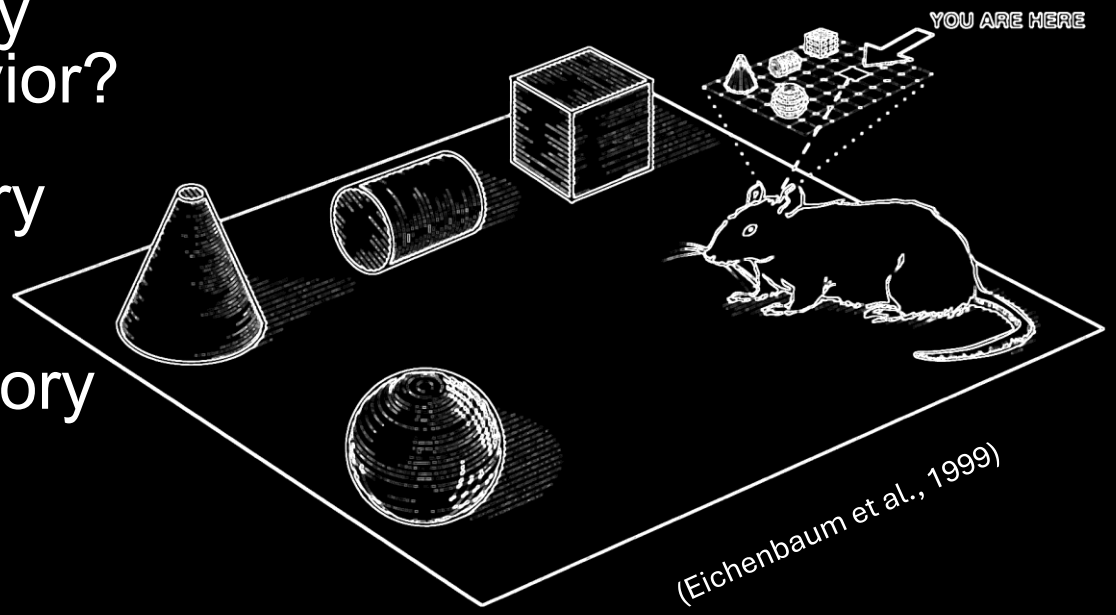
Clickbait + Ephys

Progress and preliminary analysis

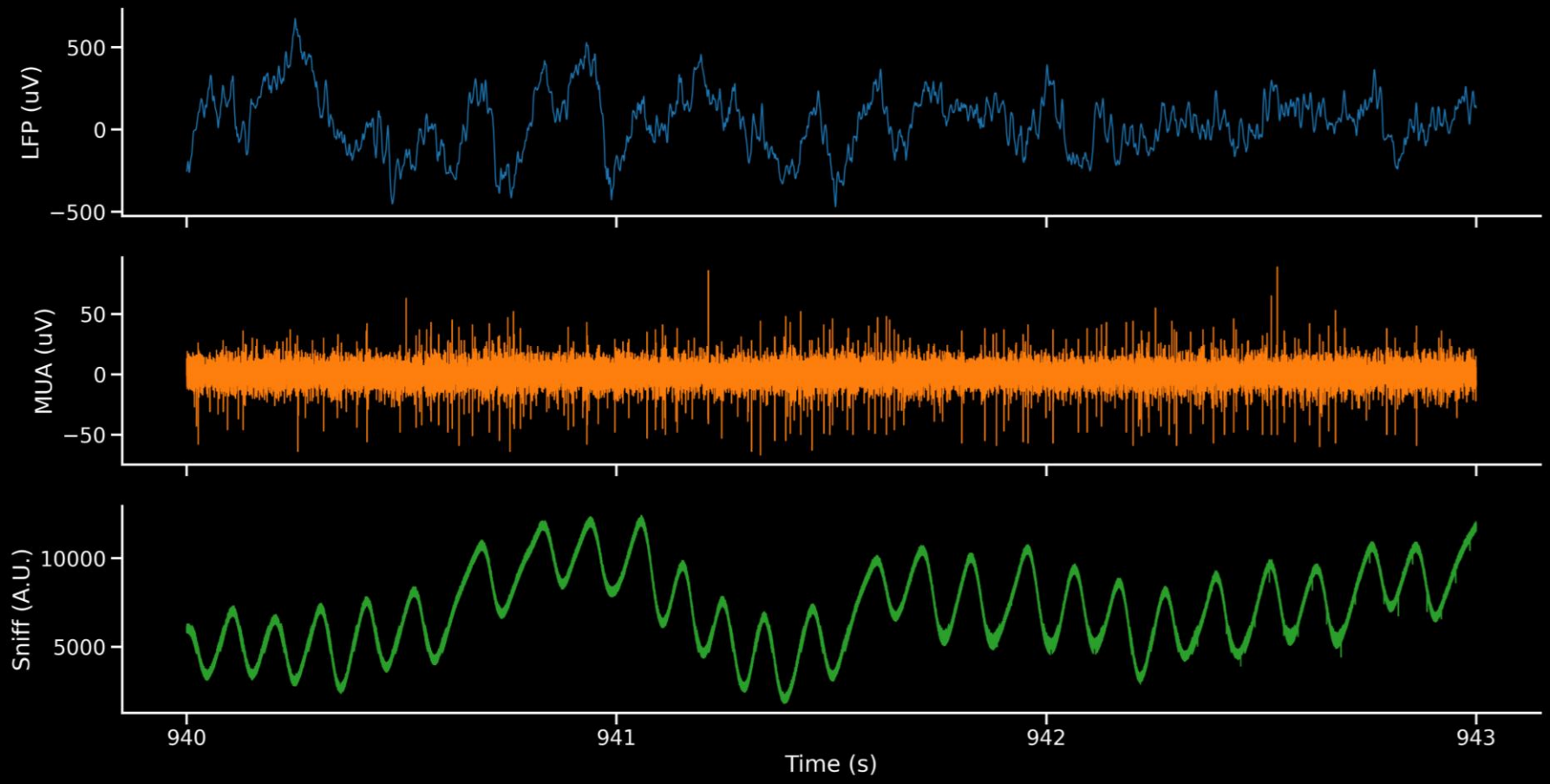
Research Questions

1. How does the brain interpret sensory inputs to generate purposeful behavior?
2. Why is place encoded in the olfactory bulb and how did it get there?
3. Is recurrence between primary sensory regions (olfactory bulb) and the hippocampus functionally relevant?
4. How might feedforward activity from olfactory bulb to hippocampus be temporally organized by local field potentials?



(Eichenbaum et al., 1999)

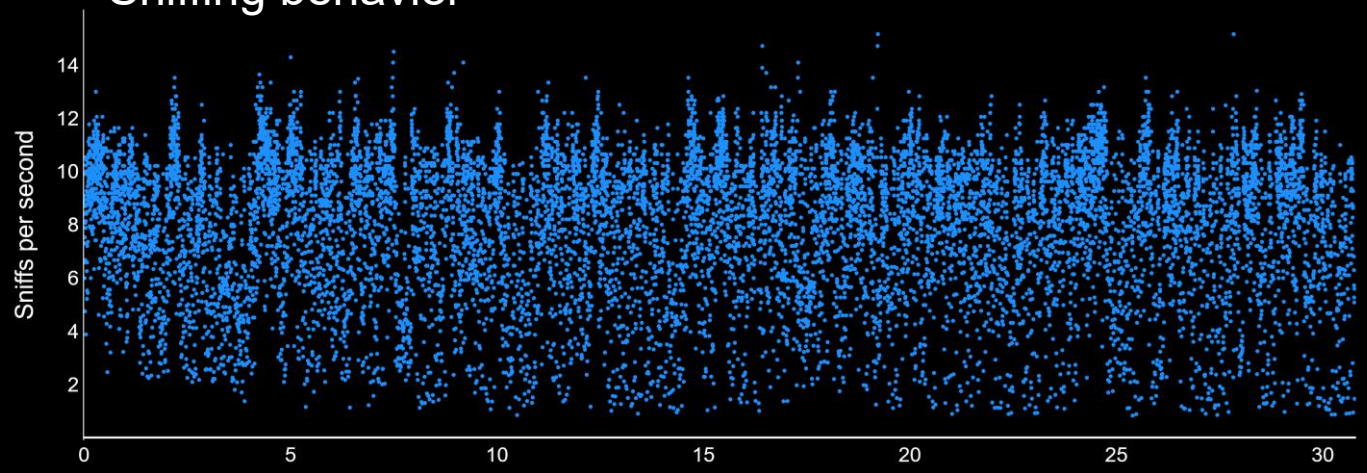
Data acquisition



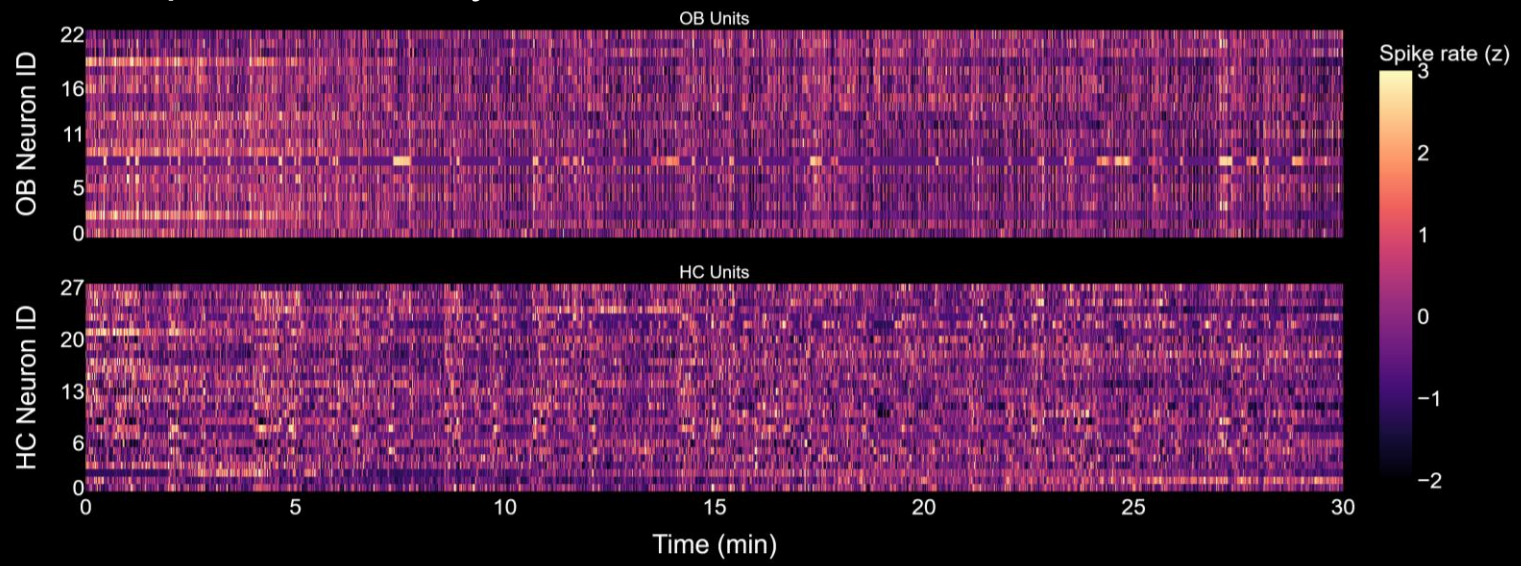
Data preprocessing

- Sniffing behavior captured with inhalation onset and sniff rate
- Position tracking from bottom-up video
- Spike sorting with Kilosort4 and manual curation in Phy2
- Smoothed and normalized spike rates

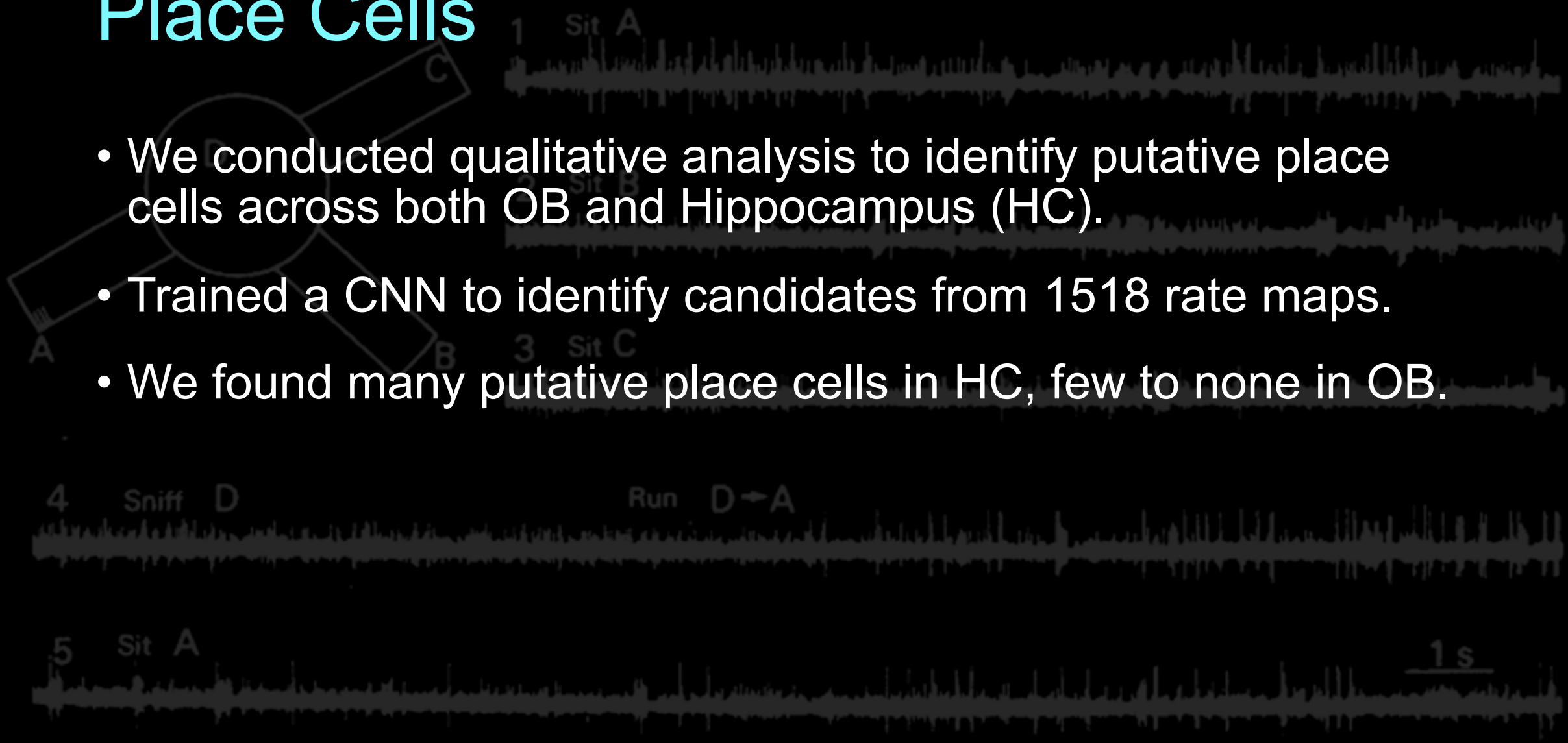
Sniffing behavior



Population activity



Place Cells

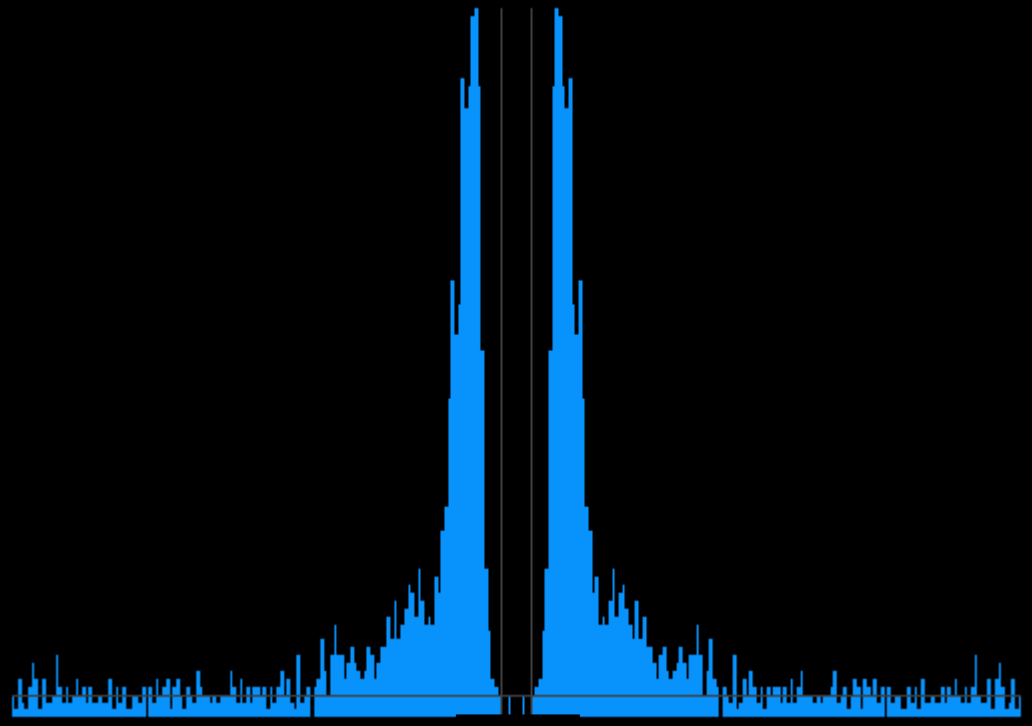


- We conducted qualitative analysis to identify putative place cells across both OB and Hippocampus (HC).
- Trained a CNN to identify candidates from 1518 rate maps.
- We found many putative place cells in HC, few to none in OB.

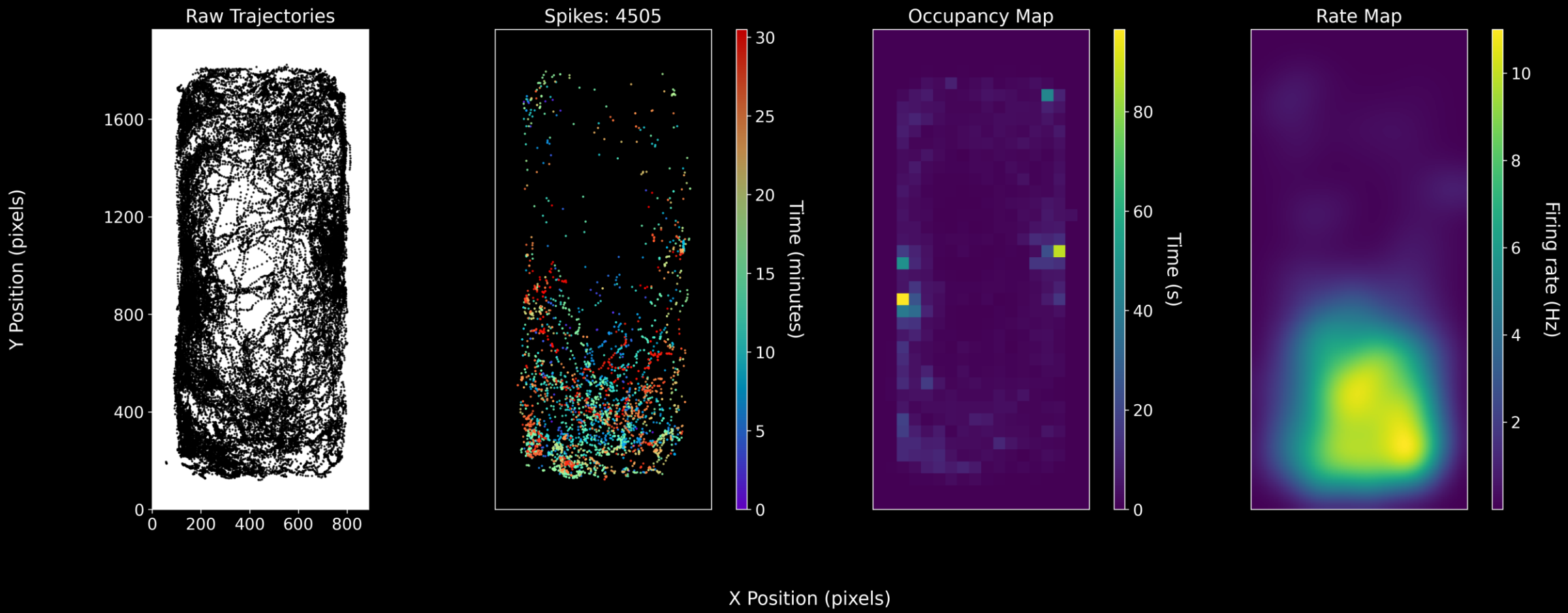
(O'Keefe & Nadel 1978)

Single Units

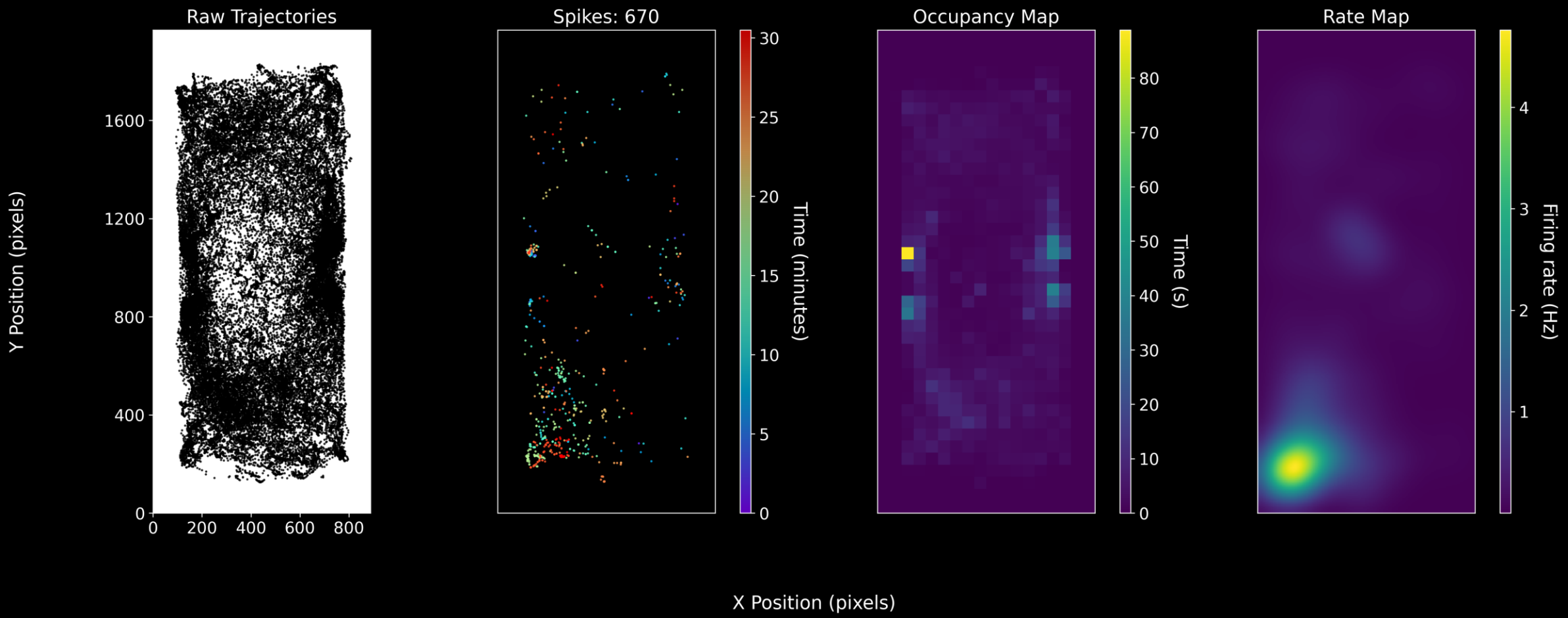
- Units detected by Kilosort4 showing few-to-zero refractory period violations.
- Single units in OB were rare in our recordings.



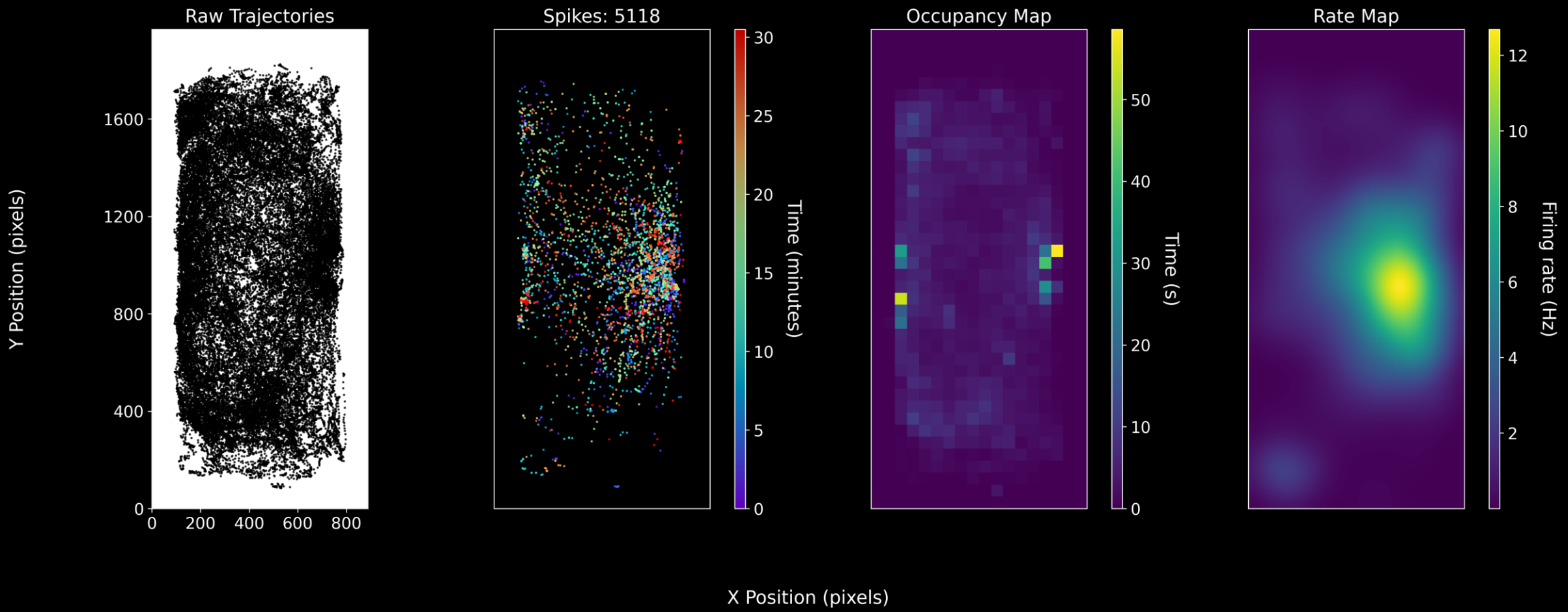
6003-13 cl13 (ch12)



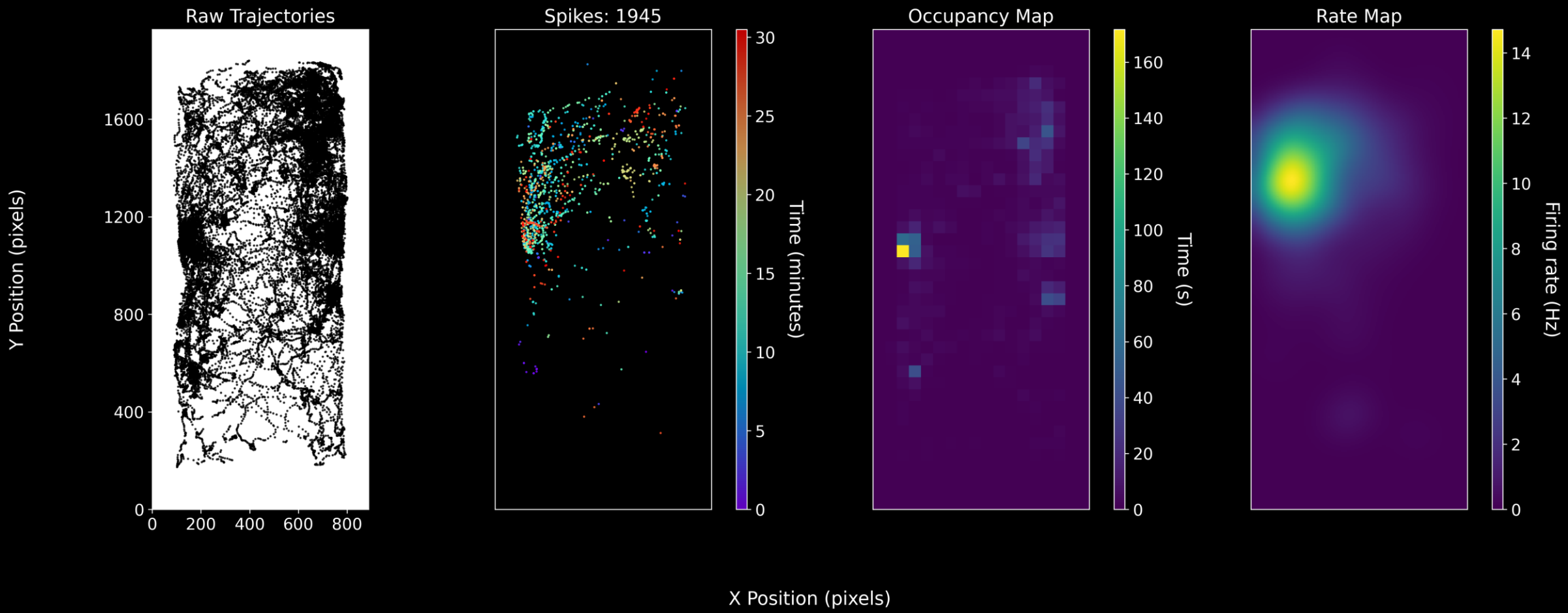
6002-10 cl15 (ch15)



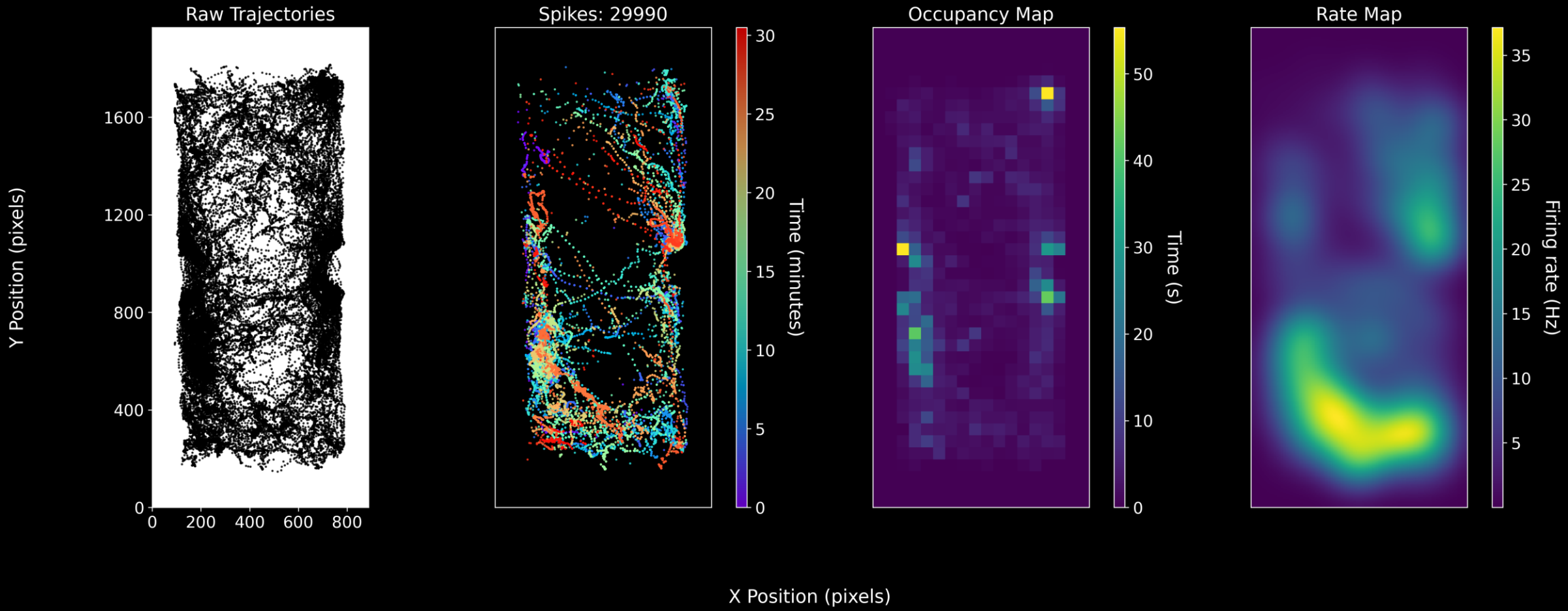
6003-12 cl20 (ch13)



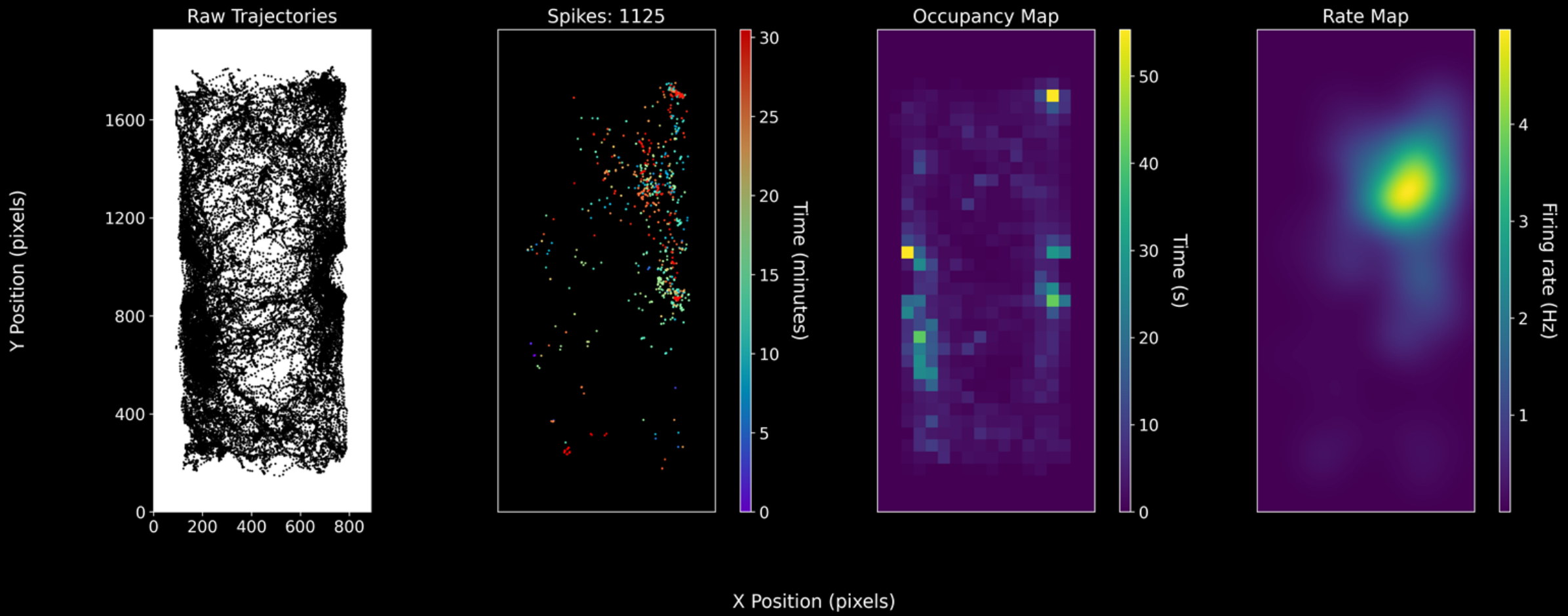
6002-6 cl11 (ch1)



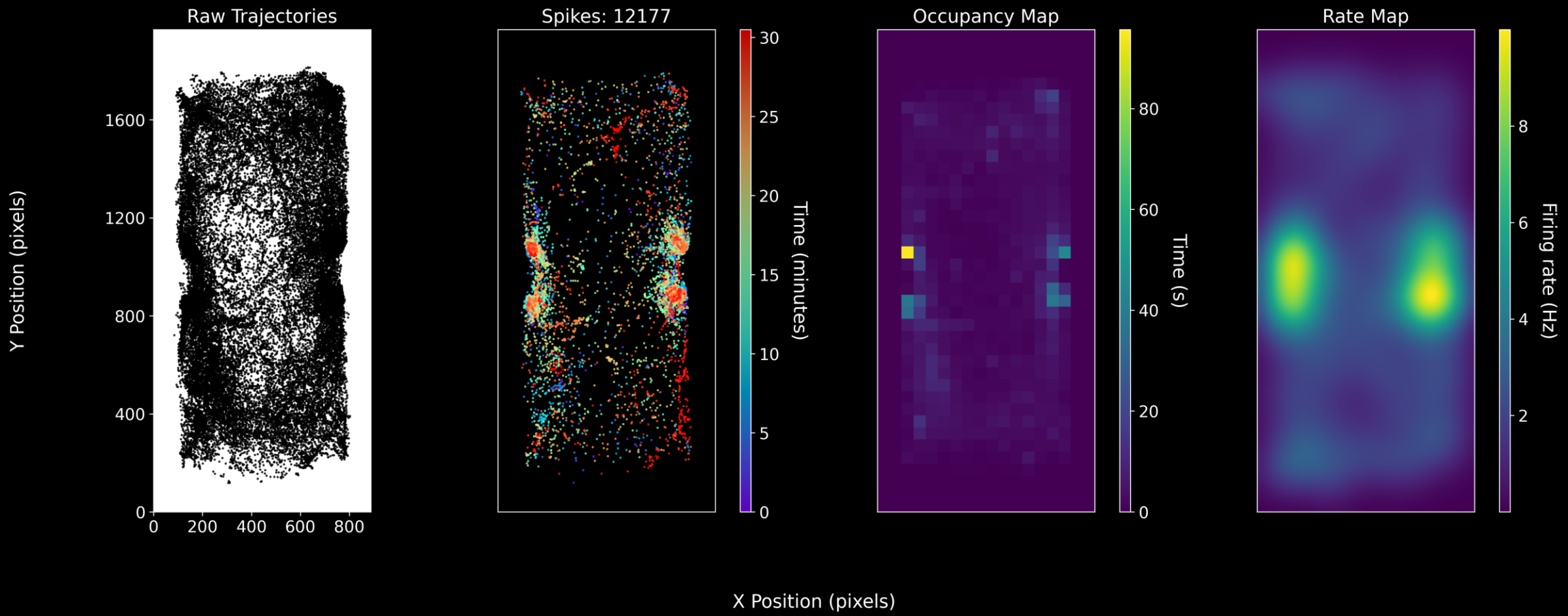
6002-8 cl32 (ch14)



6002-8 cl12 (ch2)

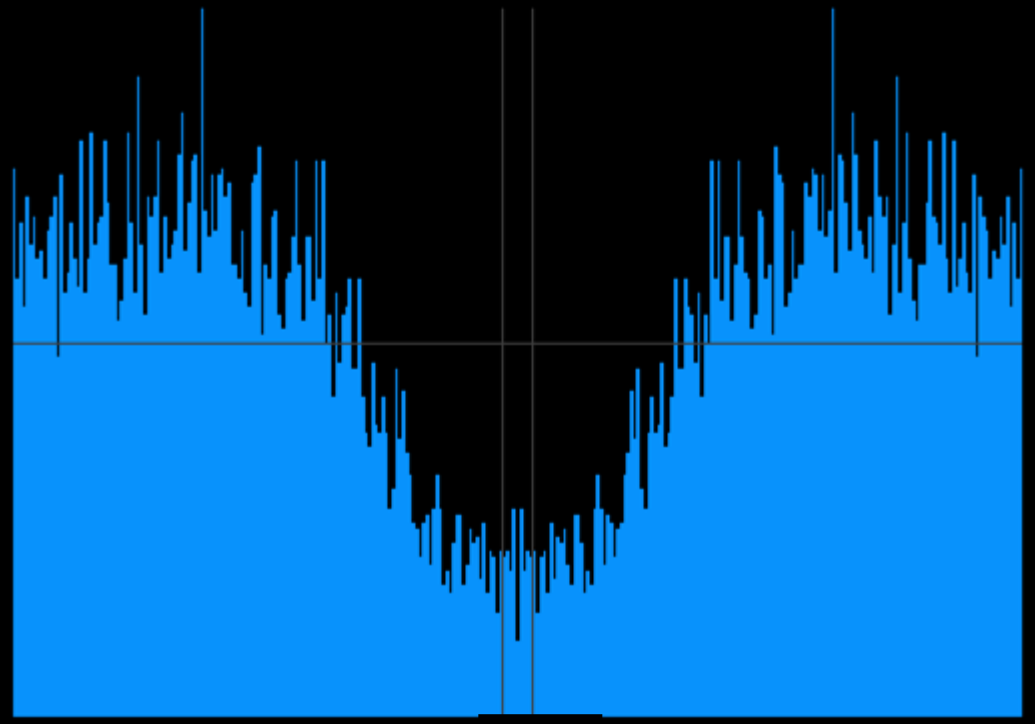


6002-9 cl21 (ch9)



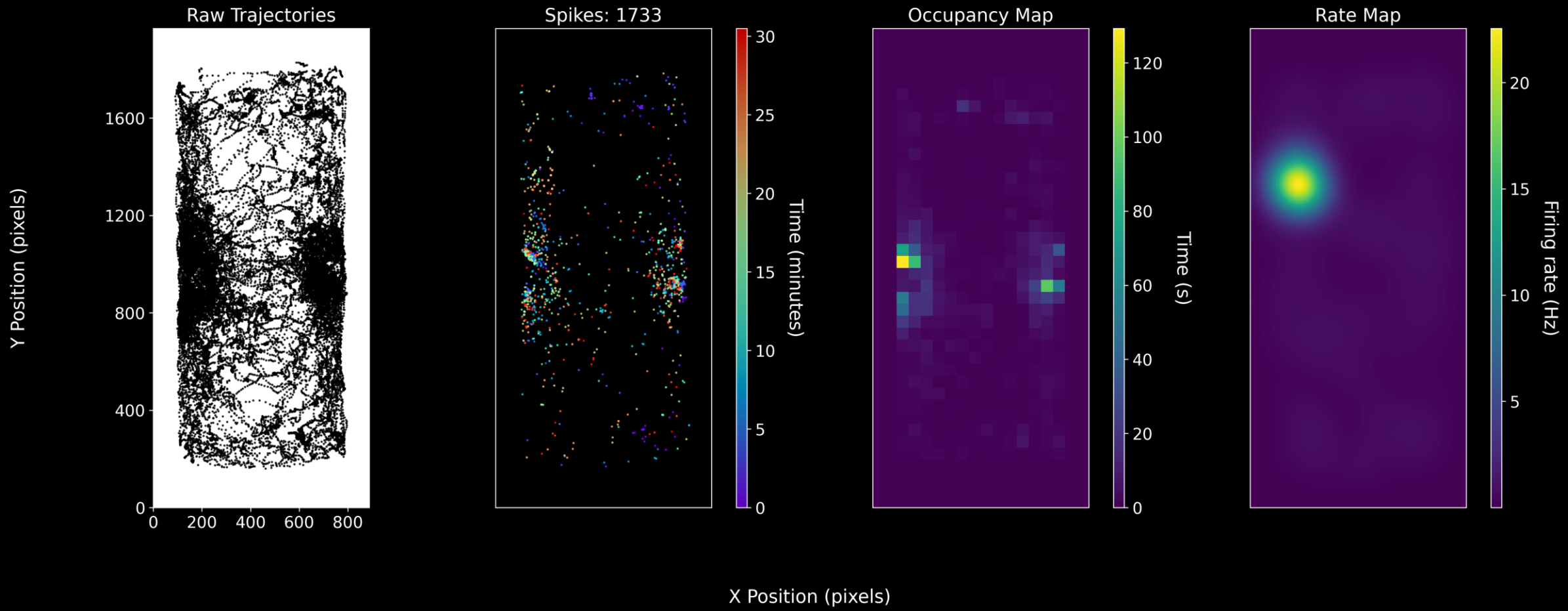
Multi Unit Activity (MUA)

- Most OB units were MUAs
- Many MUAs showed place tuning, but they were in HC.
- Some OB MUAs showed spatiotemporally localized firing, but did not appear to be place cells.

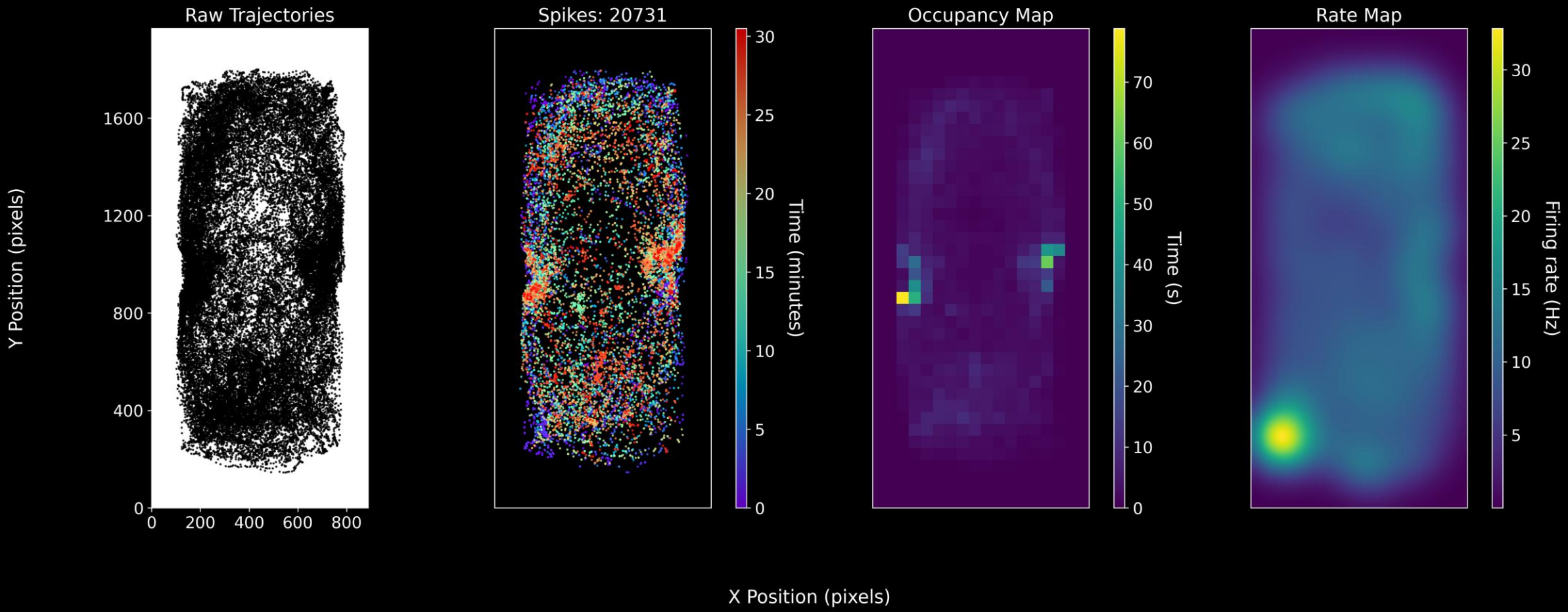


150.0 ms (0.5 ms)

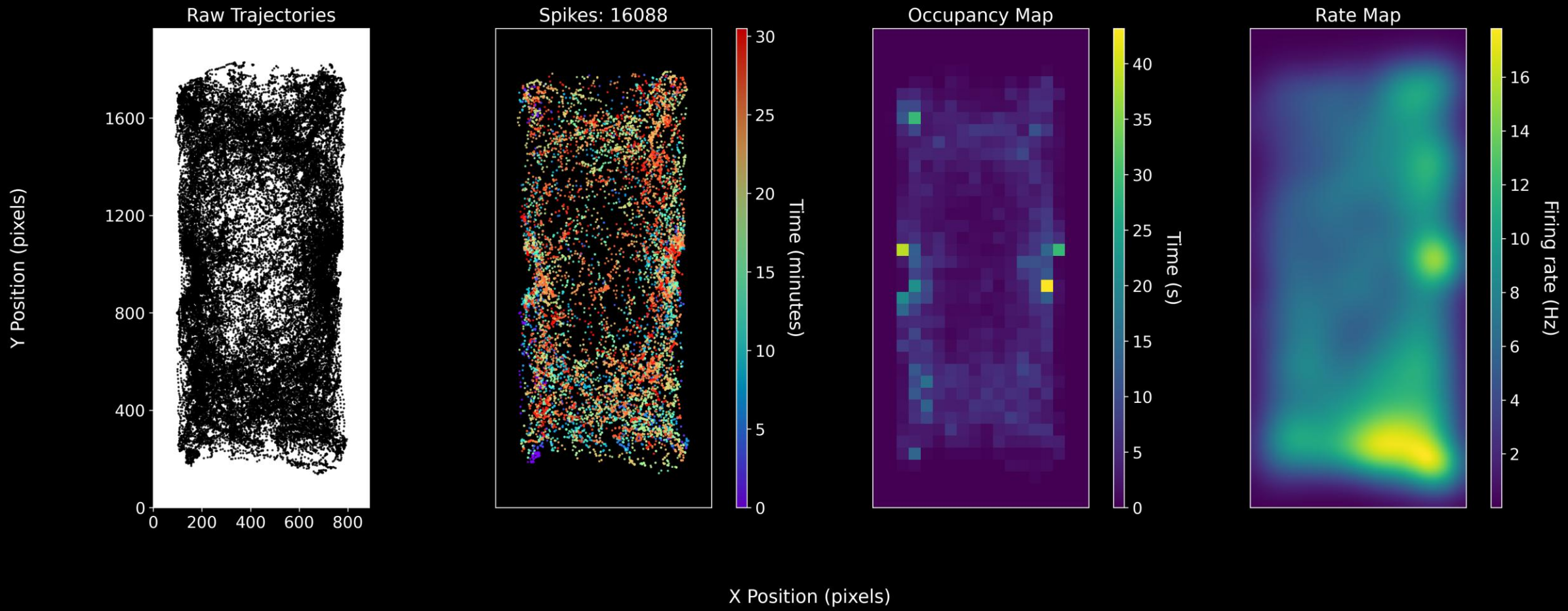
6001-6 cl25 (ch24)



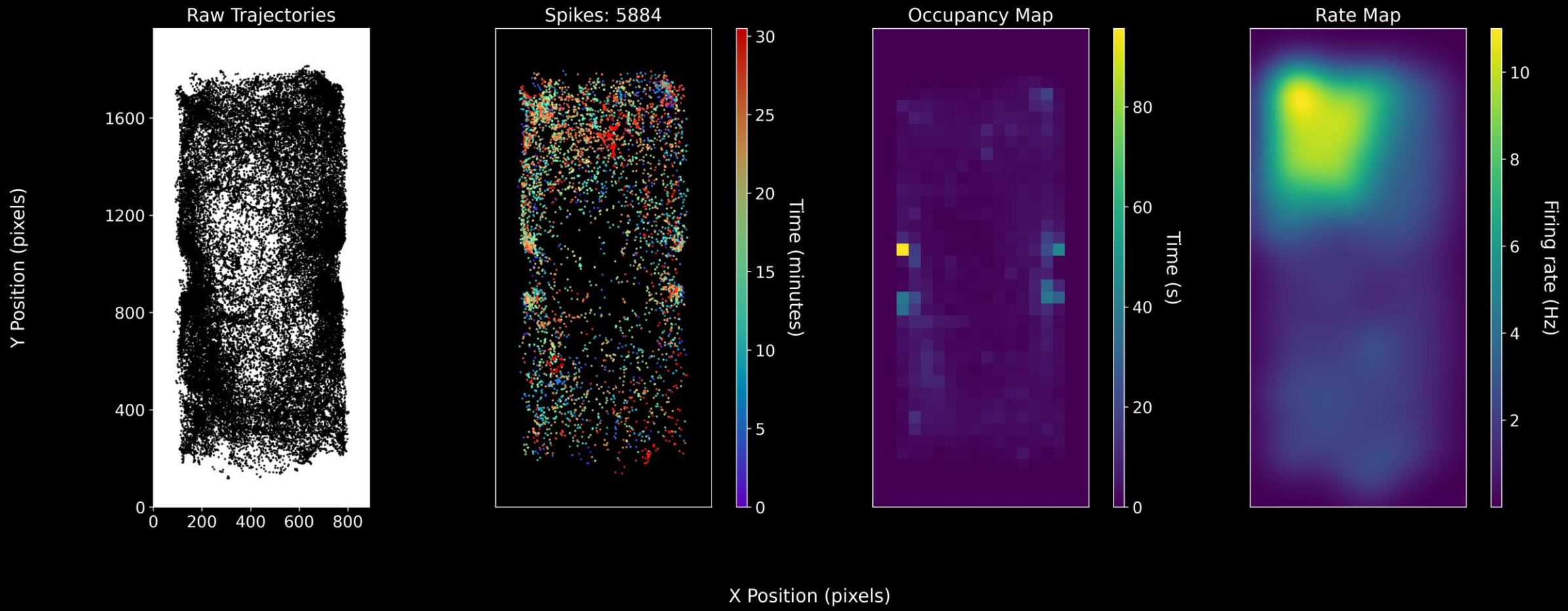
6000-9 cl41 (ch24)



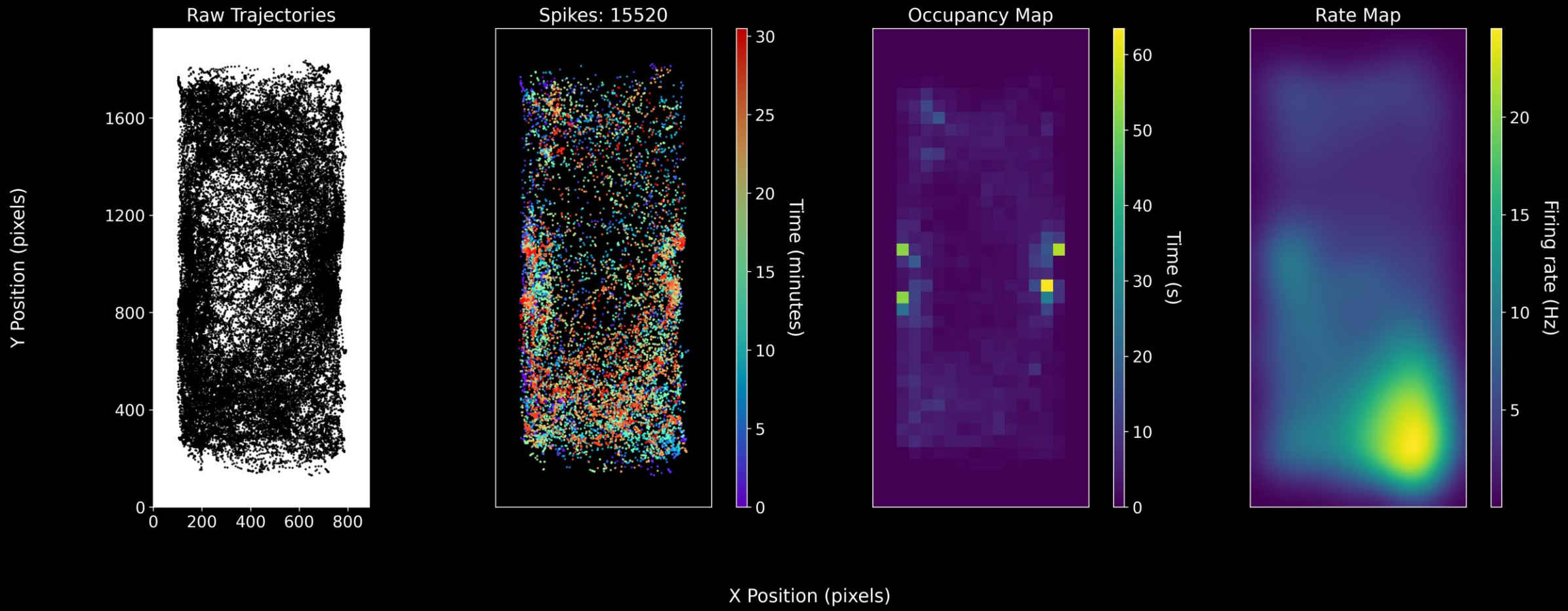
6002-13 cl27 (ch24)



6002-9 cl29 (ch8)

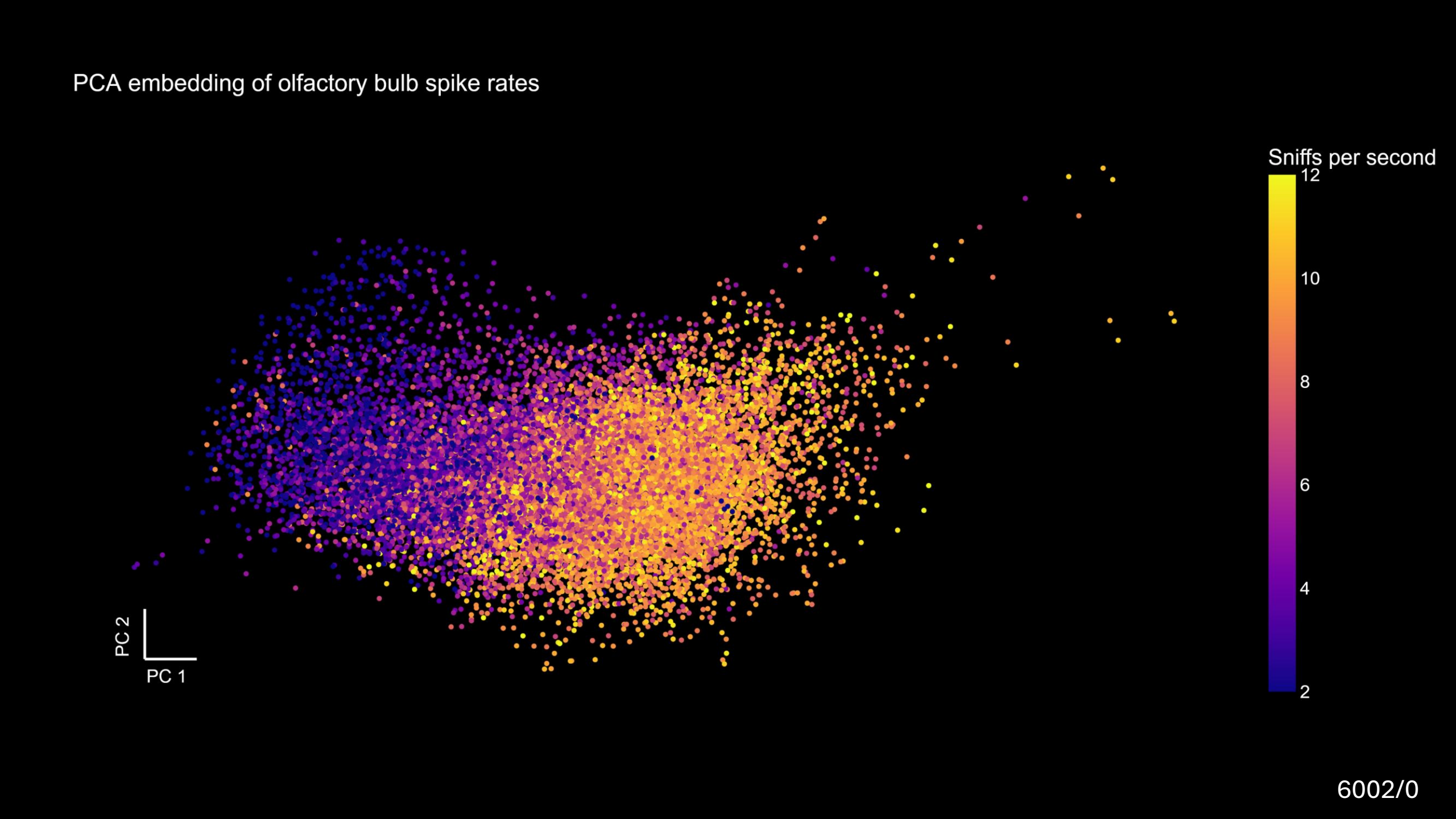


6002-12 cl12 (ch9)

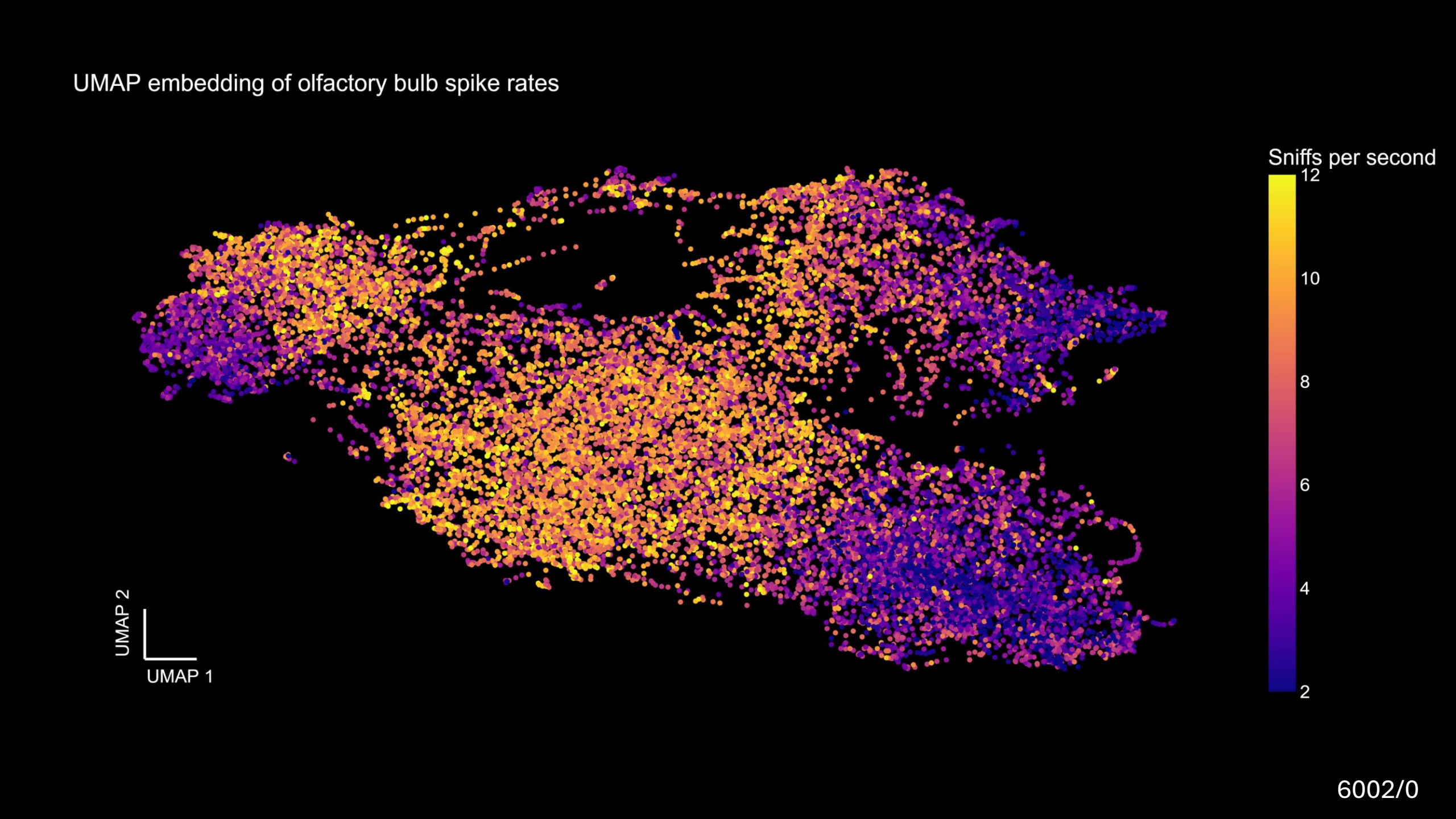


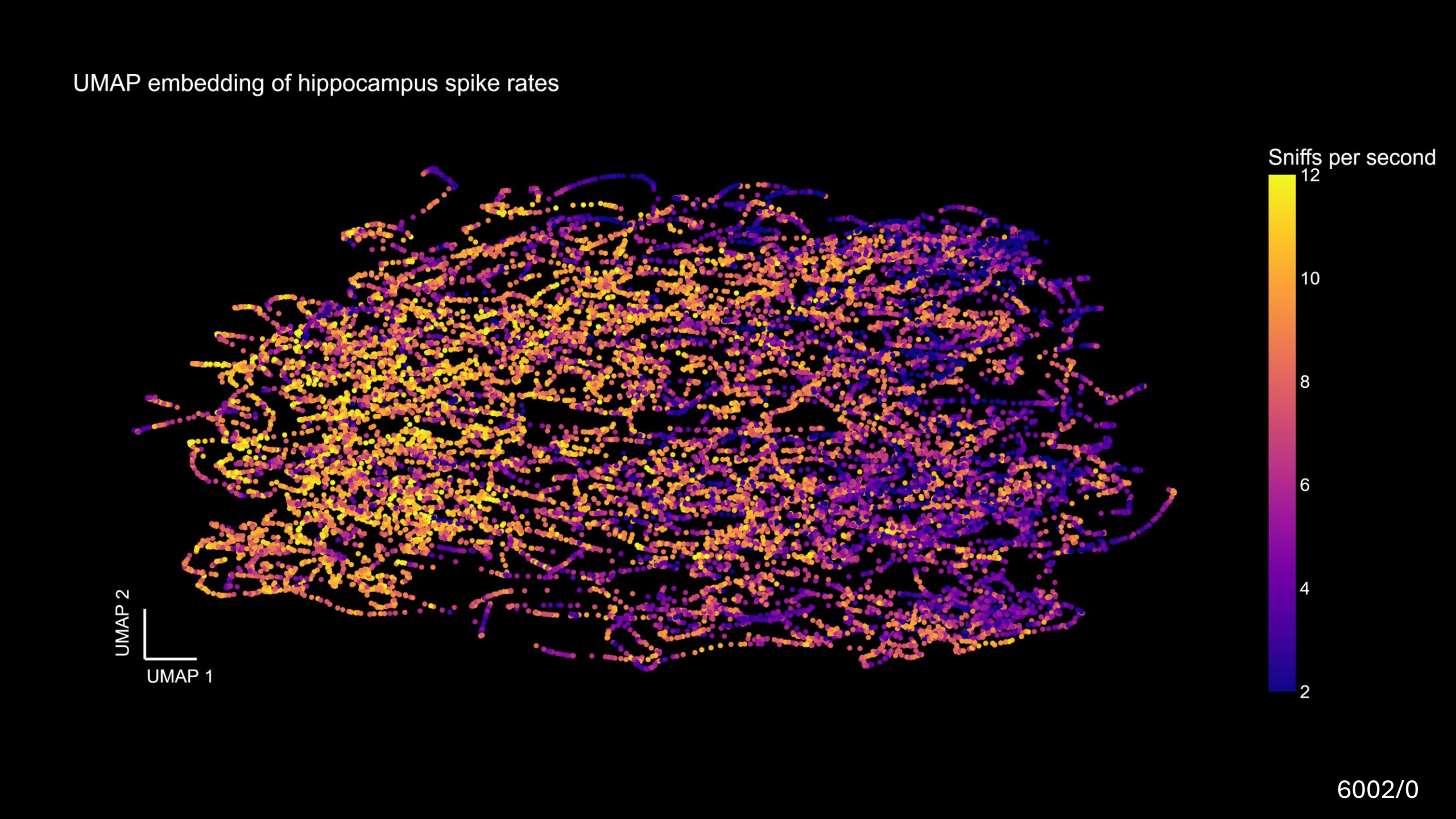
Population embeddings

- Neural firing rates were computed in 100ms bins and smoothed with a gaussian filter ($\sigma = 2.5$)
- Population firing rate vectors were embedded onto lower dimensional space
- PCA reduces the dimensionality by maximizing the explained variance in the linear sense
- UMAP utilizes a graph-based algorithm to preserve structure in a predefined metric space (cosine distance)

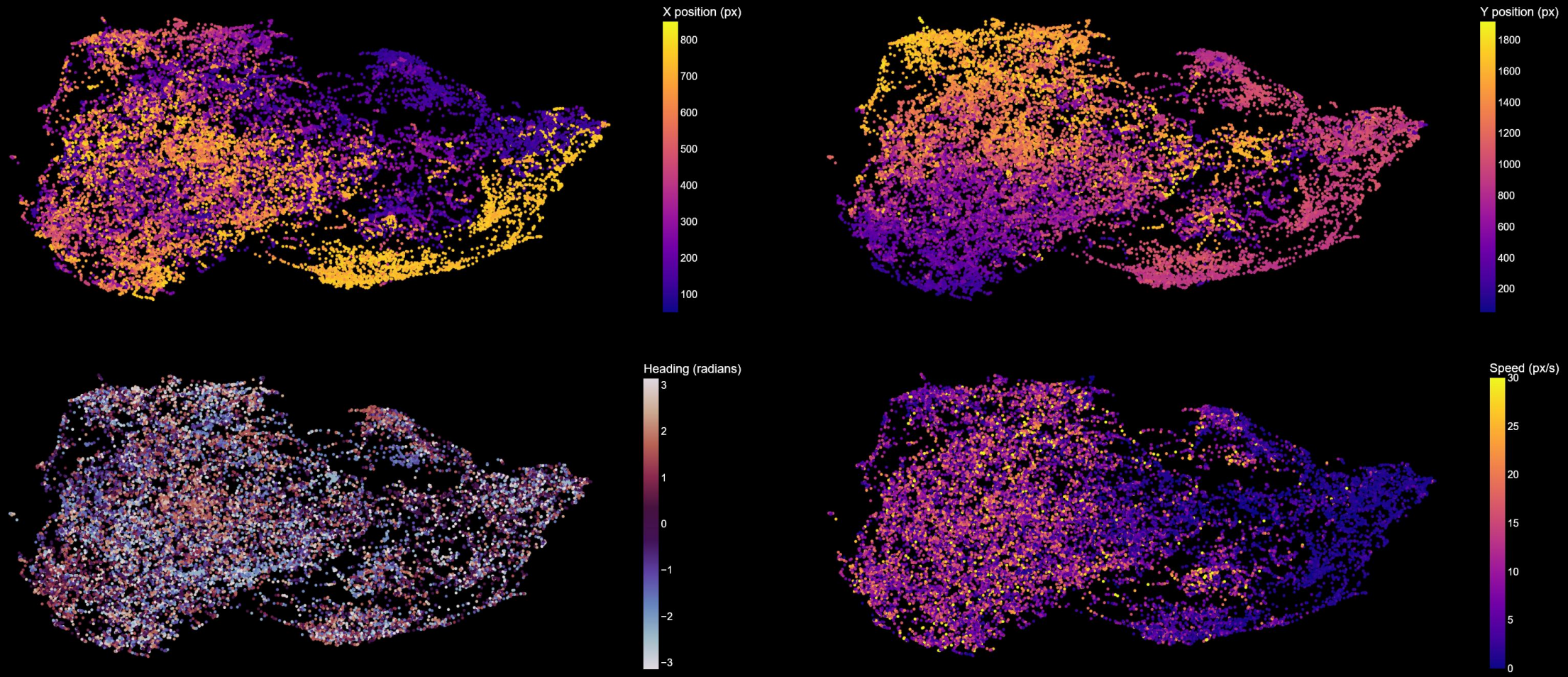

PCA embedding of olfactory bulb spike rates
Sniffs per second
12
10
8
6
4
2
PC 2
PC 1
6002/0

PCA embedding of hippocampus spike rates
Sniffs per second
12
10
8
6
4
2
PC 2
PC 1
6002/0

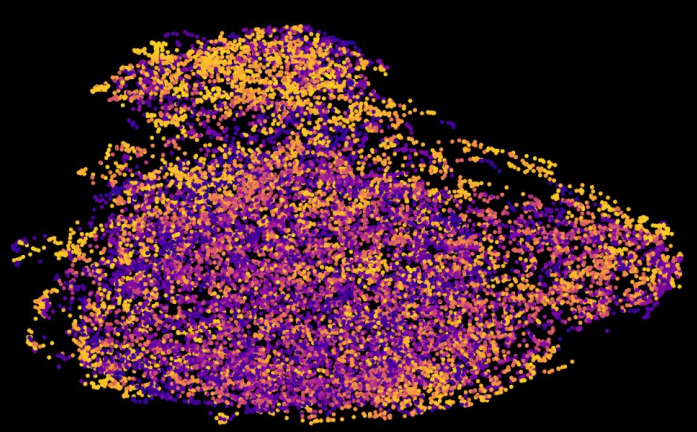

UMAP embedding of olfactory bulb spike rates
Sniffs per second
12
10
8
6
4
2
UMAP 2
UMAP 1
6002/0

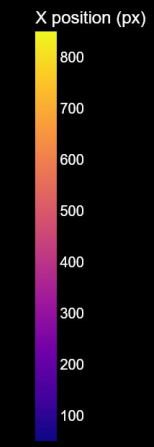

UMAP embedding of hippocampus spike rates
Sniffs per second
12
10
8
6
4
2
UMAP 2
UMAP 1
6002/0

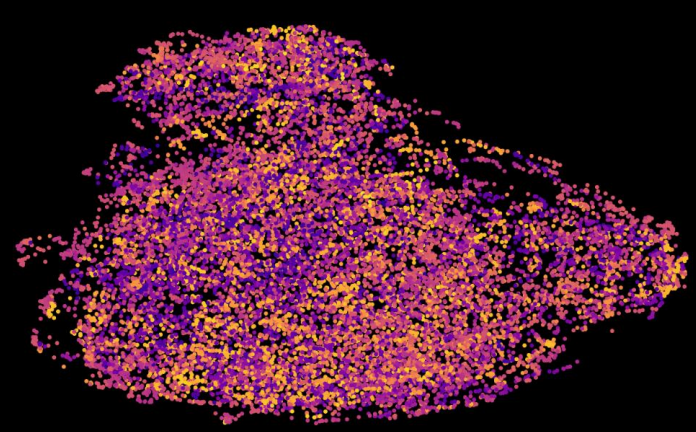
The hippocampus as a cognitive map

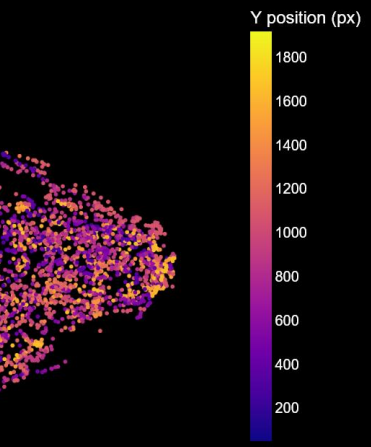


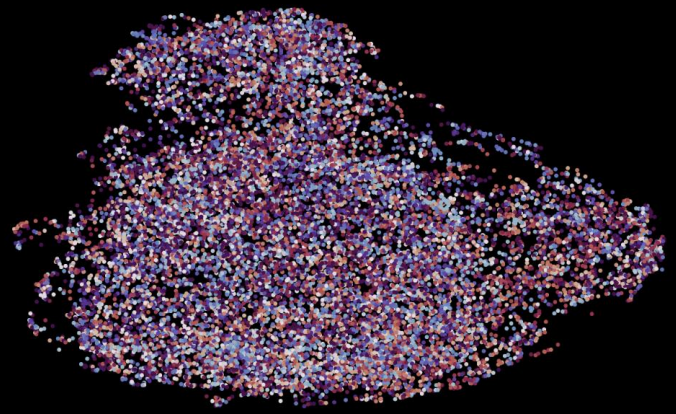
Olfactory bulb population activity

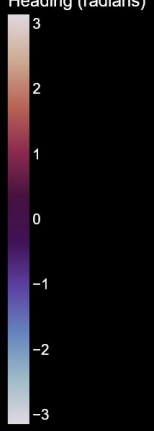


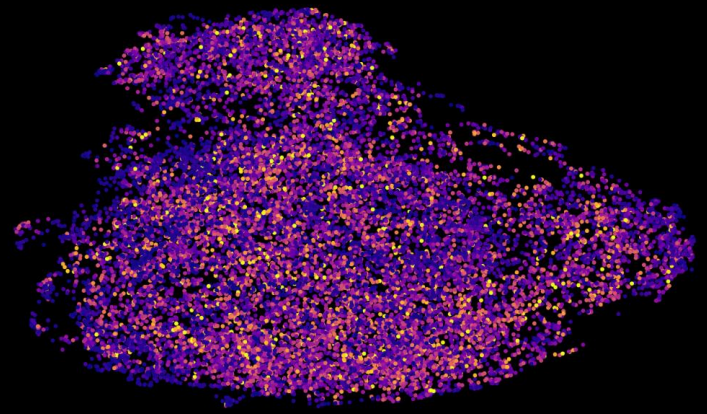




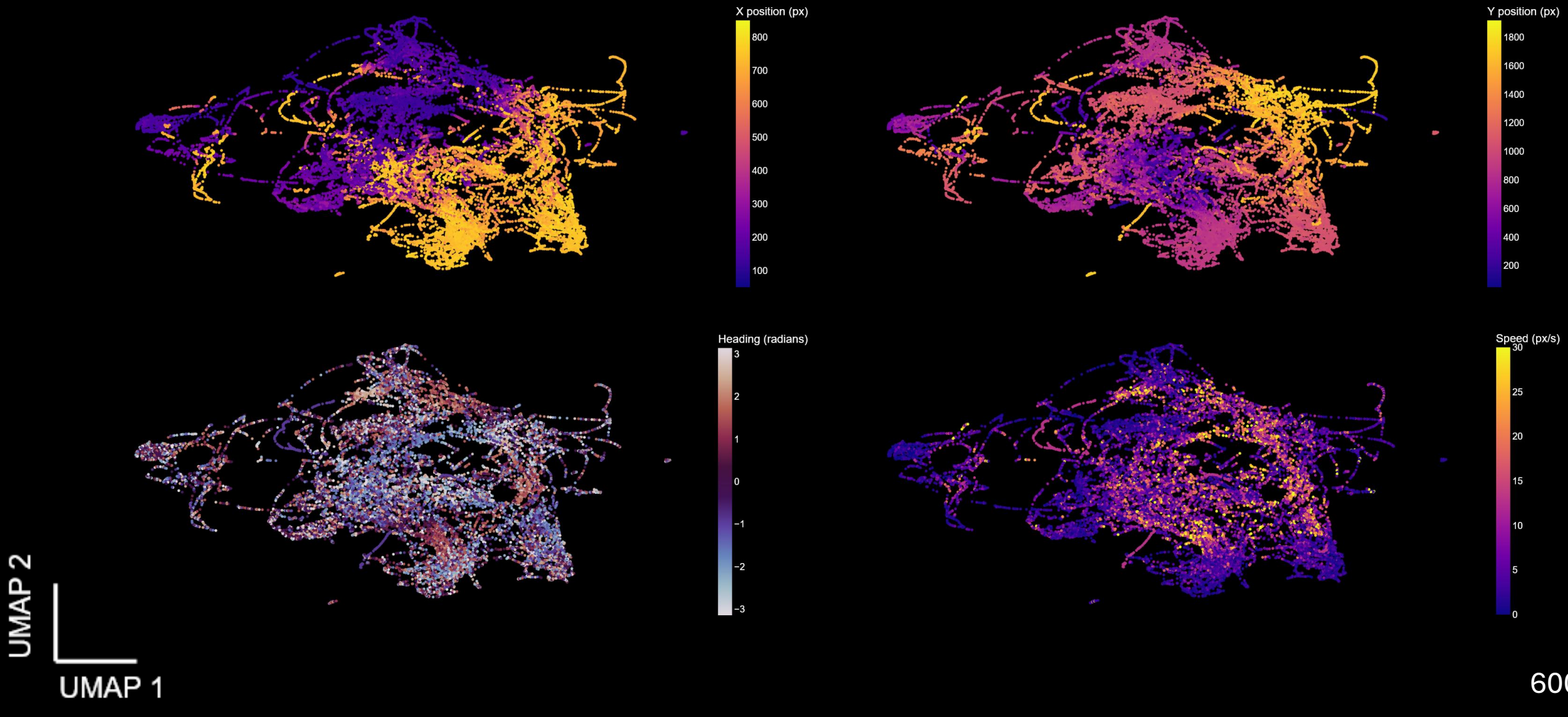




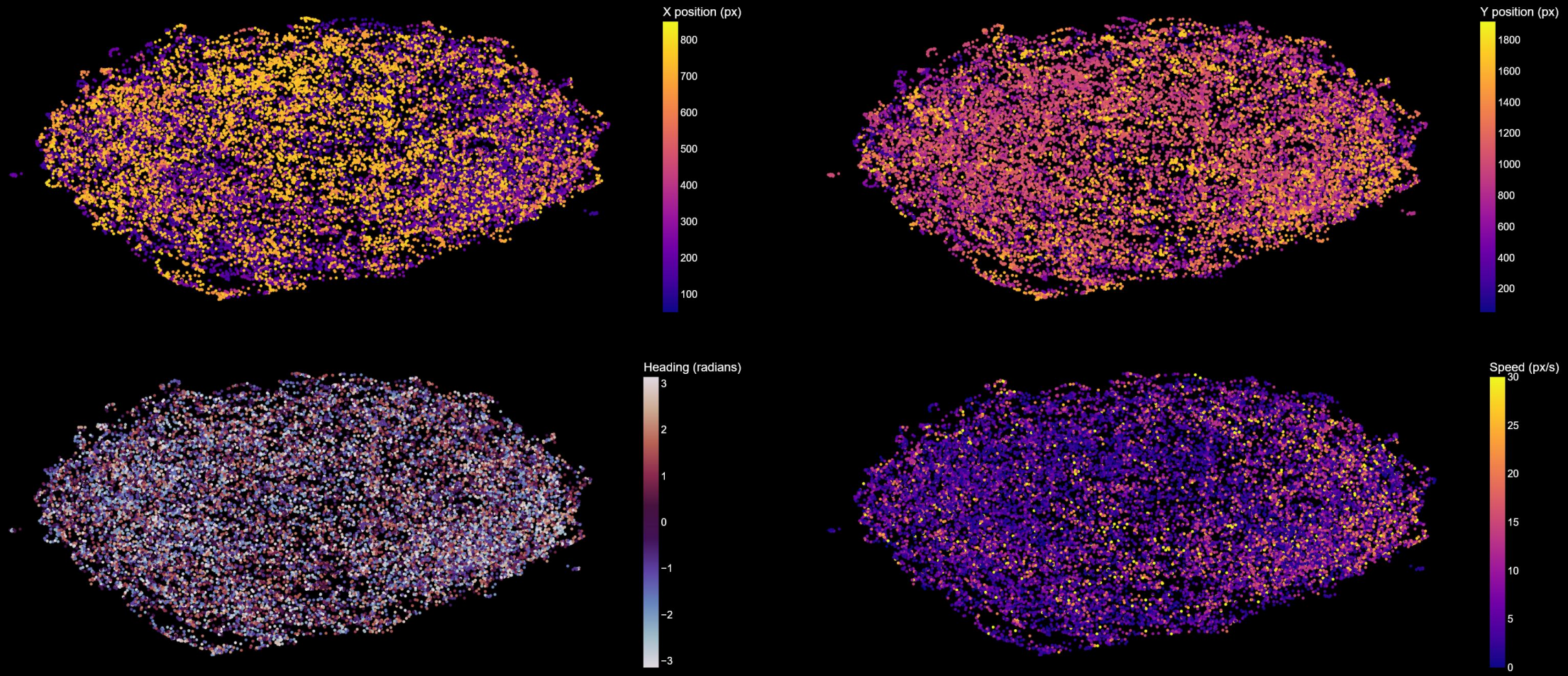




The hippocampus as a cognitive map



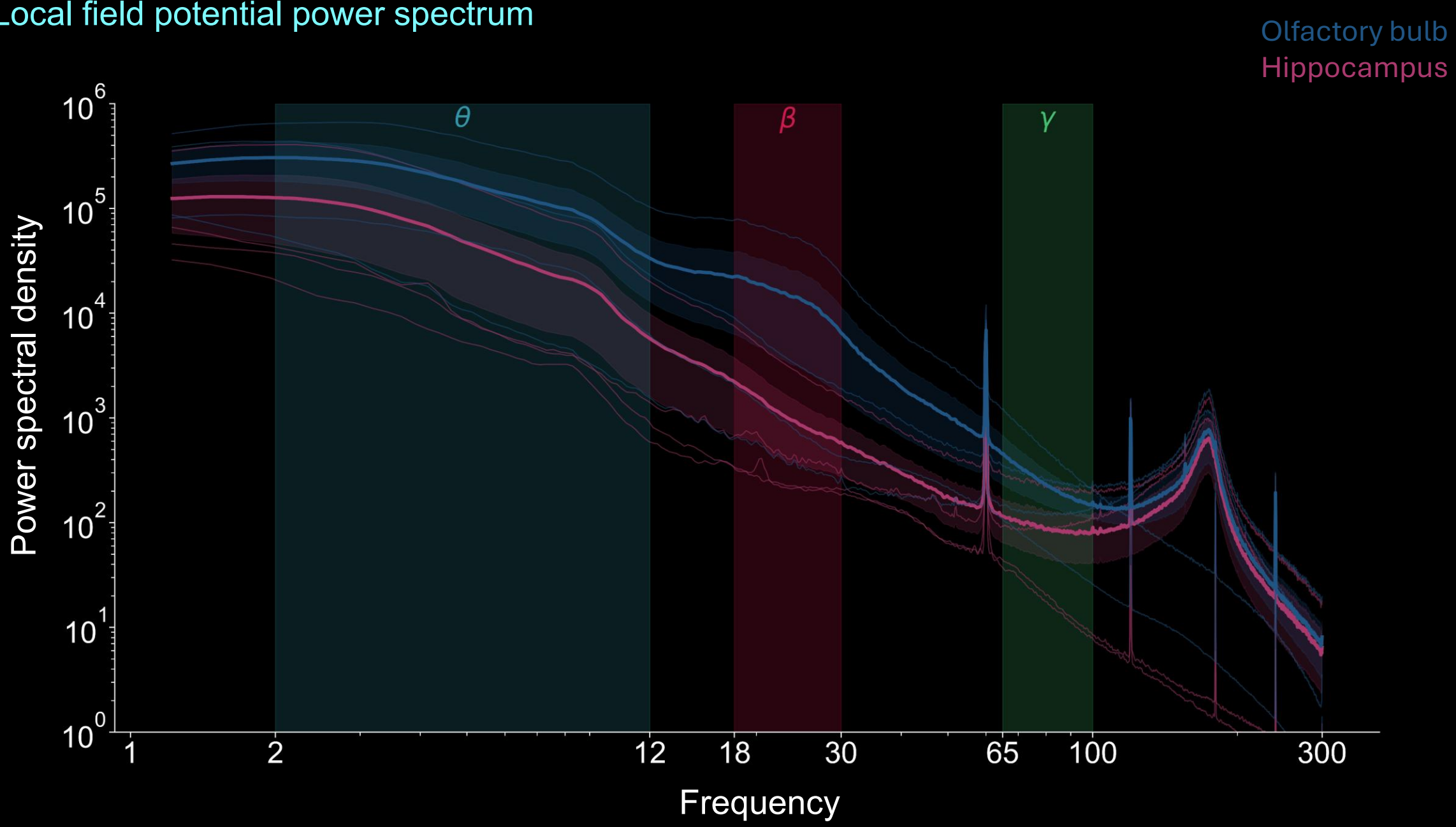
Olfactory bulb population activity



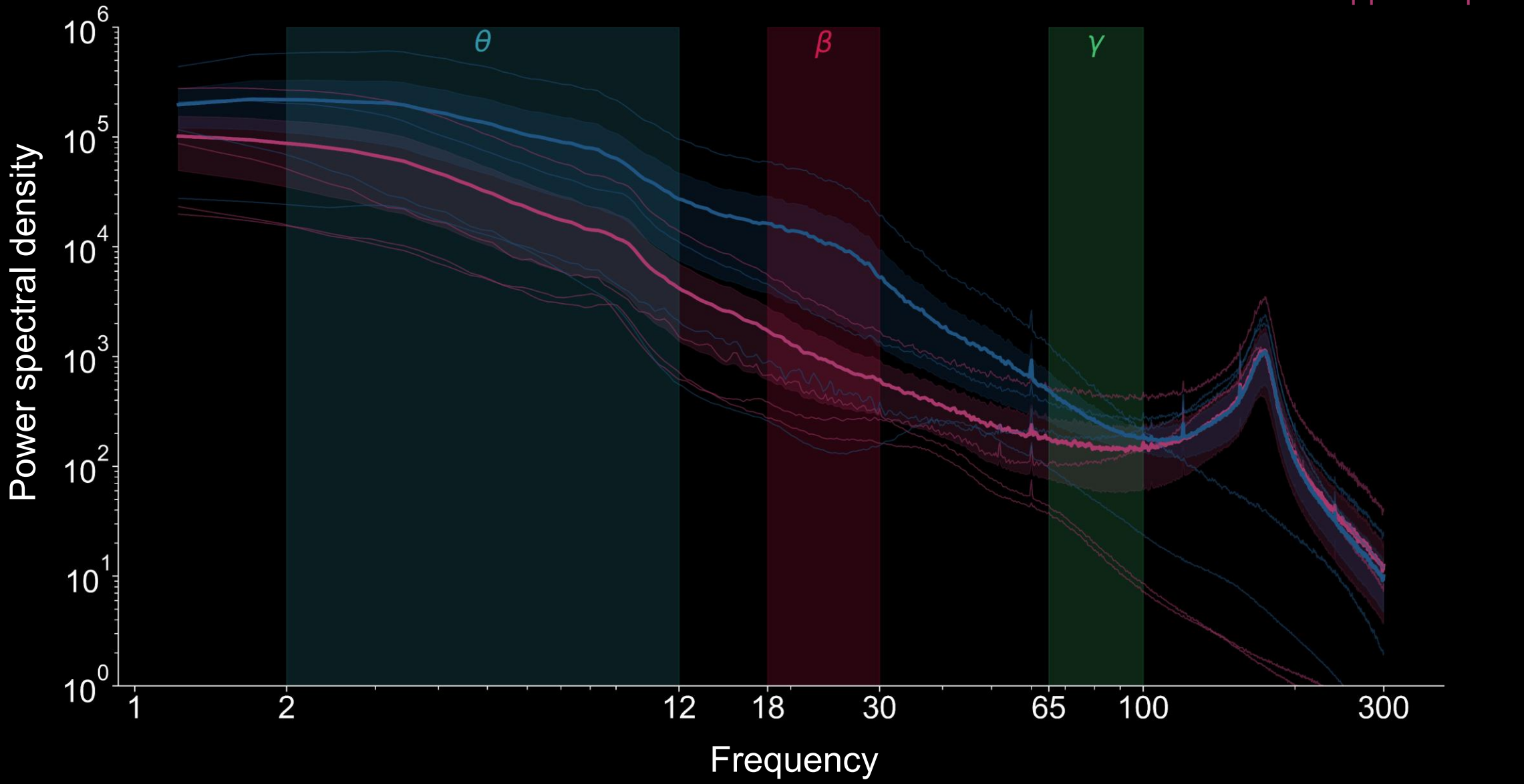
Local field potentials

- LFPs were extracted with an order 4 Butterworth filter and down sampled to 1Khz
  - Theta (θ): 2-12Hz
  - Beta (β): 18-30Hz
  - Gamma (γ): 65-100Hz
- PSD was estimated using Welch's method in 4s windows with 50% overlap
- The envelope was estimated by taking the absolute value of the Hilbert transformed signal

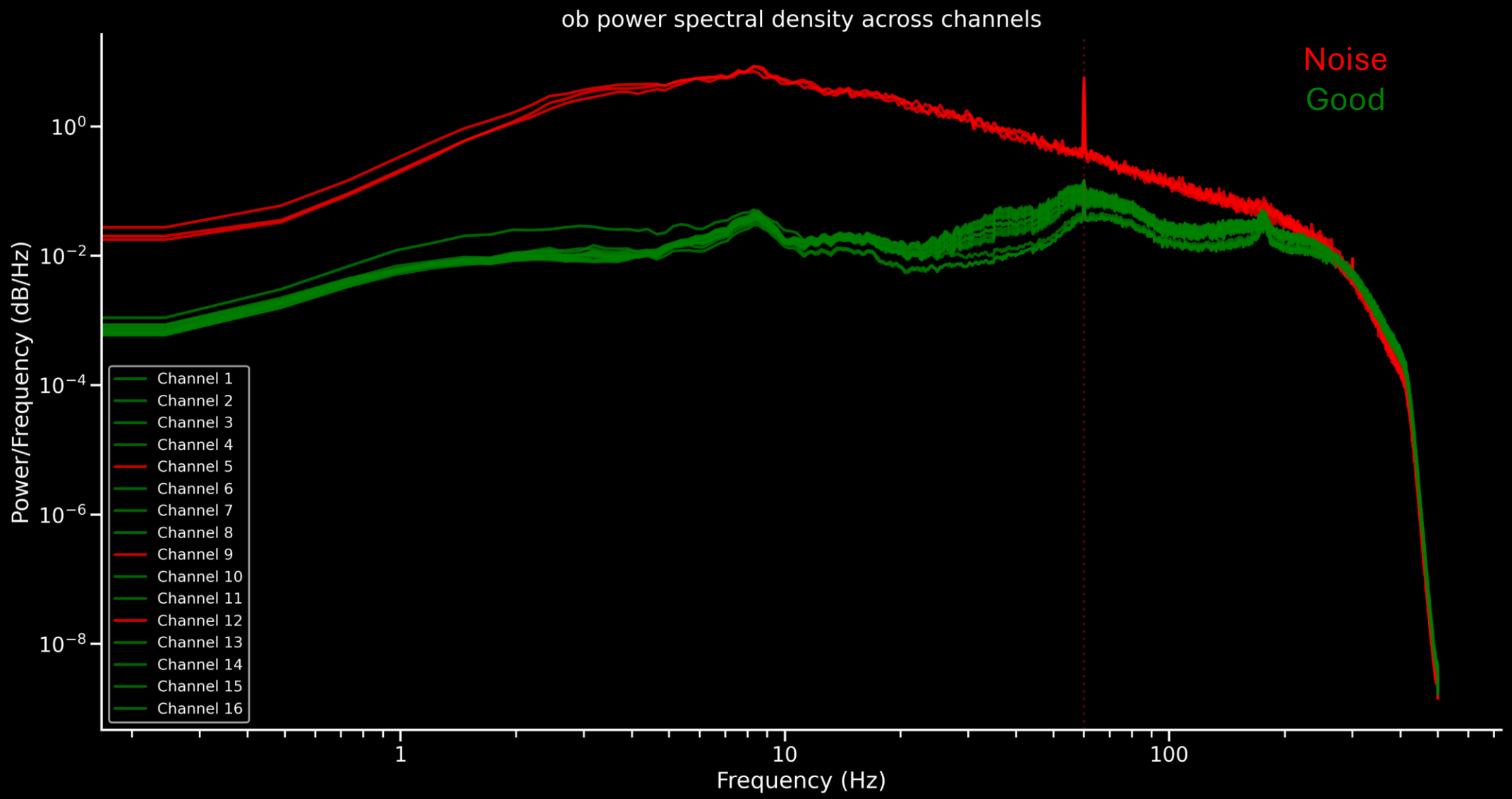
Local field potential power spectrum



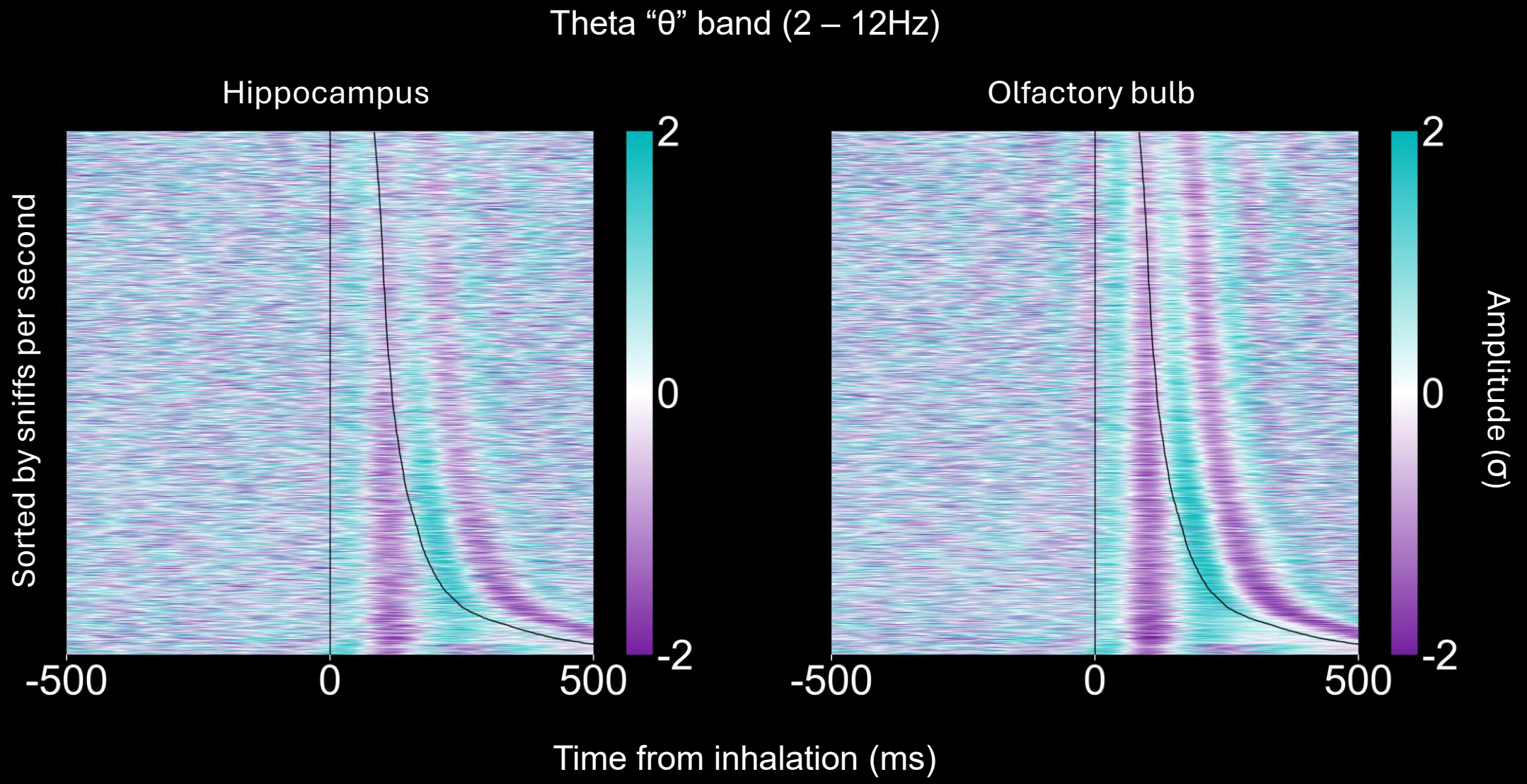
Local field potential power spectrum



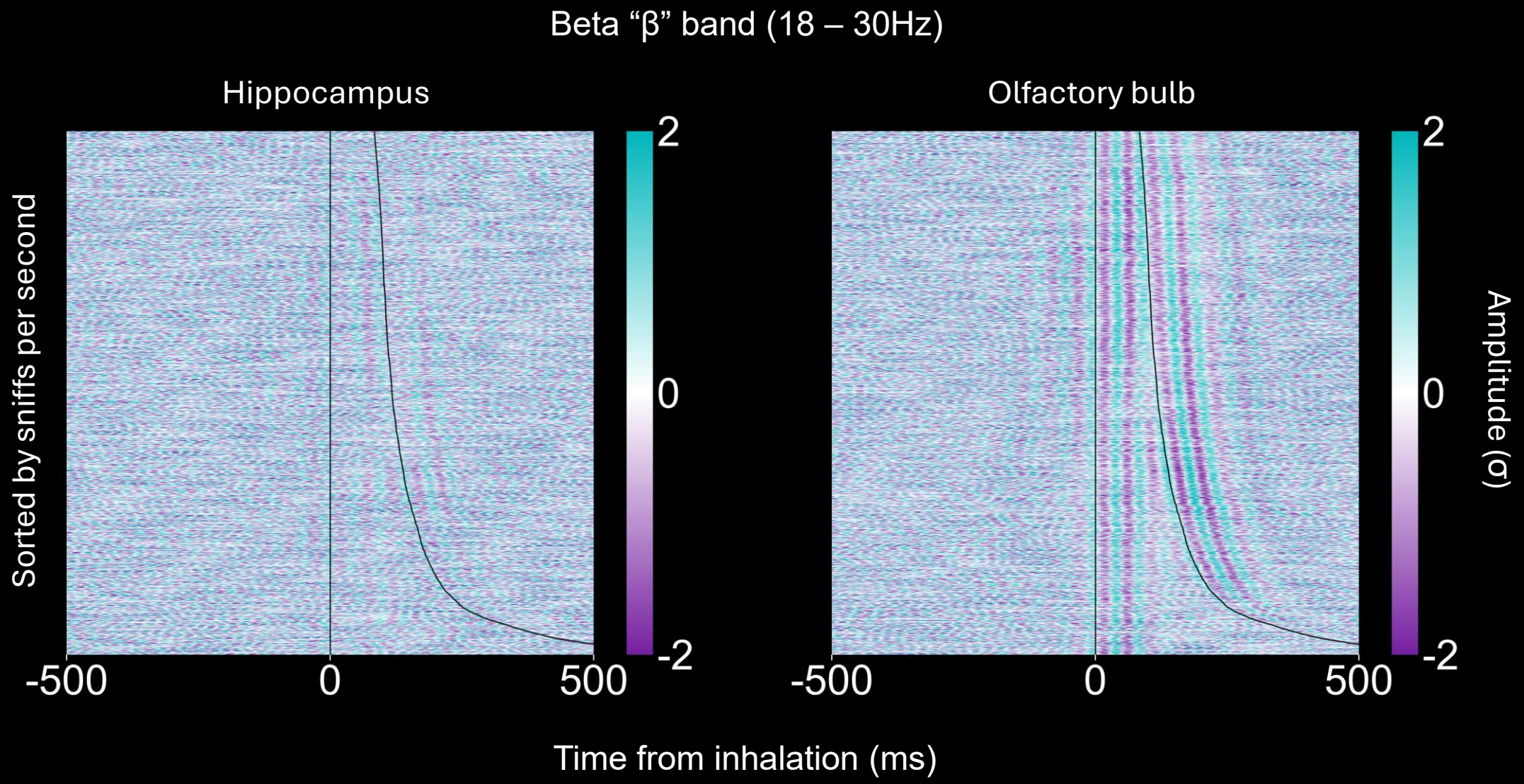
Local field potential power spectrum



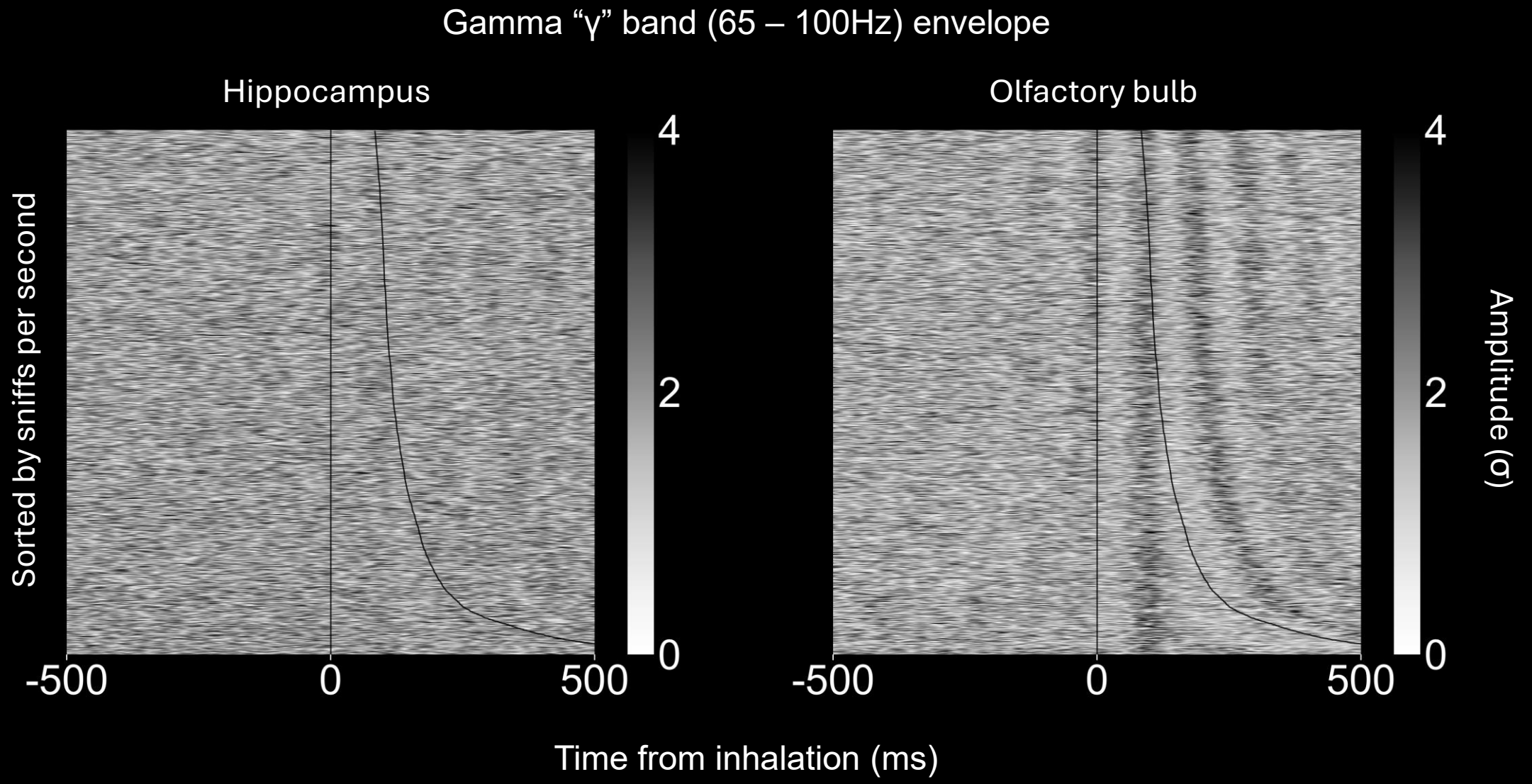
Inhalation aligned local field potentials



Inhalation aligned local field potentials

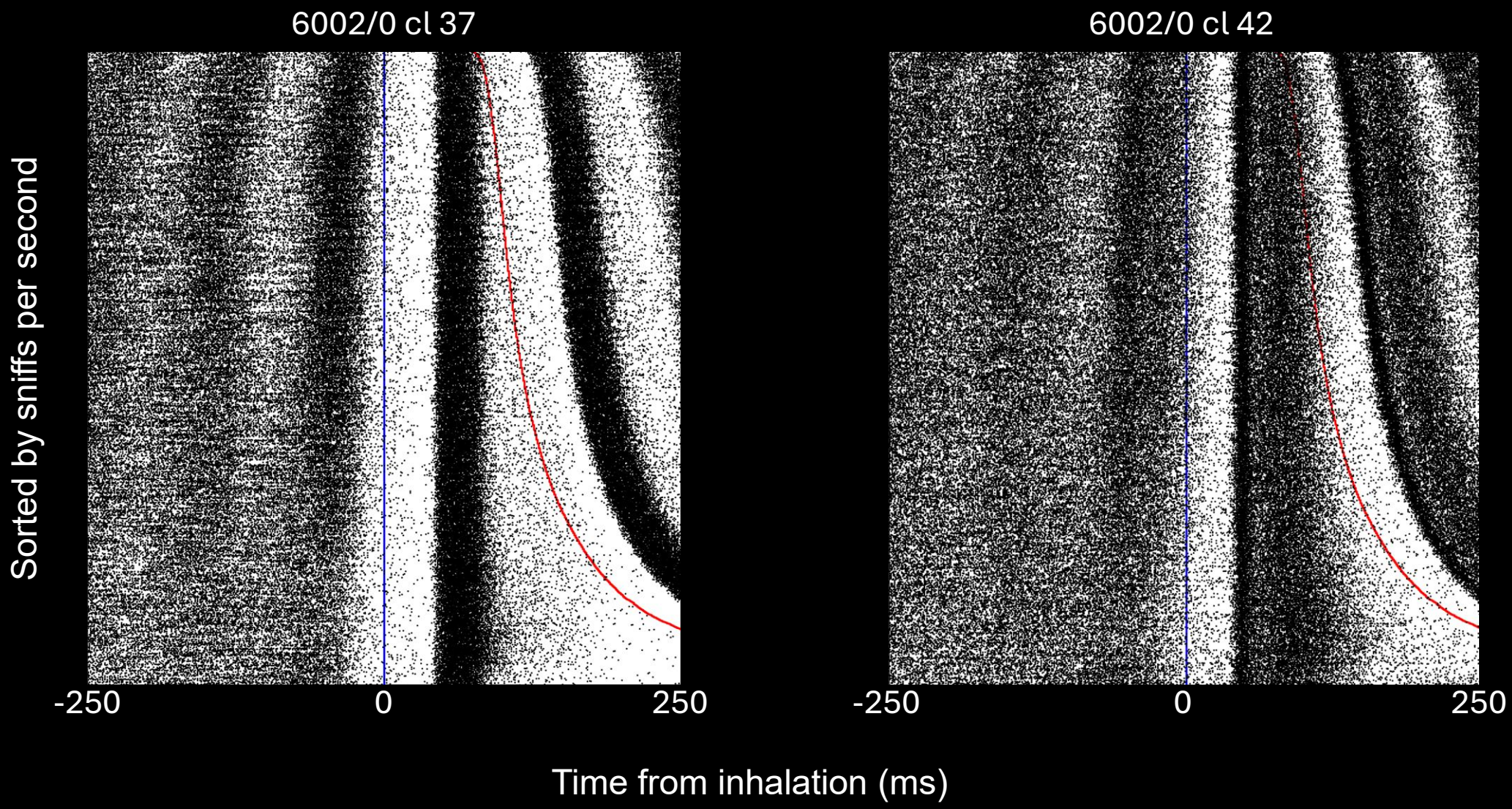


Inhalation aligned local field potentials



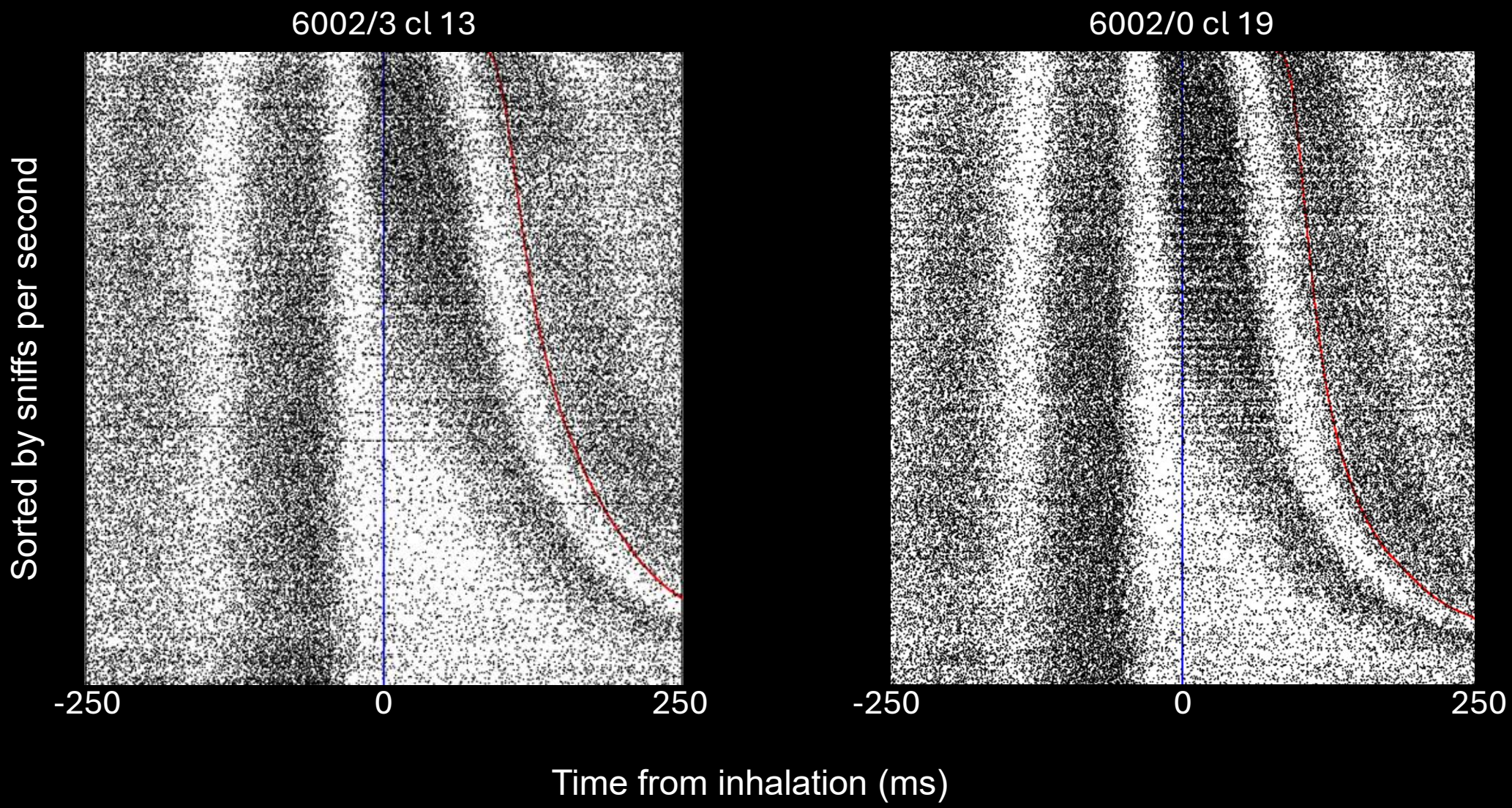
Inhalation aligned olfactory bulb spiking activity

Inhalation onset
Next inhalation



Inhalation aligned hippocampal spiking activity

Inhalation onset
Next inhalation



Current and Future Directions

Olfaction/Anosmia and Depression

1: How does disrupting olfactory inputs affect OB and HC activity?

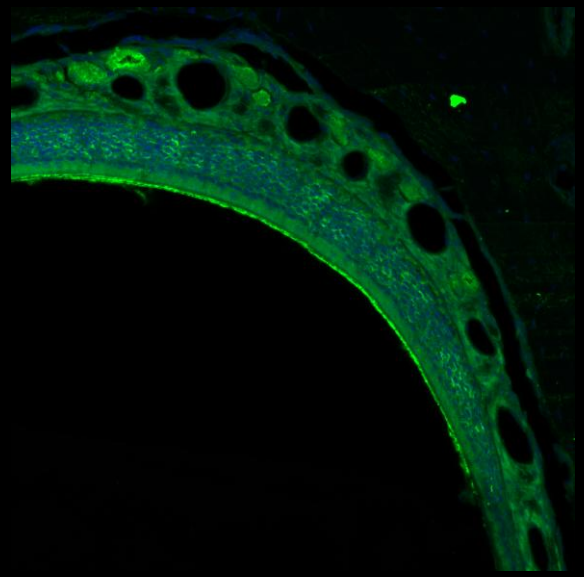
- What activity are we disrupting? Does place information come through the nose? Is it part of the recurrent network with the HC?

2: Is this disruption correlated with or causing depressive symptoms?

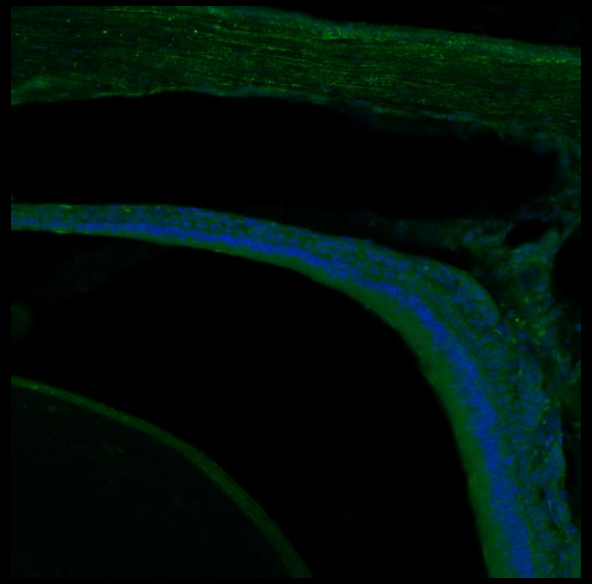
- Are LFP and spikes still aligned to inhalation? Does disrupting synchrony affect brain states?

Injections

- 100 mg/kg methimazole (MMZ)
  - Ablated olfactory epithelium

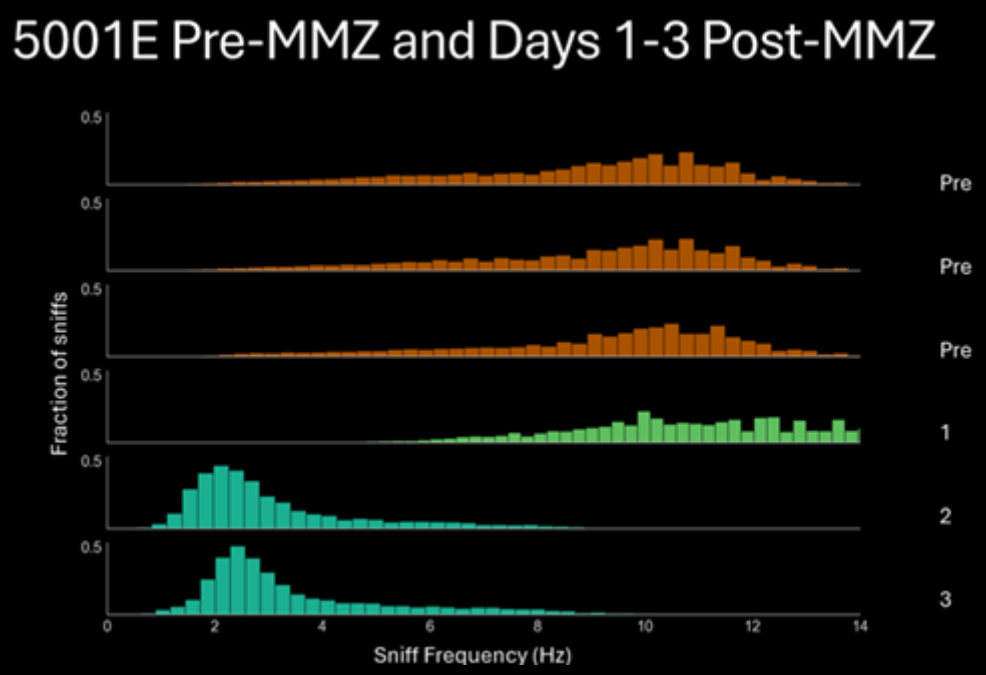


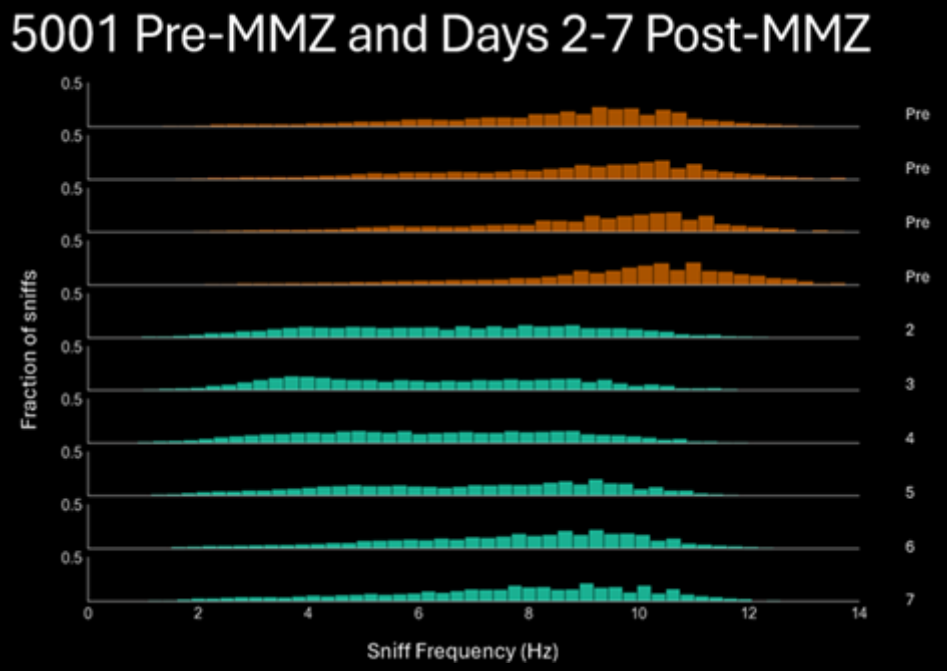
pre-injection



48 hours post-injection

MMZ affects sniffing behavior (previous results)





Behavioral Observations/Confounds

- Mice move, eat, and drink much less, sniff less frequently, and are lethargic post injection.
- Possible factors:
  - Ablation is causing disruption in neural activity
  - MMZ side effects
    - Acute toxicity can lead to myxedema coma (severe hypothyroidism)
  - Happening simultaneously?

Next Steps

- Quantify place contribution to spike rates with GLM.
- Decode place with Kalman filter, SVM, neural network.
- Analyze LFPs, spiking, and behavior in post-injection data and compare with current findings.
- SLEAP tracking
- Cohort 2
  - Powered commutator
  - VR room rotation