

1. C3D model to decode future action (lick left / right /false left/ false right) from facial recording videos. The decoding accuracy between different sides exhibited asymmetric distribution.
2. Automatic classification to identify the reliable neuron traces for downstream analysis. The classifier was implemented via SVM with a linear kernel. The prominent features were as follows: estimated raw trace baseline standard deviation, the regularity of weight and max-projection images, the maximal and minimal value of raw trace.
3. Estimate the neural activity. The numerical  $\text{Ca}^{2+}$  events were identified by a local peak discovery function with a standard deviation threshold. Then these discrete events were fitted by histogram to approximate continuous firing curves. This step was used to reduce the dimensionality of fitted traces and generated tuning curve underlying the smooth assumption.
4. The construction of similarity graph and extraction of simplicial skeleton to run UMAP (visualize neural population) and graph-based clustering (to assign discrete category). Unlike the hierarchy or k-means clustering, the Louvain algorithm computed the best partition of the population, without a prior about the number of neighbors. Therefore, the method could capture variety of neural response and generate comparable neuron clusters from datasets obtained in different experiments.
5. Cluster-based analysis: continuous neural dynamics -> discrete category (clusters)
6. A precise quantification approach designed for visualizing the response preference of the cortical neurons. For each neuron, the nearest neurons were collected and the imbalance index was calculated, which provided a local diversity measure. Furthermore, a statistical test could be applied to identify significant spatial response preference.
7. Lasso-solver or orthonormal pursuit method to quantify the local encoding of global information. A sparse linear combination using adjacent 50 neurons was enough to recover a large scale of neural activity among more than 4500 neurons. Moreover, the pattern of combination was conserved between two sequential sessions and different time periods.
8. Inferring confluctuation from paired traces. For each neuron-pair,  $\text{Ca}^{2+}$  trace confluctuation AUC was computed, then confluctuation AUC was normalized by the total AUC for individual neuron. This method provided an asymmetric metric for neuron communication and could be refined to be a symmetric to construct a undirect graph further.
9. Comparable approaches for joint analysis among different experiments. As previous described, the clustering algorithm and visualization were confined to a single dataset since the mismatch dimensionality impeded data integration among different experiment time and design. A plausible way was to divide the whole time period into equally long fragments and to align time periods to key time points. However, there was still a significant response shift after alignment even for sequential sessions, which indicated the importance to align the latent features rather than the trace itself.

Here, the clustering results and principal components were aligned and compared by mathematical and computational methods. Among eigen-trace (a trace for each cluster) obtained in different experiment, a similarity graph could be constructed using the trimmed-DTW metric, which revealed a dose-dependent neural dynamic difference. The principal components in the state space were transformed by a rotation matrix obtained by an orthonormal Procrustes solver. Then the Frobenius norm could be a metric to compare the difference between the reference PCs and query PCs, quantifying the global dynamics variety among different trials. The combined PCA trajectory plot was fitted by 2-D spline.