Neural correlates of sniffing and place in simultaneous recordings from the olfactory bulb and hippocampus

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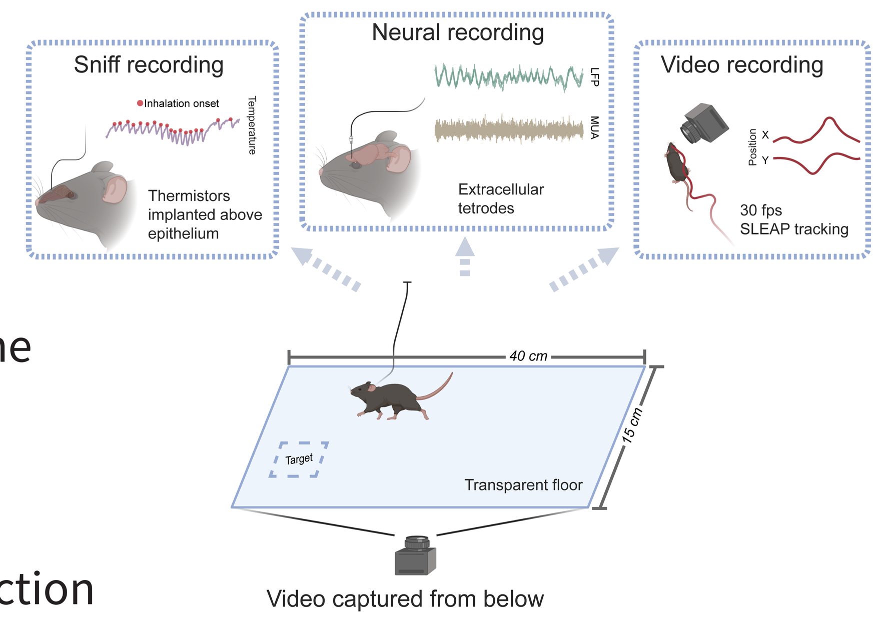
Abstract

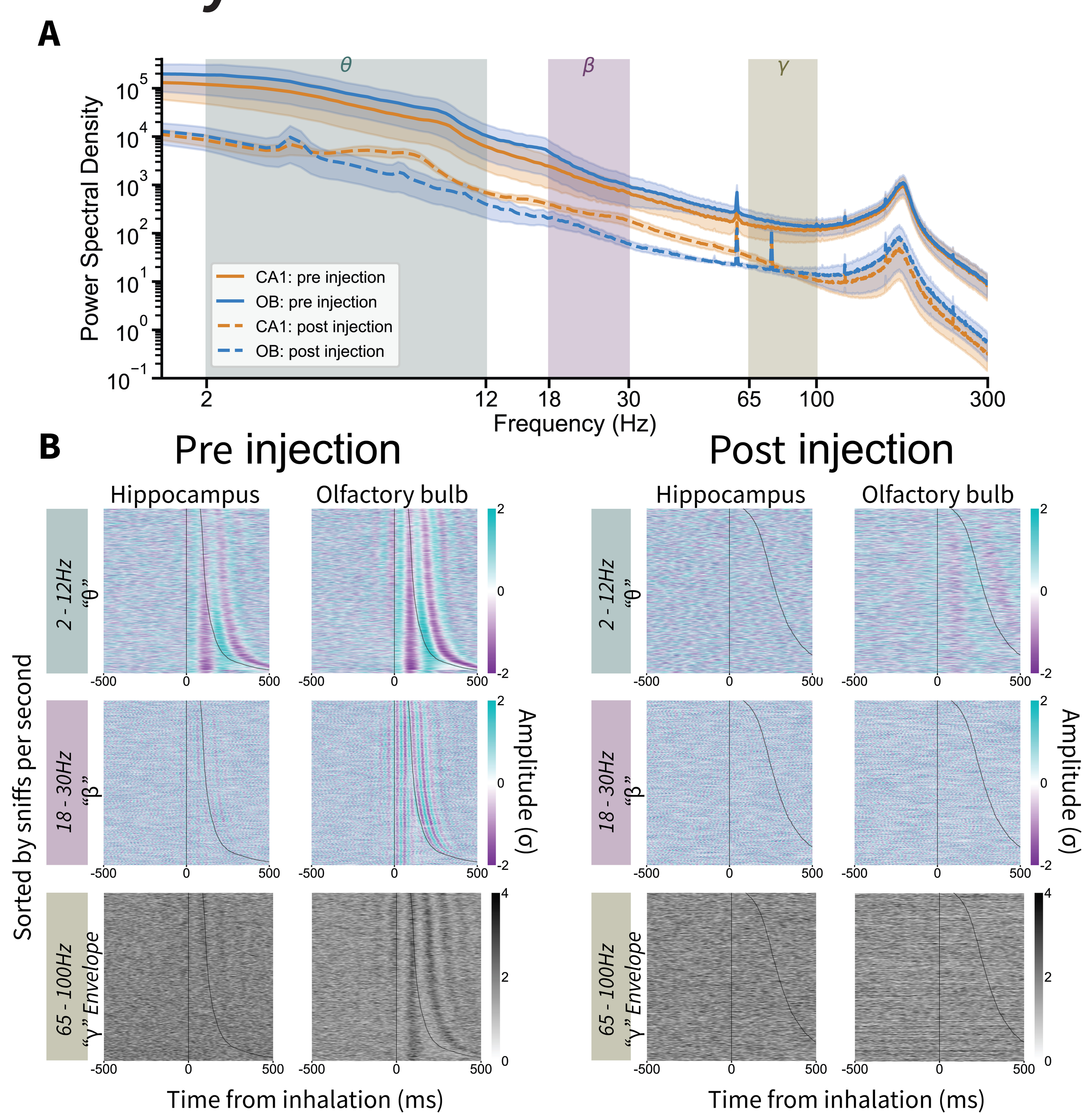
Rodents sniff to sample odors, enabling them to actively sense the chemical world. These odor samples support the identification of objects, as well as the localization of events in space and time. However, there is no receptor for place or time. To enable goal-directed behavior, mice must contextualize odor information with signals about when, where, and how they sniffed. Recent work from our lab has shown that neuronal activity in the olfactory bulb (OB) reflects spatial location and breathing rhythms. Here, we asked how these contextual signals depend on feed-forward input from olfactory sensory neurons (OSNs). We simultaneously recorded from the OB and hippocampus area CA1 in freely foraging mice before and after injecting methimazole (MMZ), a drug that ablates OSNs. We show that OSN input is required for the synchrony between sniffing and local field potentials in the OB and CA1. Further, MMZ injections eliminate neural correlates of breathing and movement while leaving spatial correspondence largely intact. Building on previous findings that sniffing synchronizes brain and behavioral rhythms, our work suggests that sniff synchronization may influence internal models of self and environment.

Methods

- Task designed to encourage foraging like behavior for water reward
- Tetrodes implanted in the olfactory bulb (OB) and hippocampus (CA1)
- Methimazole (MMZ) injection ablates olfactory sensory neurons
  - *14 sessions pre injection followed by 10 sessions post injection*
- Spike sorting in Kilosort4 manual curation in phy2
  - *across 4 mice we recorded from 186 OB and 827 CA1 single units, 537 OB and 565 CA1 multiunits*

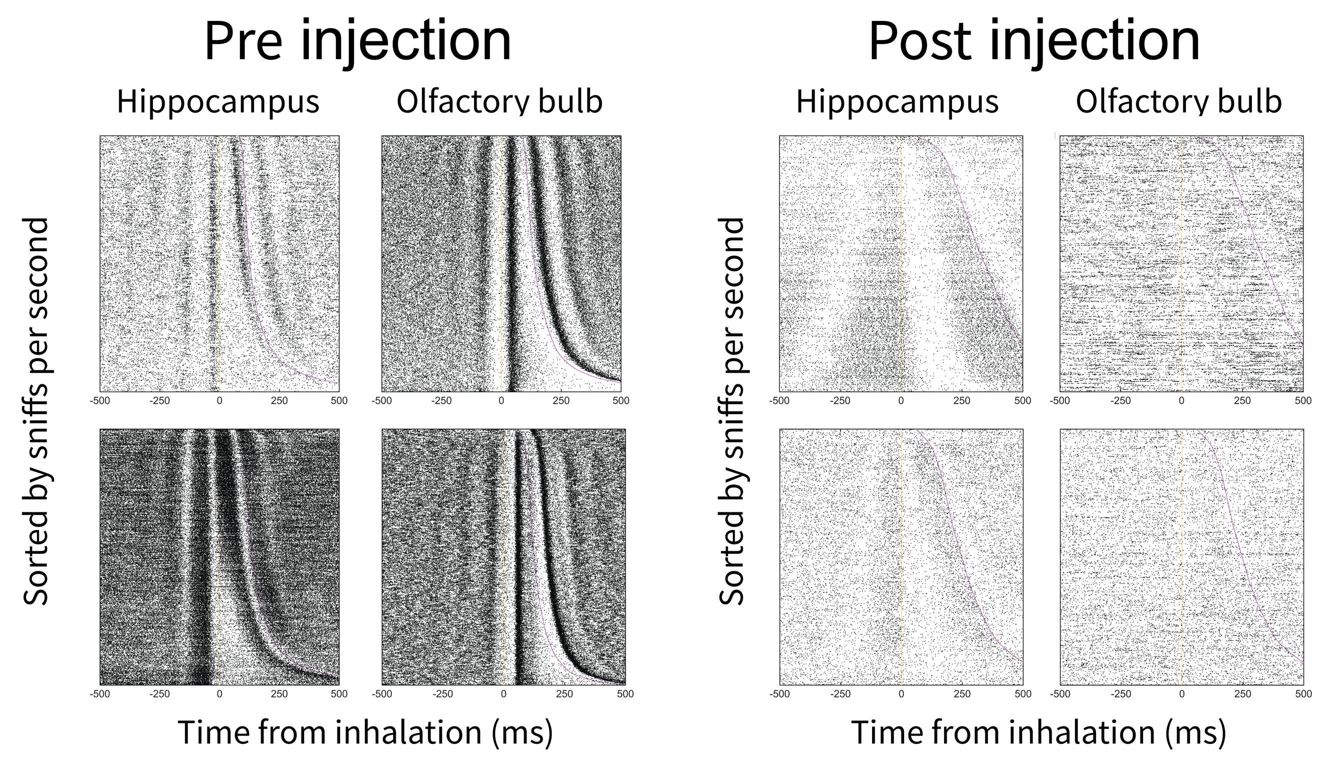


Sniff synchronous LFPs

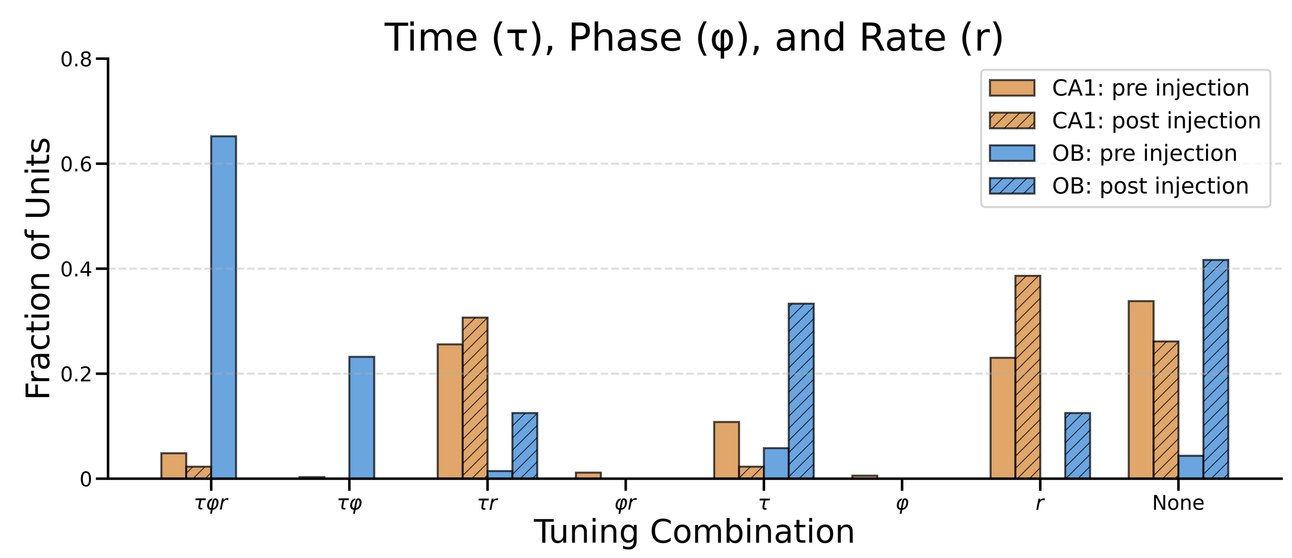


Alignmnet between LFPs and respiration is disrupted by MMZ injection. A) Power spectral density estimated using Welch's method in 4s windows. **B)** Rasters are constructed by aligning 1s epochs of LFPs to inhalation times and using color to represent amplitude. Rows are sorted such that the slowest sniffs are at the bottom, and the fastest are at the top of the rasters.

Sniff synchronous spiking



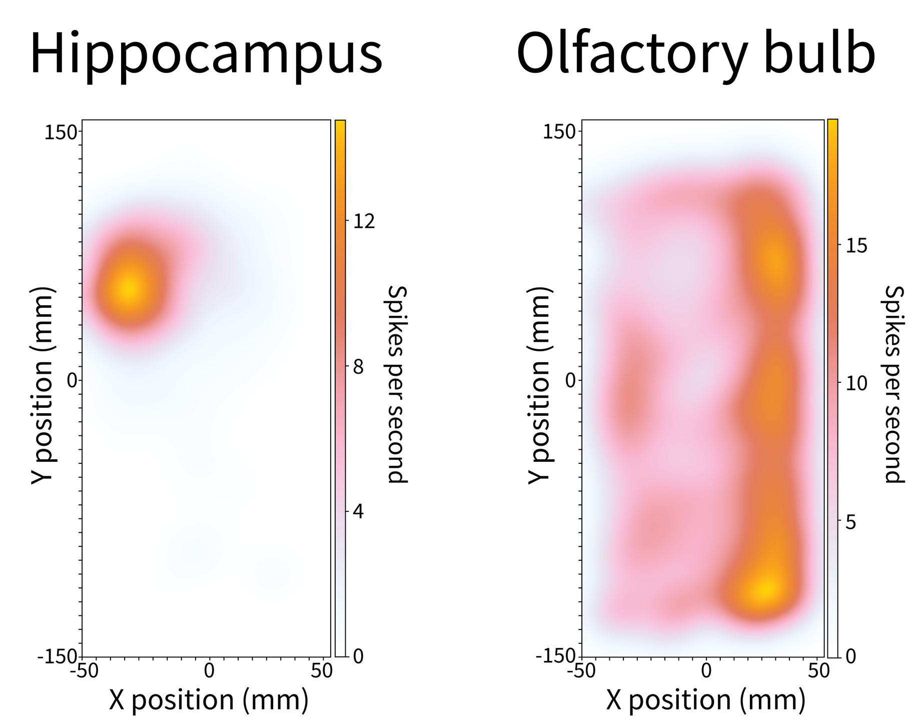
Single units in OB and CA1 are aligned to inhalation onset. Each row represents a 1s epoch centered on an inhalation time with a tick plotted for each spike. Rows are sorted such that the slowest sniffs are at the bottom, and the fastest are at the top of the rasters.

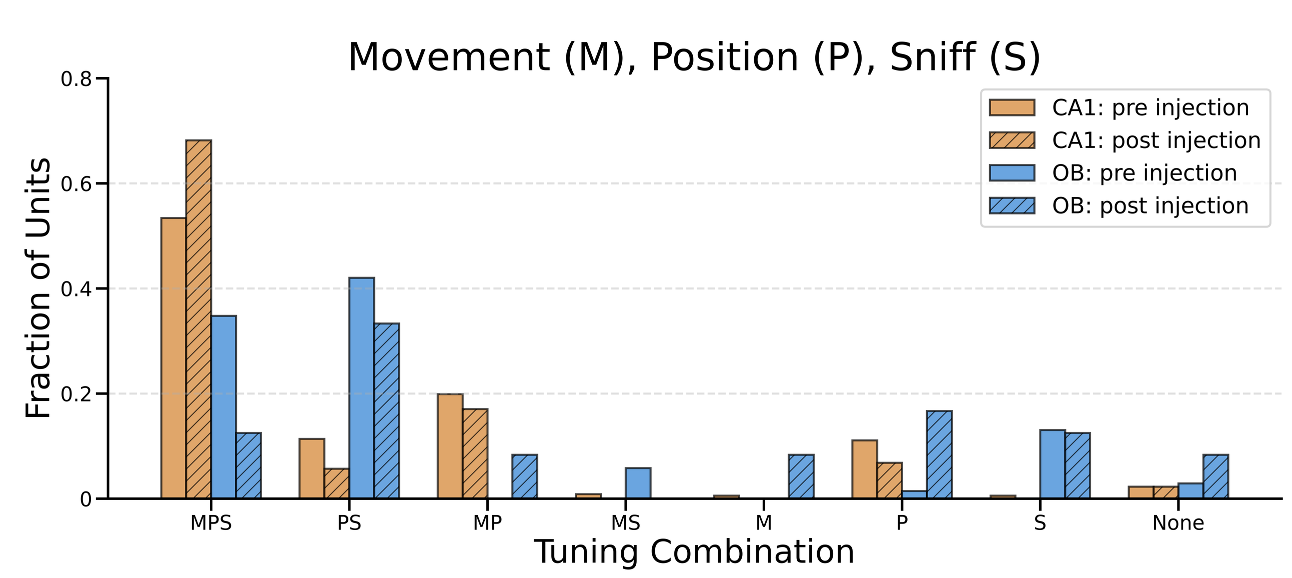


MMZ disrupts single unit tuning in OB and CA1 to sniffing parameters. Tuning combinations were estimated using a poisson generalized additive model (PGAM)[1] in which a basis of spline functions for each parameter was fit to the spike counts in 6ms bins. **τ** represents time from inhalation, **φ** the phase of the sniff cycle, and **r** the sniff rate.

Spatial olfactory code

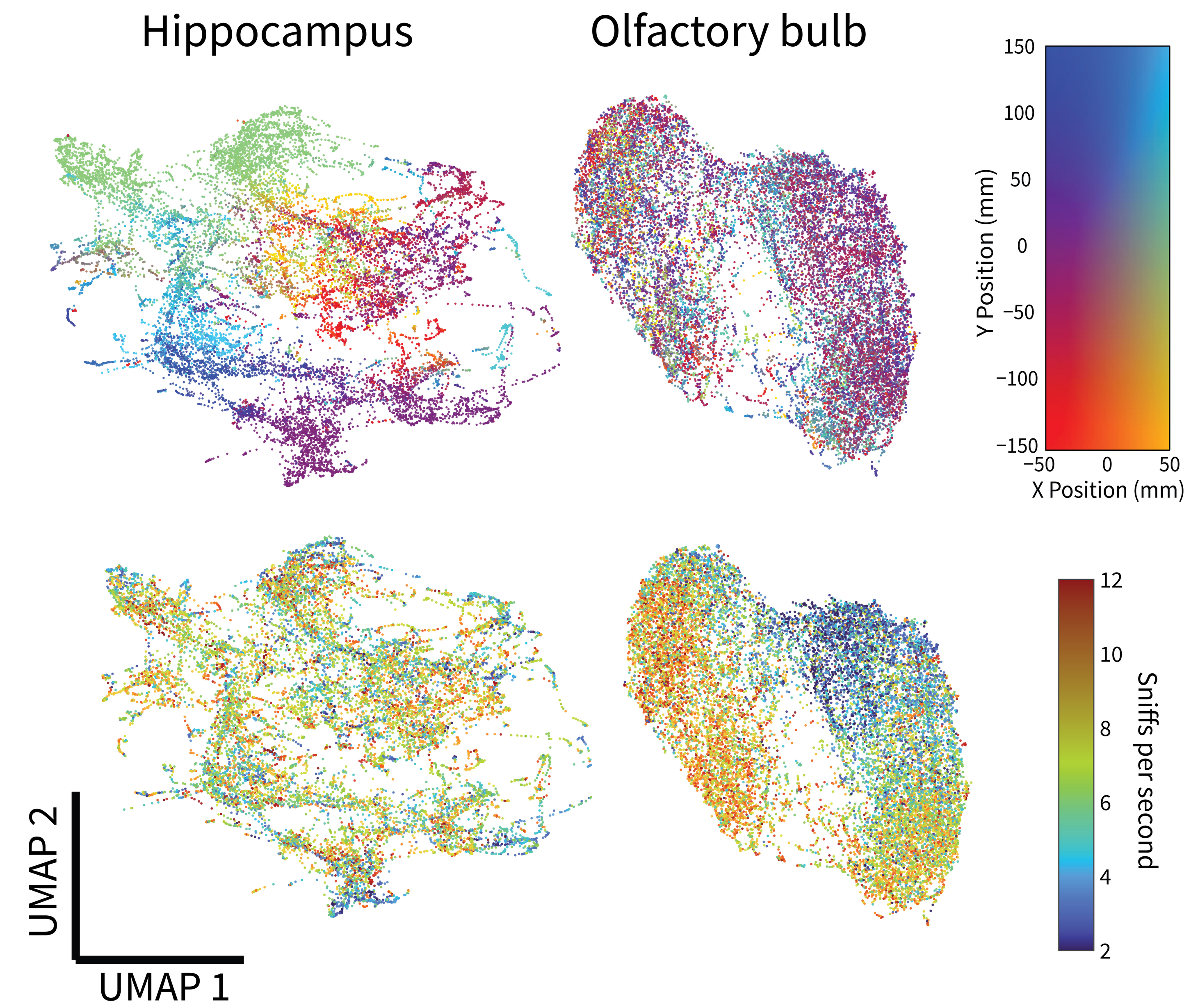
- 78% OB and 97% of CA1 neurons spatially tuned
- 38% OB and 77% of CA1 neurons tuned to movement speed
- OB & CA1 neurons multiplex sniffing parameters with spatial information
- Small decrease in spatially tuned OB units post MMZ



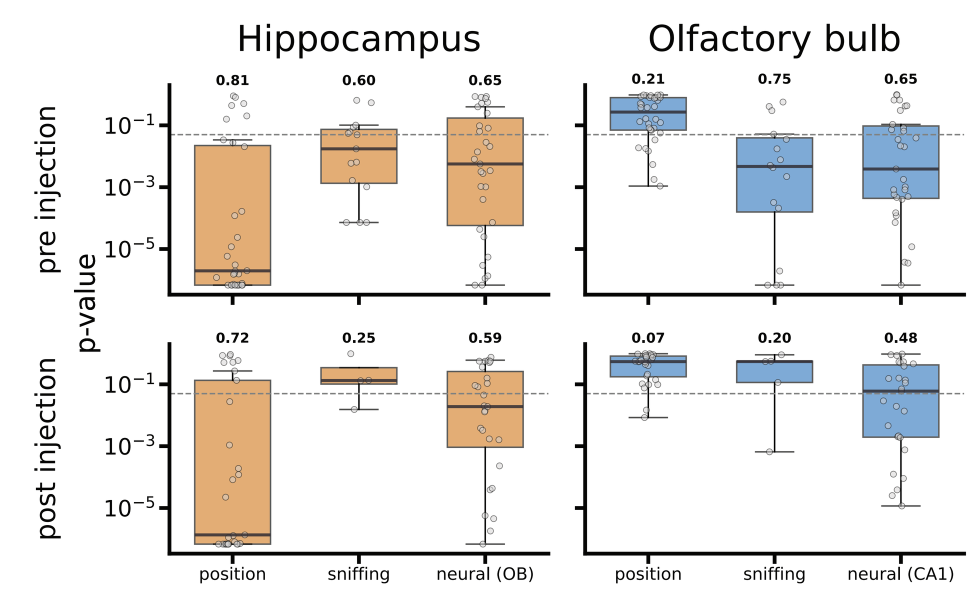


MMZ disrupts single unit tuning in OB and CA1 to spatial parameters. M represents movement, **P** spatial tuning, and **S** sniffing parameters including rate, time and phase.

Population correlations

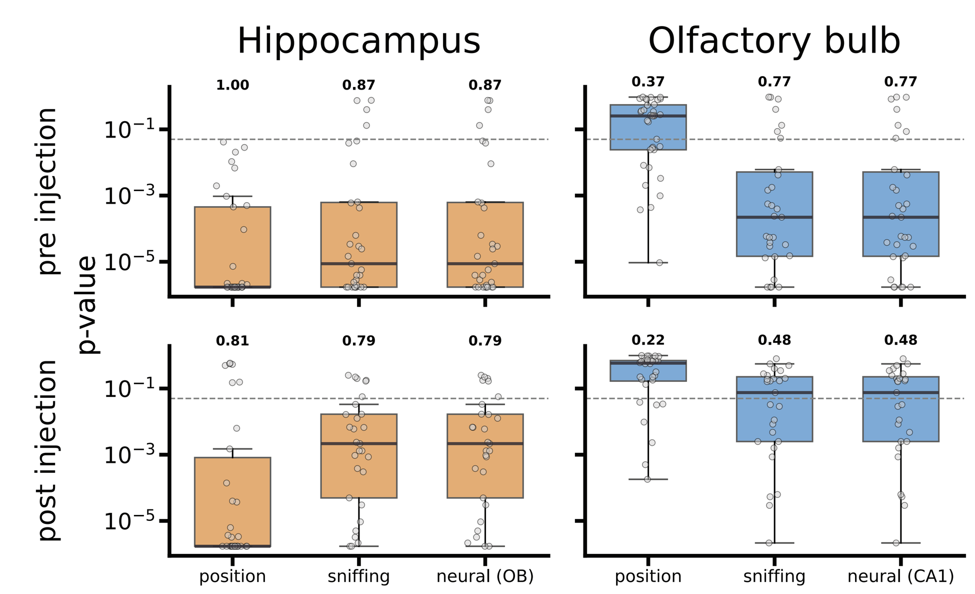


Population activity reflects spatial location and sniff rate. Uniform manifold approximation projection (UMAP)[2] embeddings of firing rate vectors in 100ms bins.



Kalman filter

- 100ms firing rate vectors
- p-values computed by 10 fold cross validation with 10 circular shifts



Long-short term memory (LSTM) model

- 1s of sequential data
- 2 hidden layers with of 64 recurrent units

Discussion

- Shared information between OB and CA1
- Population encodes place and self movement
- Spiking jointly tracks sniffing and place
- LFP rhythms are synchronous with sniffing

References

1. Balzani, E., Lakshminarasimhan, K., Angelaki, D. E., Savin, C. (2020). Efficient estimation of neural tuning during naturalistic behavior.
2. Zutshi, I., Apostolelli, A., Yang, W., Zheng, Z. (Sam), Dohi, T., Balzani, E., Williams, A. H., Savin, C., & Buzsáki, G. (2024). Hippocampal Neuronal Activity Is Aligned with Action Plans.