Embedding Analysis of Neuron Responses under Various Stimuli in dLGN and SC

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Cells in **dLGN** from **Multiple FOVs** with **36-Stim Set**
PCA & UMAP (reduce **neurons** dim)

Cells in **dLGN** from **Multiple FOVs** with **36-Stim Set**
PCA, UMAP, Manifold Embedding (reduce **stimuli** dim)

Cells in **dLGN** from **Multiple FOVs** with **48-Stim Set**
PCA & UMAP (reduce **neurons** dim)

Cells in **dLGN** from **Multiple FOVs** with **48-Stim Set**
PCA, UMAP, Manifold Embedding (reduce **stimuli** dim)

Cells in **SC** from **Multiple FOVs** with **48-Stim Set**
PCA & UMAP (reduce **neurons** dim)

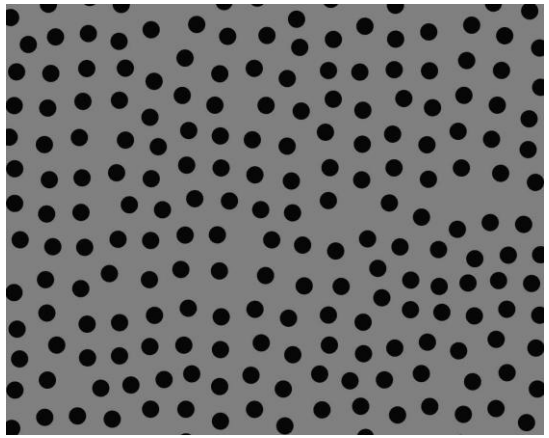
Cells in **SC** from **Multiple FOVs** with **48-Stim Set**
PCA, UMAP, Manifold Embedding (reduce **stimuli** dim)

Cells in **dLGN** from **Multiple FOVs** with **36-Stim Set**
PCA & UMAP (reduce **neurons** dim)

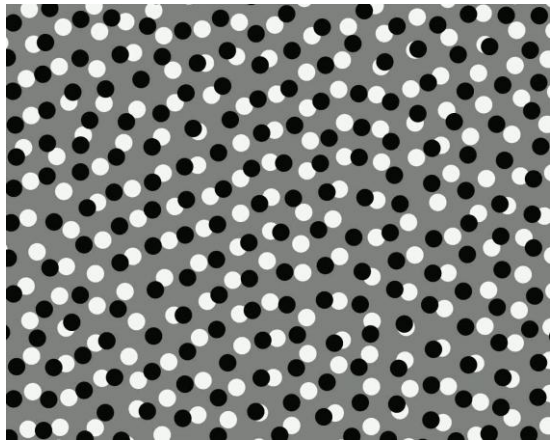
Stimuli

```
# dir: 0, 90, 180, 270
Gratings
neg_1flows
pos_1flows
neg_3flows
pos_3flows
pos_oppdir
neg_oppdir
posneg_samedir
posneg_oppdir
```

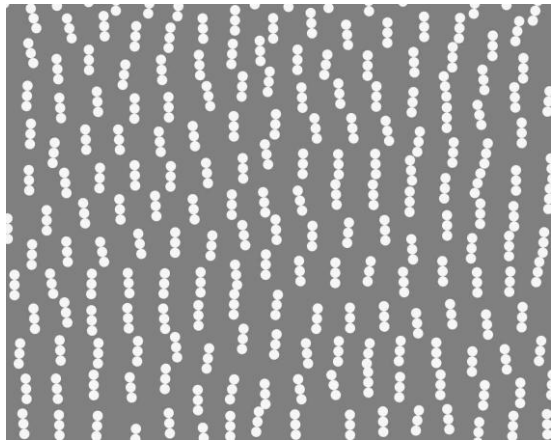
```
# 36 timuli
label_names = [
    'neg_1flows_270', 'posneg_oppdir_270', 'pos_1flows_180', 'neg_3flows_180',
    'posneg_samedir_270', 'neg_oppdir_180', 'gratings_90', 'pos_oppdir_0',
    'pos_3flows_180', 'neg_1flows_0', 'pos_1flows_270', 'gratings_270',
    'posneg_oppdir_0', 'neg_3flows_90', 'pos_oppdir_90', 'posneg_samedir_180',
    'neg_oppdir_270', 'pos_3flows_270', 'neg_3flows_0', 'gratings_0',
    'posneg_samedir_90', 'pos_3flows_0', 'neg_1flows_90', 'posneg_oppdir_180',
    'neg_oppdir_0', 'pos_1flows_0', 'pos_oppdir_180', 'pos_oppdir_270',
    'pos_1flows_90', 'posneg_oppdir_90', 'posneg_samedir_0', 'gratings_180',
    'neg_1flows_180', 'neg_3flows_270', 'neg_oppdir_90', 'pos_3flows_90'
]
```



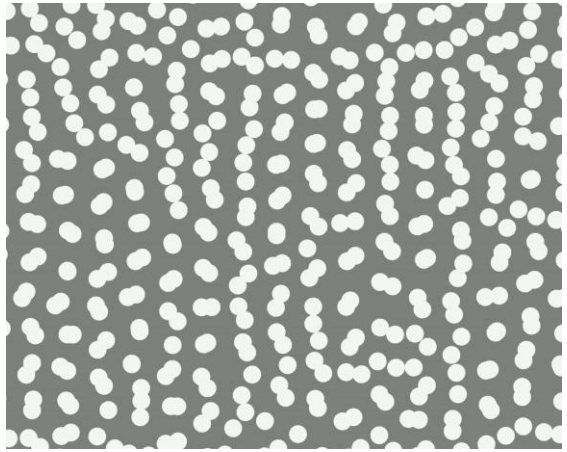
neg_1flows_180



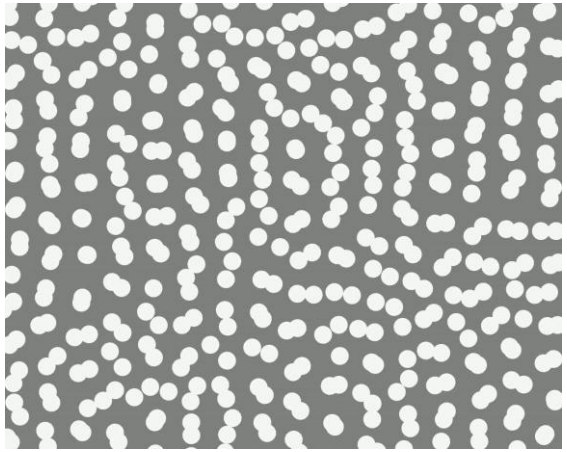
posneg_samedir_0



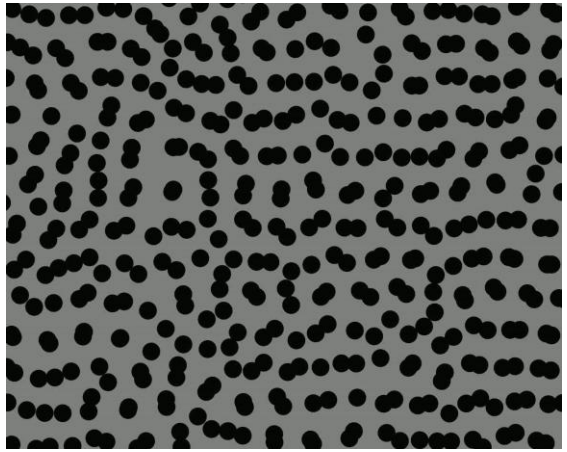
pos_3flows_0



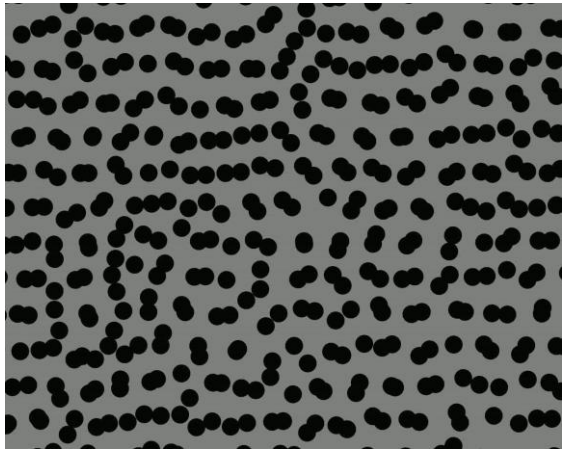
pos_oppdir_0



pos_oppdir_180



neg_oppdir_90



neg_oppdir_270

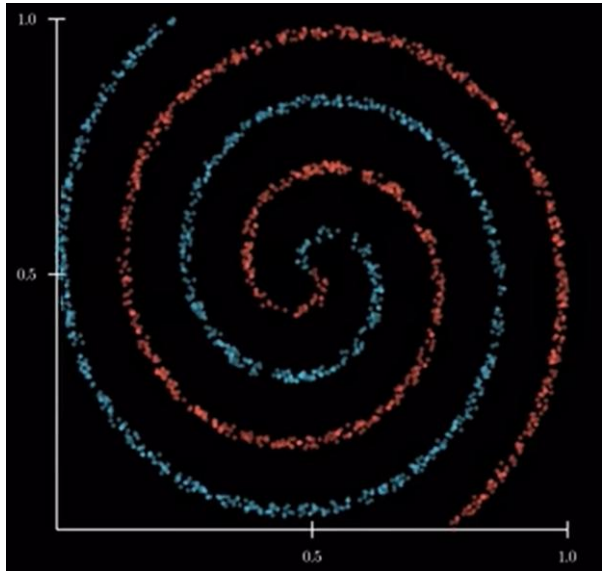
Preprocessed Data for one FOV:
2-D Matrix
N_STIMS*N_SESSIONS*N_REPS by N_NEURONS

Multiple FOVs – stack together

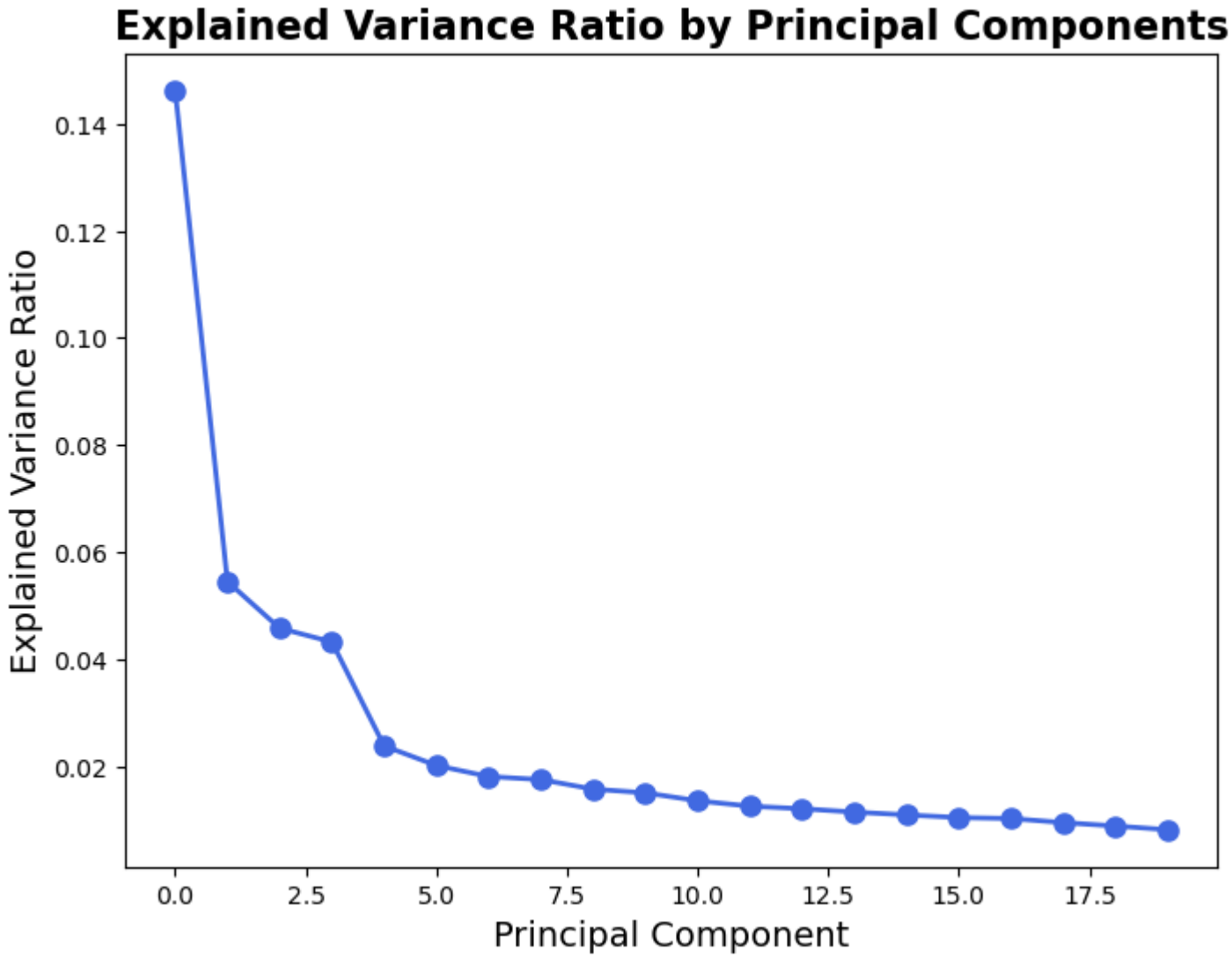
```
exps_dLGN_36 = [
    'CC182_240905_ThresholdedNaN3_Combined',
    'CC182_240906_ThresholdedNaN3_Combined',
    'CC182_240911_ThresholdedNaN3_Combined',
    'CC182_240912_ThresholdedNaN3_Combined',
    'CC182_240913_ThresholdedNaN3_Combined',
    'CC185_240916_ThresholdedNaN3_Combined',
    'CC185_240917_ThresholdedNaN3_Combined',
    'CC185_240919_ThresholdedNaN3_Combined'
]
```

Why PCA & UMAP?

UMAP (Uniform Manifold Approximation and Projection) focuses on preserving the topological structure of the data. It constructs a graph of nearest neighbors in the original space and optimizing a low-dimensional embedding to maintain the graph's structure.

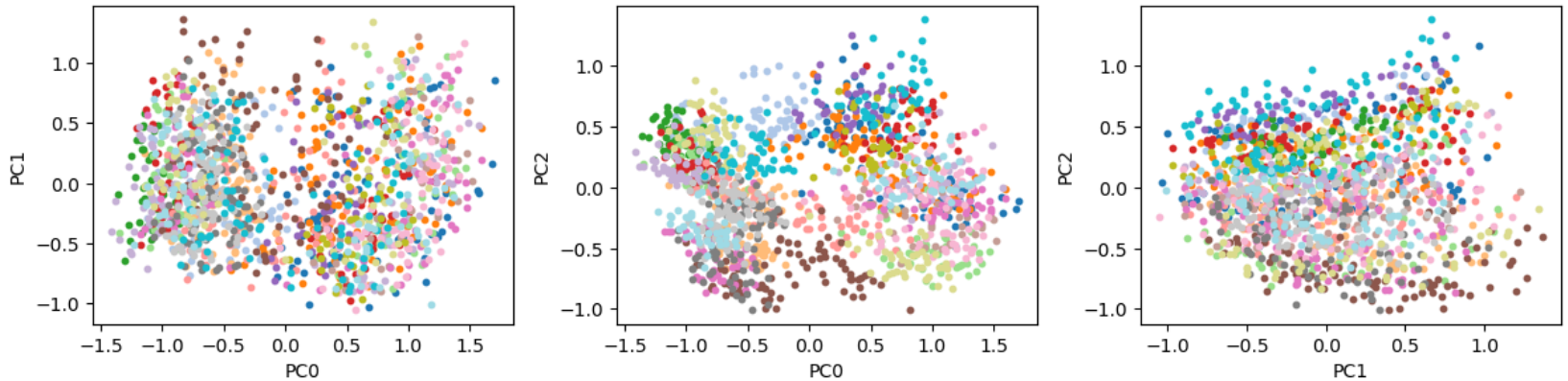


E.g., UMAP can capture the above structure (NONLINEARITY) in 1-D and PCA can't.

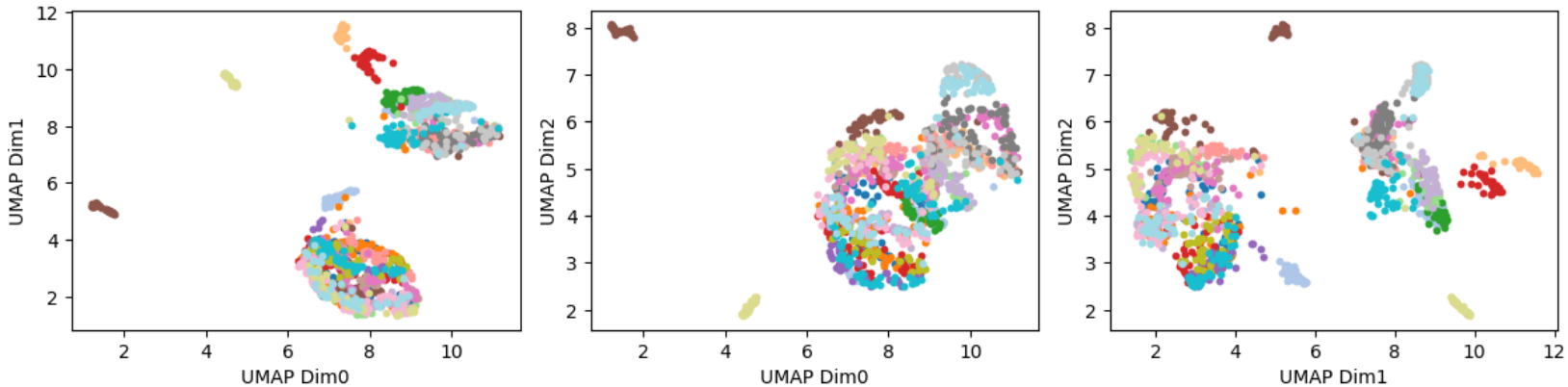


We use the first 3 PCs for plotting.

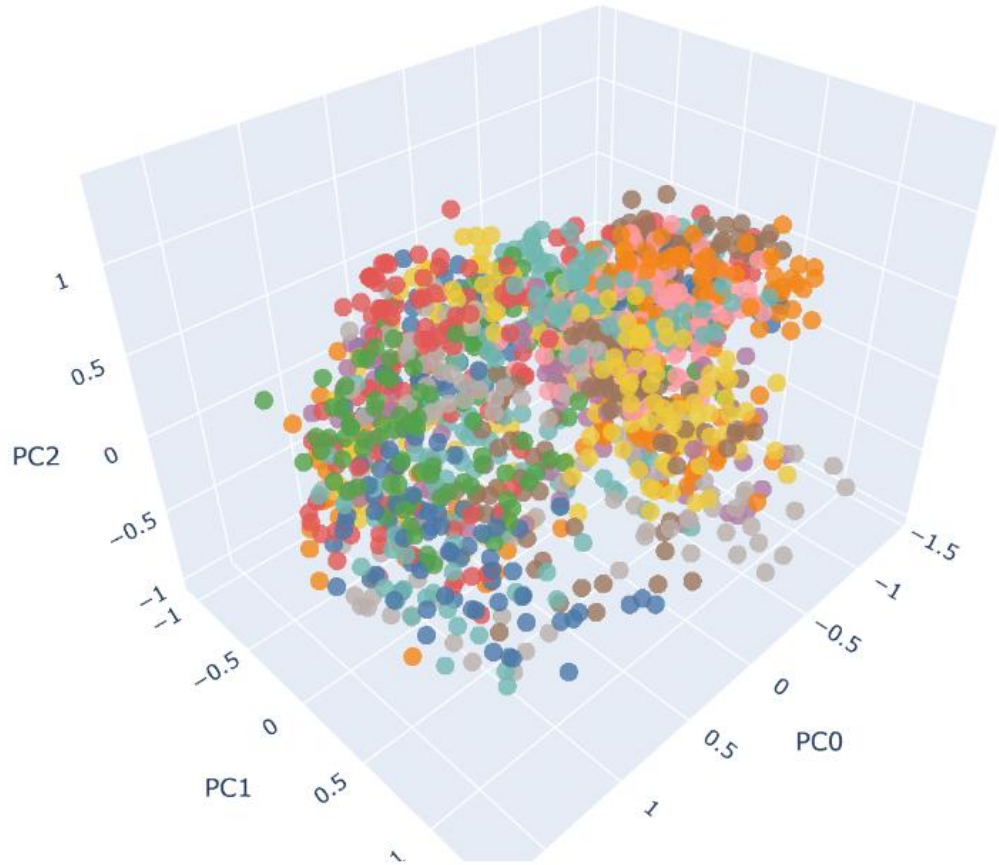
PCA: All Stimuli with Labels



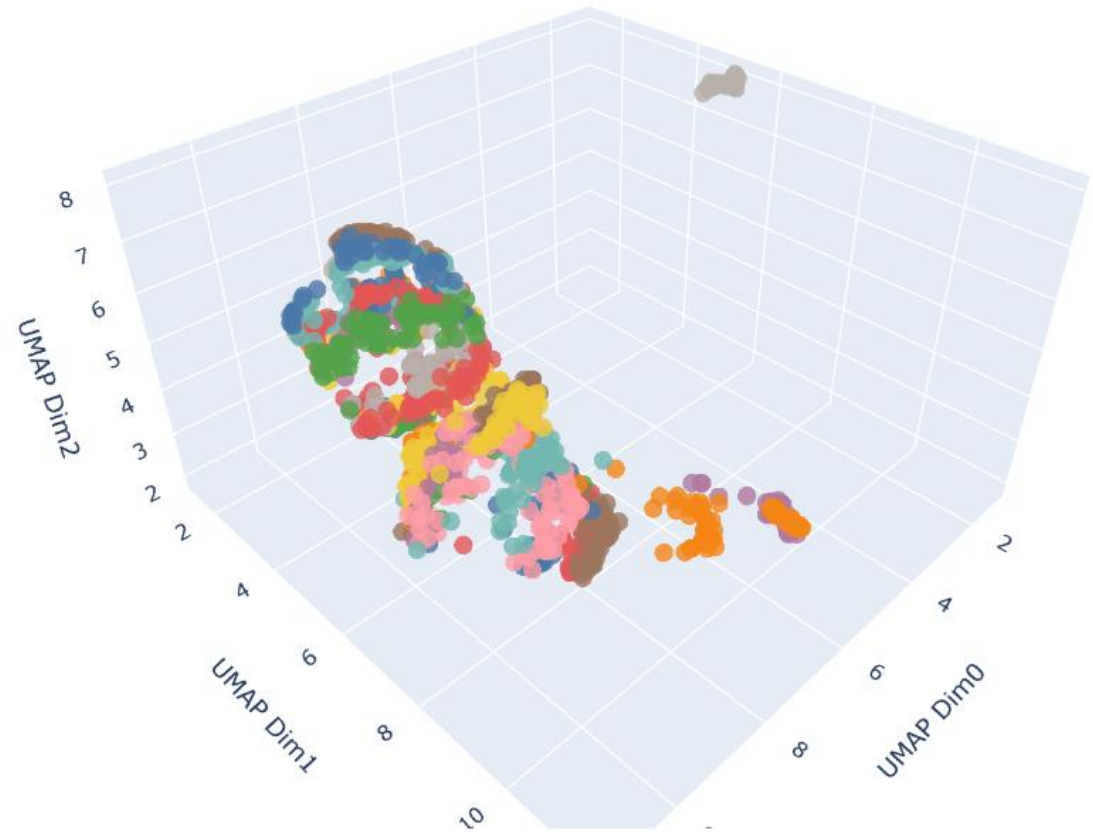
UMAP: All Stimuli with Labels

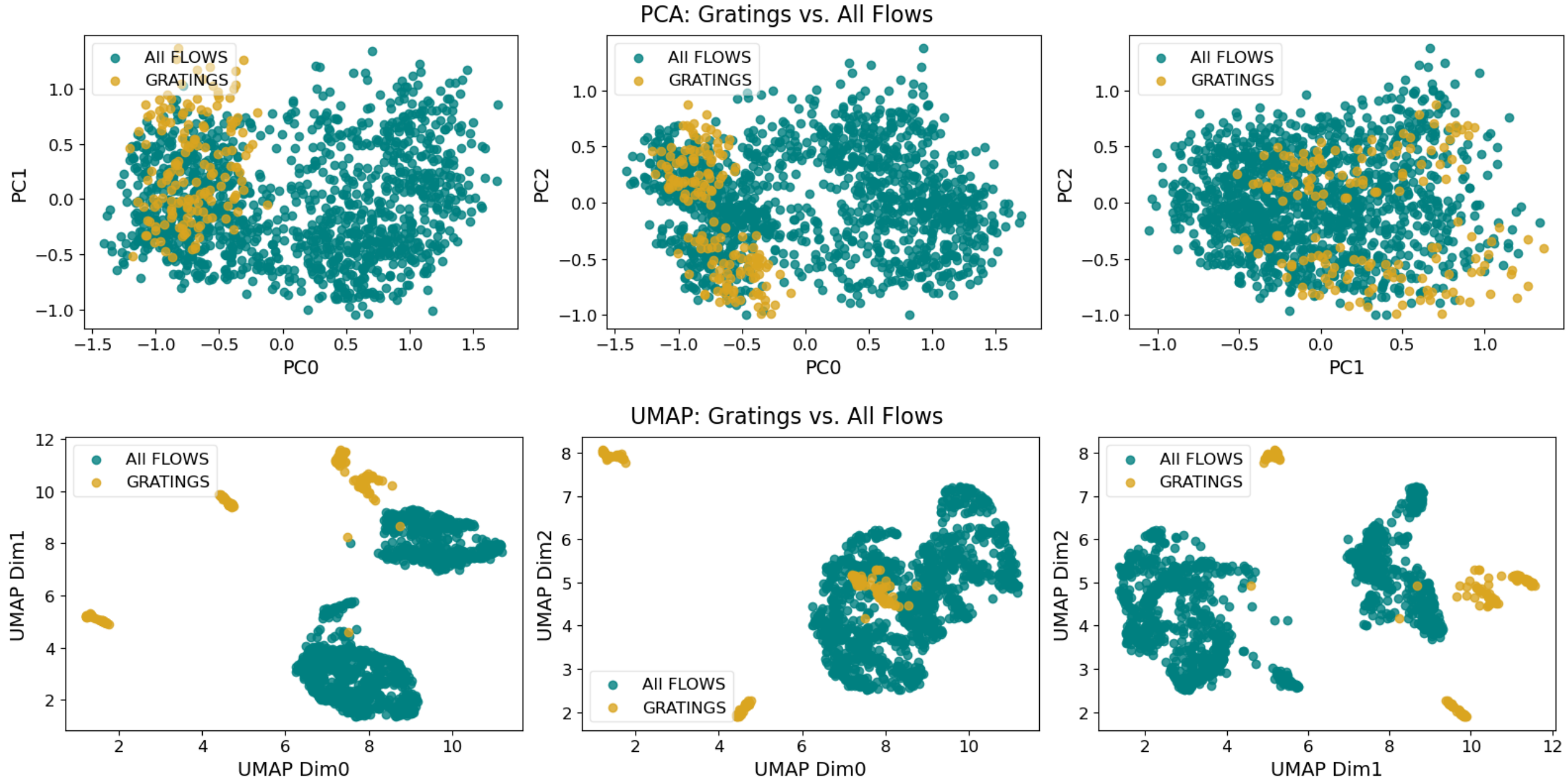


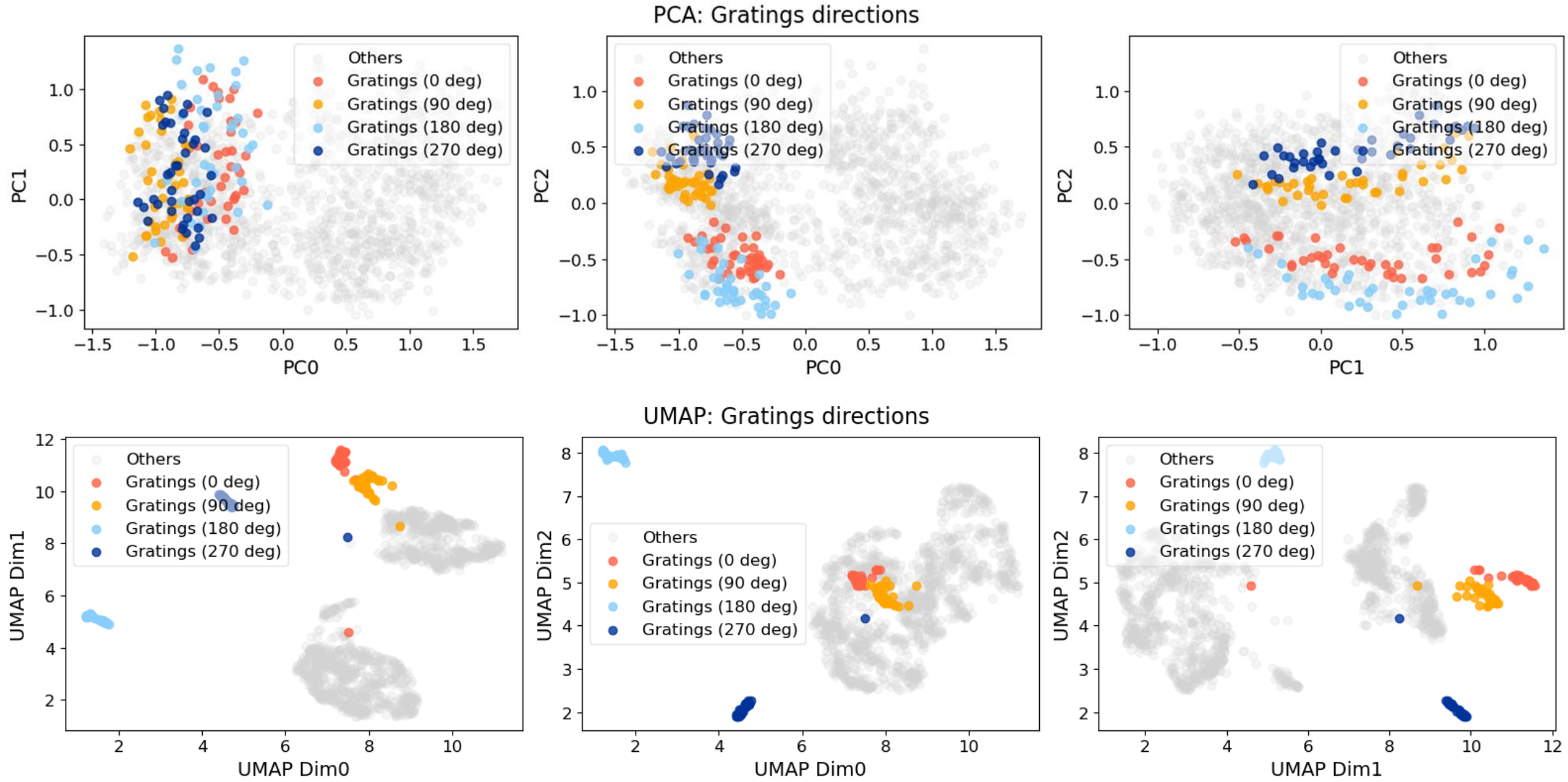
PCA: Interactive 3D Plot of All Stimuli

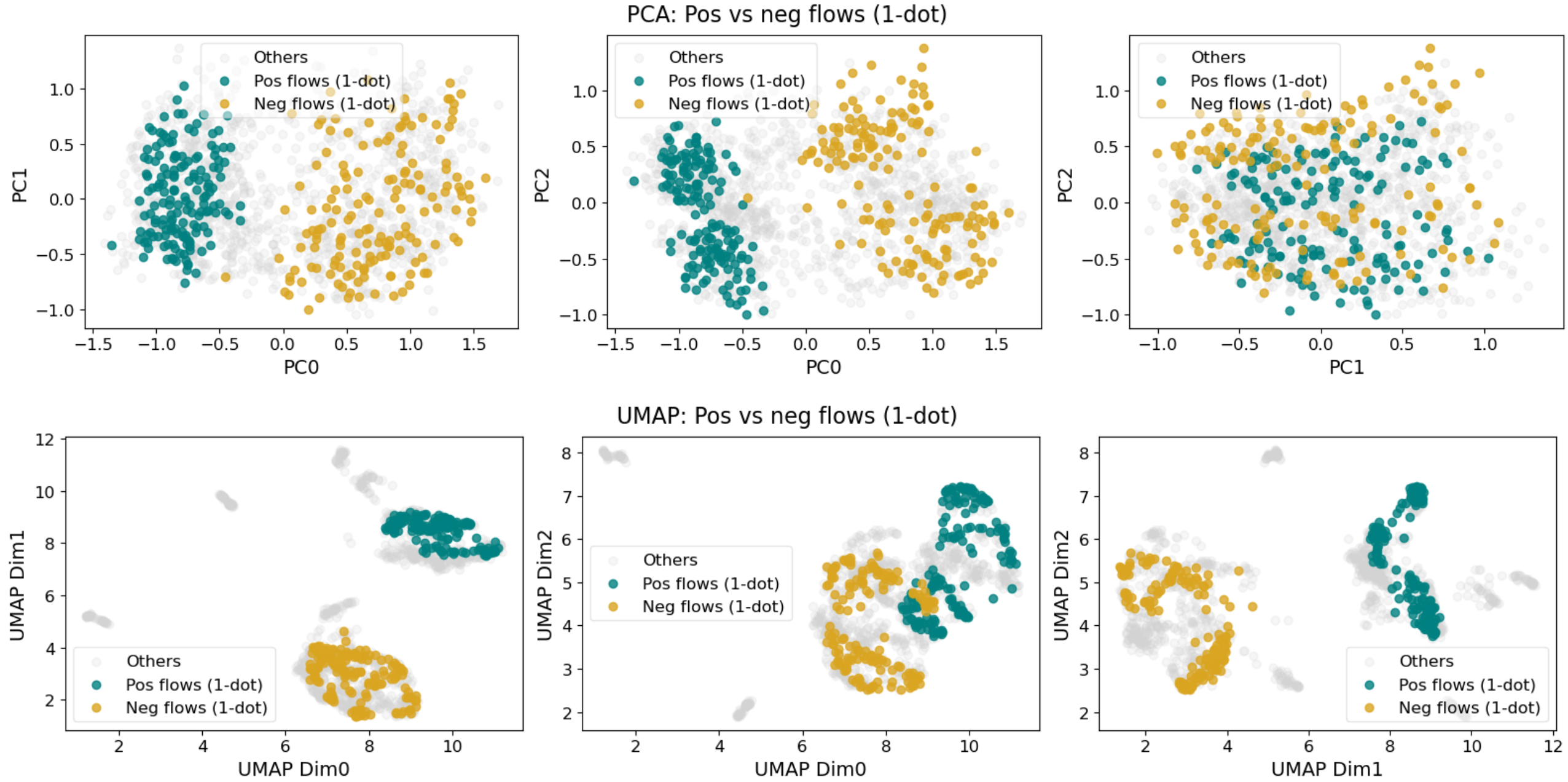


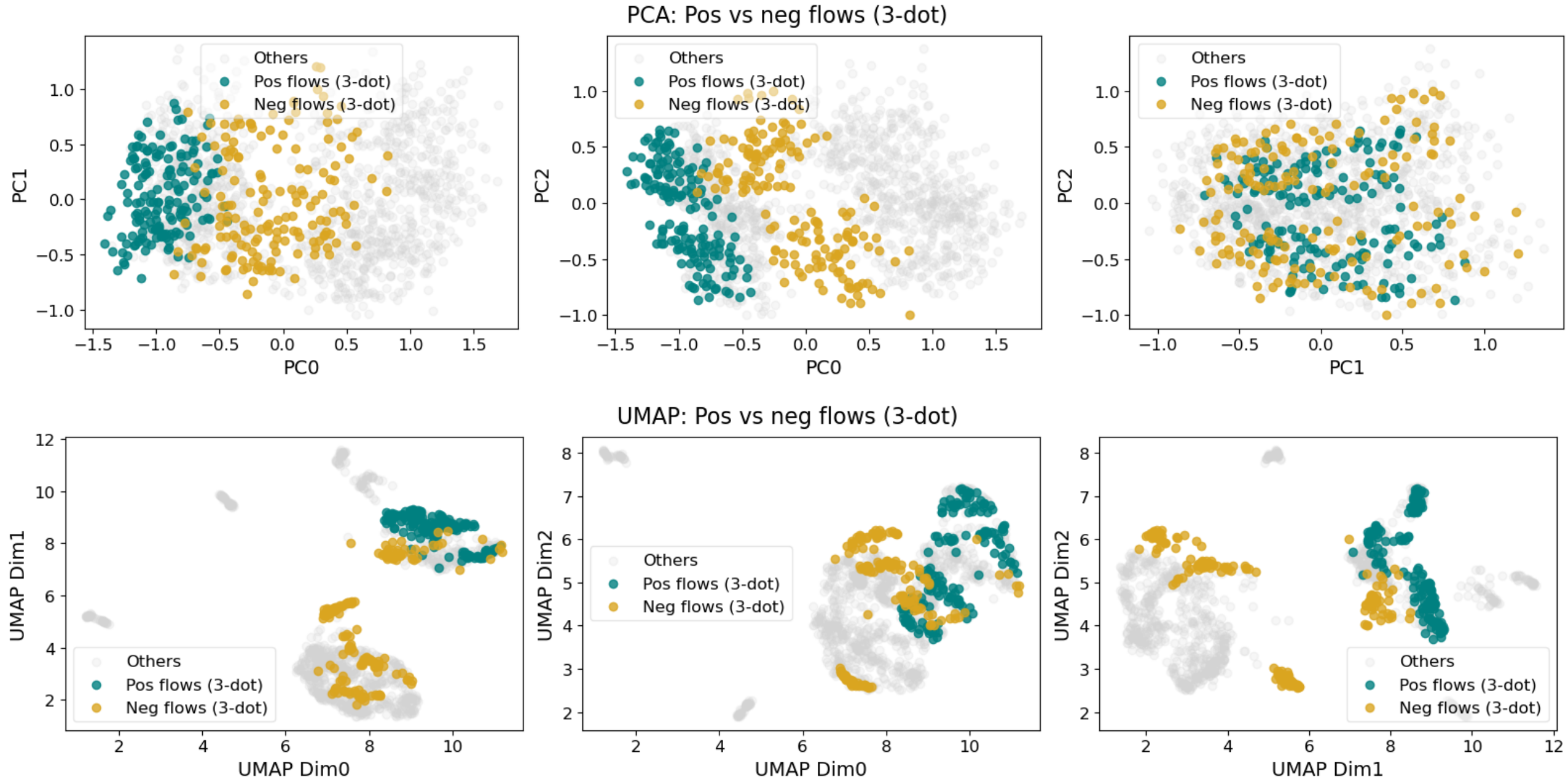
UMAP: Interactive 3D Plot of All Stimuli



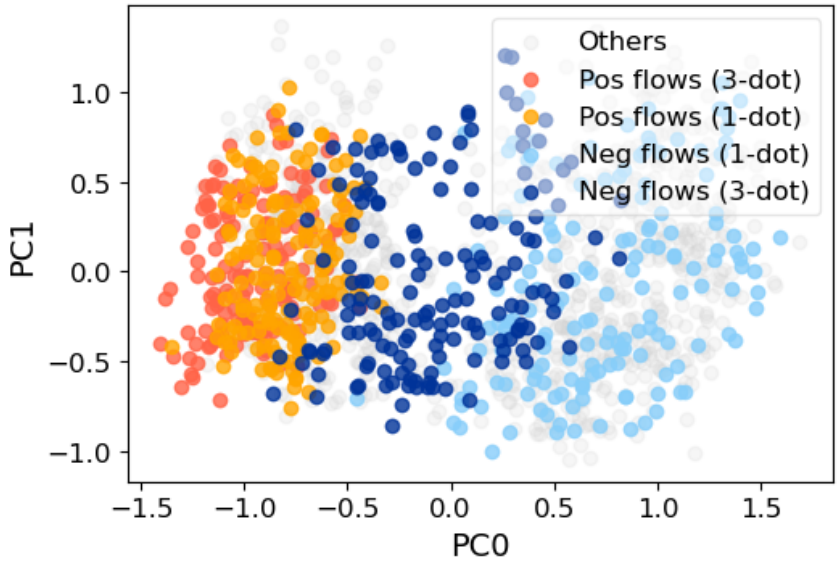

PCA: Gratings vs. All Flows
All FLOWS
GRATINGS
PC0
PC1
PC2
UMAP: Gratings vs. All Flows
UMAP Dim0
UMAP Dim1
UMAP Dim2

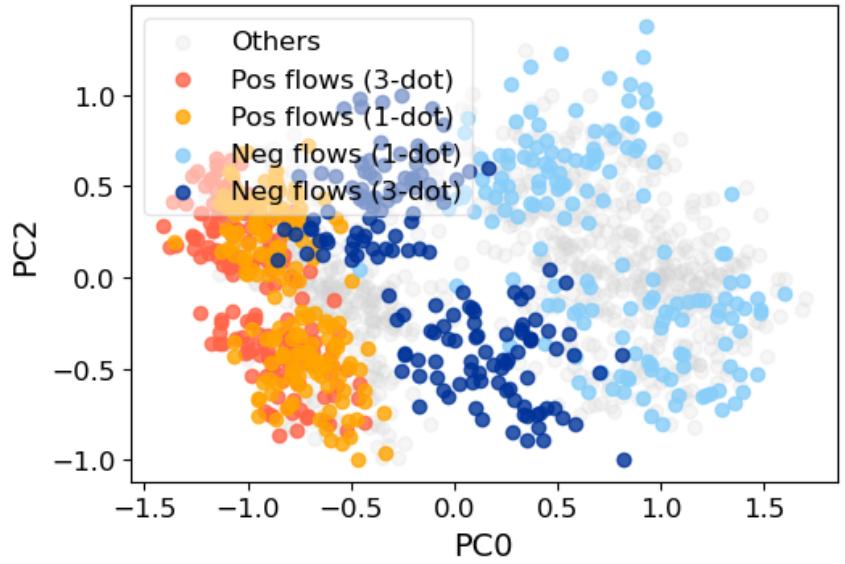

PCA: Gratings directions
Others
Gratings (0 deg)
Gratings (90 deg)
Gratings (180 deg)
Gratings (270 deg)
PC0
PC1
PC2
UMAP: Gratings directions
UMAP Dim0
UMAP Dim1
UMAP Dim2

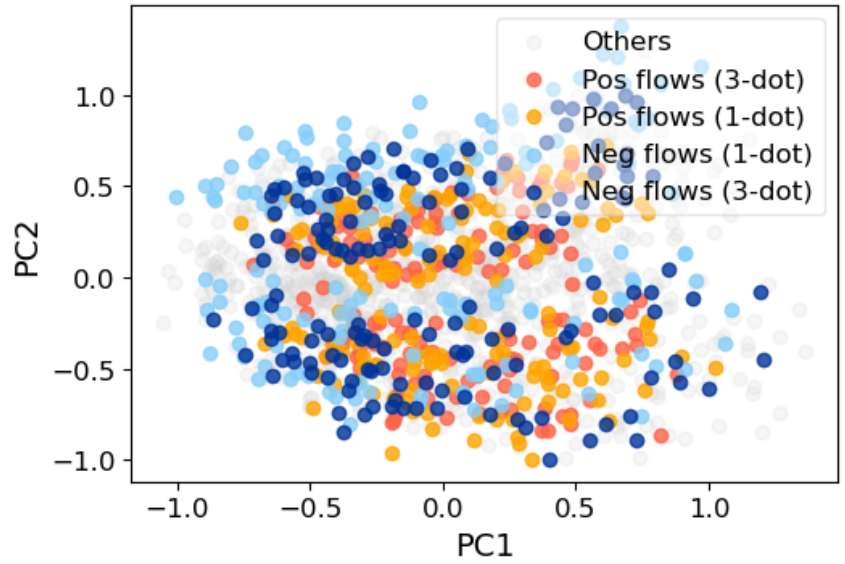

PCA: Pos vs neg flows (1-dot)
Others
Pos flows (1-dot)
Neg flows (1-dot)
PC0
PC1
PC2
UMAP: Pos vs neg flows (1-dot)
UMAP Dim0
UMAP Dim1
UMAP Dim2


PCA: Pos vs neg flows (3-dot)
Others
Pos flows (3-dot)
Neg flows (3-dot)
PC0
PC1
PC2
UMAP: Pos vs neg flows (3-dot)
UMAP Dim0
UMAP Dim1
UMAP Dim2

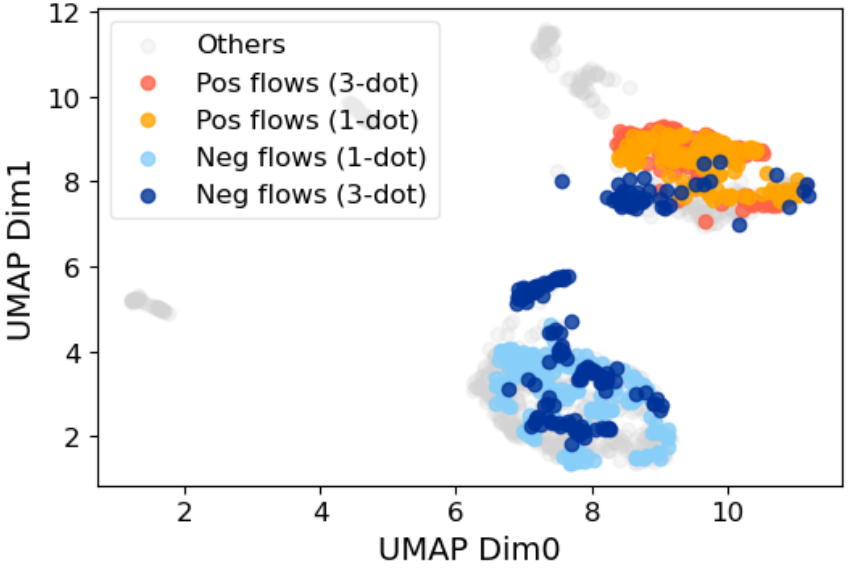
PCA: Pos vs neg flows (1 & 3-dot)

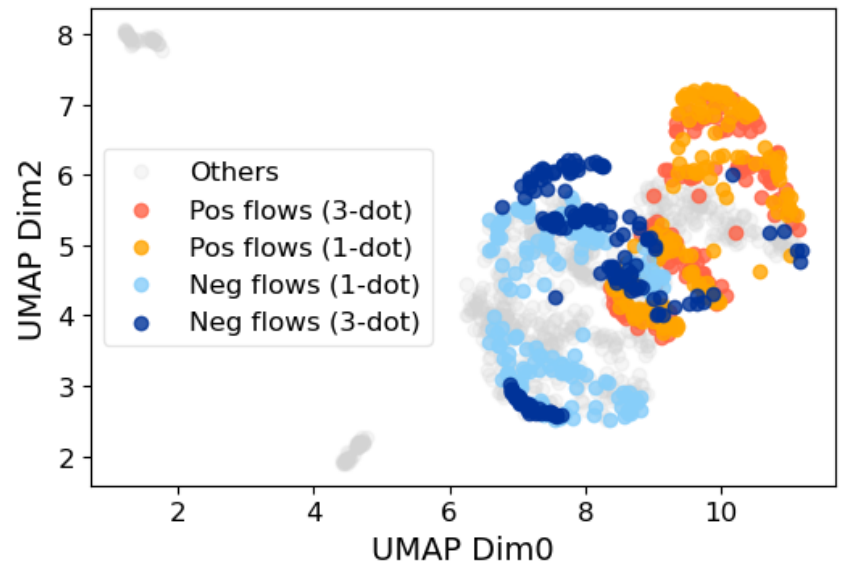


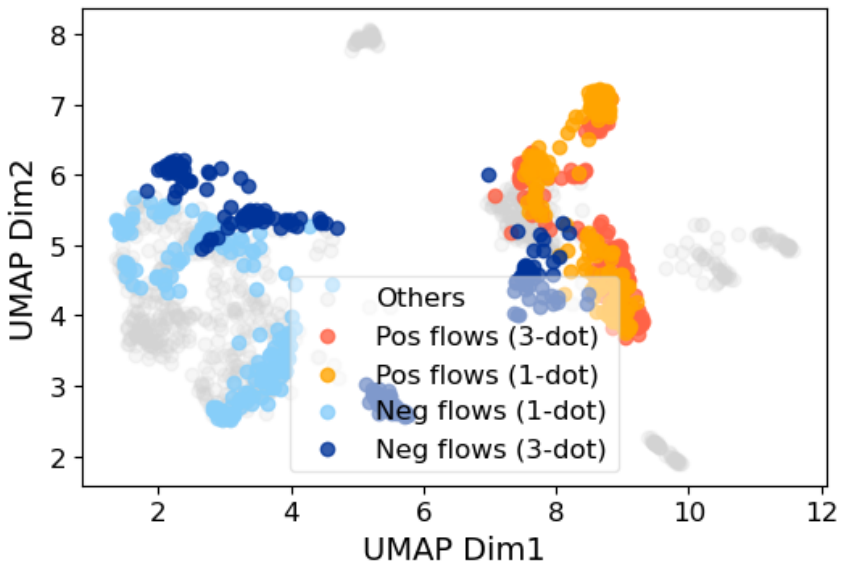


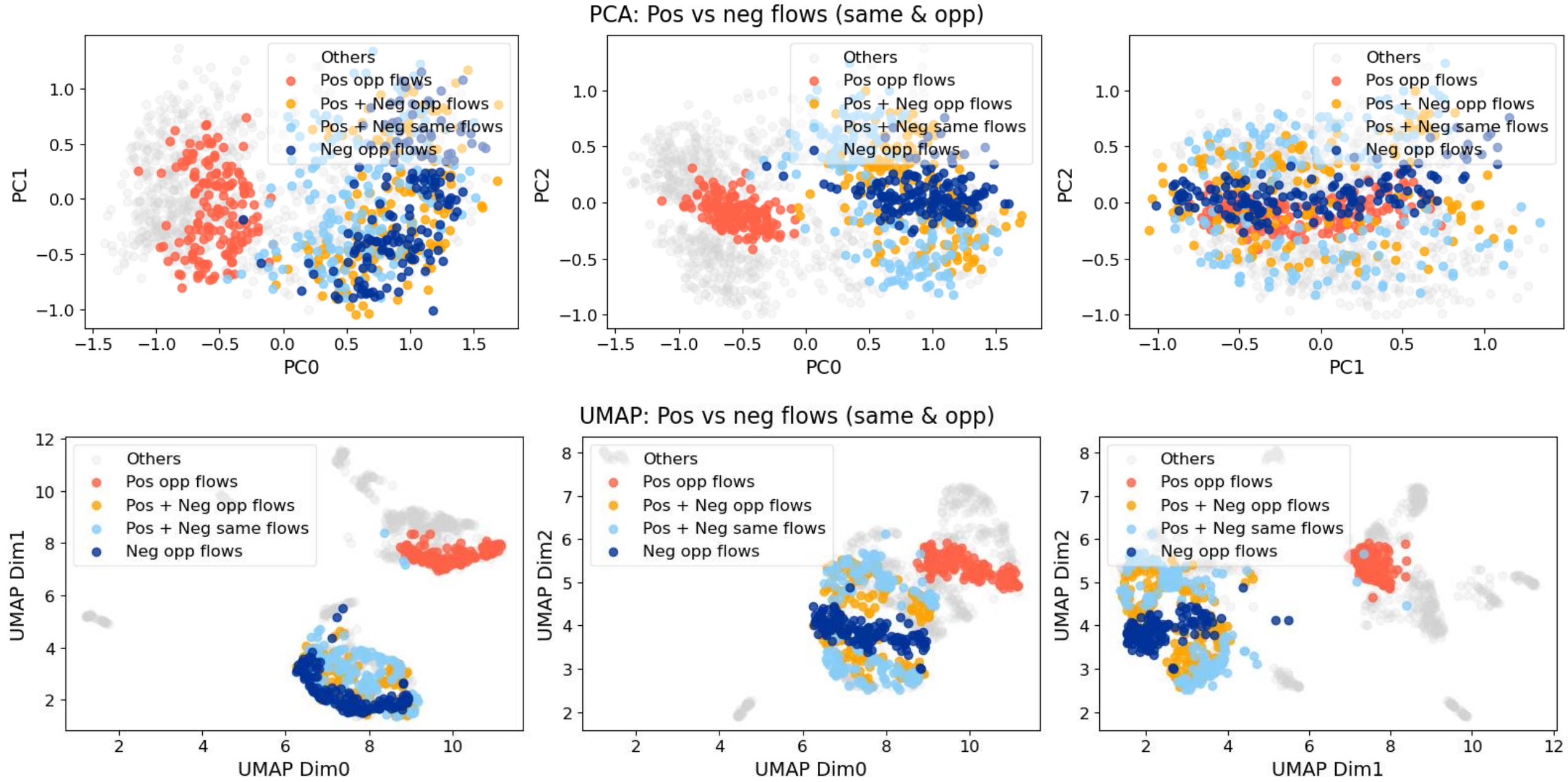


UMAP: Pos vs neg flows (1 & 3-dot)



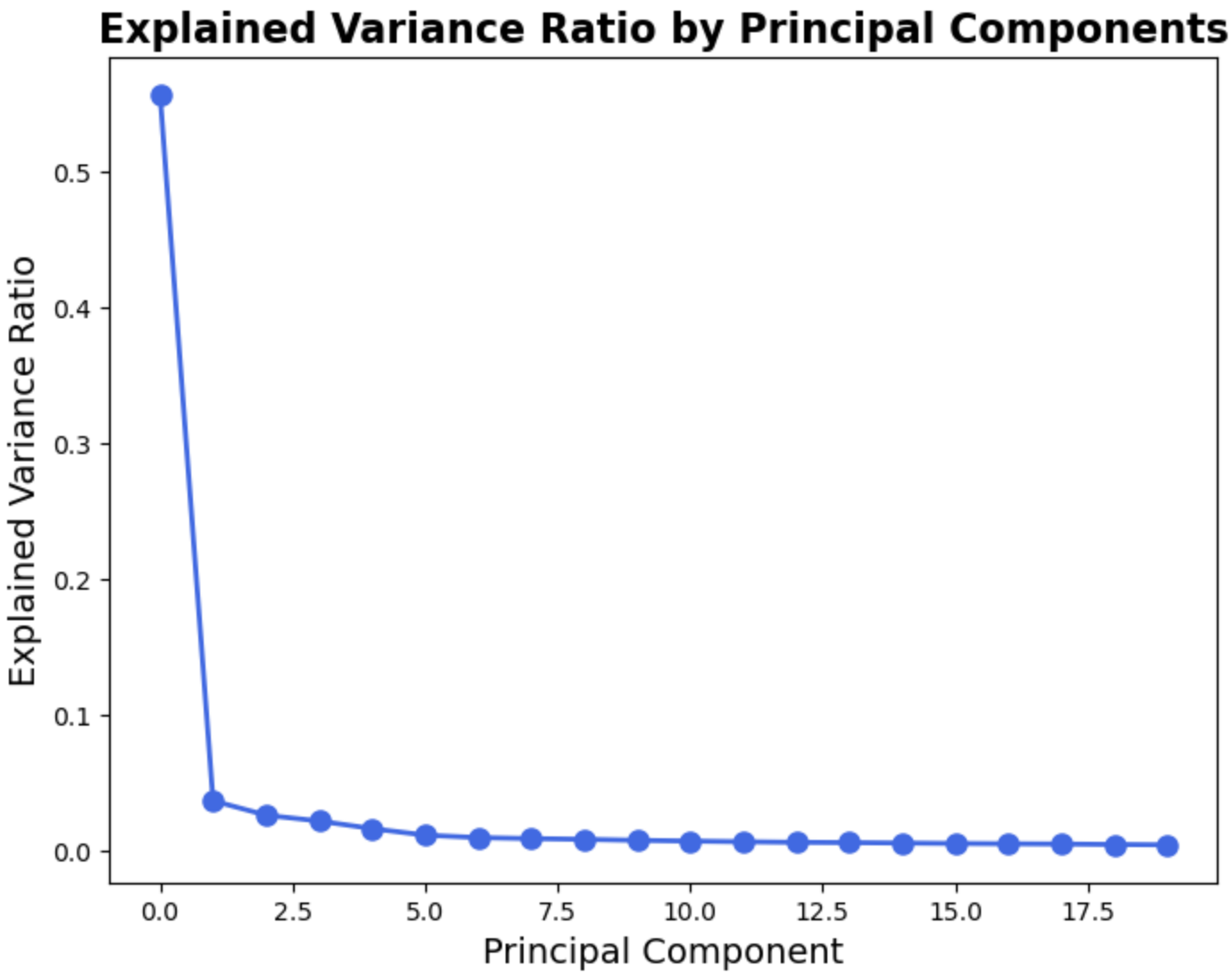





PCA: Pos vs neg flows (same & opp)
Others
Pos opp flows
Pos + Neg opp flows
Pos + Neg same flows
Neg opp flows
PC0
PC1
PC2
UMAP: Pos vs neg flows (same & opp)
UMAP Dim0
UMAP Dim1
UMAP Dim2

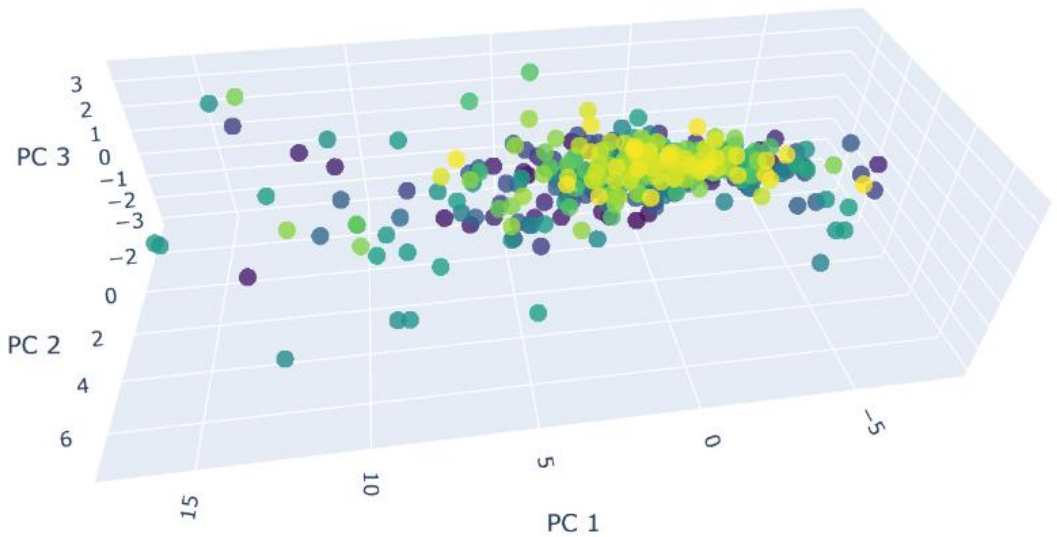
Cells in **dLGN** from **Multiple FOVs** with **36-Stim Set**

PCA, UMAP, Manifold Embedding (reduce **stimuli** dim)

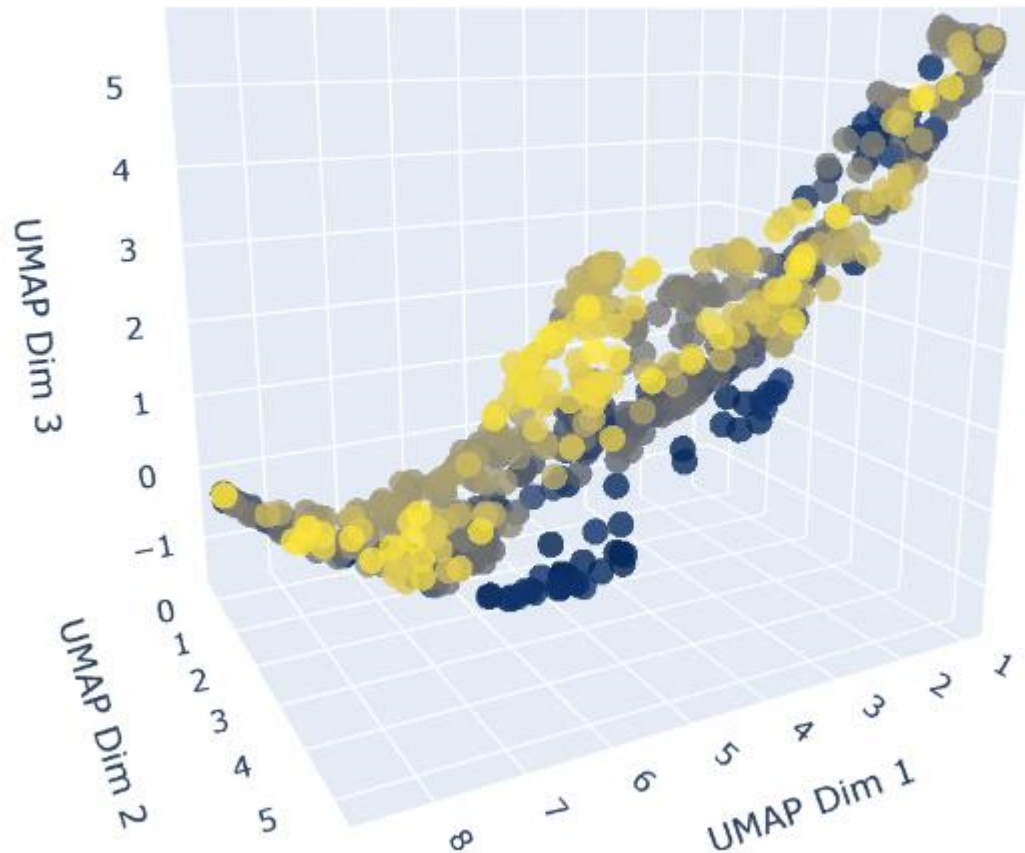


We use the first 3 PCs for plotting.

PCA: Neurons in 3D

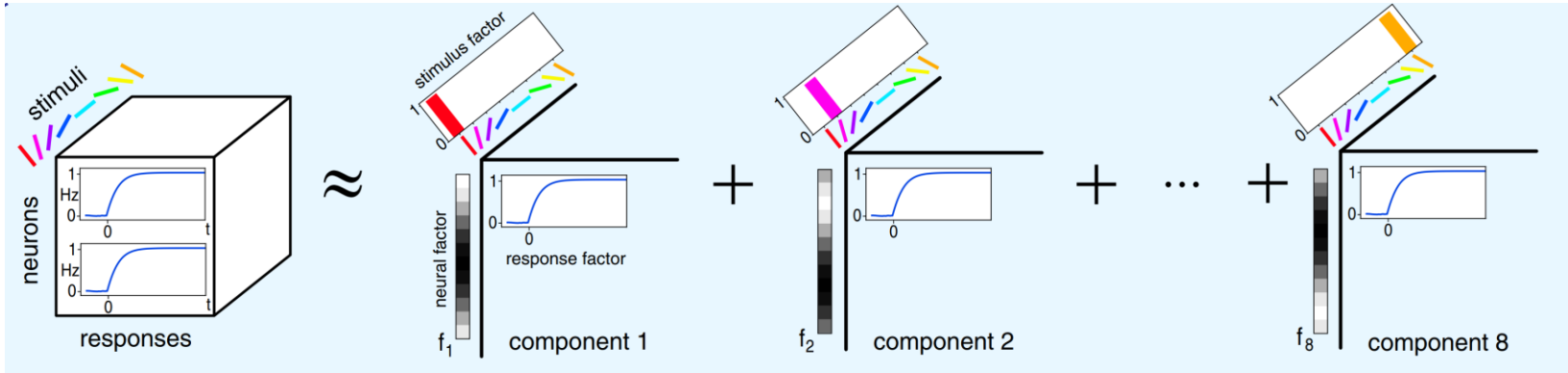


UMAP: Neurons in 3D



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.

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

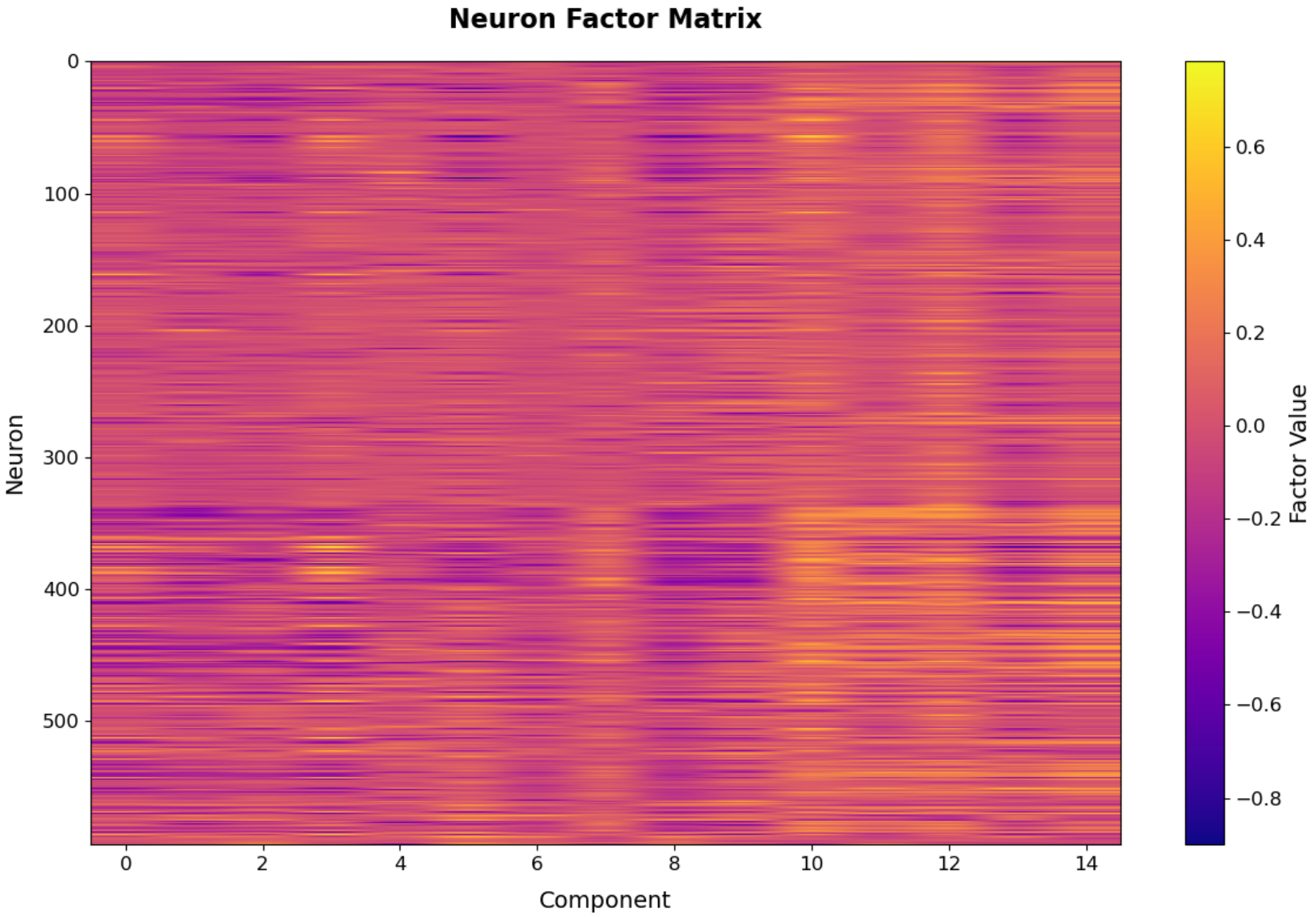
where R is the rank of the decomposition (i.e., the number of hidden components), and the number of columns R represents the number of latent factors.

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

Iterative Optimization:

Since the problem is non-convex and involves multiple variables, an **iterative optimization** approach is used. A common method is **Alternating Least Squares (ALS)** or **gradient-based methods**. Here's the general idea:

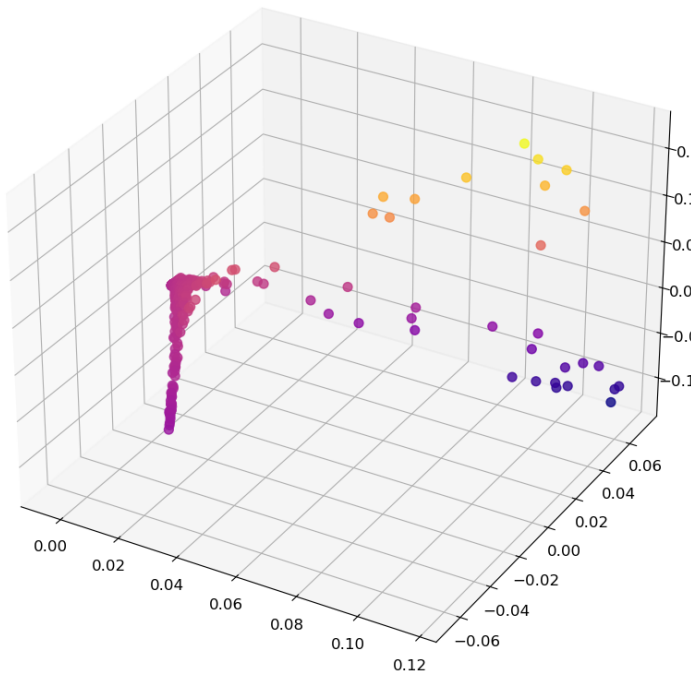
- **Initialization**: Start by initializing the factor matrices N, S, and R randomly with non-negative values.
- **Iterative Updates**:
  - Fix S and R, then solve for N by minimizing the objective with respect to N.
  - Fix N and R, then solve for S.
  - Fix N and S, then solve for R.

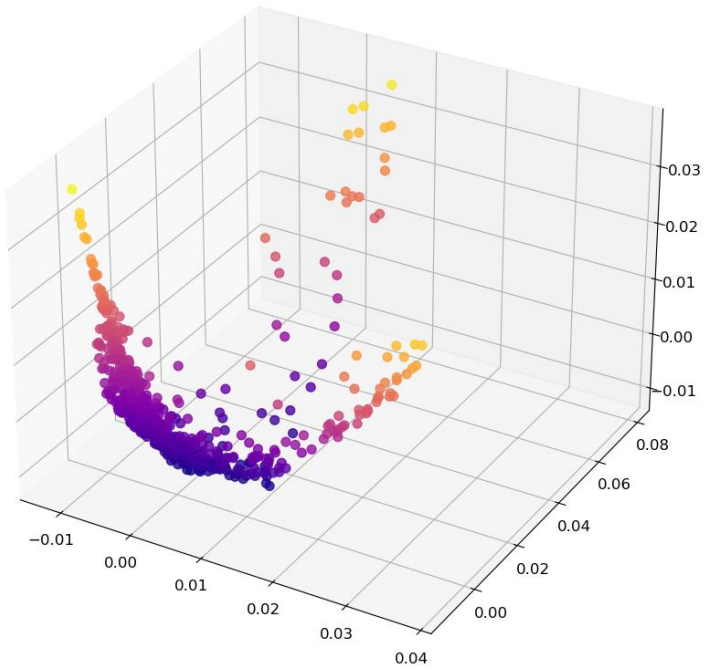


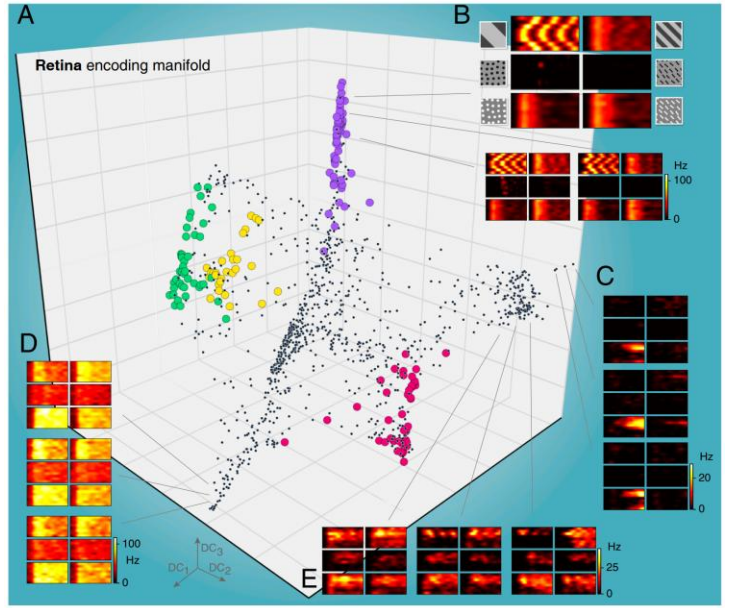
Use the neuron factor matrix to calculate pairwise distance.

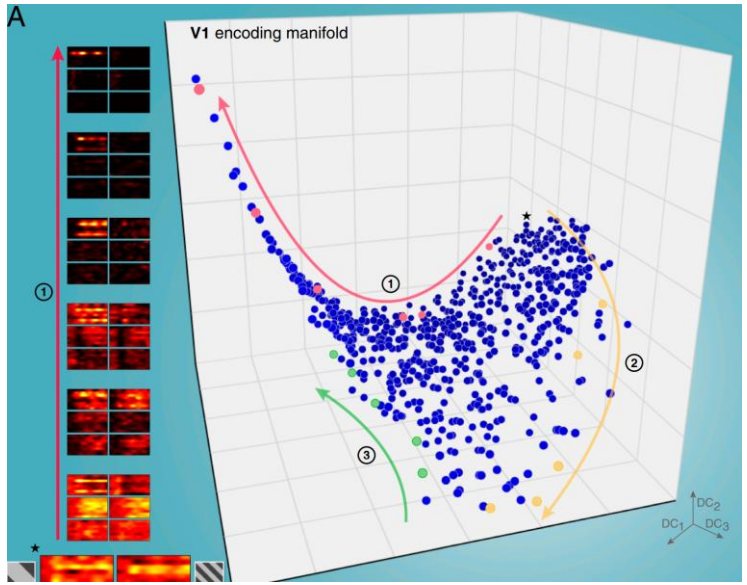
Compute Iterated Adaptive Neighborhoods (IAN kernel), where nonlinearity comes from, from pairwise distances, obtaining data graphs (unweighted and weighted)

1. Compute the similarity matrix D.
2. Normalize the similarity matrix to obtain the **diffusion matrix** P.
3. Compute the eigenvectors and eigenvalues of the diffusion matrix.
4. Use the top eigenvectors as coordinates in the low-dimensional space, generating the **manifold embedding** of neurons.









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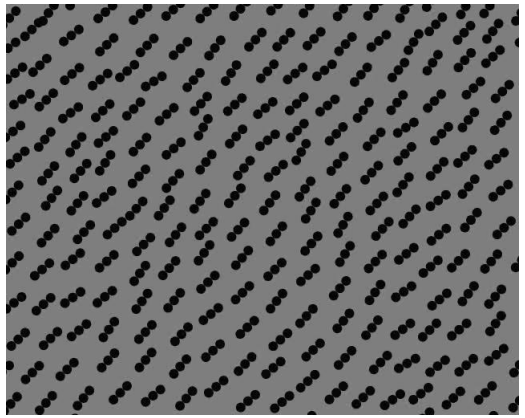
Cells in **dLGN** from **Multiple FOVs** with **48-Stim Set**
PCA & UMAP (reduce **neurons** dim)

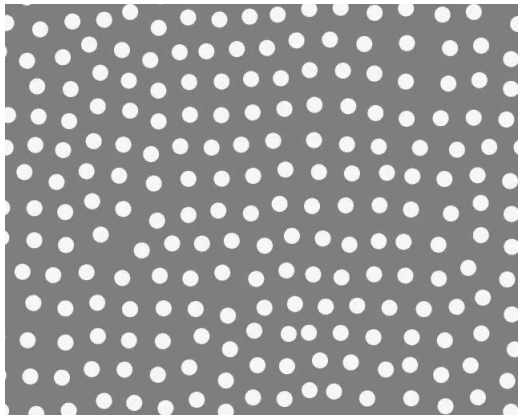
Stimuli

```
# 0, 45, 90, 135, 180, 225, 270, 315
gratings_lf
gratings_hf
neg_1flows
pos_1flows
neg_3flows
pos_3flows
```

```
# 48 timuli
label_names = [
    "neg_3flows_45", "gratings_lf_90", "gratings_hf_45", "neg_1flows_270",
    "pos_1flows_135", "pos_3flows_180", "pos_1flows_45", "neg_3flows_315",
    "gratings_hf_270", "gratings_lf_0", "pos_3flows_45", "neg_1flows_45",
    "neg_1flows_0", "pos_1flows_0", "pos_3flows_0", "gratings_lf_225",
    "gratings_hf_90", "neg_3flows_180", "gratings_hf_0", "neg_1flows_135",
    "pos_3flows_225", "pos_1flows_315", "neg_3flows_135", "gratings_lf_180",
    "pos_3flows_90", "gratings_lf_135", "pos_1flows_180", "neg_3flows_0",
    "gratings_hf_225", "neg_1flows_180", "gratings_hf_135", "pos_3flows_315",
    "pos_1flows_225", "gratings_lf_270", "neg_1flows_225", "neg_3flows_270",
    "neg_1flows_315", "gratings_hf_180", "pos_3flows_270", "neg_3flows_225",
    "pos_1flows_270", "gratings_lf_45", "pos_1flows_90", "neg_1flows_90",
    "gratings_hf_315", "gratings_lf_315", "pos_3flows_135", "neg_3flows_90"
]
```

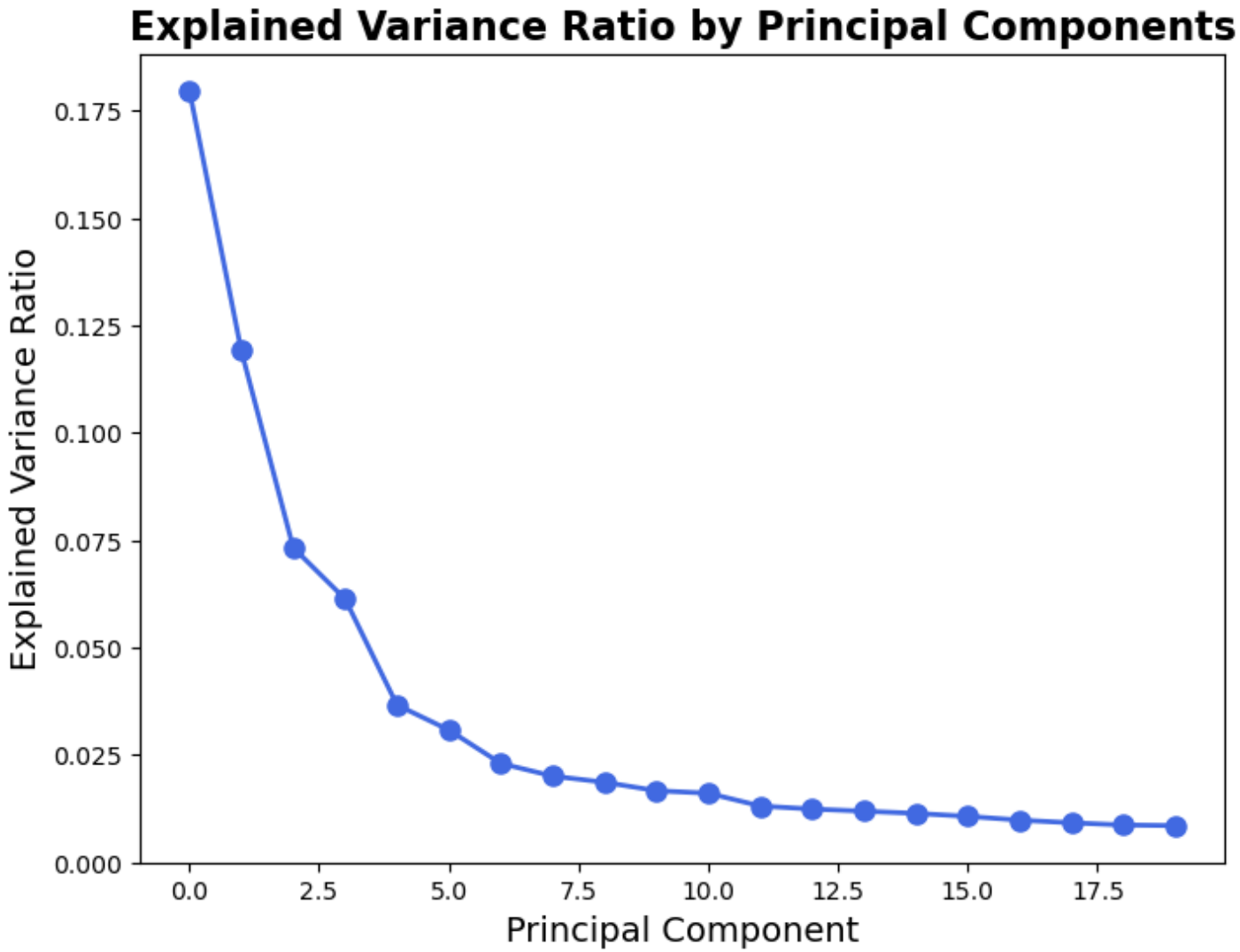


neg_3flows_315

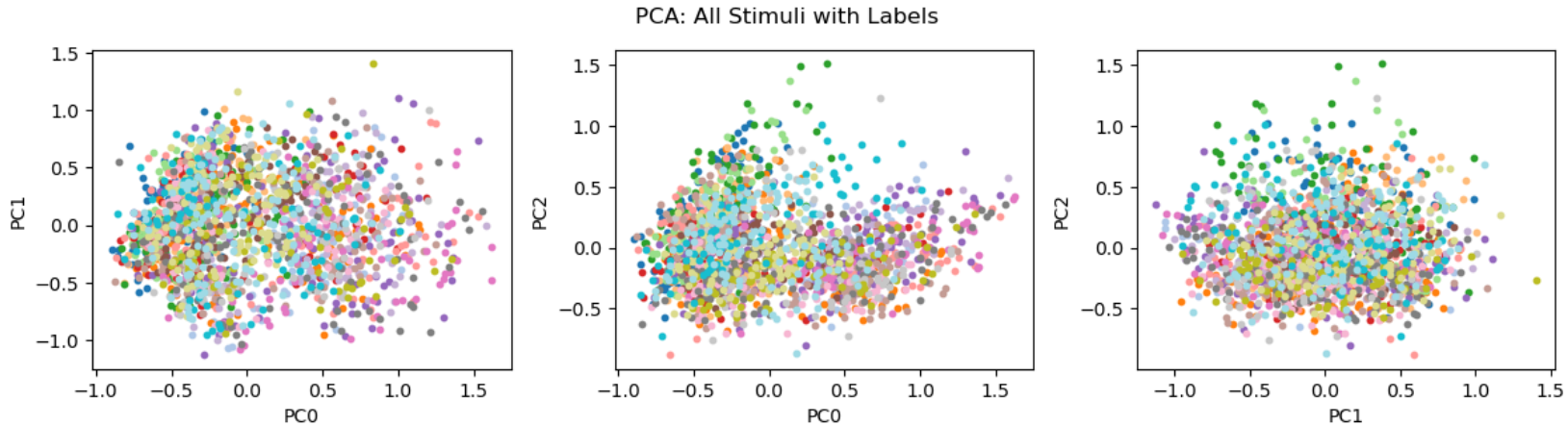


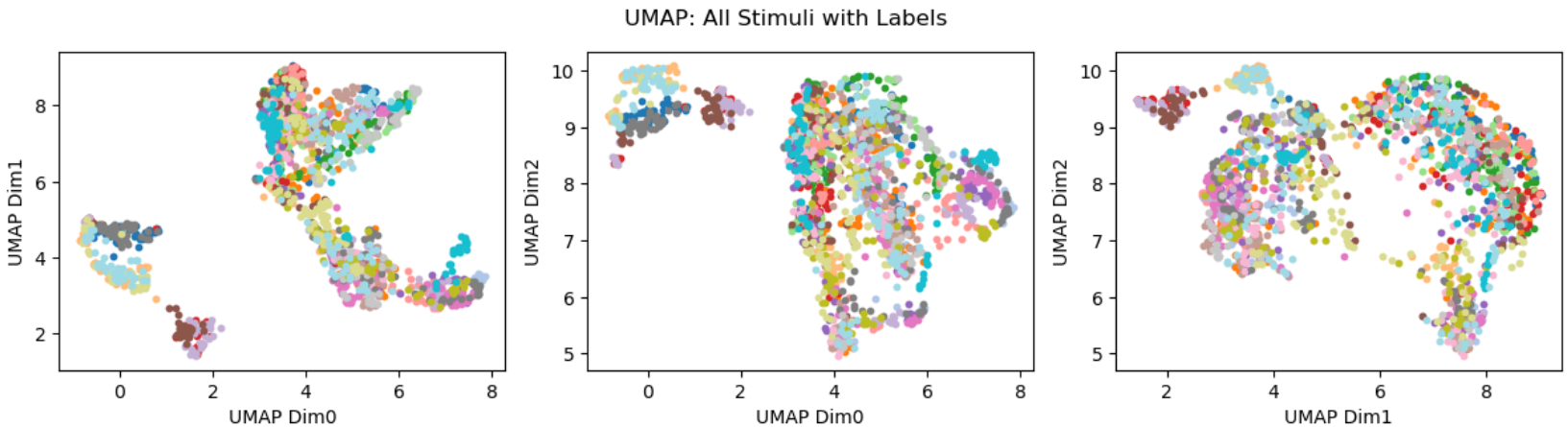
pos_1flows_225

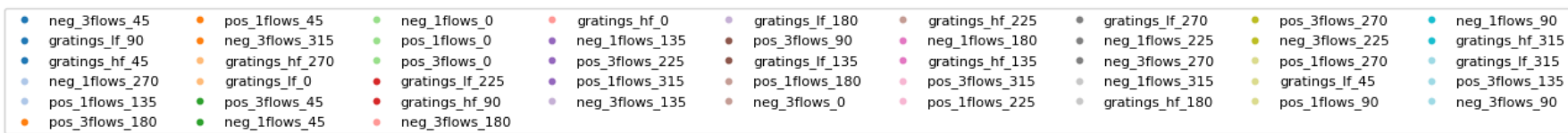
gratings_lf_45



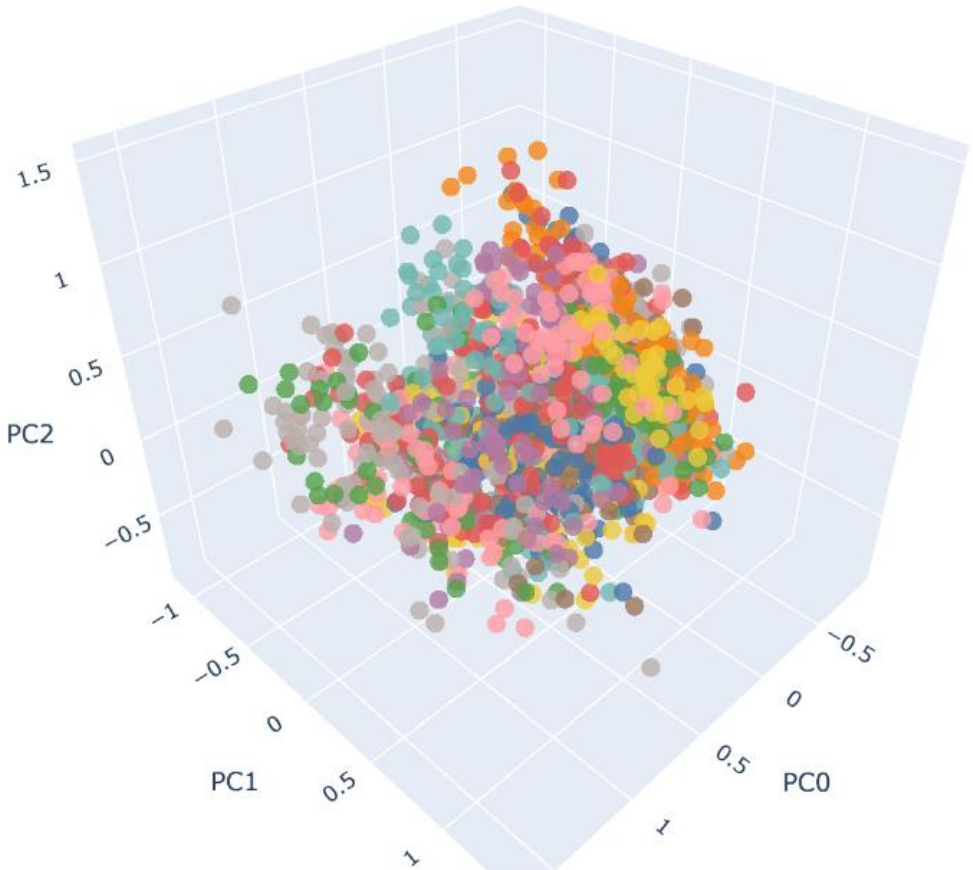
We use the first 3 PCs for plotting.


PCA: All Stimuli with Labels
PC1
PC0
PC2
PC0
PC2
PC1

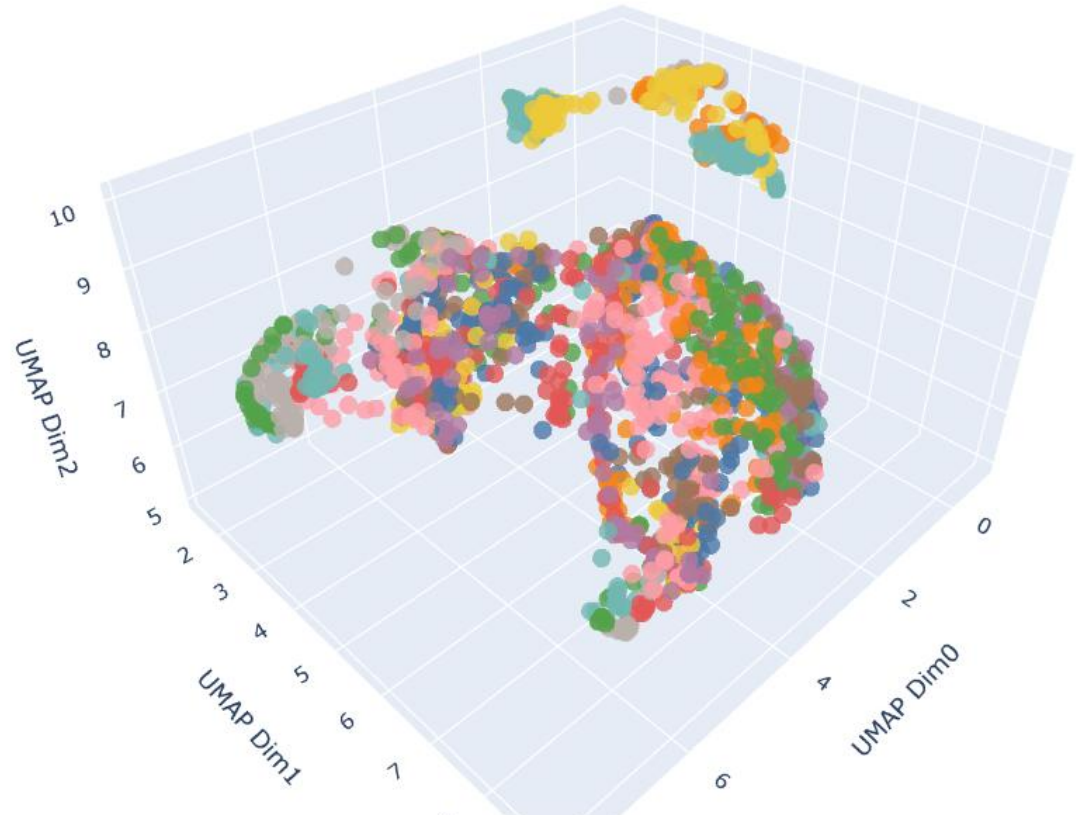

UMAP: All Stimuli with Labels
UMAP Dim1
UMAP Dim0
UMAP Dim2
UMAP Dim0
UMAP Dim2
UMAP Dim1

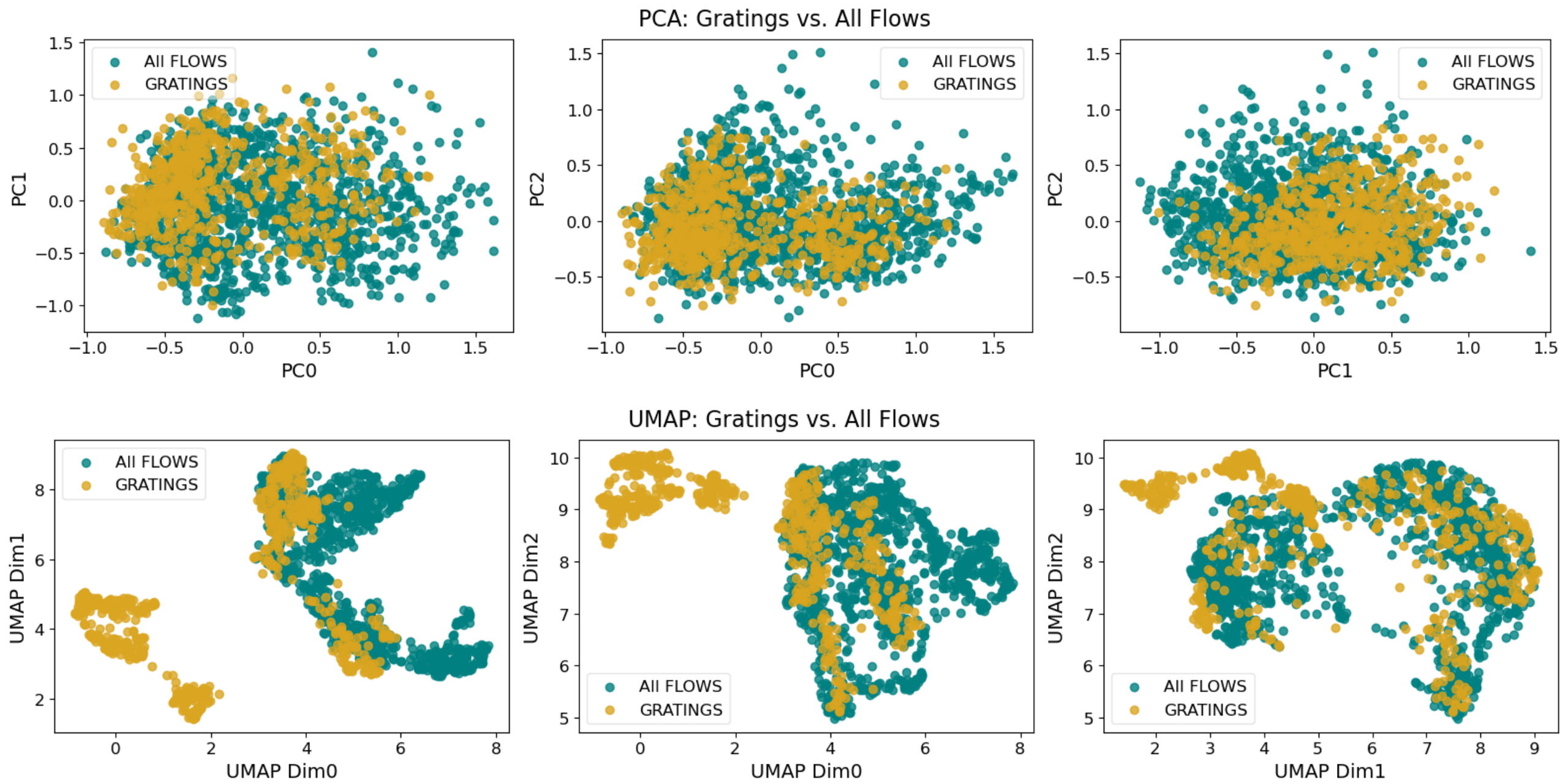

neg_3flows_45
gratings_lf_90
gratings_hf_45
neg_1flows_270
pos_1flows_135
pos_3flows_180
pos_1flows_45
neg_3flows_315
gratings_hf_270
gratings_lf_0
pos_3flows_45
neg_1flows_45
neg_1flows_0
pos_1flows_0
pos_3flows_0
gratings_lf_225
gratings_hf_90
neg_3flows_180
gratings_hf_0
neg_1flows_135
pos_3flows_225
pos_1flows_315
neg_3flows_135
gratings_lf_180
pos_3flows_90
gratings_lf_135
pos_1flows_180
neg_3flows_0
gratings_hf_225
neg_1flows_180
gratings_hf_135
pos_3flows_315
pos_1flows_225
gratings_lf_270
neg_1flows_225
neg_3flows_270
neg_1flows_315
gratings_hf_180
pos_3flows_270
neg_3flows_225
pos_1flows_270
gratings_lf_45
pos_1flows_90
neg_1flows_90
gratings_hf_315
gratings_lf_315
pos_3flows_135
neg_3flows_90

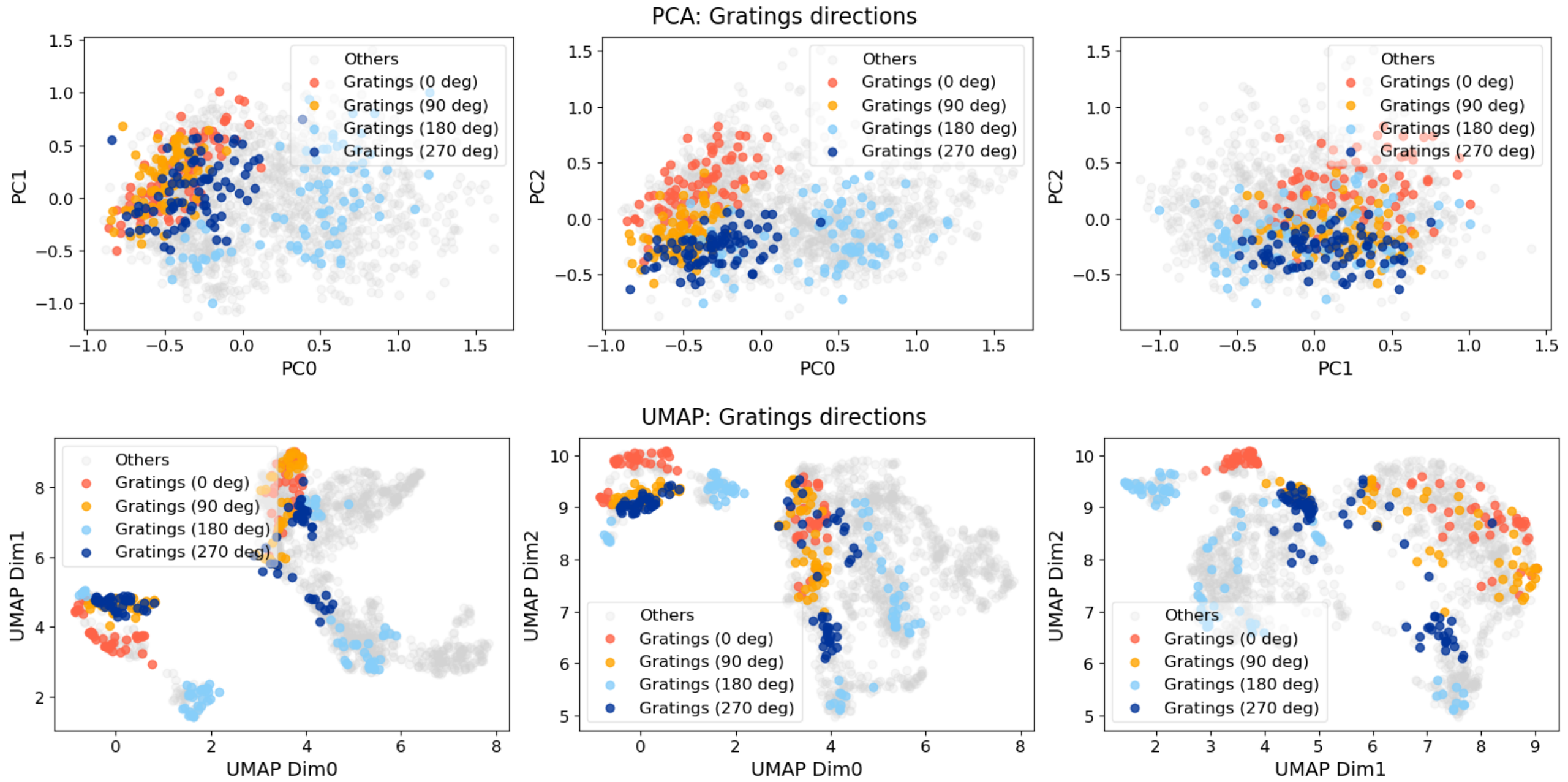
PCA: Interactive 3D Plot of All Stimuli

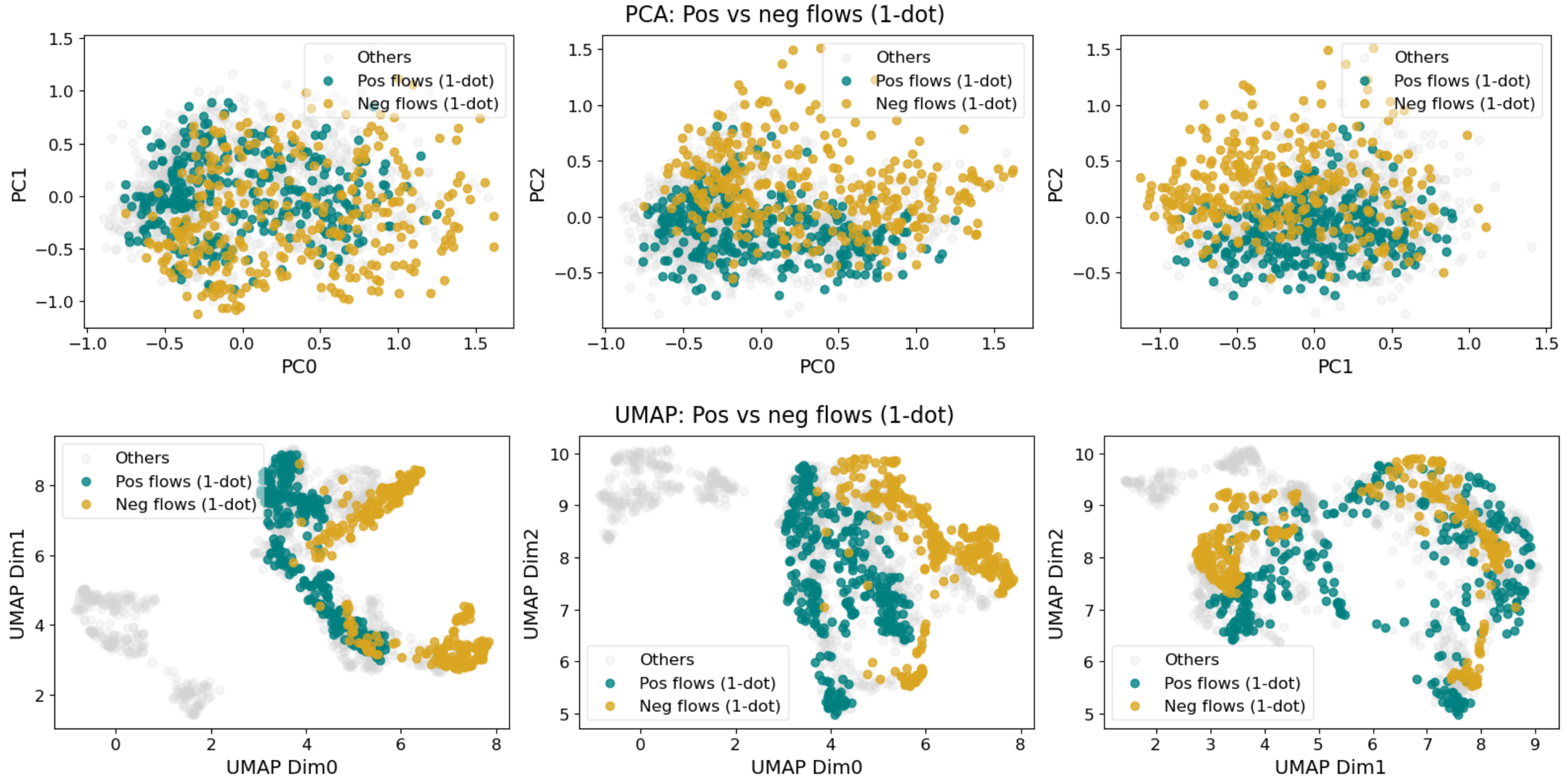


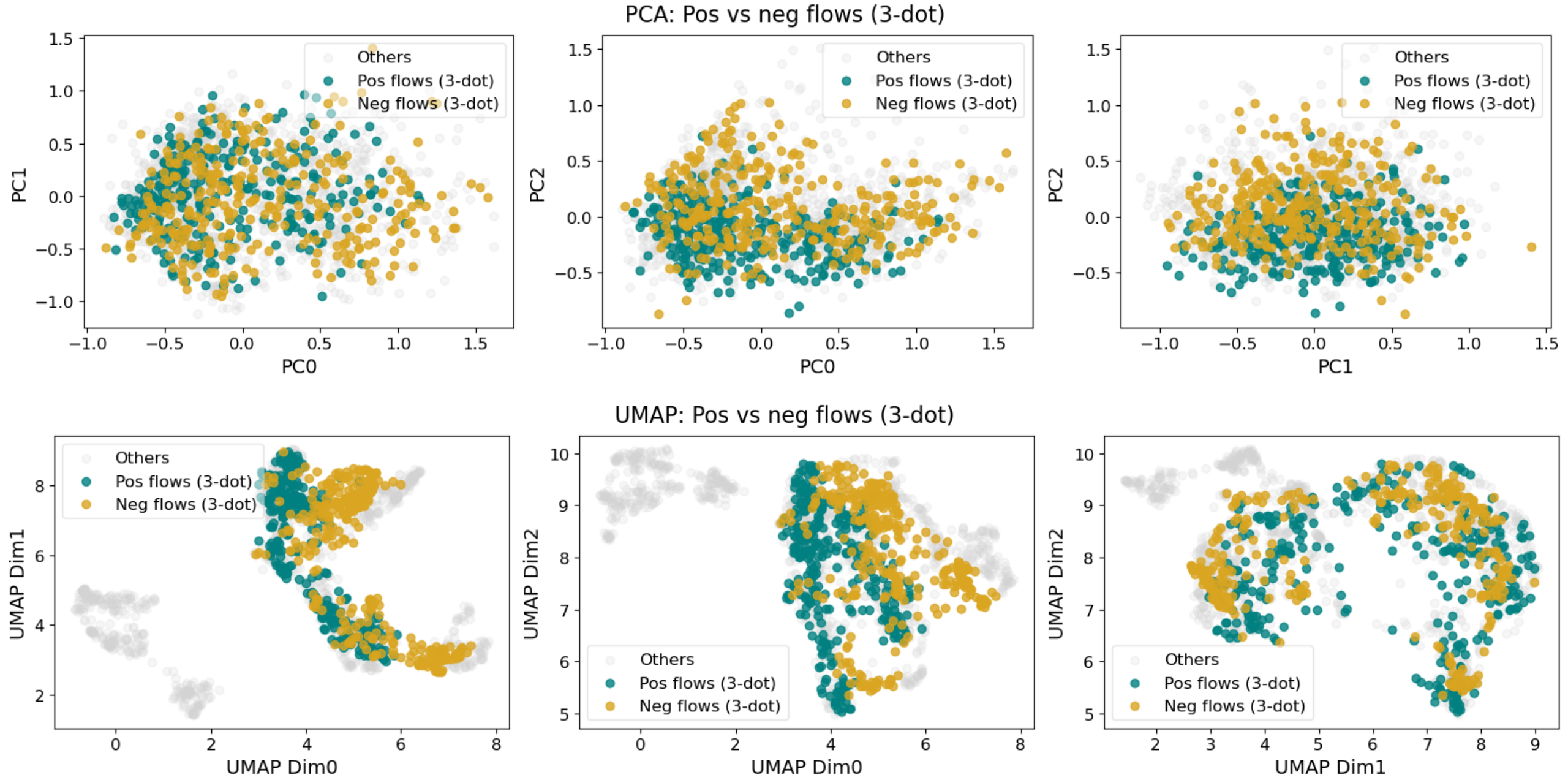
UMAP: Interactive 3D Plot of All Stimuli

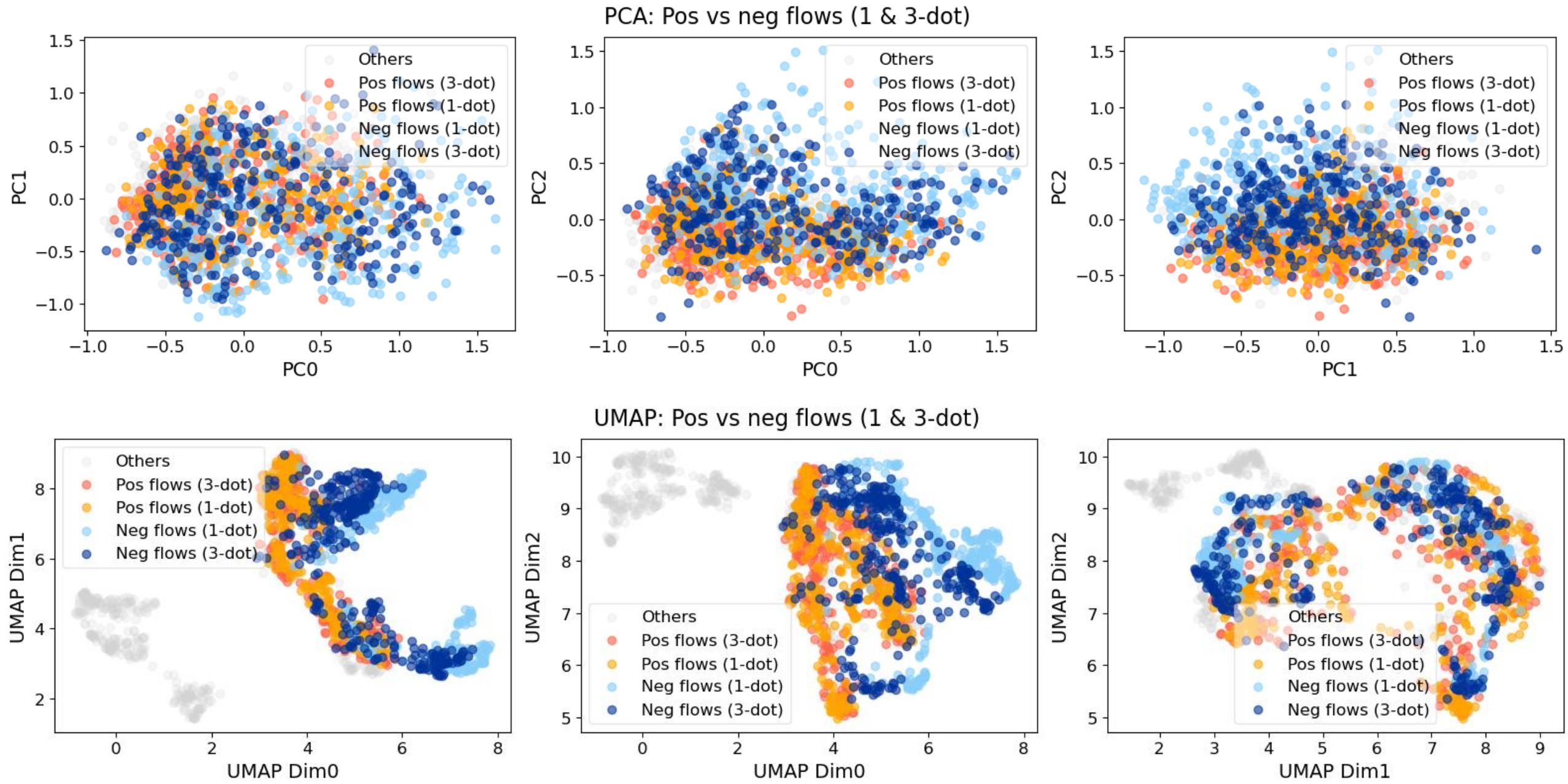



PCA: Gratings vs. All Flows
All FLOWS
GRATINGS
PC0
PC1
PC2
UMAP: Gratings vs. All Flows
UMAP Dim0
UMAP Dim1
UMAP Dim2


PCA: Gratings directions
Others
Gratings (0 deg)
Gratings (90 deg)
Gratings (180 deg)
Gratings (270 deg)
PC0
PC1
PC2
UMAP: Gratings directions
UMAP Dim0
UMAP Dim1
UMAP Dim2

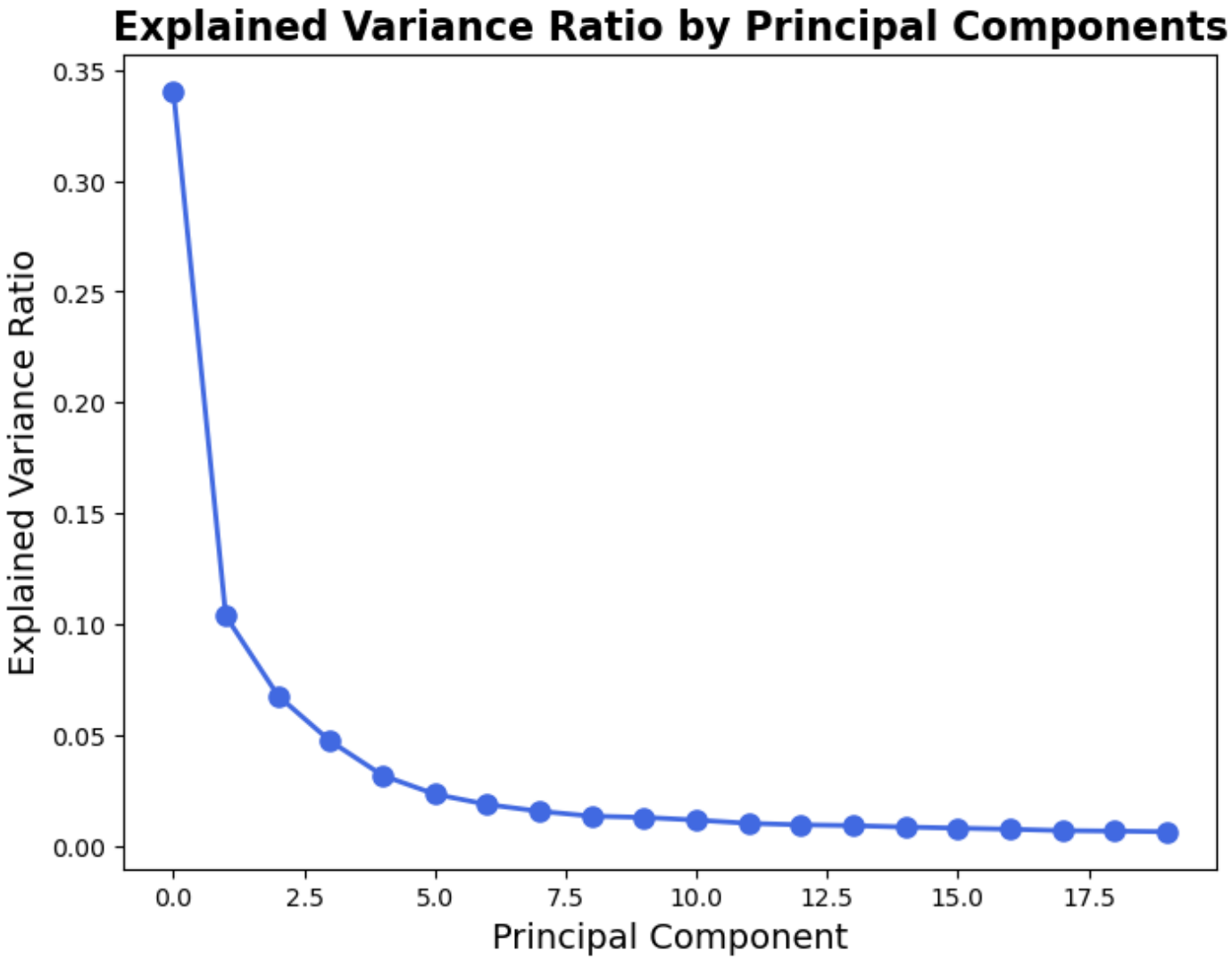

PCA: Pos vs neg flows (1-dot)
Others
Pos flows (1-dot)
Neg flows (1-dot)
PC0
PC1
PC2
UMAP: Pos vs neg flows (1-dot)
UMAP Dim0
UMAP Dim1
UMAP Dim2


PCA: Pos vs neg flows (3-dot)
Others
Pos flows (3-dot)
Neg flows (3-dot)
PC0
PC1
PC2
UMAP: Pos vs neg flows (3-dot)
UMAP Dim0
UMAP Dim1
UMAP Dim2


PCA: Pos vs neg flows (1 & 3-dot)
Others
Pos flows (3-dot)
Pos flows (1-dot)
Neg flows (1-dot)
Neg flows (3-dot)
PC0
PC1
PC2
UMAP: Pos vs neg flows (1 & 3-dot)
UMAP Dim0
UMAP Dim1
UMAP Dim2

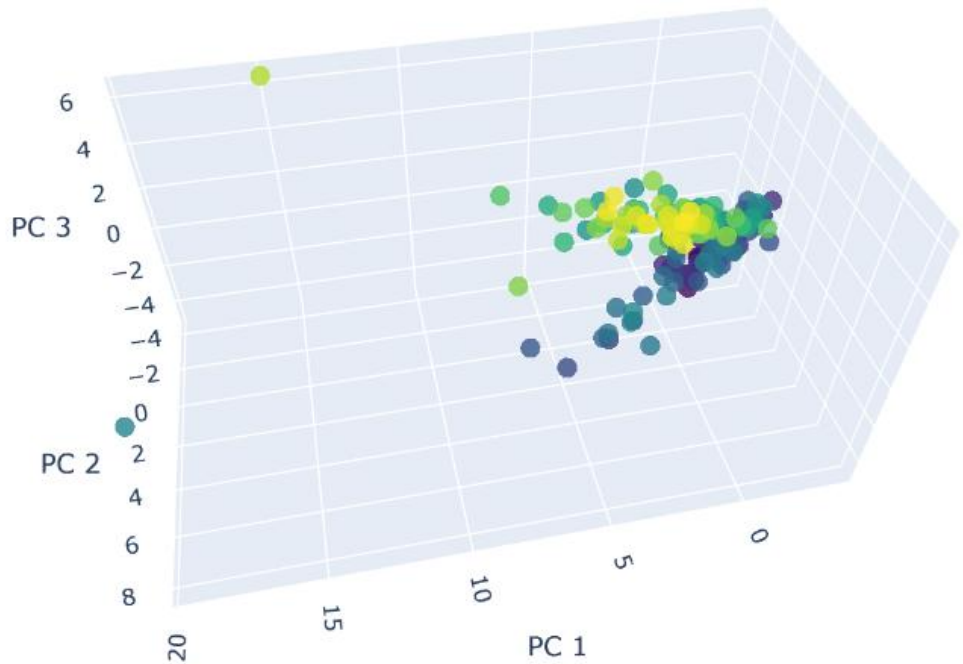
Cells in **dLGN** from **Multiple FOVs** with **48-Stim Set**

PCA, UMAP, Manifold Embedding (reduce **stimuli** dim)

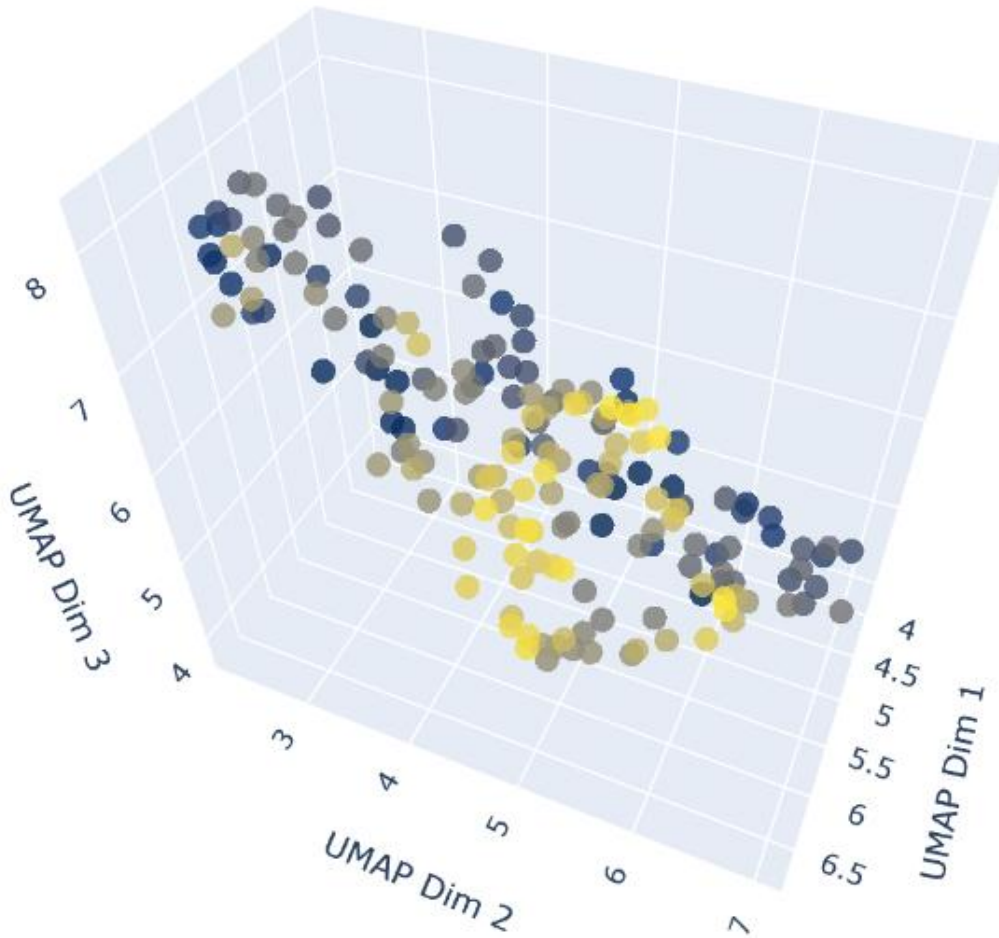


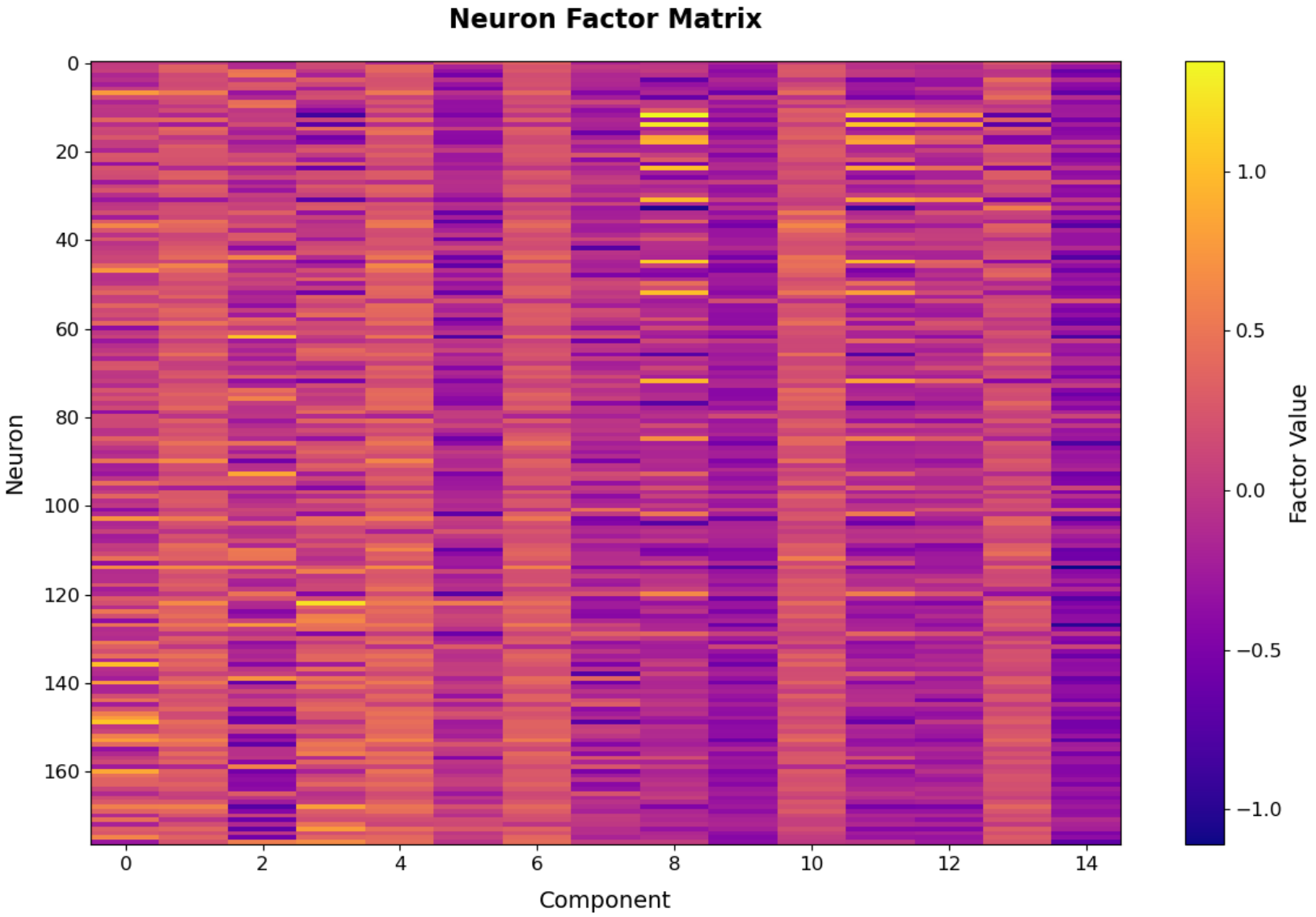
We use the first 3 PCs for plotting.

PCA: Neurons in 3D



UMAP: Neurons in 3D

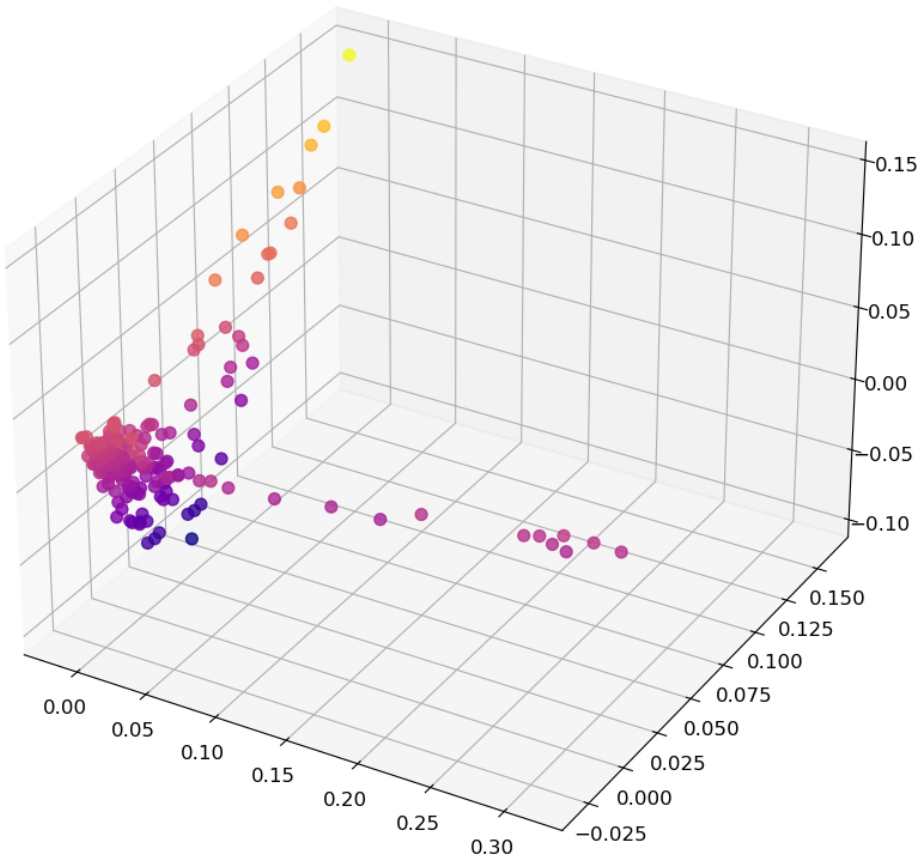




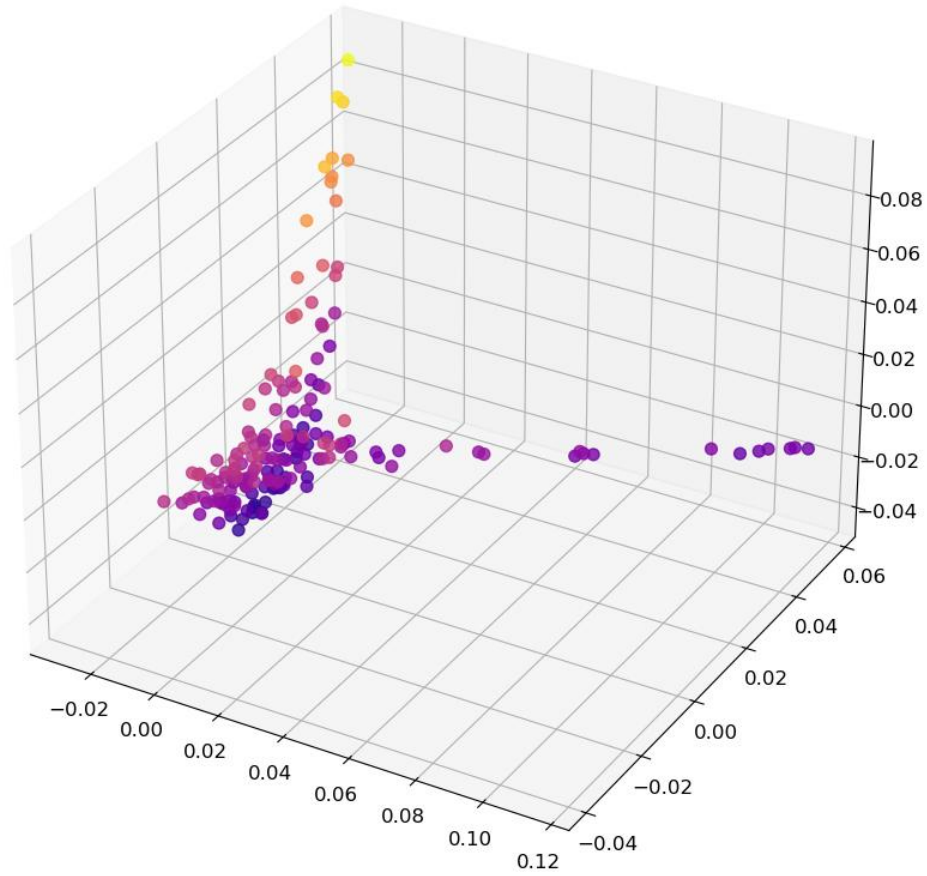
Use the neuron factor matrix to calculate pairwise distance.

Compute Iterated Adaptive Neighborhoods (IAN kernel) from pairwise distances, obtaining data graphs (unweighted and weighted)

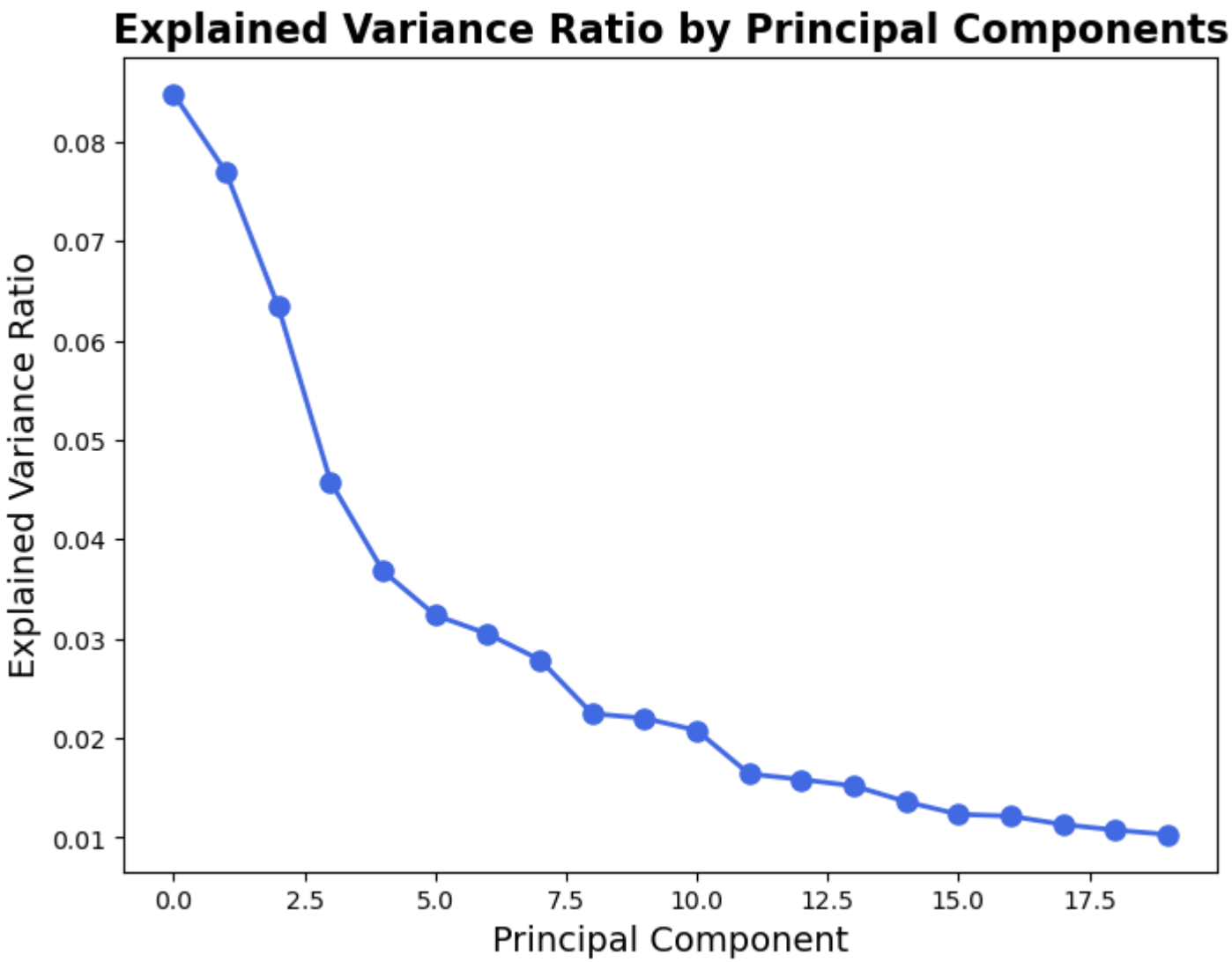
Neuron Diffusion Map (Weighted)



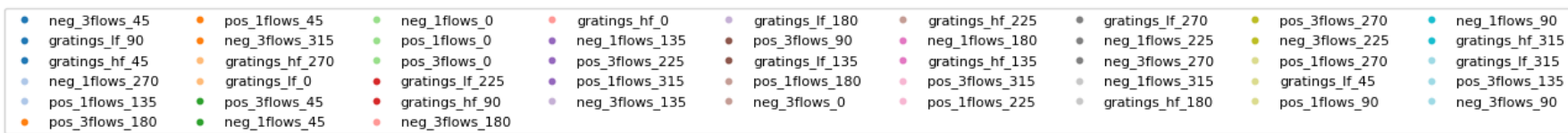
Neuron Diffusion Map (Unweighted)



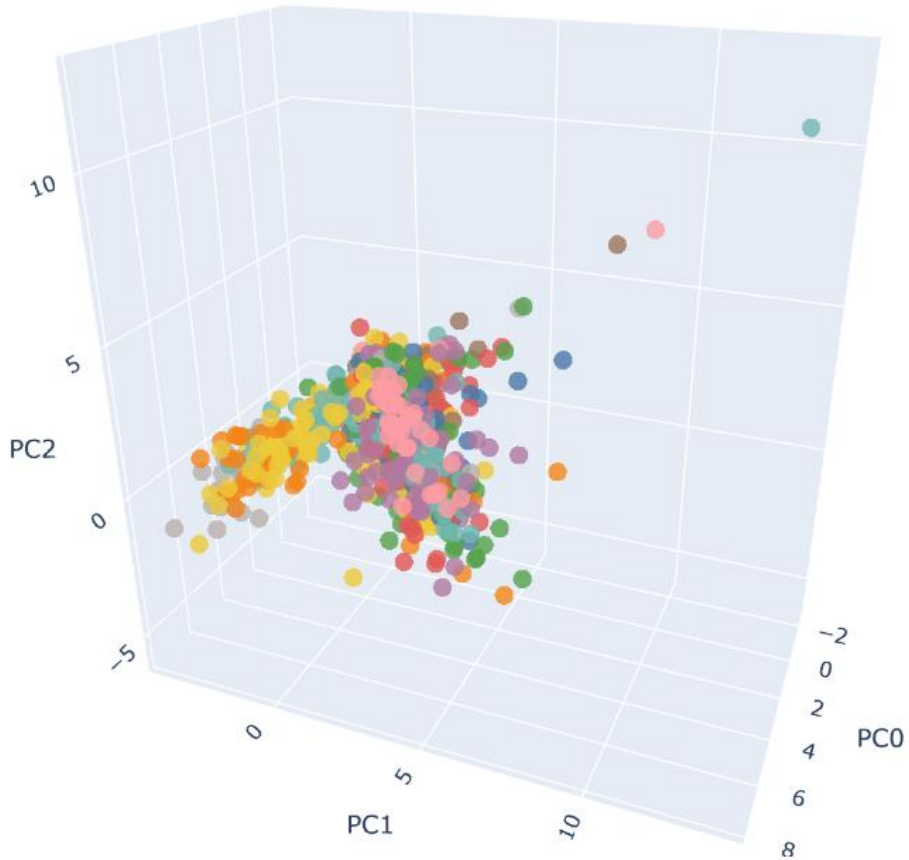
Cells in **SC** from **Multiple FOVs** with **48-Stim Set**
PCA & UMAP (reduce **neurons** dim)


Explained Variance Ratio by Principal Components
Explained Variance Ratio
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0.0
2.5
5.0
7.5
10.0
12.5
15.0
17.5
Principal Component

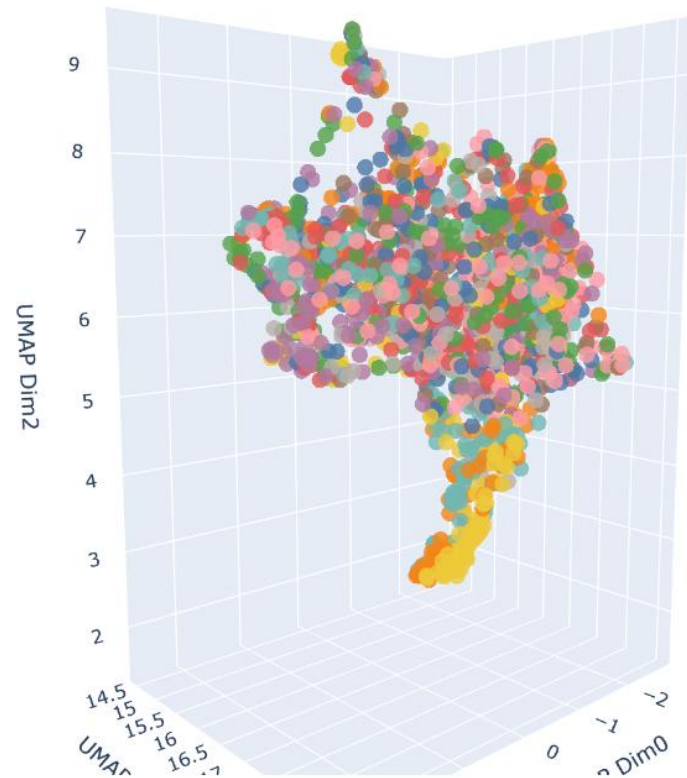

PCA: All Stimuli with Labels
PC1
PC0
PC2
PC0
PC2
PC1
UMAP: All Stimuli with Labels
UMAP Dim1
UMAP Dim0
UMAP Dim2
UMAP Dim0
UMAP Dim2
UMAP Dim1

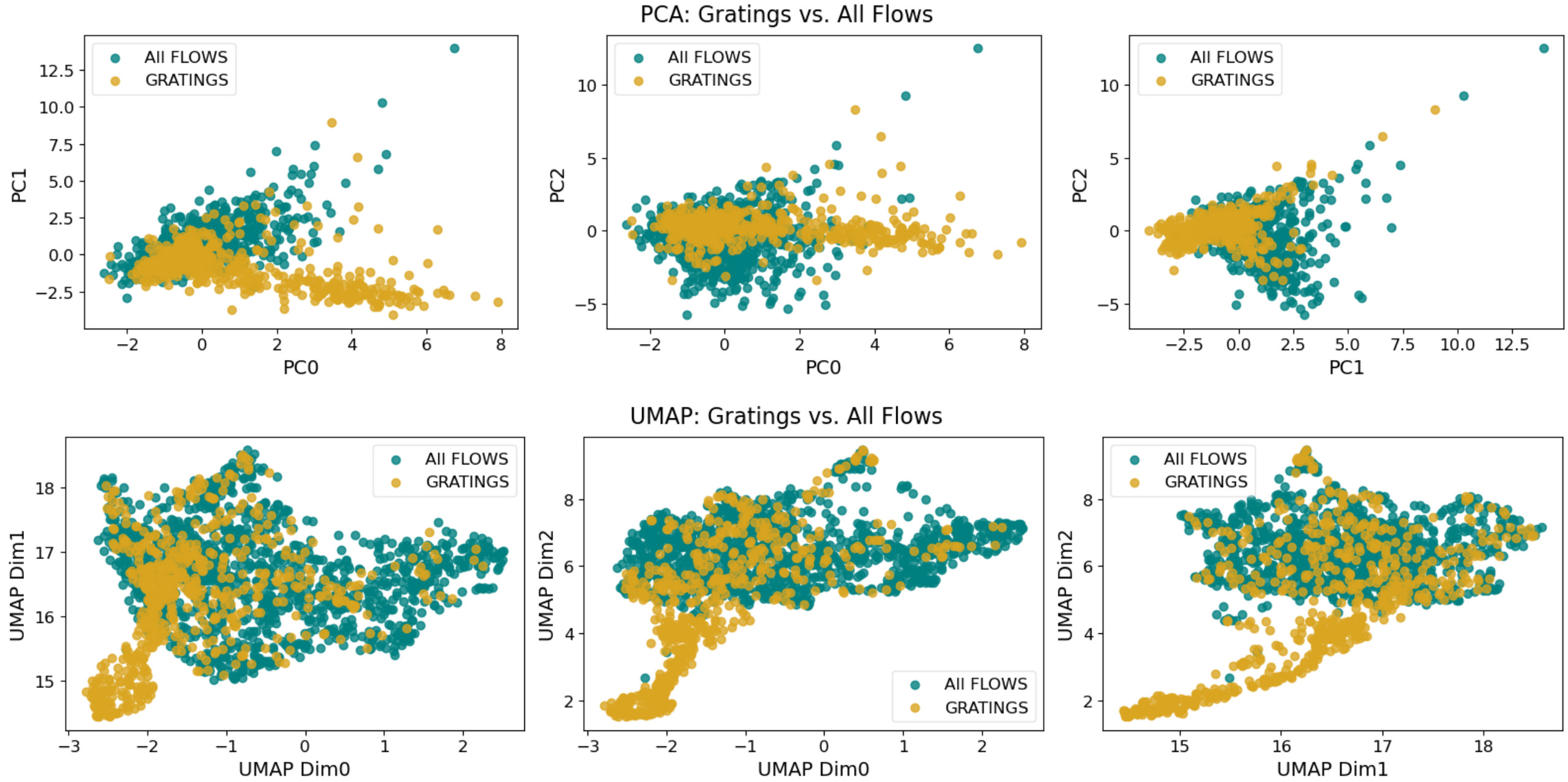

neg_3flows_45
gratings_lf_90
gratings_hf_45
neg_1flows_270
pos_1flows_135
pos_3flows_180
pos_1flows_45
neg_3flows_315
gratings_hf_270
gratings_lf_0
pos_3flows_45
neg_1flows_45
neg_1flows_0
pos_1flows_0
pos_3flows_0
gratings_lf_225
gratings_hf_90
neg_3flows_180
gratings_hf_0
neg_1flows_135
pos_3flows_225
pos_1flows_315
neg_3flows_135
gratings_lf_180
pos_3flows_90
gratings_lf_135
pos_1flows_180
neg_3flows_0
gratings_hf_225
neg_1flows_180
gratings_hf_135
pos_3flows_315
pos_1flows_225
gratings_lf_270
neg_1flows_225
neg_3flows_270
neg_1flows_315
gratings_hf_180
pos_3flows_270
neg_3flows_225
pos_1flows_270
gratings_lf_45
pos_1flows_90
neg_1flows_90
gratings_hf_315
gratings_lf_315
pos_3flows_135
neg_3flows_90

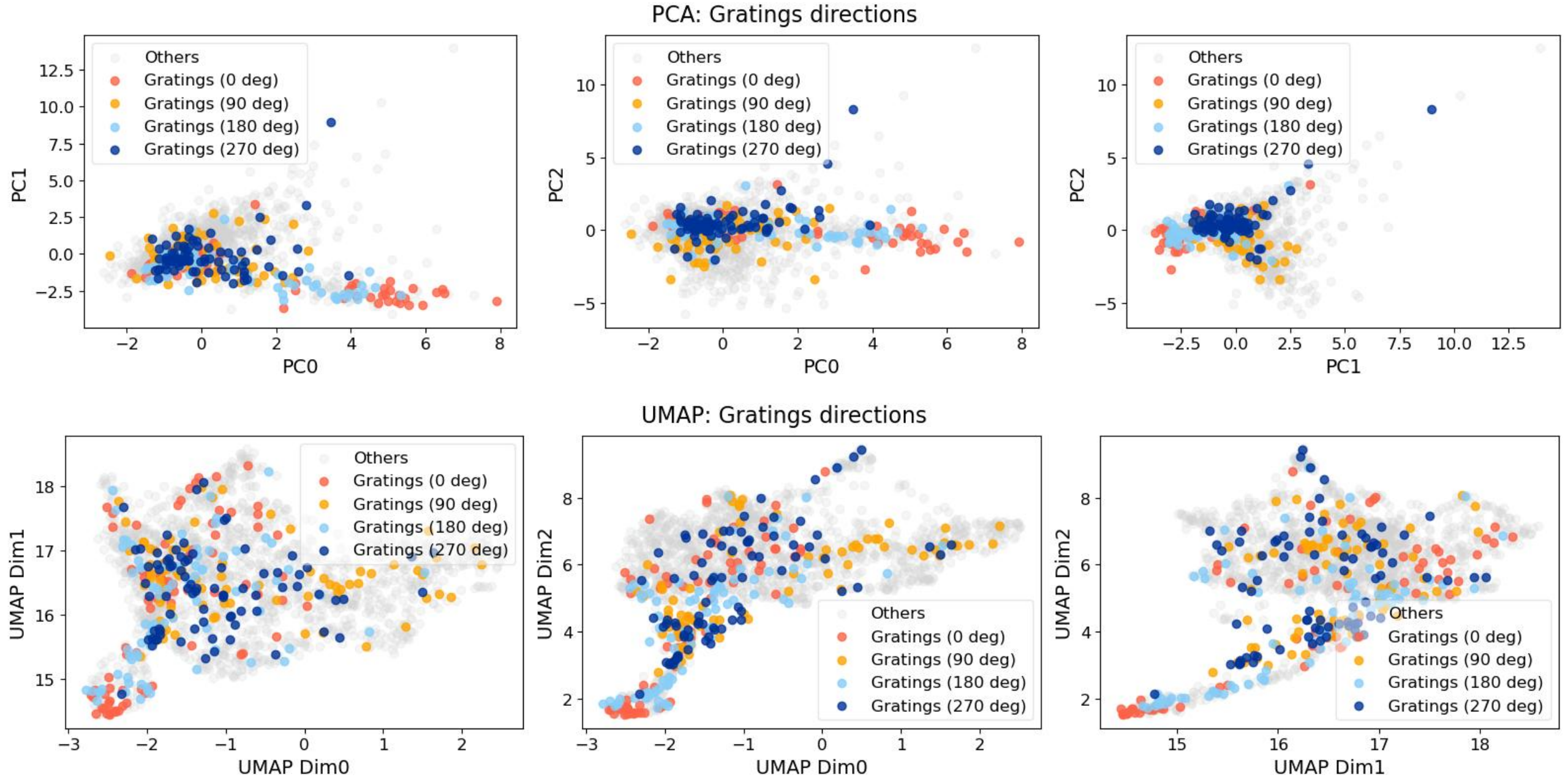
PCA: Interactive 3D Plot of All Stimuli

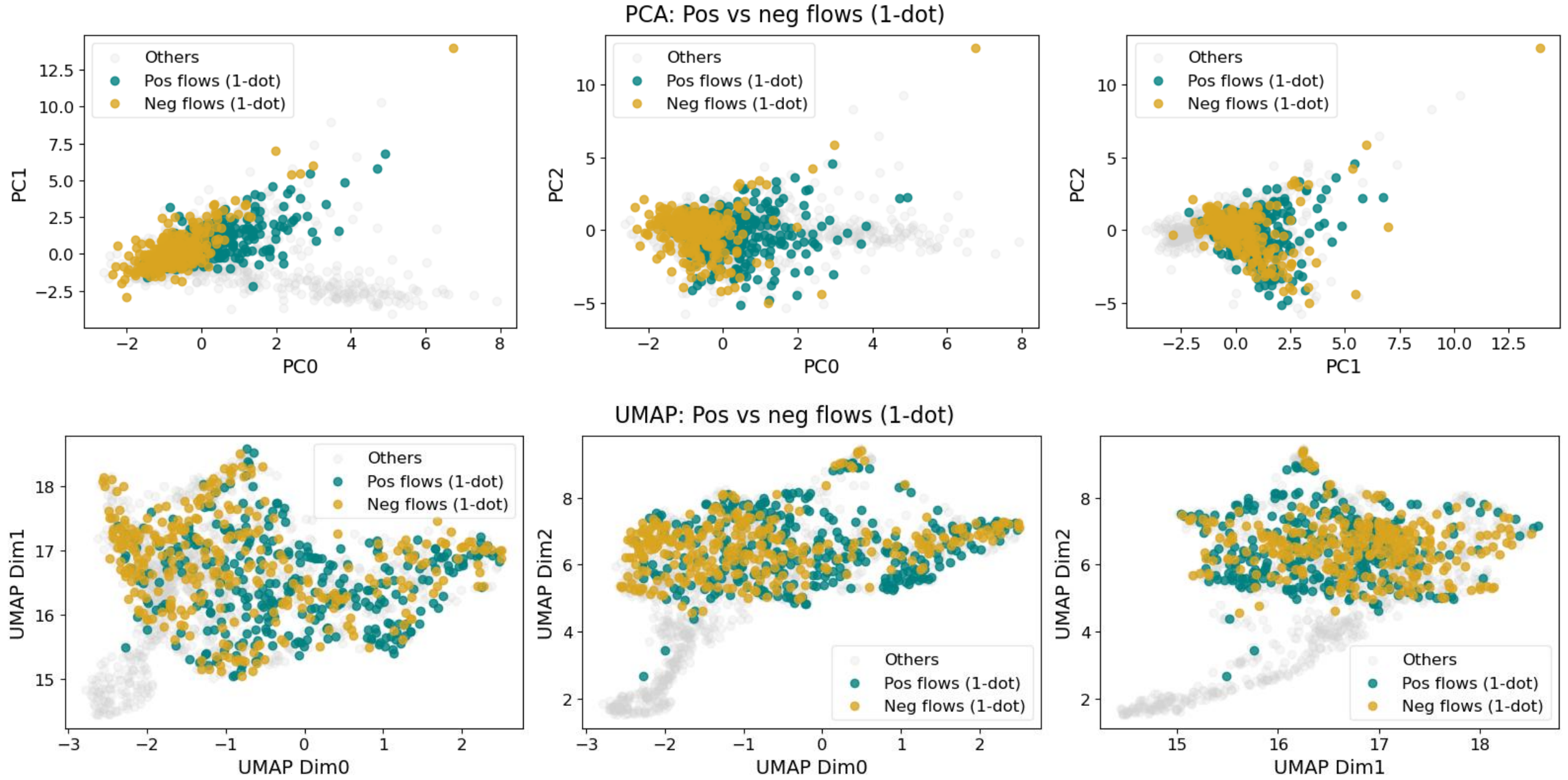


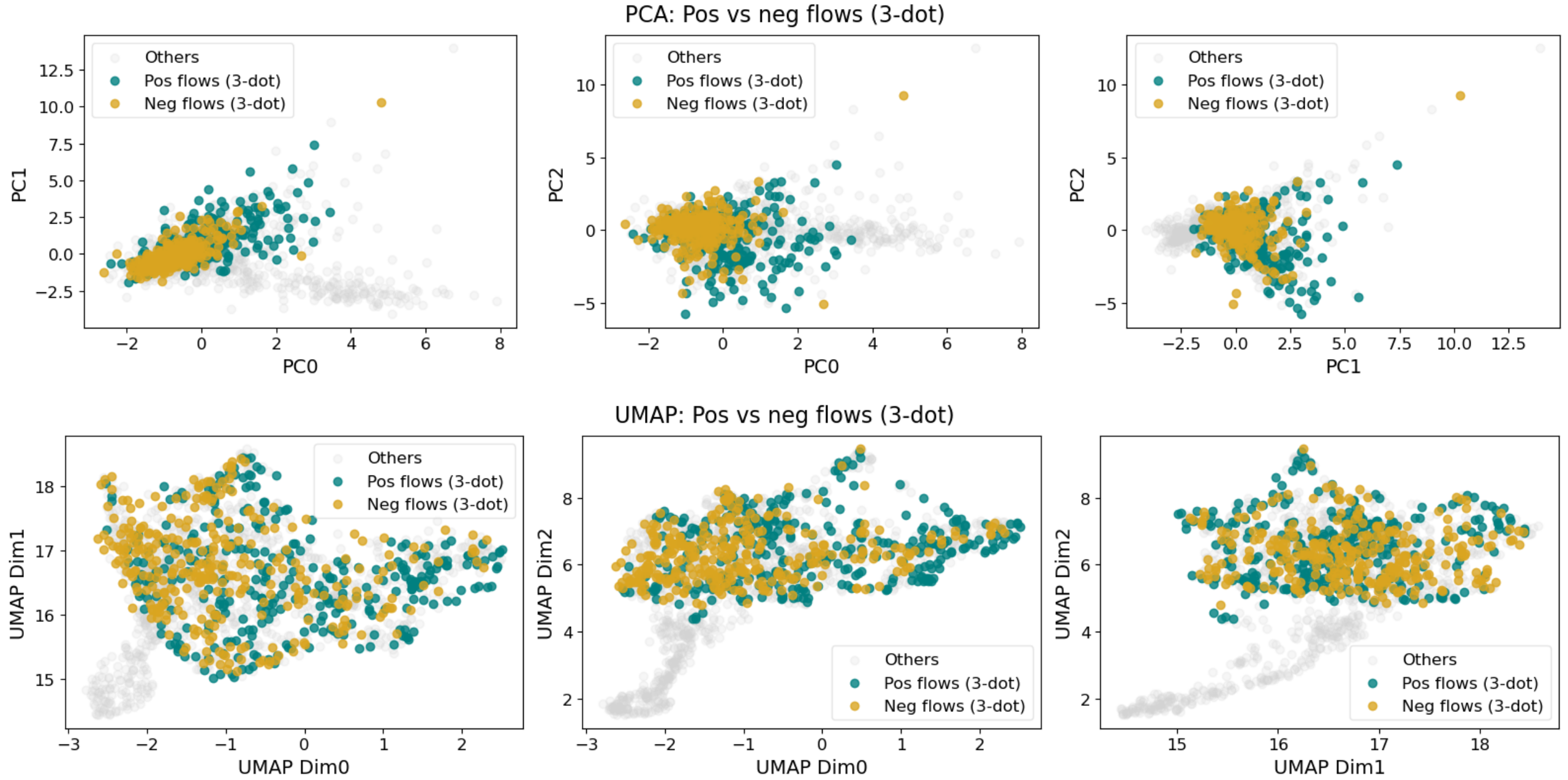
UMAP: Interactive 3D Plot of All Stimuli

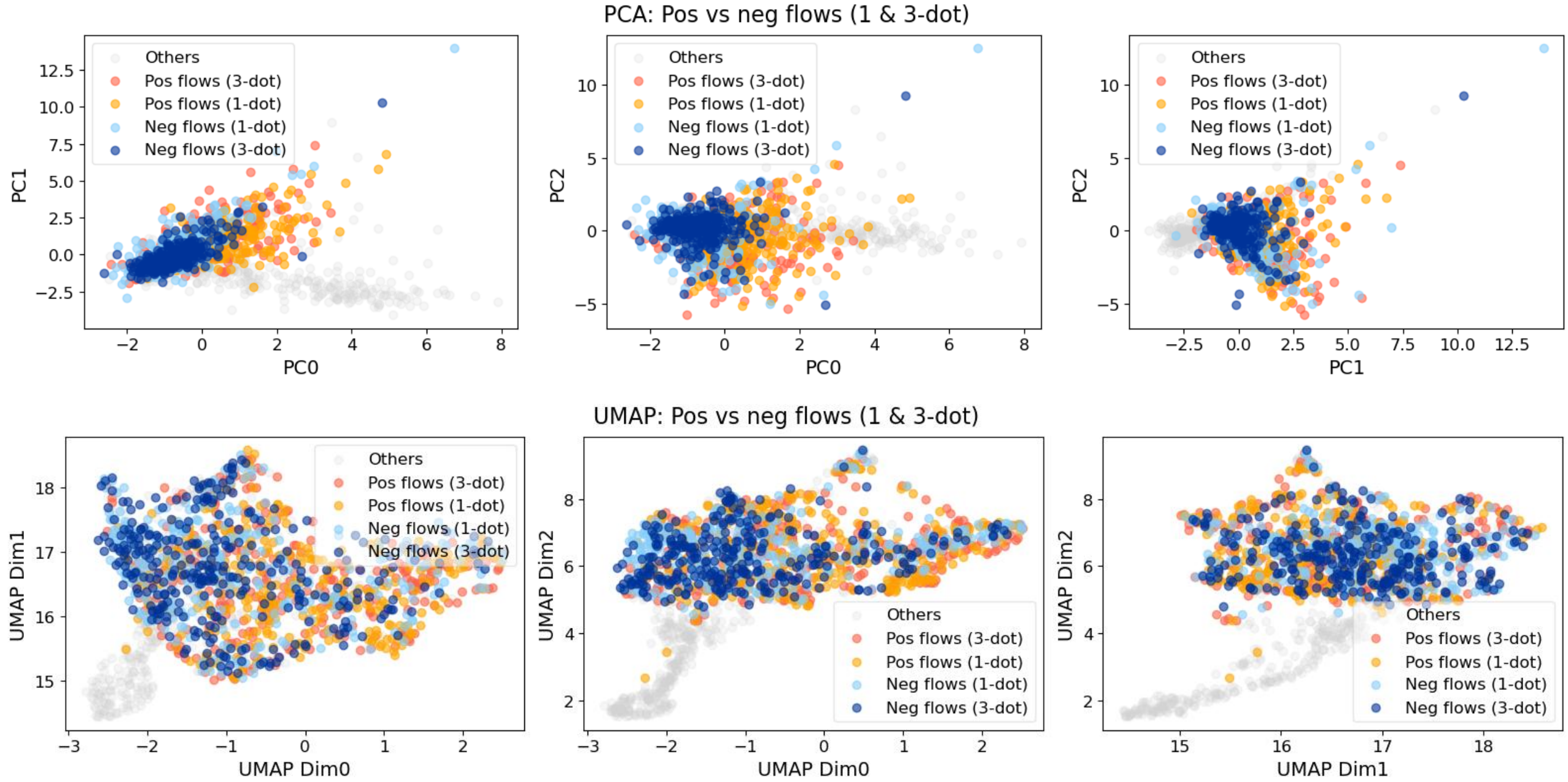



PCA: Gratings vs. All Flows
All FLOWS
GRATINGS
PC1
PC0
PC2
PC0
PC2
PC1
UMAP: Gratings vs. All Flows
UMAP Dim1
UMAP Dim0
UMAP Dim2
UMAP Dim0
UMAP Dim2
UMAP Dim1


PCA: Gratings directions
Others
Gratings (0 deg)
Gratings (90 deg)
Gratings (180 deg)
Gratings (270 deg)
PC0
PC1
PC2
UMAP: Gratings directions
UMAP Dim0
UMAP Dim1
UMAP Dim2

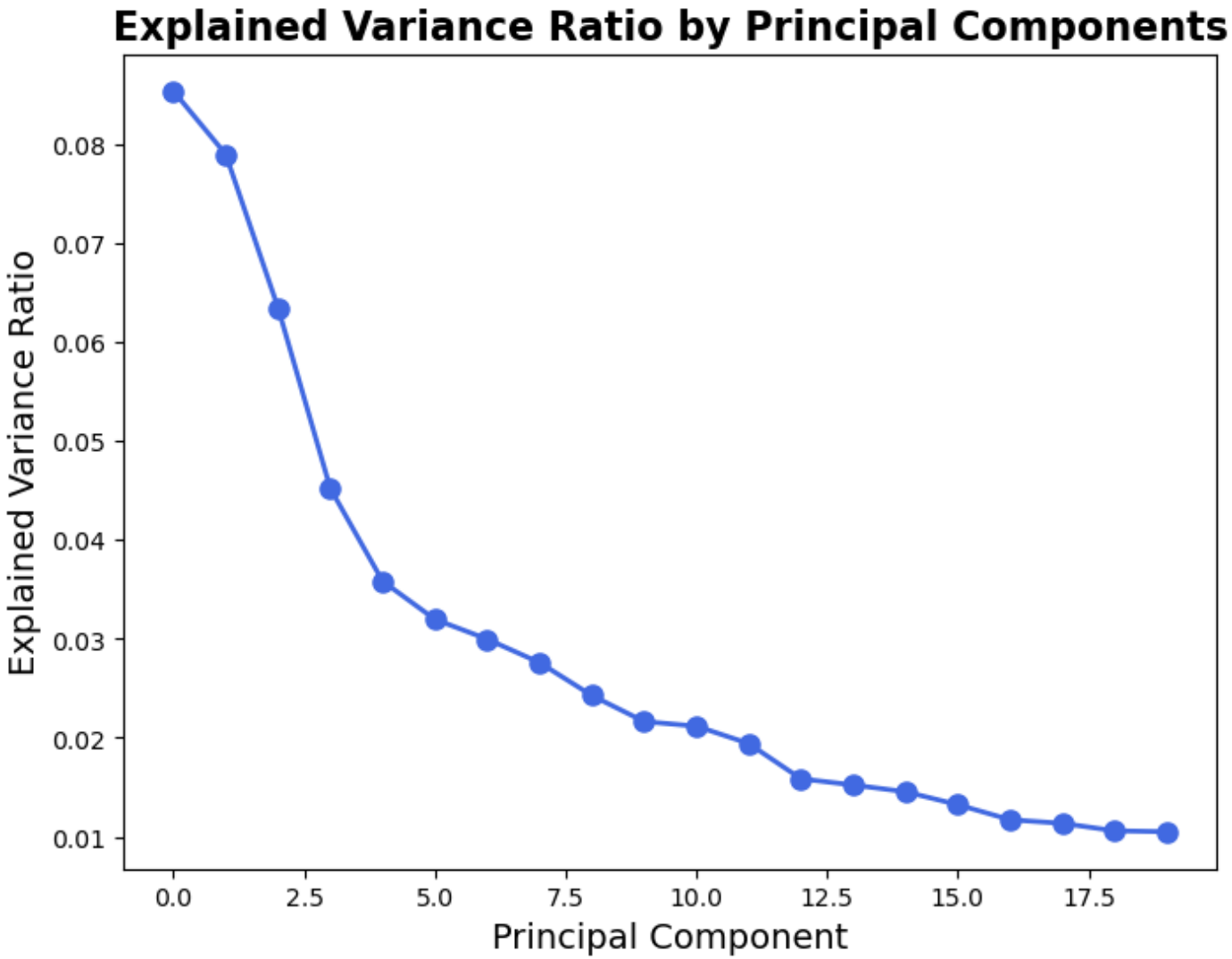

PCA: Pos vs neg flows (1-dot)
Others
Pos flows (1-dot)
Neg flows (1-dot)
PC0
PC1
PC2
UMAP: Pos vs neg flows (1-dot)
UMAP Dim0
UMAP Dim1
UMAP Dim2


PCA: Pos vs neg flows (3-dot)
Others
Pos flows (3-dot)
Neg flows (3-dot)
PC0
PC1
PC2
UMAP: Pos vs neg flows (3-dot)
UMAP Dim0
UMAP Dim1
UMAP Dim2

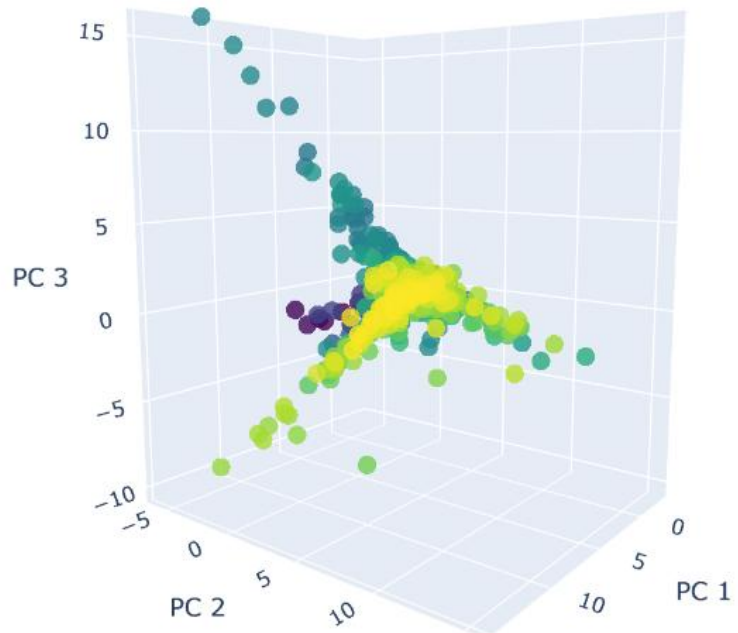

PCA: Pos vs neg flows (1 & 3-dot)
Others
Pos flows (3-dot)
Pos flows (1-dot)
Neg flows (1-dot)
Neg flows (3-dot)
PC1
PC0
PC2
PC0
PC2
PC1
UMAP: Pos vs neg flows (1 & 3-dot)
UMAP Dim1
UMAP Dim0
UMAP Dim2
UMAP Dim0
UMAP Dim2
UMAP Dim1

Cells in **SC** from **Multiple FOVs** with **48-Stim Set**

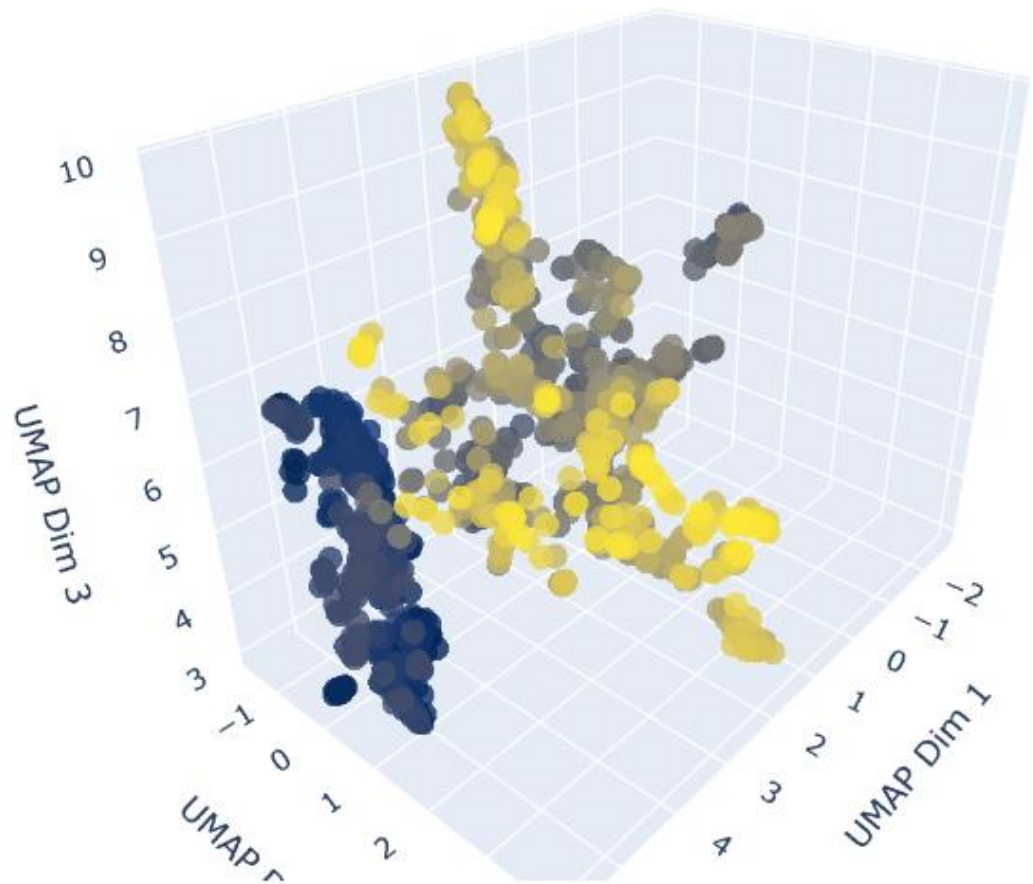
PCA, UMAP, Manifold Embedding (reduce **stimuli** dim)

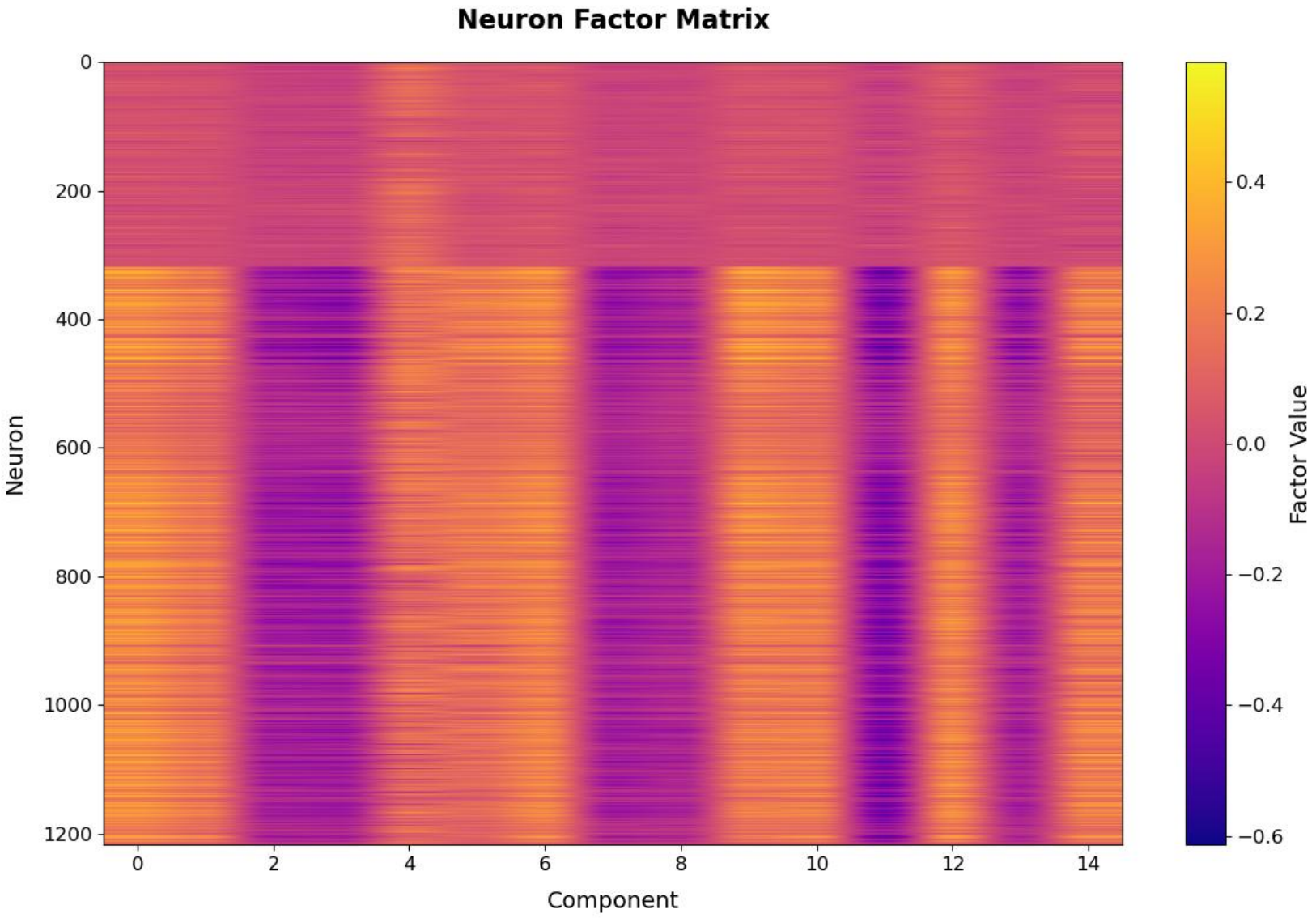

Explained Variance Ratio by Principal Components
Explained Variance Ratio
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0.0
2.5
5.0
7.5
10.0
12.5
15.0
17.5
Principal Component

PCA: Neurons in 3D



UMAP: Neurons in 3D



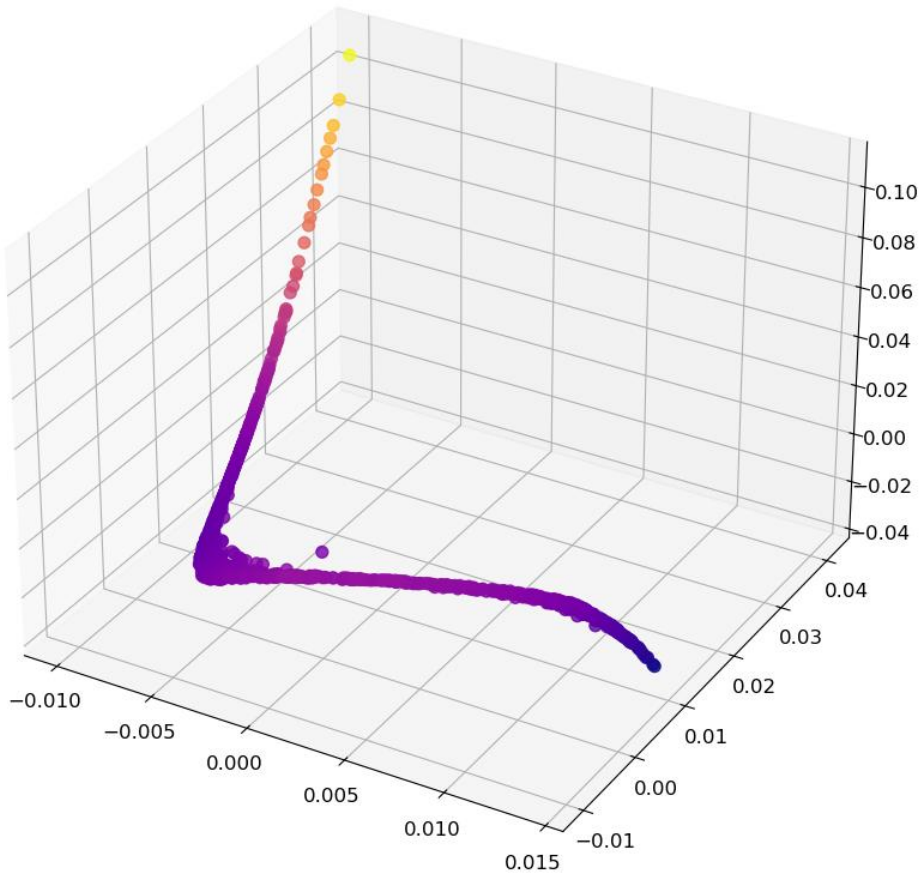


Two types of neurons

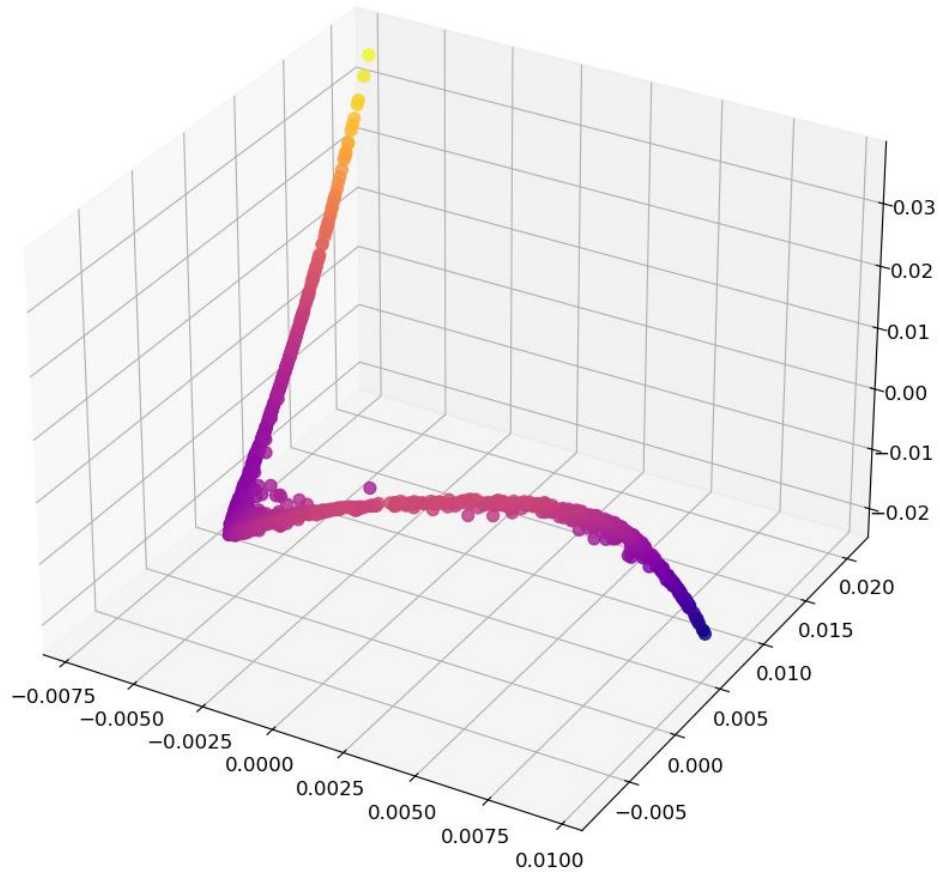
Use the neuron factor matrix to calculate pairwise distance.

Compute Iterated Adaptive Neighborhoods (IAN kernel) from pairwise distances, obtaining data graphs (unweighted and weighted)

Neuron Diffusion Map (Weighted)



Neuron Diffusion Map (Unweighted)



Thanks