Population Activity of Auditory Cortical Cells Codes Stimulus Information during Sleep Spindles

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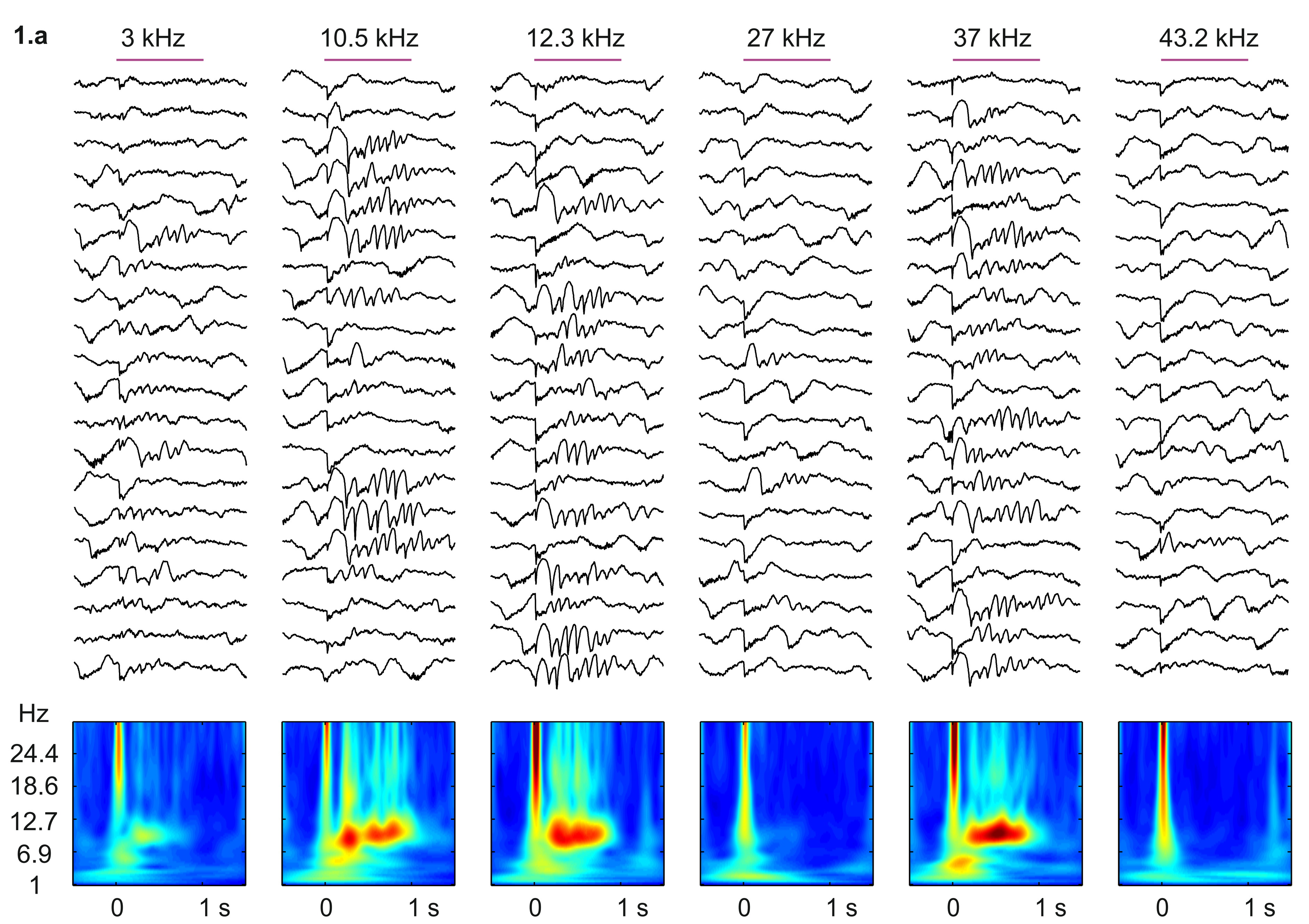
INTRODUCTION

- Sleep spindles are 10-15 Hz transient oscillations, prevalent mainly during stage II. sleep. They have a role in memory consolidation, they correlate with intelligence, and it is already known that several pathological brain states alter spindle activity.
- Spindles are generated in the thalamus by the interplay of excitatory thalamocortical and inhibitory thalamic reticular neurons; from here the rhythm is transmitted to the neocortex, which provides feedback to both generating cell types. Although the basic mechanism of spindle generation is well established, **it is unclear how spindles are involved in information processing**, especially compared to other thalamocortical network oscillations.

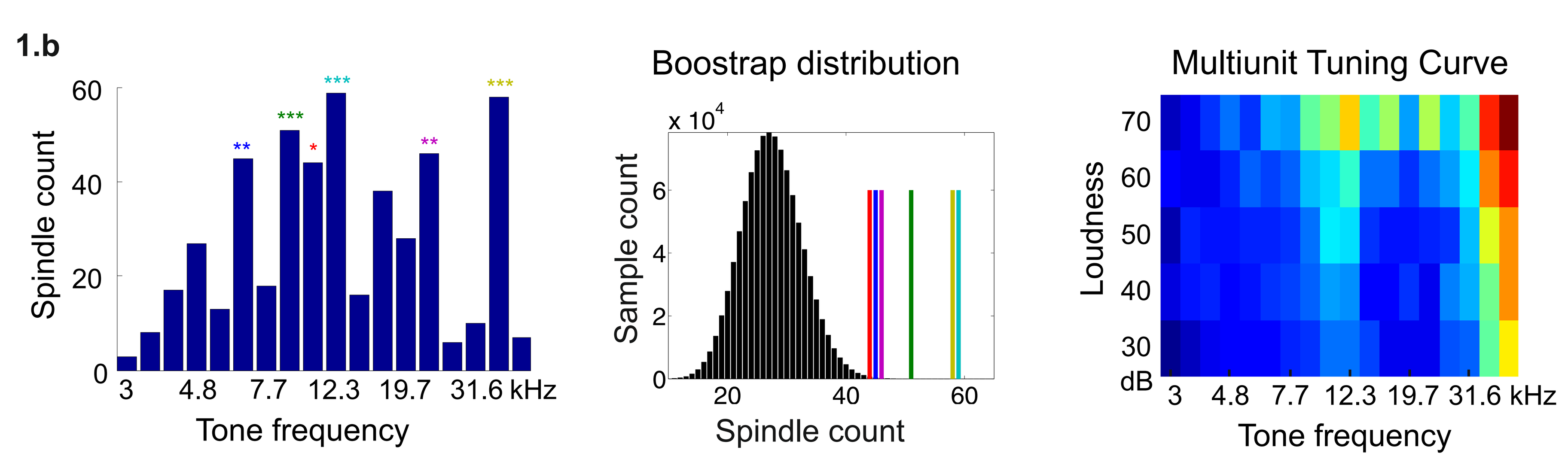
CONTRIBUTION

- **We studied the functional aspects of sleep spindles on the population level**. Specifically, we investigated auditory information content of neural populations during spindles and other sleep rhythms, such as up-down states as well as the population firing patterns of participating cells during sensory stimuli presentation.

1. AUDITORY STIMULI EVOKE SPINDLES IN A STIMULUS SPECIFIC MANNER

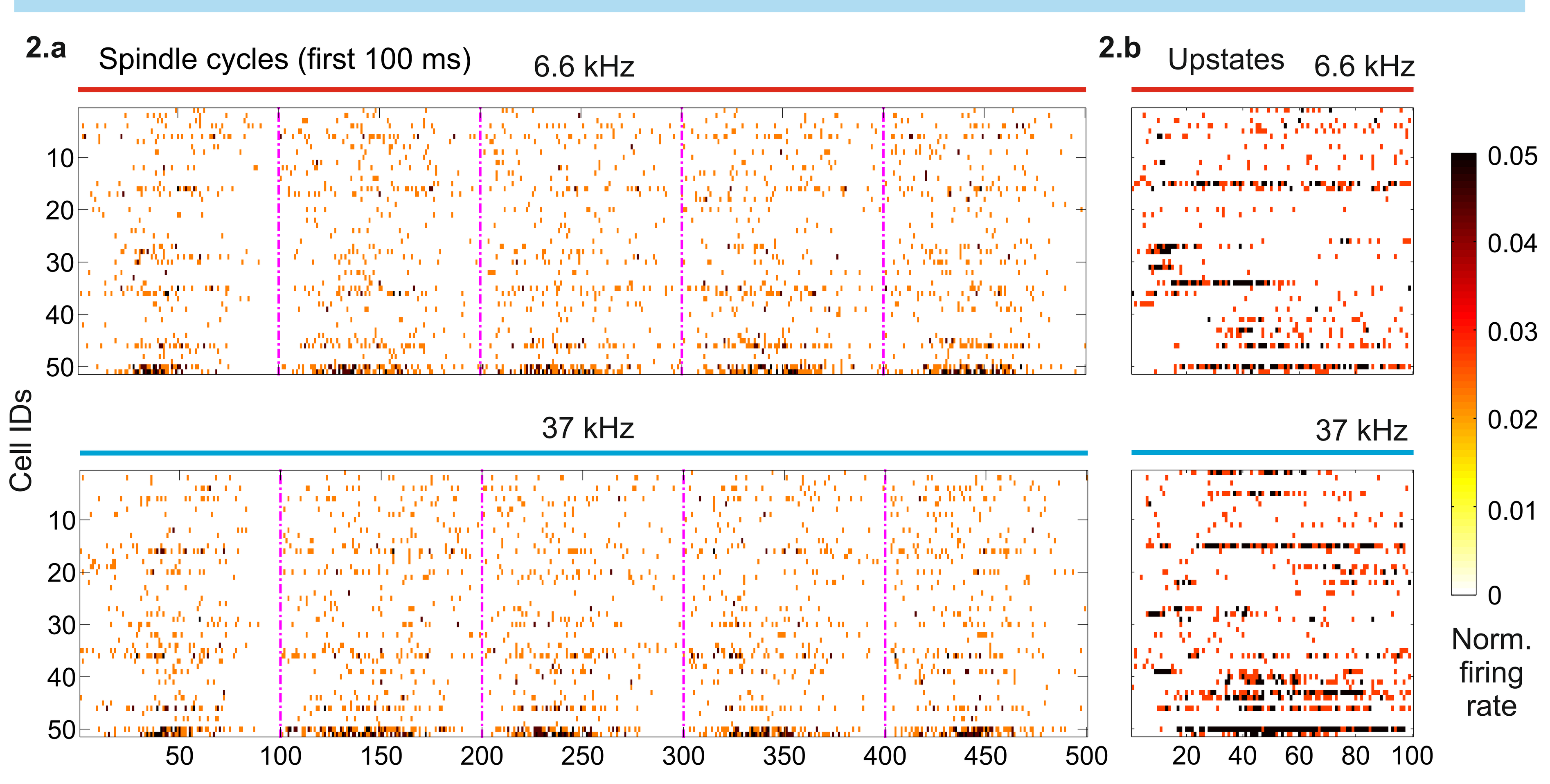


1.a Local field potential of cortical responses for repeated presentations of pure tone stimuli (top). **Wavelet transform** of averaged response shows strong 10-15 Hz spindle power during some tone frequencies but not others (bottom).



1.b Histogram of evoked spindles by different tone stimuli (left). Some tone frequencies evoke significantly more spindles than expected. Significance is determined by a bootstrap distribution with Bonferroni correction (middle). The multiunit tuning curve shows some correlation with spindle evoking tone frequencies (right).

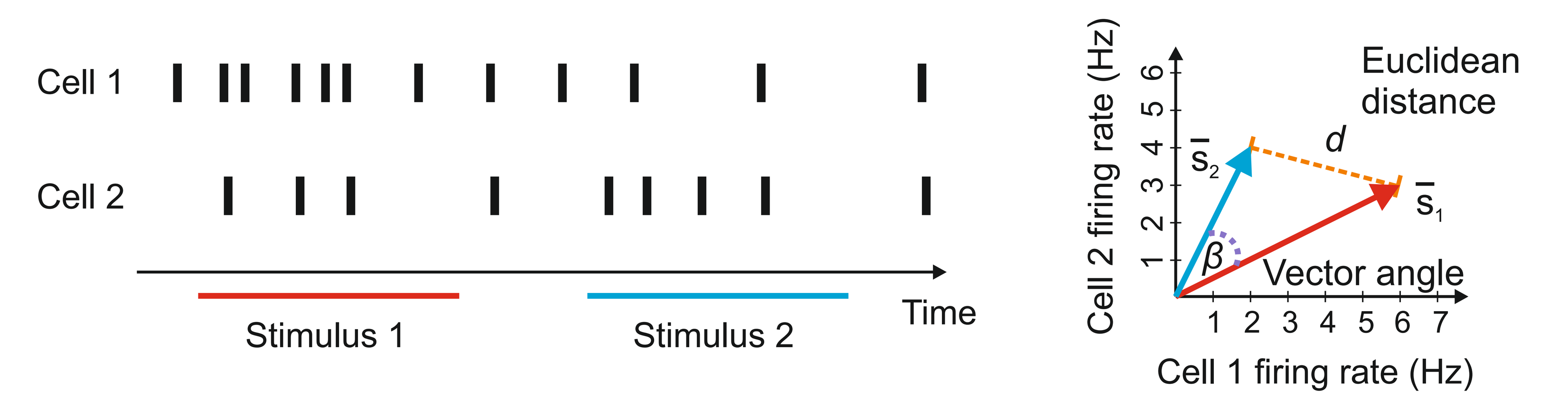
2. STIMULUS EVOKED SPINDLES AND UPSTATES HAVE CHARACTERISTIC FIRING PATTERNS



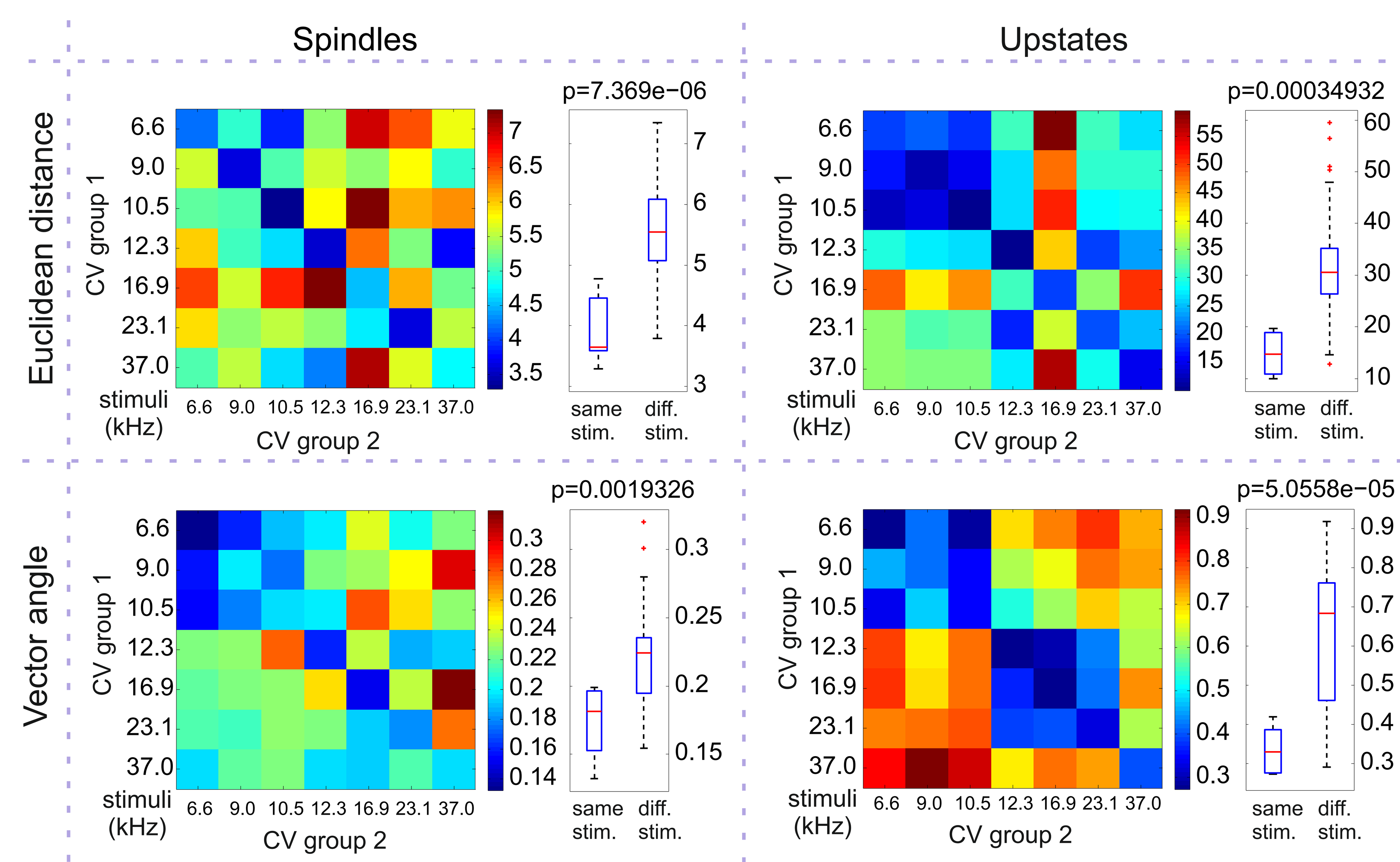
2.a Averaged population firing patterns during the first 5 cycles of 45 evoked spindles are markedly distinct for different stimuli. **Normalized firing rate** indicates that for repeated presentation of stimuli how much cells fired at the same time in response to the stimuli. **2.b** Averaged firing patterns for evoked upstates (37 ups. for each stimulus).

3. POPULATION ACTIVITY IS REPRESENTED AS FIRING RATE VECTORS

To analyze population activity in the auditory cortex, first we clustered electrophysiological multiunit cell activity into single cell firing. Peri-stimulus firing of individual cells were then averaged within stimuli (left). Finally, population activity was represented as firing rate vectors ($\bar{s}_i$) with *n* dimensions, where *n* equals the number of single cells in the population (right). As a first approximation, similarity between population firing patterns under different stimuli was measured as the Euclidean distance (*d*) and angle (*β*) between the population vectors.

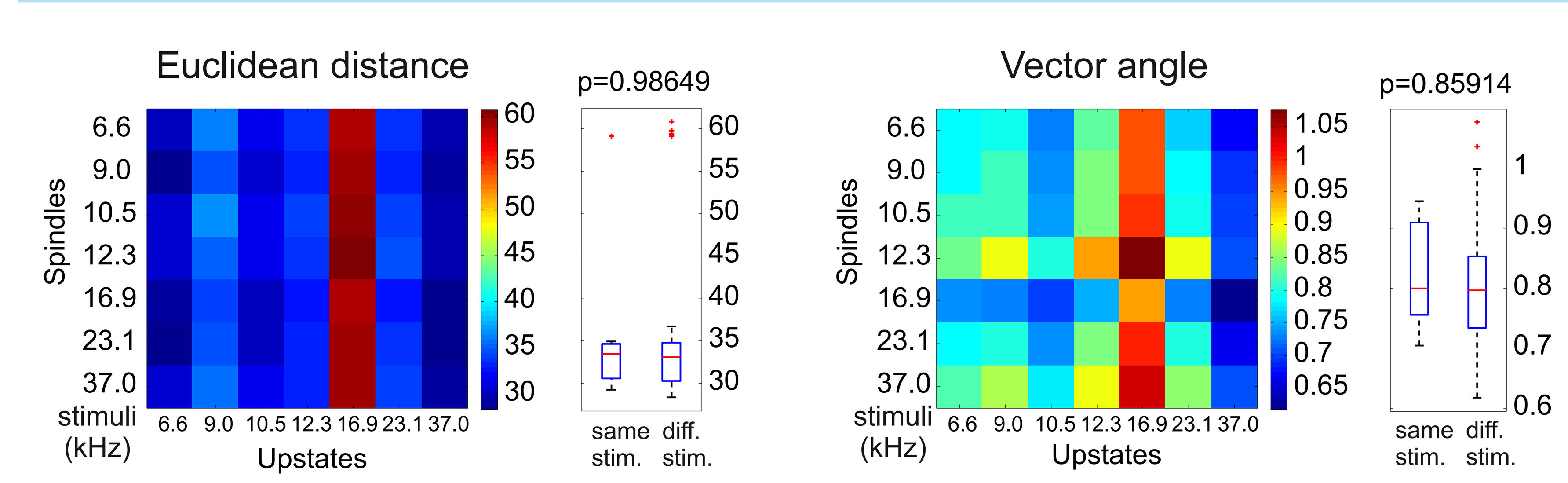


4. POPULATION ACTIVITY CONTAINS STIMULUS SPECIFIC INFORMATION DURING SLEEP OSCILLATIONS



Cross validated Euclidean distance (top row) and vector angle (bottom row) of population firing rate vectors under stimuli evoked **spindles** (left column) and **upstates** (right column) show that **population activity is more similar within same stimulus (diagonal) than between different stimuli (off-diagonal)**.
Cross validation is done by taking population vectors under a given stimulus into two randomly separated (CV) groups. Statistical significance is shown by paired t-test.

5. SPINDLES CONTAIN DISTINCT POPULATION INFORMATION COMPARED TO UPSTATES



Similarly as before, but stimulus evoked population vectors are compared under spindles vs. upstates. With this simple comparison method we found no significant similiarity in same stimulus evoked population activity under the different sleep oscillations. (*Note the lack of similarity in the diagonal.*)

METHODS

We simultaneously recorded extracellular electrophysiological activity of auditory cortical neurons (n=27-70) in four Wistar rats (180-500 g) under light urethane anaesthesia (1.5 g/kg) with 32-channel Buzsaki type silicon probes (4 and 8 shanks) during randomized repeated presentation of pure tones (1.7-67.6 kHZ). Signal was amplified and digitized with an Intan RHD2000 system. Clustering of single units was done with general semi-automatic clustering methods (KlustaSuite). Spindles were detected with automatic filtering methods (Bartho et al., Neuron, 2014) and then manually checked and refined. Upstate onsets were detected as the time when the smoothed multiunit activity crossed a standardized threshold after 60 ms of inactivity and remained over threshold for at least 60 ms. All analysis was done in MATLAB.

DISCUSSION

- Our results show that **auditory stimuli can evoke spindles in a stimulus specific manner**.
- The tuning of evoked spindles showed only small correlation with the tuning of the local multiunit.
- We found that the **population activity during spindles contained information about the ongoing stimulus**, but **the representation was markedly different from of upstates occurring during the same stimulus type**.
- Our results indicate that **information processing might work through distinct mechanisms during different neural oscillations**.

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