Olfactory bulb local field potentials track breathing rhythms at multiple time scales

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Abstract

Odors carry useful navigational and episodic information, but most of the chemical world cannot be accessed without actively sampling the environment. To optimally orient by olfactory information, the brain must unify odor-driven activity with representations of self-movement and context. Studies in other sensory modalities demonstrate that contextual signals are common in primary sensory areas, and it has long been known that olfactory bulb (OB) local field potentials (LFP) are coupled with behavior. Our lab has found that individual olfactory bulb neurons track the long-timescale rhythmic structure of breathing, in the absence of experimenter applied stimuli or tasks. To better understand the coupled rhythms of breath and OB population activity dynamics, we analyzed local field potentials. During free movement, respiration is rhythmically organized into discrete states lasting minutes, whereas these states are not apparent during head fixation. In the OB, low frequency LFP oscillations correlate with sniff frequency and LFP waveforms in multiple frequency bands are aligned to inhalation. Further, LFP amplitudes in various frequency bands are associated with sniff frequency. Thus, OB LFP tracks information about timing and frequency of the respiratory cycle, and the amplitude may encode behavioral state. We propose that these contextual signals, particularly those dependent on active sampling, facilitate the incorporation of olfactory information into cognitive maps of self and environment.

Ongoing behavior and neural dynamics

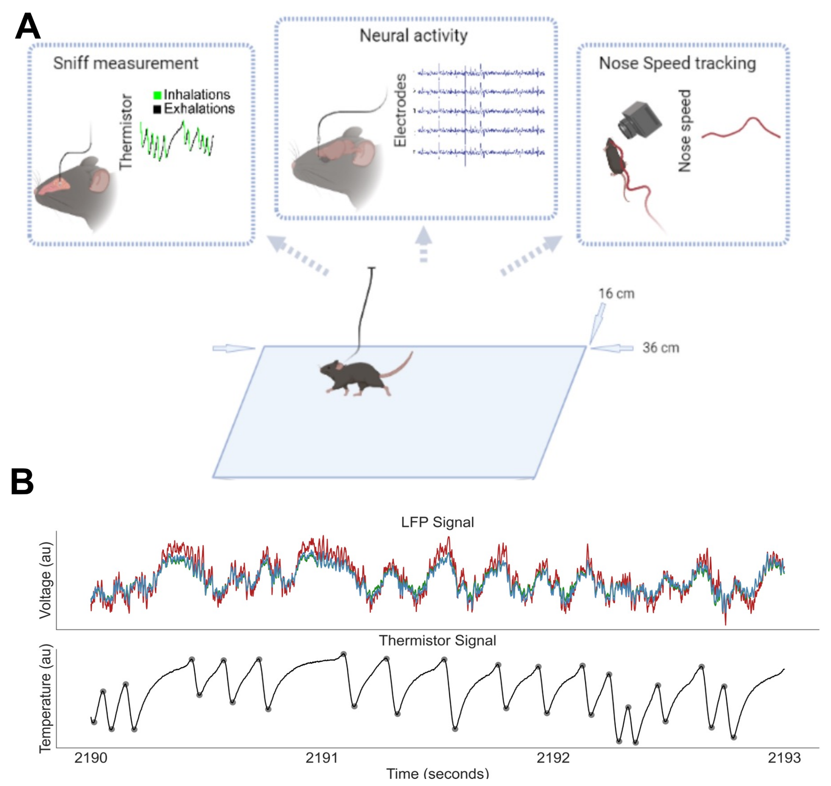

Figure 1. Recording ongoing behavior and neural dynamics in freely-moving mice. A. We recorded breathing with a thermistor (McAfee et al, 2016; Findley et al, 2021), neural activity with silicon probes (Neuronexus 16 channel and Diagnostic Biochips 64 channel), and video with a Blackfly camera (100 fps). **B.** (Top) To analyze local field potentials, we filtered and downsampled neurophysiological signals to 1 kHz. Signals from two electrodes are overlaid. (Bottom) Thermistor signals are also downsampled and smoothed, and we detected inhalation onset and offset times using a peak detection algorithm.

Multimodal distributions of sniff frequencies

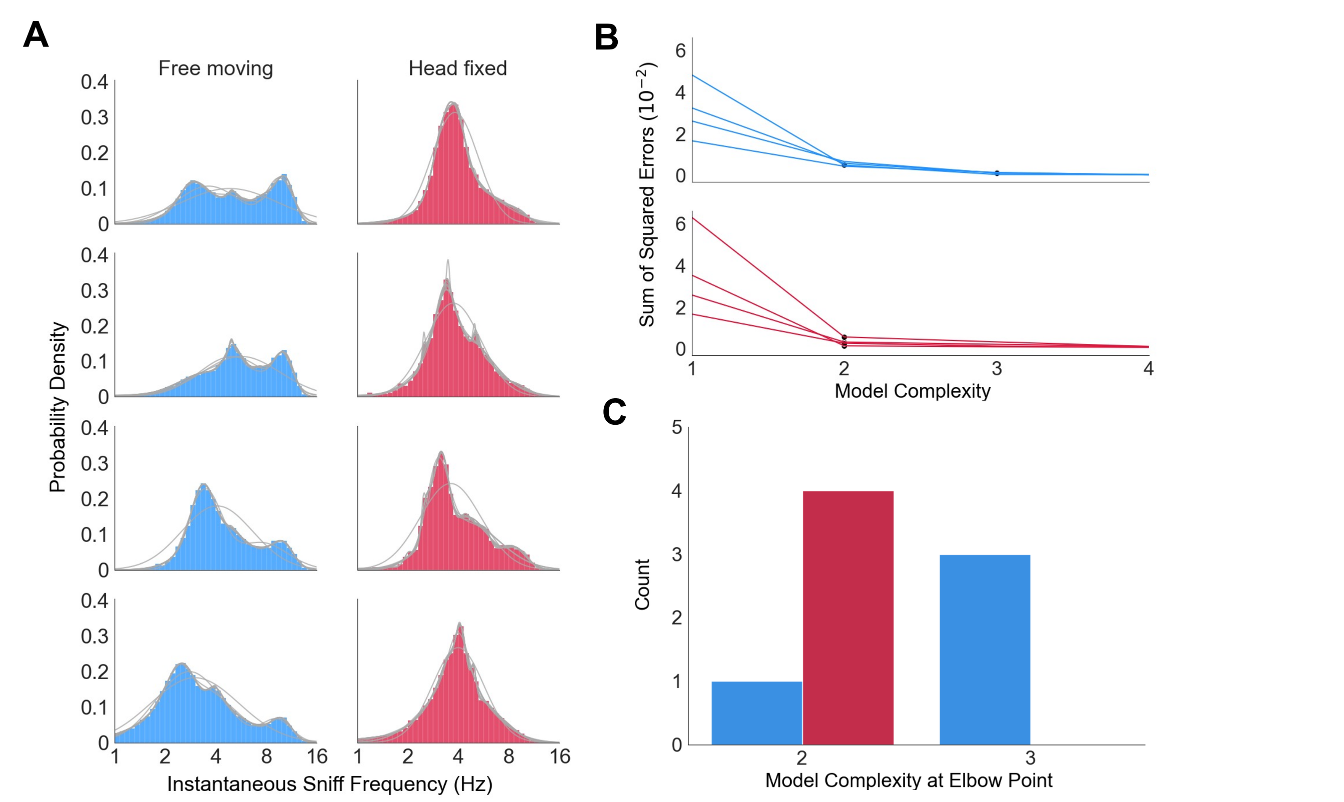

Figure 2 Analysis of sniff frequencies between head fixed and freely moving mice explains variation in sniffing behavior and informs behavioral/neural state modeling. A) Sniff frequency histograms for four mice in freely moving and head fixed conditions. Overlayed log-normal mixture distribution fitting. **B)** Error as function of model complexity. **C)** Optimal complexity supports three state model (Satopaa et al, 2011).

Sniff-aligned LFPs in head-fixed and freely-moving

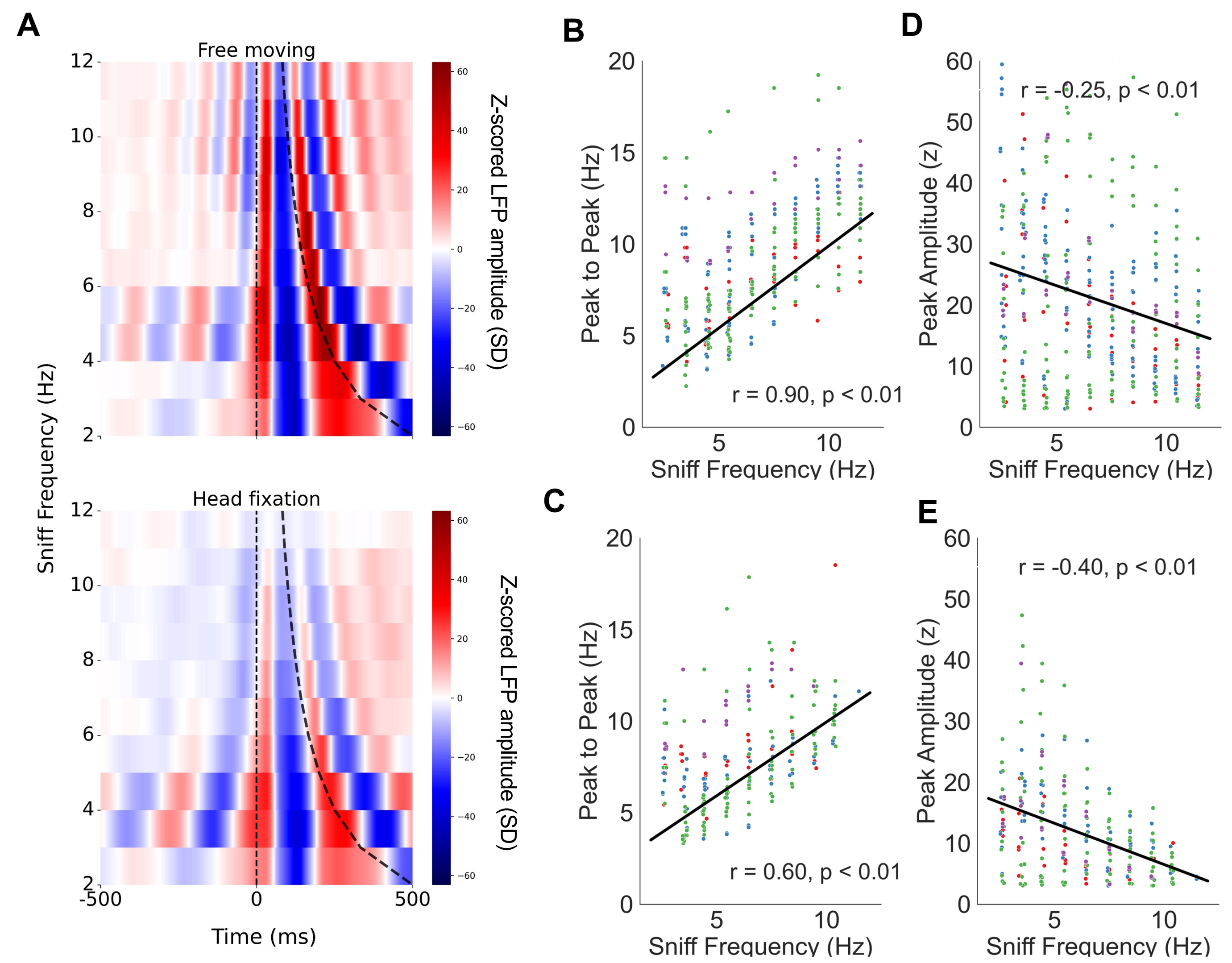

Figure 3 Aligning low pass filtered (24Hz) LFP epochs to inhalation times in head fixation and free moving conditions reveals linear correlations and neural event latencies. A) We aligned LFPs to inhalation times and pooled across breaths in 1 Hz bins. Amplitudes are expressed as z-scores in standard deviations of a null distribution formed from circular shifts of inhalation times relative to LFP **B & C)** demonstrate that LFP frequencies, calculated from peak-to-peak times, correlate with sniff frequency. **C & D)** Show LFP amplitude negatively correlated with sniff frequency.

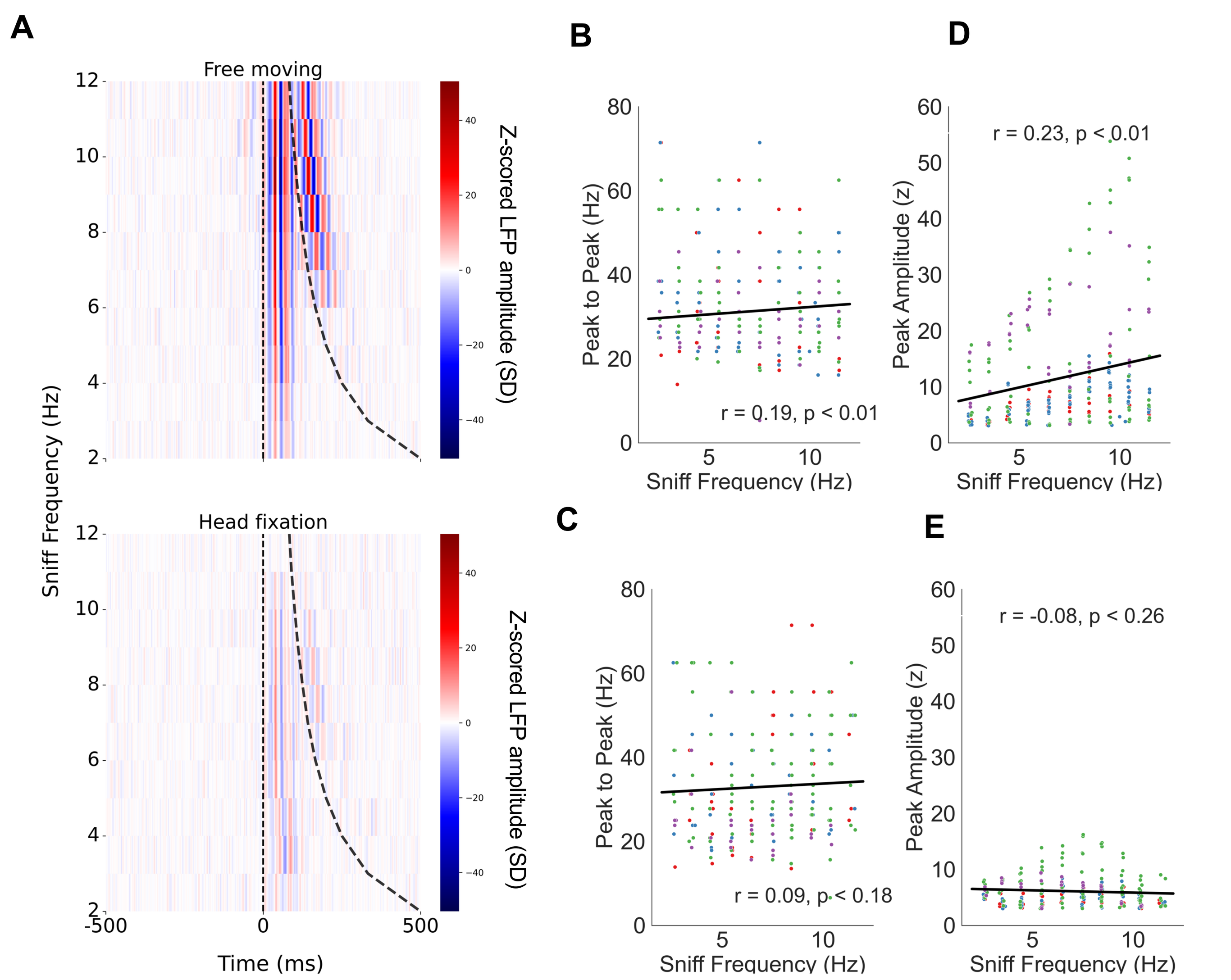

Figure 4 Aligning high pass filtered (24Hz) LFP epochs to inhalation times reveals alignment, and reduction in head fixation. A) We aligned, pooled, and z-scored high pass filtered LFPs as in Figure 3 **B & C)** demonstrate LFP beta frequencies, calculated from peak-to-peak times, are aligned but uncorrelated with sniff frequency. **D)** Positive correlation between sniff frequency and high-frequency power **E)** Sniff-aligned high-frequency power is reduced during head fixation.

Long-timescale rhythms in freely moving mice

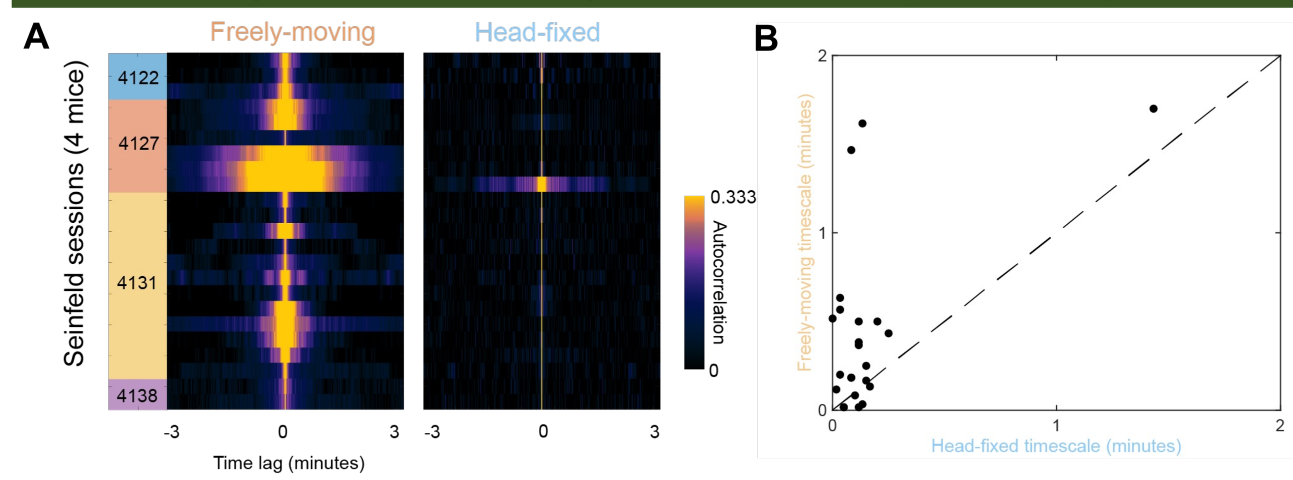

Figure 5 Autocorrelation demonstrates long timescale structure in sniffing behavior which is absent in head fixation. A) We calculated autocorrelation values of the sniff frequency time-series. Each row indicates one session from one mouse. **B)** To quantify timescales, we used the time constant of an exponential fit to the autocorrelation function.

Behavioral and neural states

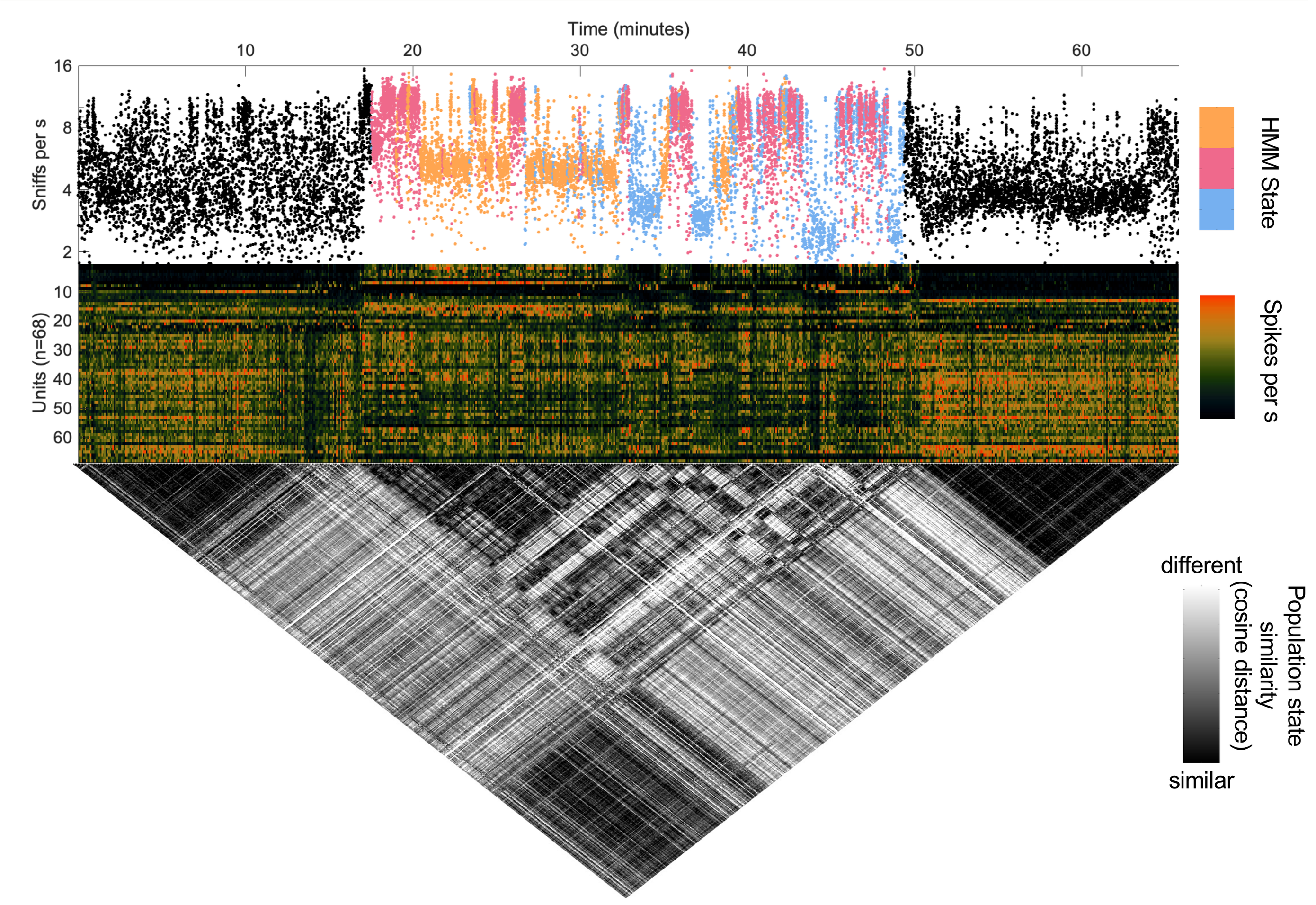

Figure 6 Olfactory bulb population dynamics track breathing rhythms and behavioral states. **Top)** Sniff frequency time series colored by Hidden Markov Model state identity. **Middle)** Single unit activity in 10s windows. **Bottom)** Cosine distance matrix representing population dynamics similarity across the session.

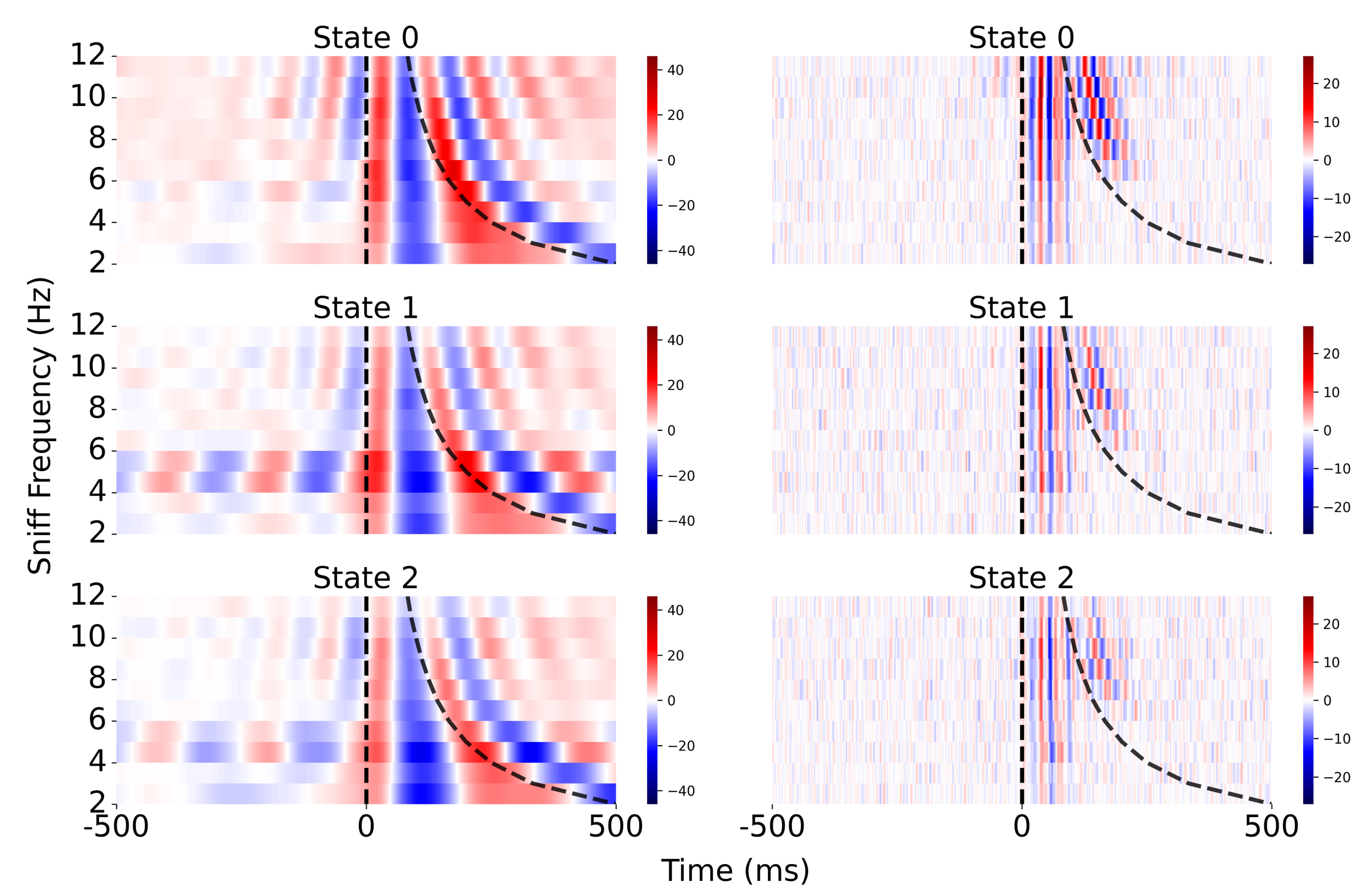

Figure 7 Sniff-centric visualization suggests that LFP does not differ across behavioral states Low-pass (Left) and High-pass (Right) filtered sniff-aligned LFP separated by HMM states.

Spectral analysis

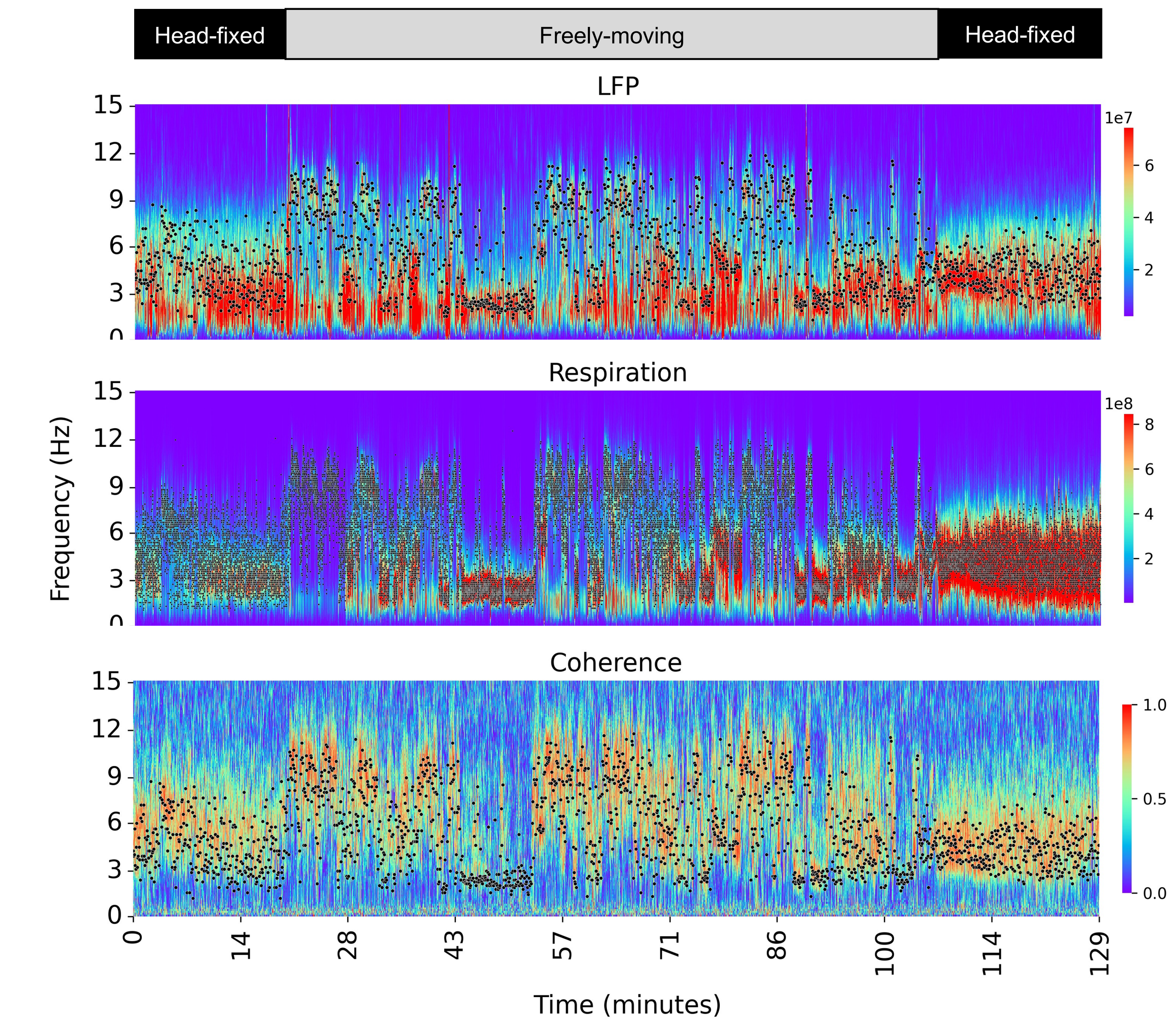

Figure 8 Spectral Analysis reveals coherence between LFP and sniff signal (after Rojas-Labano et al, 2014). Spectrograms were computed using Thompson's multitaper method using five tapers in 4s windows sliding in 400ms increments. Black scatter overlay represents instantaneous sniff frequency calculated from peak times. Color bar shows head fixation (red) and free moving (blue). Example session is shown **Top)** Power spectral density (PSD) of LFP. **Middle)** PSD of thermistor signal. **Bottom)** Spectral coherence between LFP and thermistor signals

Preliminary conclusions and future directions

- **Sniff-centric visualization of LFPs provides a complementary perspective for understanding population dynamics**
- **High-frequency LFP components track inhalation time, maintain constant timing across breath frequencies**
- **LFPs may track long-timescale breathing rhythms less than unit activity**
- Analyze the relationship between single unit activity and LFP phase (using the Hilbert transform and aligning signals bidirectionally to various peaks).
- Further explore spectral analysis using wavelet transforms to compare LFP frequency, power, and phase with respiration
- Understand the relationship between LFP frequency bands not aligned with inhalation times (gamma), respiration and behavioral HMM state.
- Predict head fixation, free moving, and behavioral HMM state from population activity using binary classification, k means clustering, and neural networks

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