Comparison of Response Characteristics in Auditory Cortex of the Awake and Anesthetized Ferret

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Supported by:
MURI # N00014-97-1-0501 from the Office of Naval Research
NIDCD T32 DC00046-01 from the National Institute on Deafness and Other Communication Disorders
NSFD CD8803012 from the National Science Foundation
American Society of Electrical Engineers

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Introduction

- The goal of our research is to understand the functional organization of Auditory Cortex by studying the cortical encoding of complex and natural sounds in the awake, behaving, ferret.
- In previous studies, we characterized the response of cells in the Ketamine-anesthetized ferret Primary Auditory Cortex (AI), using dynamic, broadband sounds.
- We have developed techniques for neurophysiological recordings from the awake restrained ferret to enable a comparison of cortical responses in awake and anesthetized conditions.
- Pure tone and moving ripple stimuli were used to measure the frequency tuning and rate level functions of the cells in AI and to derive their Spectro-Temporal Response Fields (STRFs).
- We also compared the pure tone responses and STRFs from units recorded simultaneously with a single electrode at the same cortical location.

Experimental Methods

- Standard extracellular techniques (with 5 MΩ tungsten electrodes) were used to record single and multi-unit responses in the auditory cortex of the awake and ketamine-anesthetized ferret.

- In order to restrain the ferret's head movements in the awake preparation, a metal post was surgically implanted on the skull so that the head could be held in a stable position.

- Neurophysiological recording sessions in the awake animal lasted 3-6 hours per day. Acute experiments on the anesthetized preparation lasted 3-4 days. In each electrode penetration, recordings were made at several cortical depths, and raw or filtered responses waveforms were sampled and stored for off-line sorting and data analysis.

- Sound stimuli were delivered through small microphones (Etymotic Research) inserted in the ear canal and calibrated in situ at the beginning of each recording session. Each stimulus set was presented at least ten times in a randomized order.

Moving Ripples

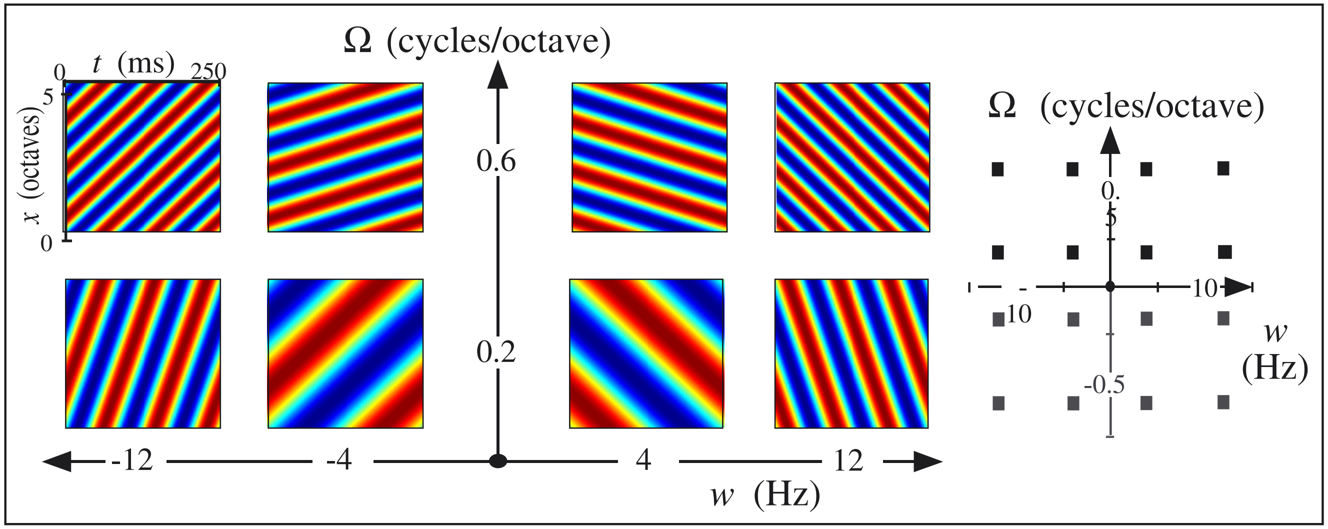
Ripples form our basis for the Fourier-domain description of dynamic spectra. At time t and frequency x, their amplitude $S(t,x)$ is given by:

$$S(t,x) = \sin[2\pi w t + 2\pi \Omega x]$$

$x = \log_2[f / f_0]$

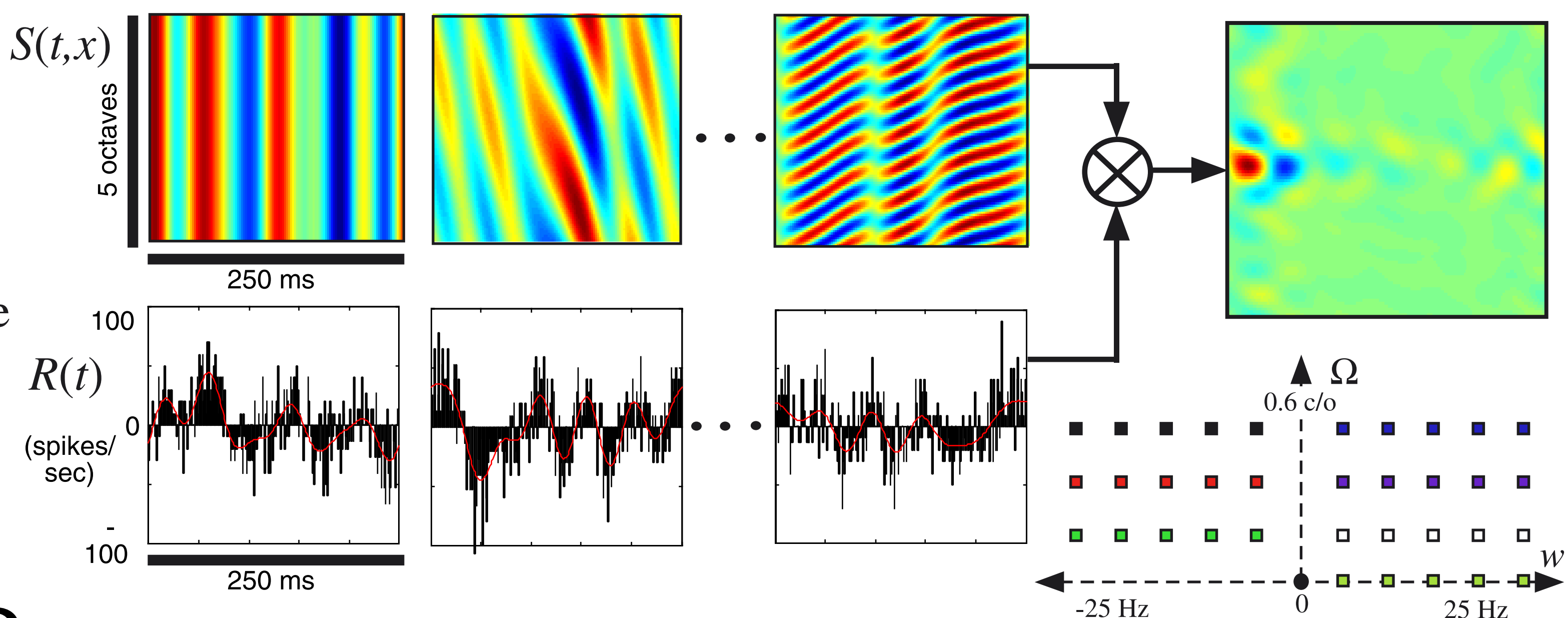
w = ripple velocity (mod rate)

Ω = ripple frequency (density)



Temporally Orthogonal Ripple Combinations (TORCs)

TORCs are made up of ripples with different modulation rates. The stimuli shown here contain ripples which cover the same range of ripple velocities, but at different ripple frequencies.



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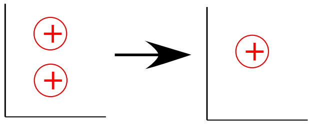
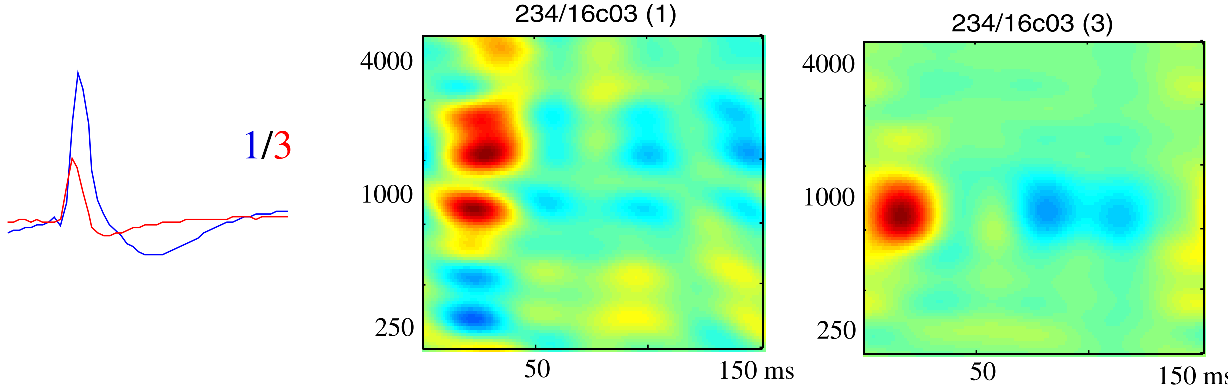
STRF Pairs (Anesthetized)

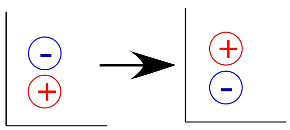
Variability

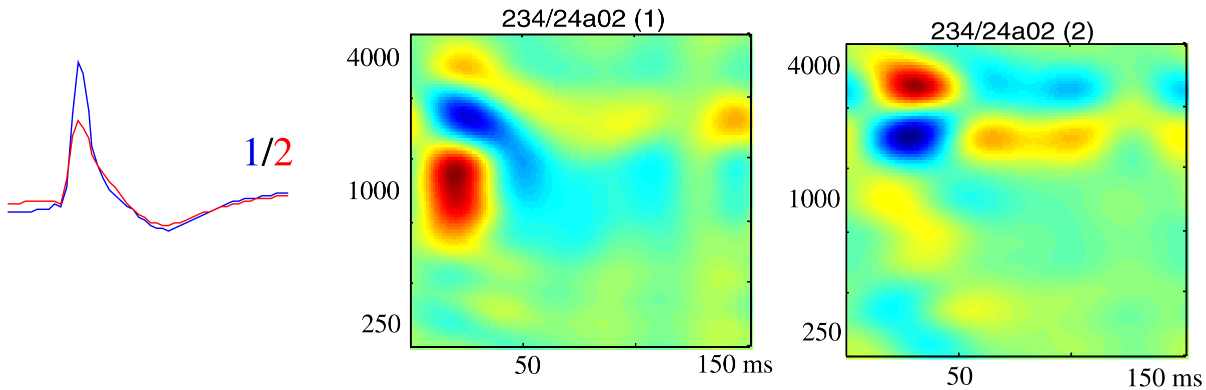
Multi Vs. Single-Peak



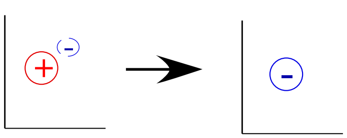


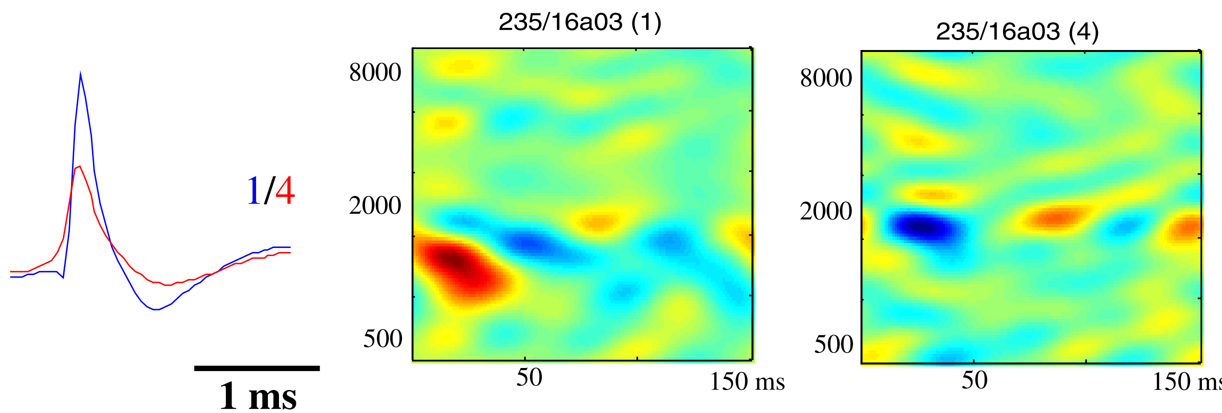
Reversed Sideband Excitation





Reversed Polarity





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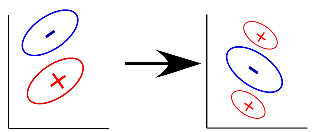
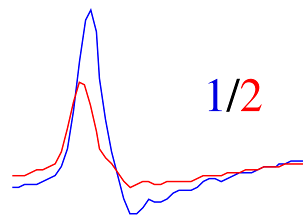
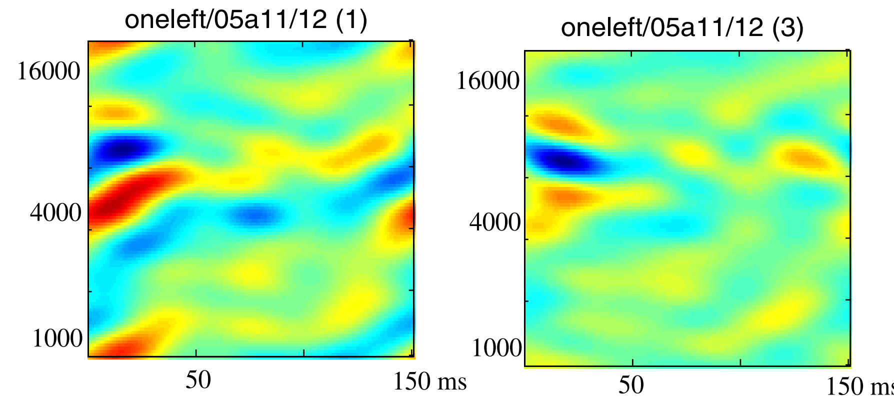
STRF Pairs (Awake)

Variability

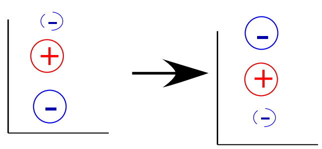
Orientation

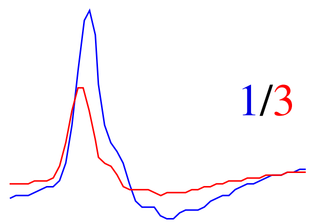


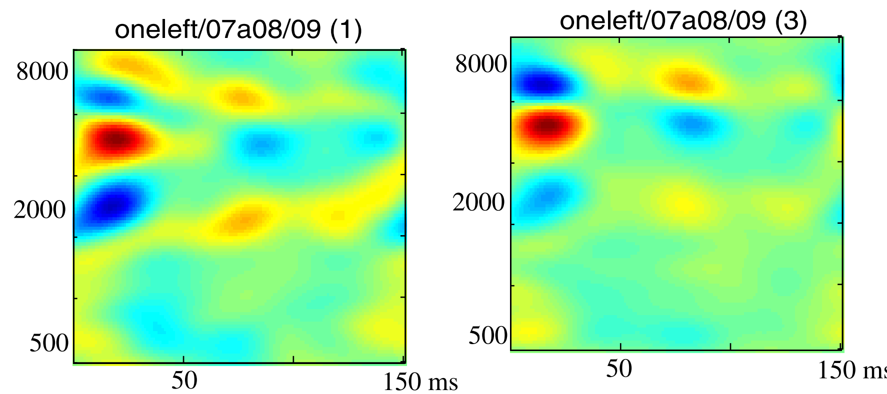




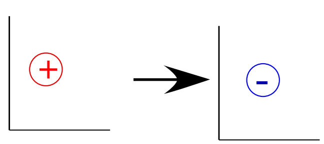
Reversed Sideband Inhibition

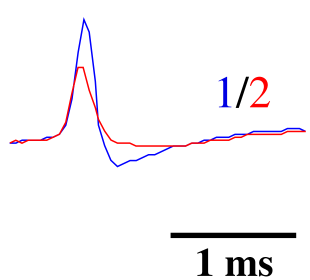


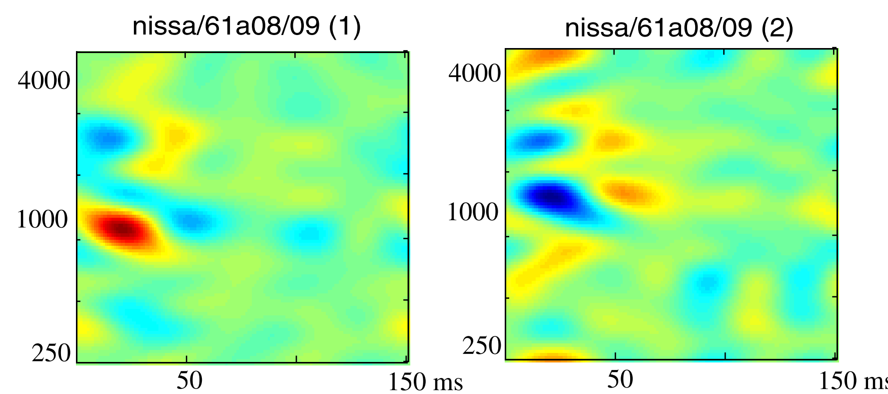




Reversed Polarity







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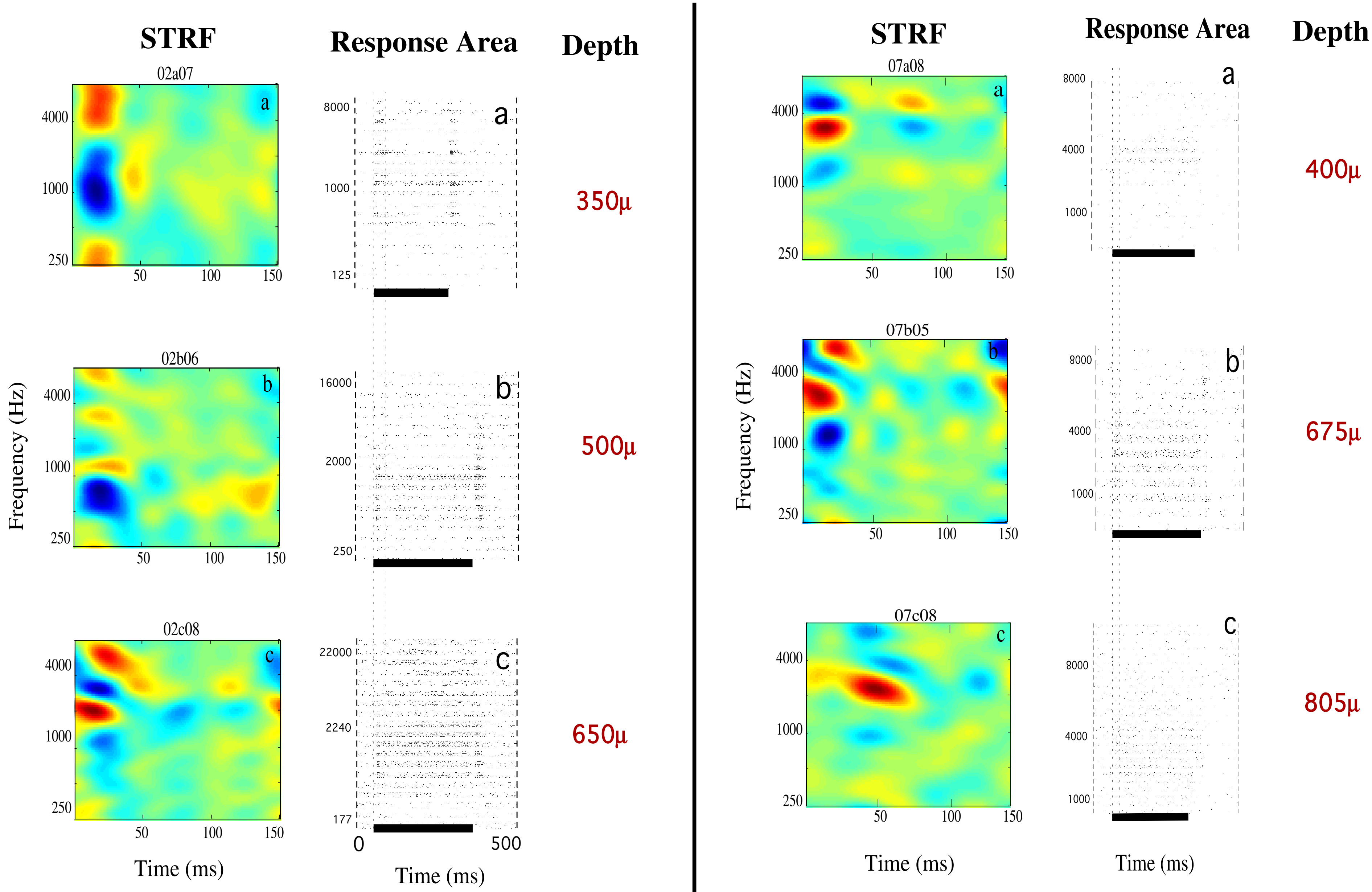
Quantifying the Fine Structure



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Response Variability

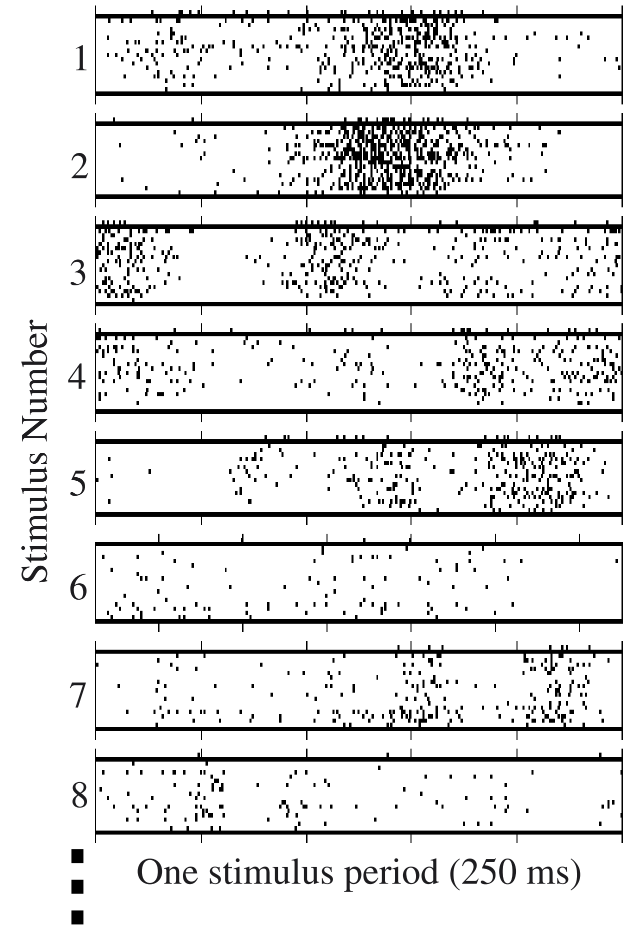
Identical stimuli do not yield identical responses. This inherent variability results in STRF variability. The expected amount of variability should be taken into account when analyzing the STRF.

The periodic nature of the stimuli allows easy evaluation of the response variability.

The mean response is an estimate of the spike rate, which has some variance.

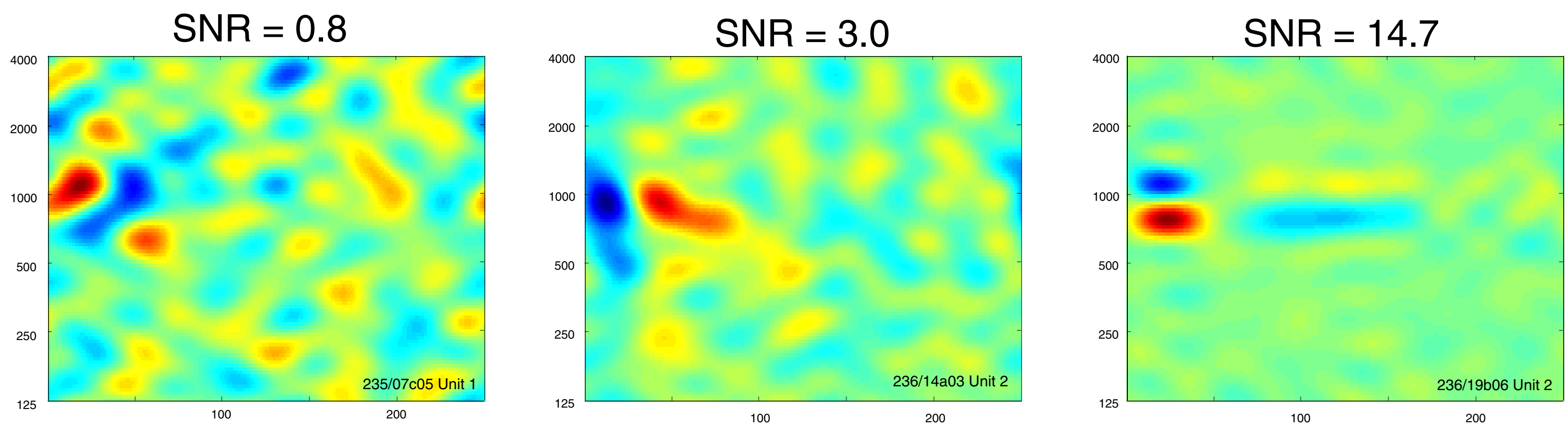
The variance is proportional to the mean, inversely proportional to the number of stimulus presentations, and is well described by Poisson statistics.

The variance can be evaluated in the time domain, or the frequency domain. The total amount of variance is equal across both domains.



STRF Variability

The response variability contributes a random, unstructured component to the measured STRF. The strength of this component, relative to the strength of the STRF, is quantified by the signal-to-noise ratio (SNR).



With TORC stimulation, the strength of the random component is trivially obtained from the response variability, since the response frequencies have a one-to-one correspondence with the STRF components.

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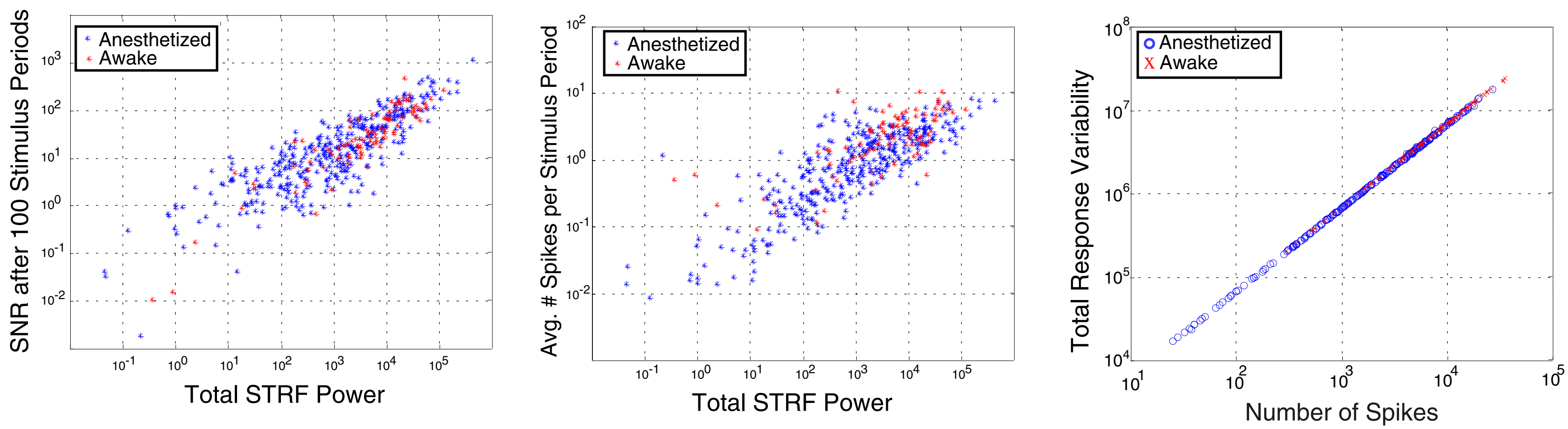
Variability: Awake vs. Anesthetized

The most obvious difference between the awake and the anesthetized responses is that under the awake condition, neurons fire more spikes on average. However, taking this difference into account, it seems that the same set of laws are governing the relations between the STRF strength, the spike rate, and the response variability.



The relations are well described by a Poisson process, plus an independent source of variability which is the same under both conditions, on average.

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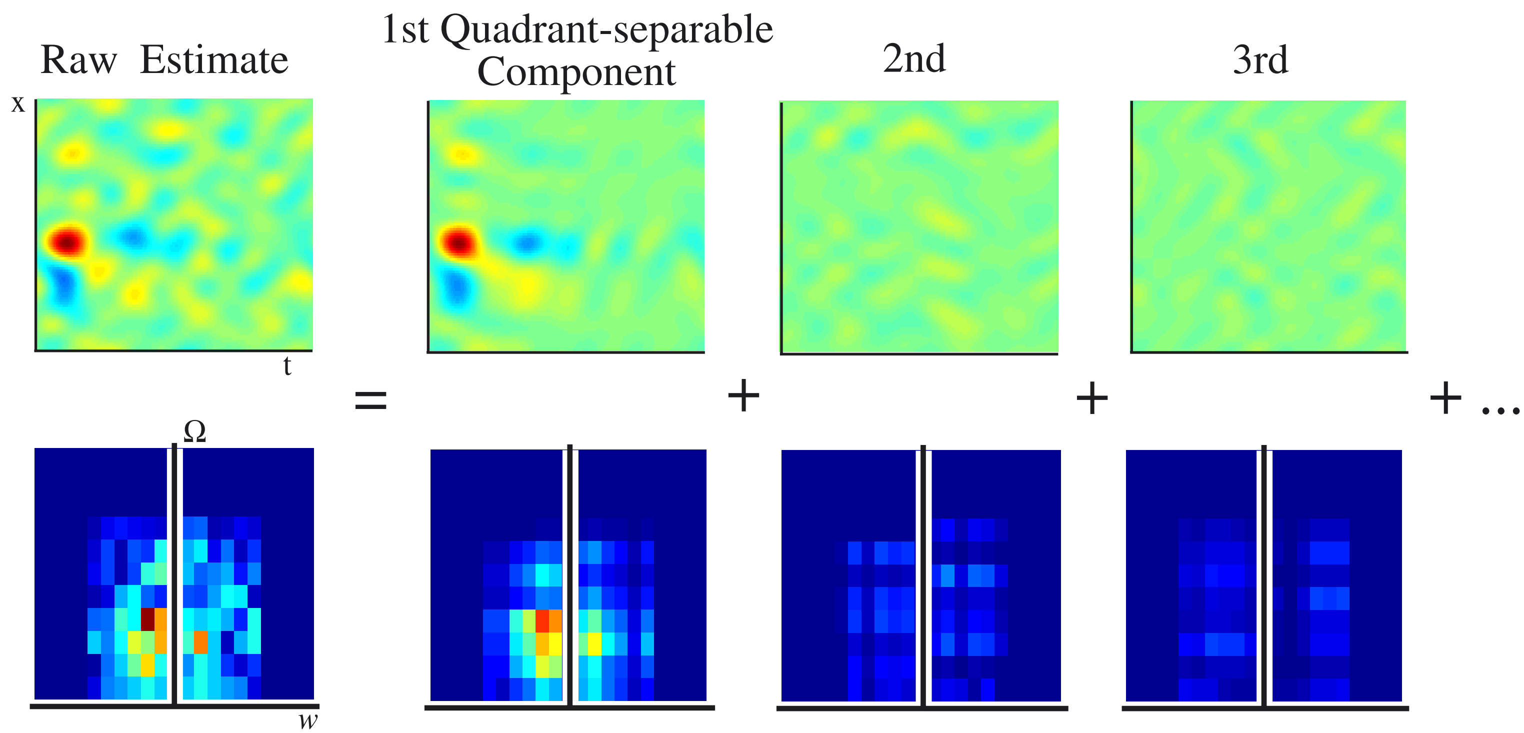
STRF Structure: Introduction

The complexity of the STRF is evaluated using the singular value decomposition (SVD), which describes the STRF as a sum of separable functions, arranged in order of overall size. The more complex the STRF structure, the less the STRF will be able to be described by a single separable function. In the same way, the complexity of the quadrants of the ripple transfer function can be assessed.



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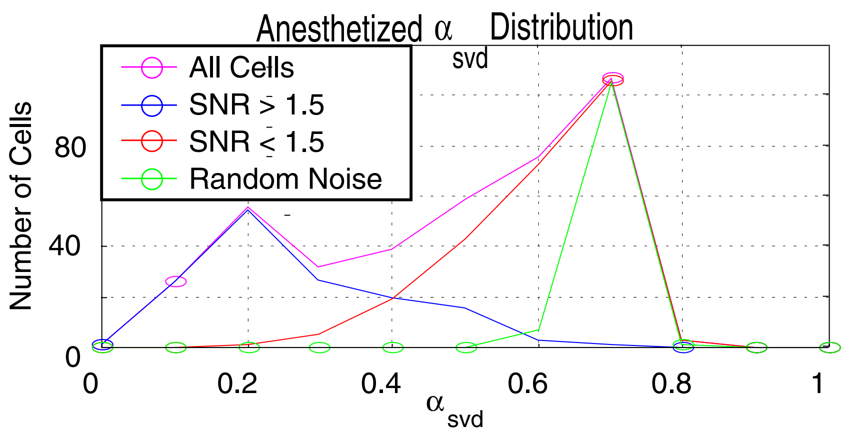
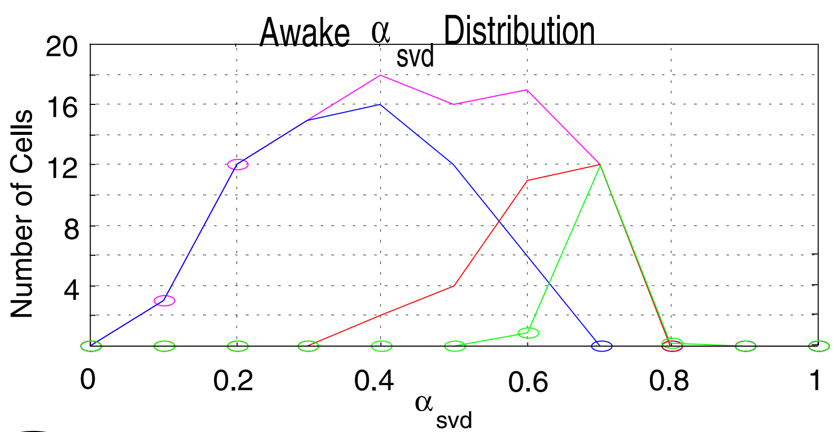
STRF Structure: Noise

The random, noisy component of the STRF increases the overall complexity. Thus, STRFs with a low SNR tend to have a high degree of complexity. The complexity is quantified by α_{svd}, which is the fraction of STRF power which cannot be described by a single separable function.





Fortunately, this noise is manifested primarily in a the lower-power SVD components. Since we know the total amount of noise to expect, we can discard those low-power components that lie below the noise threshold, effectively removing a large amount of the noise. The complexity of the noise-cleaned STRF is then assessed.

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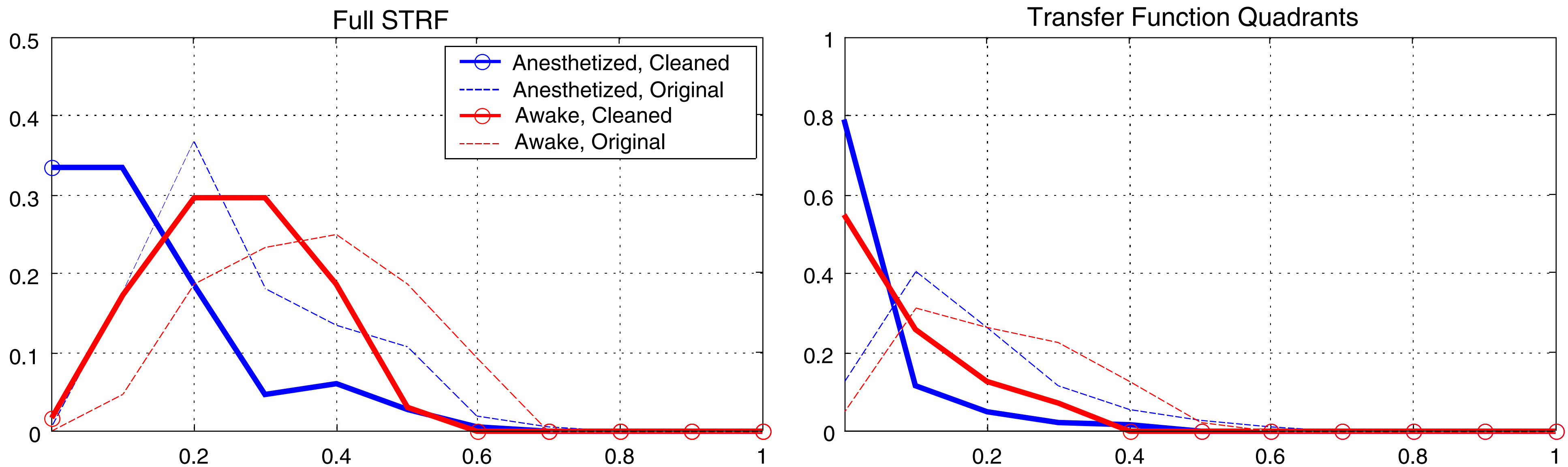
Structure: Awake vs. Anesthetized

The complexity of the STRFs measured in the awake ferret is higher than in the anesthetized ferret, on average. However, the transfer-function quadrants have a similar degree of complexity in the two conditions; most STRFs are still well described by quadrant-separable transfer functions.

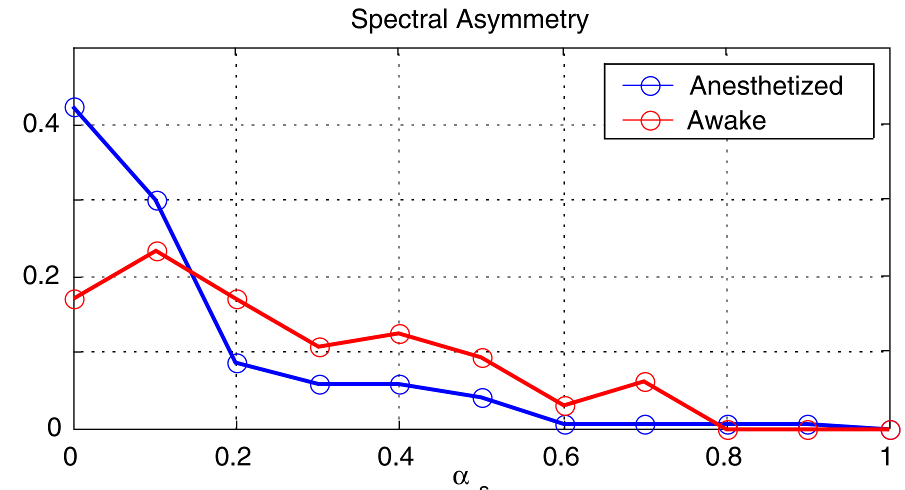


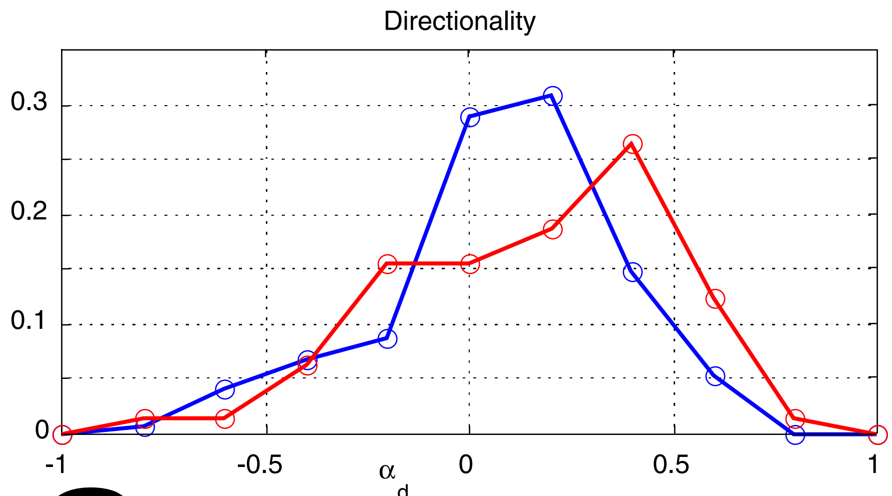
Therefore, the increased STRF complexity in the awake condition must be due to different relationships between the quadrants of the transfer function.

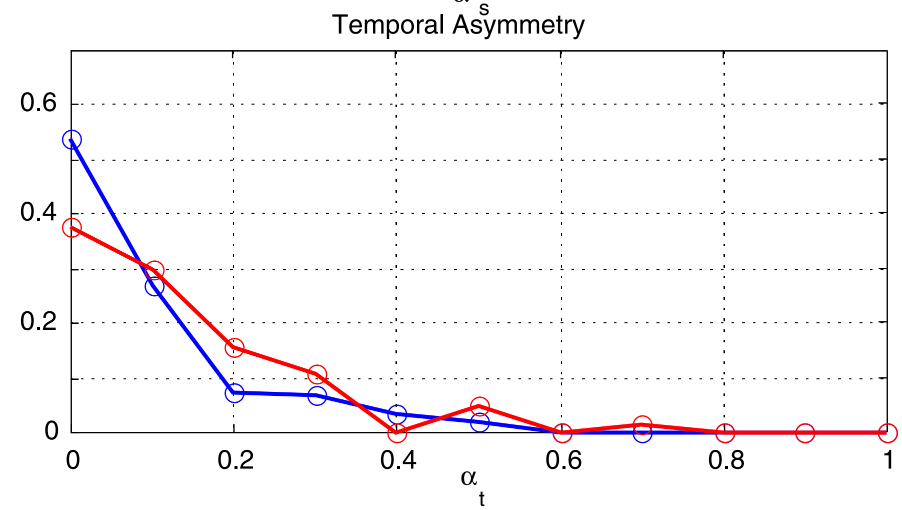
Transfer Function Structure

If a ripple transfer function is quadrant separable, then an increase in STRF complexity corresponds to increased differences between the quadrants. Each quadrant is described by a single spectral transfer function, temporal transfer function, and overall power.

Therefore, these differences are fully described by the spectral asymmetry α_s, the temporal asymmetry α_t, and the directionality (overall power asymmetry) α_d.







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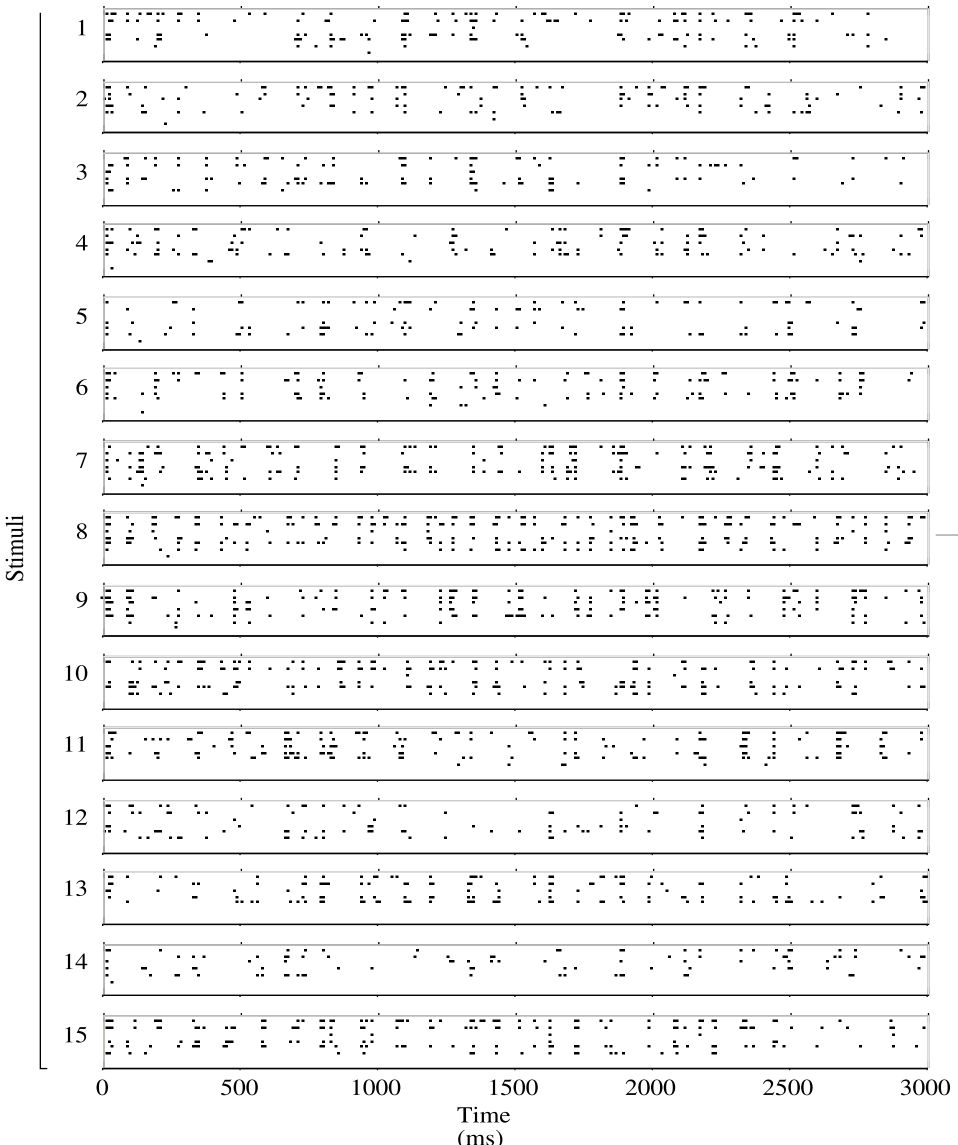
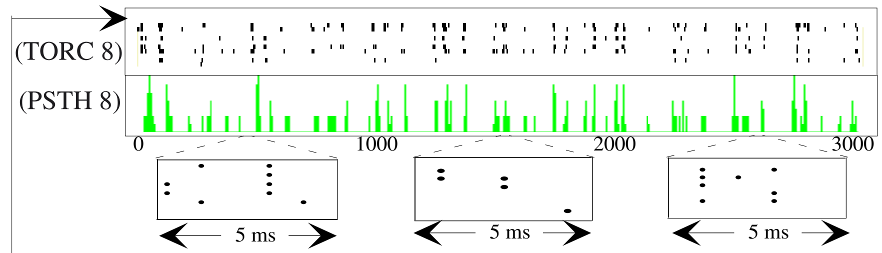
Fine Structure Responses

(Anesthetized Data)

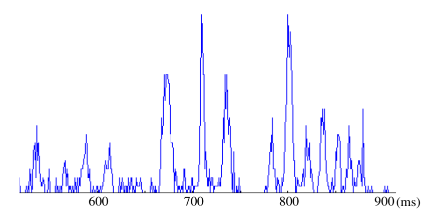


234/17a03(2)

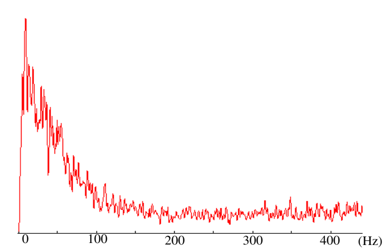
3691 spikes, 80 dB, 7 sweeps
(showing half the stimuli)



PSTH
(average of all stimuli)



Fourier Transform



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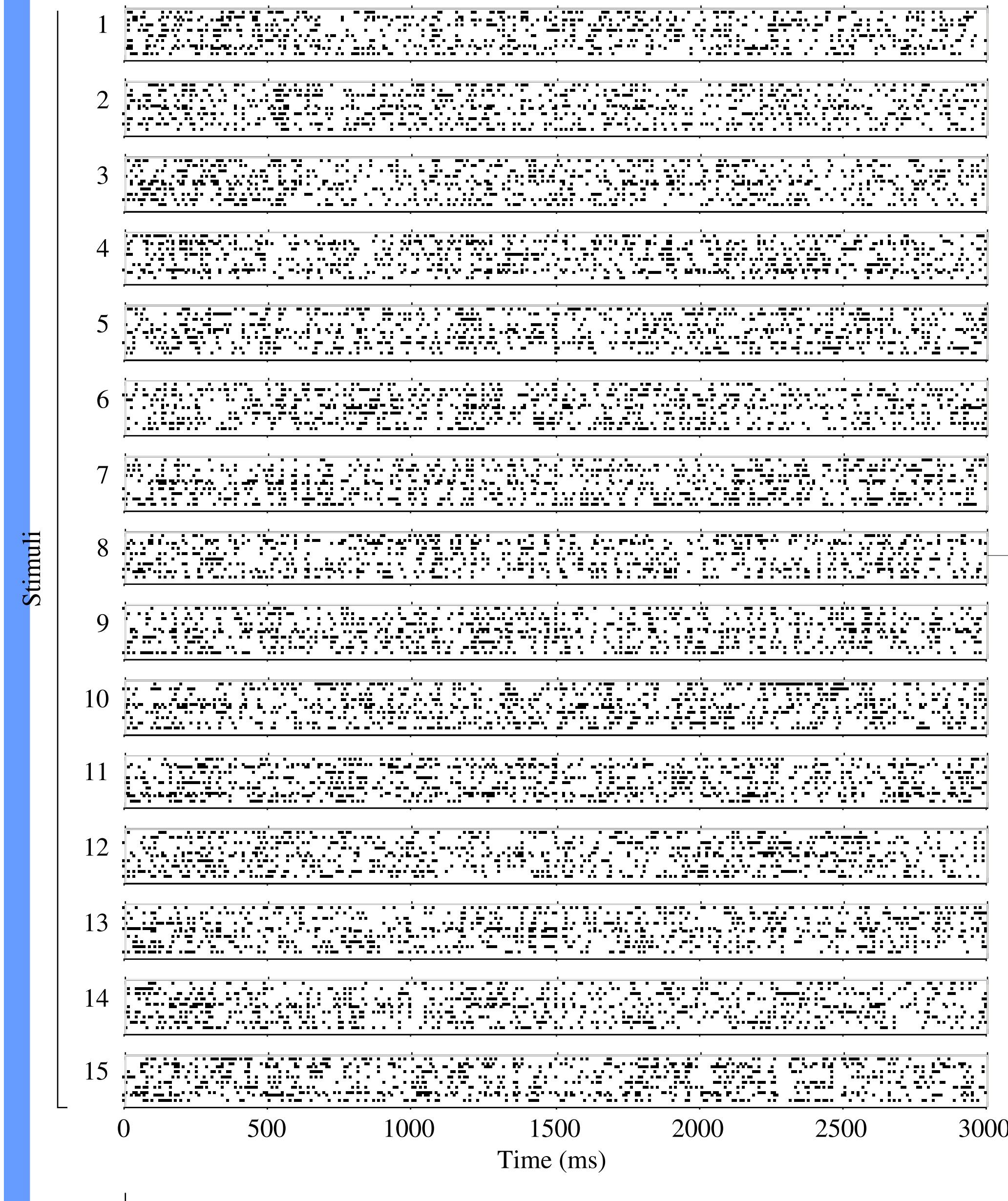
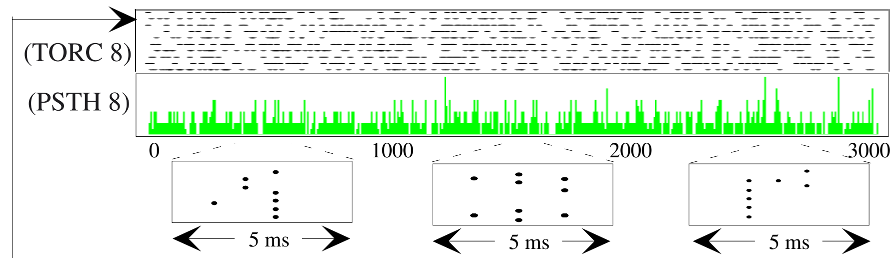
Fine Structure Responses

(Awake Data)

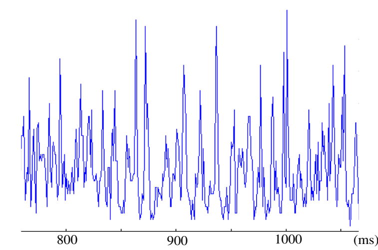


oneleft/09a04/05(2)

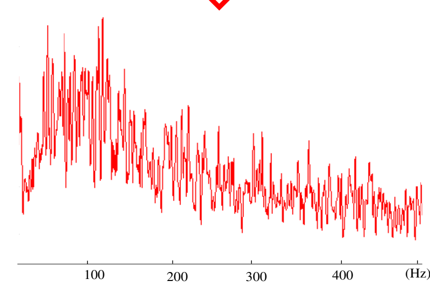
14619 spikes, 40 dB, 10 sweeps
(showing half the stimuli)



PSTH
(average of all stimuli)



Fourier Transform



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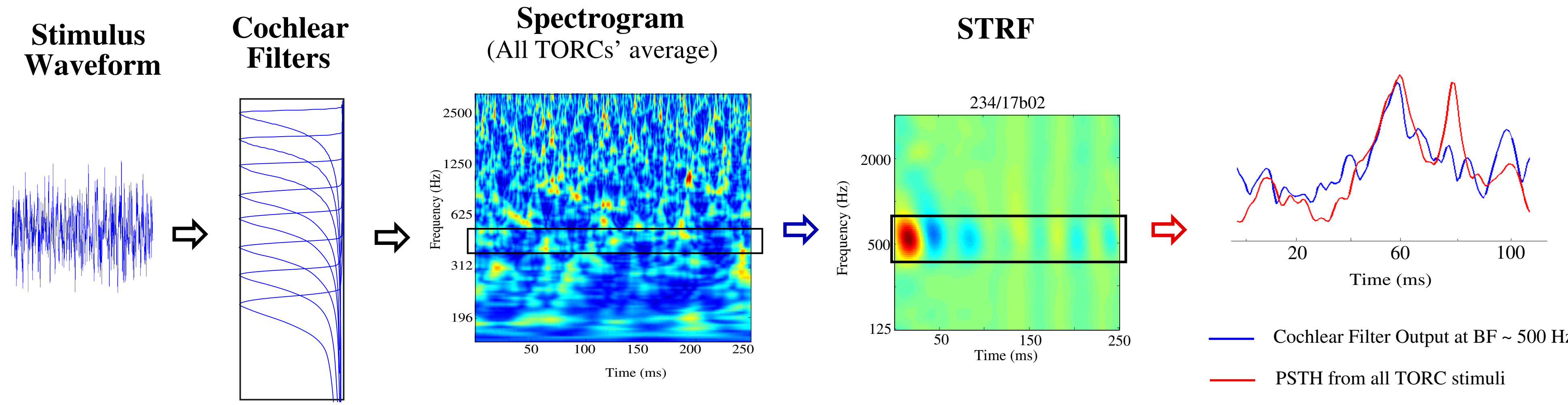
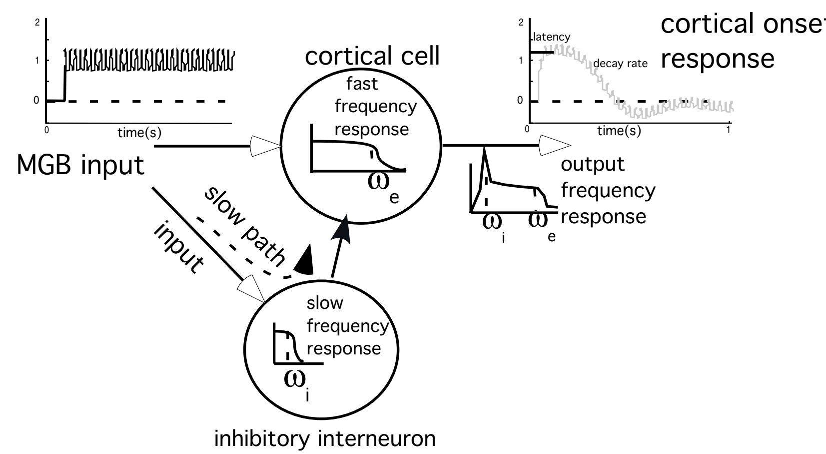
Explaining the Phenomenon



A schematic model of the excitatory and inhibitory dynamics in a cortical cell.



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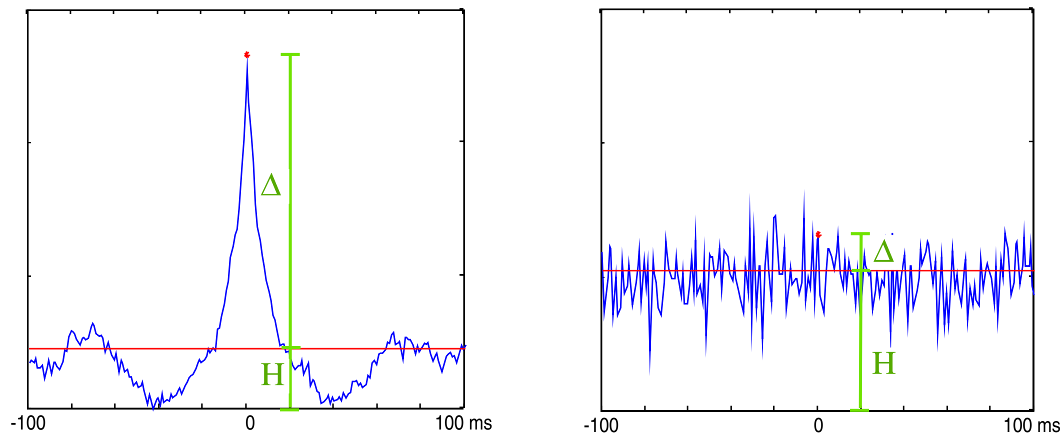
Quantifying the Fine Structure

Spike Time Correlations

Fine Structure indicator

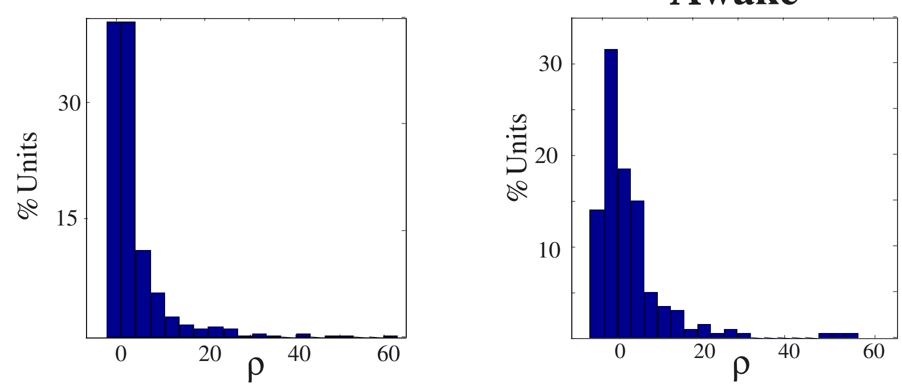
$$\rho \sim \Delta / H$$



Strong locking **Zero locking**

We compute the correlation between 2 PSTHs corresponding to 2 sets of randomly chosen stimuli combinations. These correlations (shown in the upper panel) can go from very strong correlation at 0-lag (left), to zero correlation (right). A ratio of the correlation peak at 0-lag (Δ) to the baseline (H), normalized by stimuli combination variability gives us an indicator (ρ) of the strength of the fine structure locking.

Anesthetized **Awake**



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Conclusions

The responses of neurons in the awake ferret show many fundamental similarities to the responses obtained from the Ketamine-anesthetized animal. These similarities include:

- The variety of basic STRF shapes observed
- The variability of STRF shapes measured at a given recording site
- The statistical laws governing the spiking behavior
- Quadrant separability of the ripple transfer function

However, the awake results show some average differences from the anesthetized results which include:

- An increased spike rate
- More complex (less separable) STRF shapes
- More complex spectral processing
- Increased selectivity to the direction of frequency modulation

In addition, about 1/4 of all cells (in both awake and anesthetized conditions) display a locking to the stimulus fine structure. These responses include higher frequencies than the 4-24 Hz range that we use to define the STRFs.

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Selected References

Spectro-Temporal Correlation Methods:

- Klein DJ, Depireux DA, Simon JZ and Shamma SA, Robust spectro-temporal reverse correlation for the auditory system: Optimizing stimulus design, J. Computational Neuroscience (2000).
- Eggermont JJ, Hearing Research 66 (1993) 177-201.

Singular Value Decomposition:

- Hansen PC, Rank-Deficient and Discrete Ill-Posed Problems, SIAM 1998.
- Press WH, Flannery BP, Teukolsky SA, and Vetterling, WT, Numerical Recipes, Cambridge University Press 1986.

Separability:

- Watson AB and Ahumada AJ, J. Opt. Soc. Am. A2(2) (1985) 322–341.
- Saul AB and Humphrey AL, J. Neurophysiol. 64 (1990) 206-224.
- Simon JZ, Depireux, DA, Klein DJ and Shamma SA, Temporal Symmetry and Quadrant Separability: Theory and Implications for Biological Network Connectivity (2001)

Related techniques and models:

- Kowalski N, Depireux D and Shamma S, J. Neurophysiol. 76 (5) (1996) 3503-3534
- Depireux DA, Simon JZ and Shamma SA, Comments in Theoretical Biology (1998).
- Wang K and Shamma SA, IEEE Trans. on Speech and Audio 2(3) (1994) 421-435, and 3(2) (1995) 382-395.
- Depireux DA, Simon JZ, Klein DJ and Shamma SA, Dynamics of Neural Responses in Ferret Primary Auditory Cortex:I. Spectrotemporal Response Characterization by Dynamic Ripple Stimuli, J Neurophysiol 85: 1220-1234, 2001.

Abstract

We recently developed an awake preparation for chronic physiological recording in the ferret (ARO Abstracts, Fritz et al, 2001) and described neural responses in auditory cortex in the awake animal to a variety of acoustic stimuli including tones, noise, ripples and their combinations. Previous neurophysiological studies of the ferret auditory cortex in our laboratory (Depireux et al, 2001) have used an anesthetized preparation which has yielded valuable insight into auditory function but may have caused depression of neural activity and inhibit cortico-cortical interactions. Hence we have continued to explore responses in auditory cortex of the awake animal in order to understand the full range of dynamic information flow, and have recorded from over 300 single units. We characterized and correlated the activity of single units from neighboring cells in a cortical column in response to these stimuli.

As we have shown in previous research, units in auditory cortex are well characterized by their responses to the envelope of moving ripples. An important property of a spectro-temporal receptive field (STRF) is its separability, i.e. whether it can be decomposed into the product of two 1-dimensional functions (temporal and spectral). We have characterized the STRFs from cortical neurons in the awake and the anesthetized preparation analyzing separability in the two populations and found an overall similarity of the STRFs in both conditions. However, we observed differences in the response pattern to pure tones in the awake vs anesthetized ferret (increased sustained on-responses and vigorous off-responses in the awake preparation) and so discuss the apparent disparity in the effects of anesthesia on cortical responses to pure tone and dynamic ripples.