What does precise spiking in AI tell us about the structure of its receptive fields?

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Abstract

Several recent investigations of cortical response characteristics have demonstrated that most cells fail to respond to rapidly changing stimuli (> 30 Hz) that evoke strong responses at all pre-cortical stages. Yet, these same cells are capable of producing precisely timed spikes (millisecond accuracy) at stimulus onsets and other instants throughout the stimulus. In this study, we tried to explore this paradox using specially designed ripple stimuli that effectively resemble broadband frozen noise with a spectro-temporally modulated envelope. The stimuli are constructed by adding hundreds of closely-spaced *carrier* tones with a slowly drifting spectro-temporal profile. Using such ripples (or combinations of ripples) it is possible to characterize the modulation transfer functions of auditory cortical cells, and to measure their Spectro-Temporal Response Fields (STRF). It is also possible however with this stimulus to observe the "*fine structure* of the responses due to the carrier tones or their interactions. We shall demonstrate in this report the existence of this "fine structure . Specifically, we demonstrate that AI responses are locked to within a millisecond accuracy, and that they likely reflect auditory-nerve responses to the interactions among the carrier tones of the ripples. The results also suggest that the slow dynamics of the STRFs are an emergent property of cortical circuits, especially its inhibitory inter-neurons.

Introduction

Mammalian auditory cortex neurons exhibit relatively slow temporal dynamics. They respond best to temporal modulations below 30 Hz (Langner 92, Schreiner and Calhoun 95, Shamma et al. 95, Depireux et al. 98). However, recent studies indicate that cortical units are also capable of fine temporal resolution (up to few hundred hertz).

These two cortical phenomena have generally been studied separately using stimuli that highlight one or the other. In this work, we explore the *coexistence* of these two properties in cortical responses, using special combinations of moving ripple stimuli.

The questions we address in this study are:

* How is the system capable of fine temporal resolution up to 1 ms, while it completely fails to follow modulations higher than 30 Hz?
* Under what circumstances do cortical units exhibit fine temporal precision?
* How do fast response properties relate to the cell's slow dynamics?
* What structures or mechanisms in the auditory cortex or sub-cortical nuclei give rise to these phenomena?

Methods

Experimental Procedure

❑ Neurophysiological data were collected from cortical recordings in 8 domestic ferrets.

❑ 3 ferrets were ketamine-anesthetized. Acute recording sessions lasted 3-4 days.

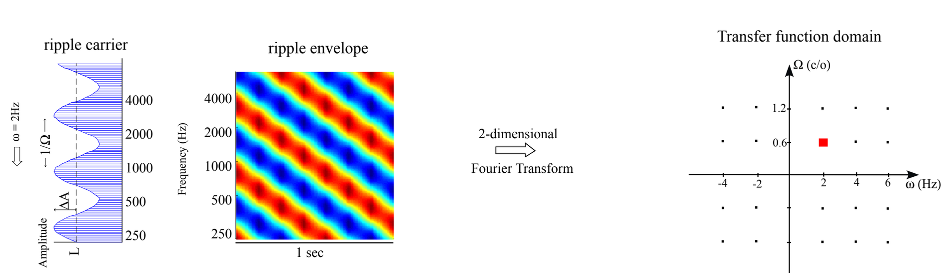
❑ 5 ferrets were awake. 2 of the them attended to a task during the recordings (ARO Poster 2003, #220), while the remaining animals were awake, but non-behaving. Awake recordings lasted 3-6 hours a day. During each session, the animal's head was restrained by a surgically implanted metal post, and the head was held in a stable position throughout the recording.

❑ Neurophysiological experiments consisted of extracellular recordings of single and multi-unit responses in the ferret's auditory cortex. Using 5 MΩ tungsten electrodes, raw or filtered responses at different cortical depths were collected. The responses were sampled at 20 KHz, and saved for further off-line sorting and analysis.

❑ The sound stimuli were delivered through small microphones (Etymotic Research) inserted in the animal's ear canal, and calibrated in situ at the beginning of each recording session. Stimuli were presented many times in a randomized order.

Stimuli

*** Single Ripples**



✓ **Ripple carrier:** broadband complex of equally-spaced tones on a logarithmic frequency axis, over 5 octaves (100 tones/octave).

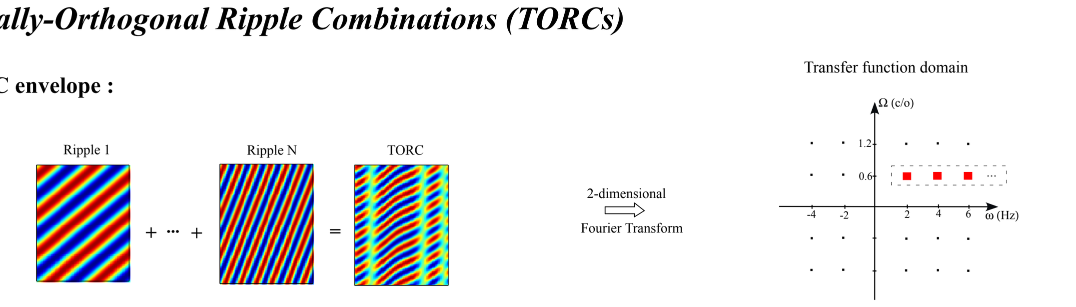
✓ **Ripple envelope :** $S(x,t) = L(1+\Delta A \sin(2\pi(\omega t + \Omega x) + \varphi))$

ω: ripple velocity (Hz)
Ω: ripple density (cycles/octave)
φ: ripple phase (rad)

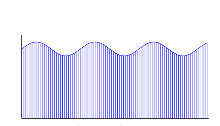
⇨ Ripples form an orthogonal basis set in the Fourier Domain for describing dynamic spectra

*** Temporally-Orthogonal Ripple Combinations (TORCs)**

✓ **TORC envelope :**



✓ **TORC carrier:** The same broadband carrier (as single ripple) is used for TORCs. It consists of logarithmically-spaced tones at exactly the *same* tone frequencies and phases for all TORC stimuli.

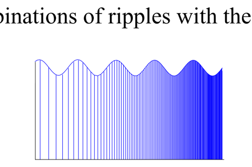


⇨ In this study, we use a set of 30 TORCs (3 seconds long), with varying modulations densities {0,±0.2,±0.4, ...,±1.4}(c/o). The ripple velocities for all TORCs are {4,8,..,24}(Hz).

*** Harmonic TORCs**

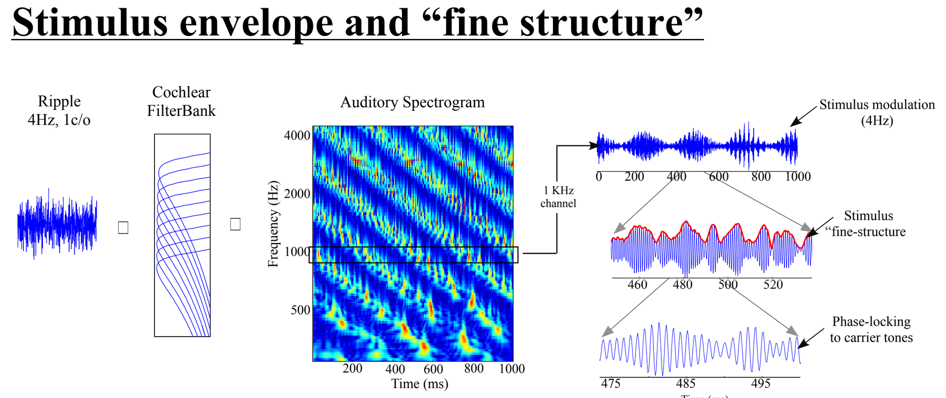
✓ **Harmonic-TORC envelope :** Same spectro-temporal envelopes as regular TORCs (i.e., combinations of ripples with the same set of ripple velocities and varying ripple densities)

✓ **Harmonic-TORC carrier:** Tones harmonically spaced (with random phases) over 5 octaves. The base frequencies tested for the harmonic sequences are = {25, 48, 50, 75, 100, 200} (Hz)



⇨ Harmonic-TORCs have a clear pitched sound quality.

Stimulus envelope and "fine structure"



The red envelope in the middle right-most panel corresponds to the stimulus "fine-structure at the 1 KHz channel. It is due to the interaction between the carrier tones.

⇨ The fine structure varies from one channel to the other depending on the channel's bandwidth, and the interaction of the tones present within that bandwidth.

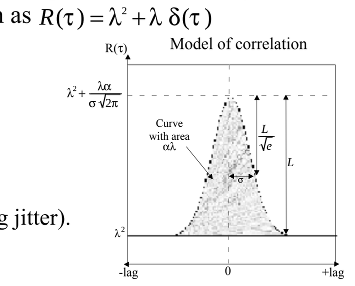
Data Analysis

Analyzing the locking to fine structure

The precision of the cells' responses can be measured from the cross-correlation of spike trains of different stimuli presentations. Using the basic theory of stochastic processes, we formulate a mathematical model in order to quantify the precision of locking in the cells' responses. We know that the correlation function of poisson impulses with rate λ can be written as $R(\tau) = \lambda^2 + \lambda\,\delta(\tau)$

We introduce a new term to account for timing jitter (σ), as well as spike deletion (α). Our model for poisson spike correlations becomes:

$$\boxed{R(\tau) = \lambda^2 + \frac{\alpha\lambda}{\sigma\sqrt{2\pi}} e^{-\tau^2/\sigma^2}}$$

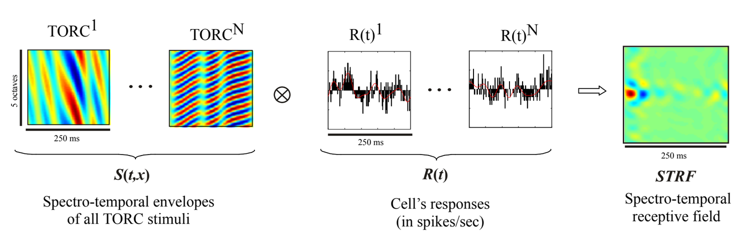


* The timing jitter is modeled by a zero-mean Gaussian function with variance σ. (for σ ≈ 0, little or no timing jitter).
* The spike deletion is modeled by a scaling of the Gaussian function. (for α ≈ 1, no spike deletion)

⇨ Based on the above correlation model, we fit our experimental correlation functions in order to derive the parameters α and σ.

Receptive fields

Standard reverse-correlation techniques are used to compute spectro-temporal receptive fields (STRFs).

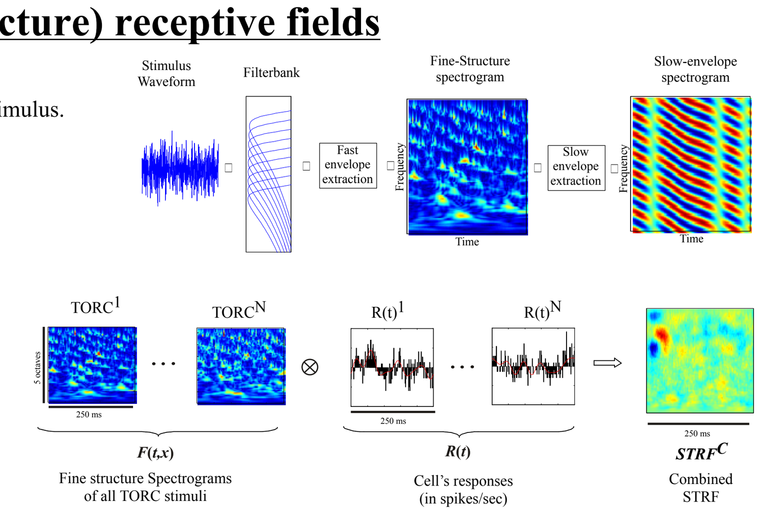


⇨ The STRFs reflect the cell's response to the stimulus envelope *only*. The dynamic range of the STRF is limited by the dynamic range of the stimuli envelopes (up to 24Hz).

Combined (envelope and fine structure) receptive fields

We first generate fine structure spectrograms for each TORC stimulus.

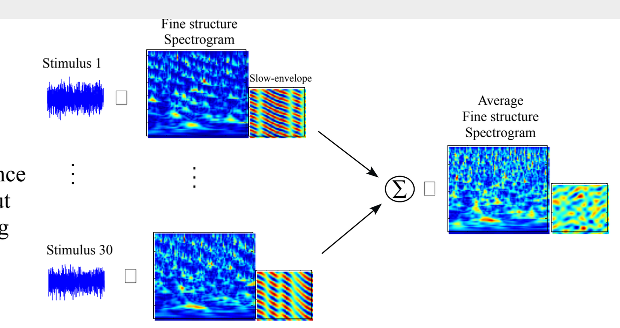
Using reverse correlation on all fine structure spectrograms, we compute the ***Combined STRFs*** ($STRF^C$)



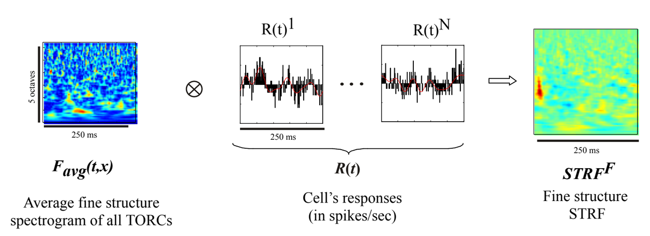
⇨ $STRF^C$s are derived from the stimuli cochlear outputs. They take into account the responses to *both* the envelope and the fine structure of the stimulus.

Fine structure receptive fields

In order to investigate the role of the fine structure *alone,* we first extract the fine structure from the TORC stimuli by eliminating the slow envelopes. Since all 30 TORCs share the *same* carrier tones (same frequencies and phases), but varying envelopes, we extract the stimuli fine structure by using an averaging technique.



Using the same average fine structure spectrogram for all 30 TORCs, reverse correlation is used to compute the ***fine structure STRF*** ($STRF^F$)



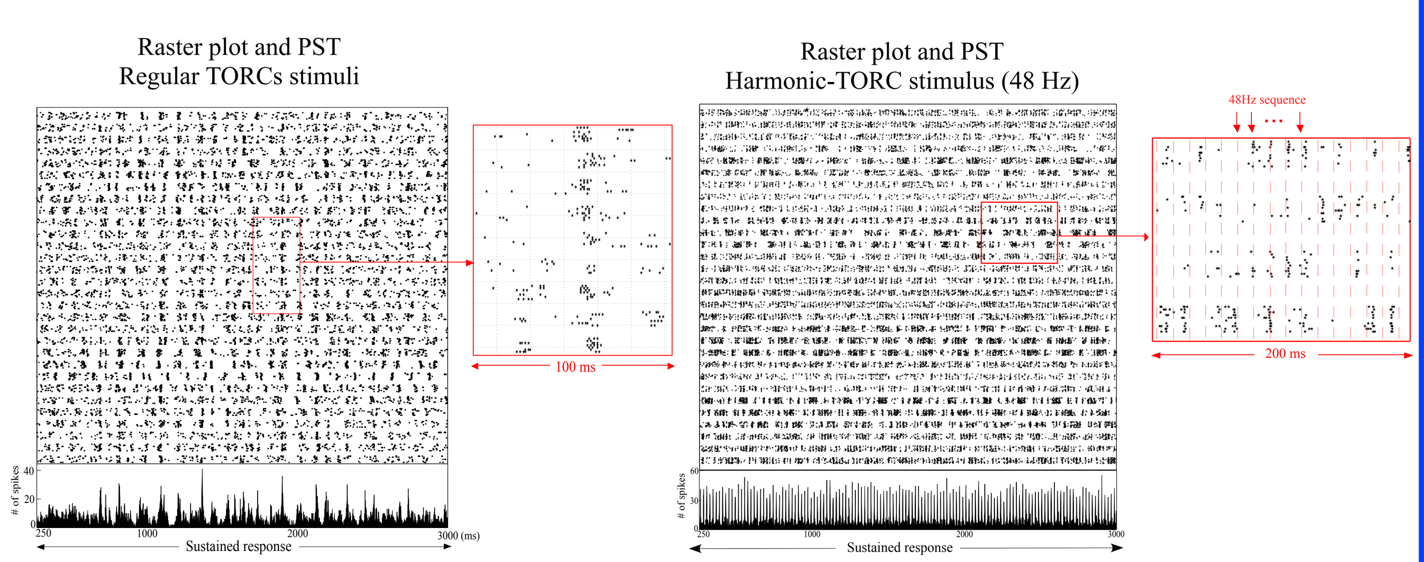
⇨ The fine structure component of the cell's response is captured by the $STRF^F$.

Note: Similar techniques for computing STRF, $STRF^C$, $STRF^F$ can be used in the case of Harmonic TORC recordings. Examples are given in the results section.

Results

We recorded from a total of 680 units. 341 were from anesthetized ferrets, while 339 from awake animals.

Examples of locked responses



⇨ Responses to regular TORCs are correlated with the envelope of each stimulus. However, it is clear that the timing of spike occurrence is highly correlated with the fine structure, which is common to all stimuli.

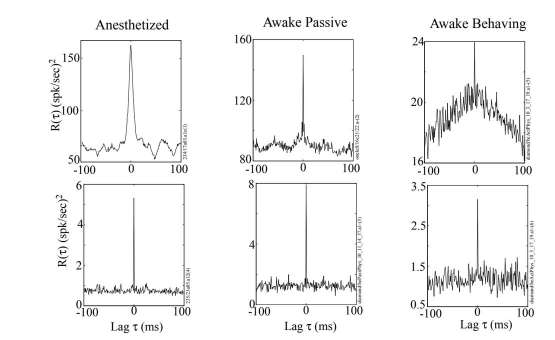
⇨ Responses to Harmonic TORCs show a clear locking to the 48 Hz base frequency of the carrier tones of the stimulus. The locking is in-phase even across stimuli.

⇨ Sustained responses (lasting more than 2.5 seconds) appear to be precisely locked to the stimulus fine structure.

Results (Cont'd)

Correlation of neuron responses

We compute the average spike correlations across stimuli, and within stimulus presentations. The response correlations are computed for all recording conditions (anesthetized, awake, and awake behaving)



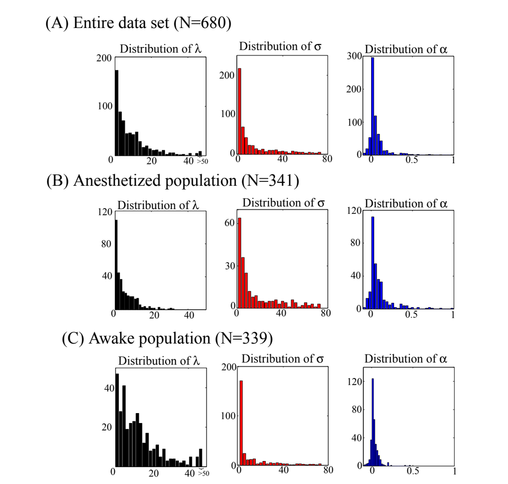
⇨ Examples of response correlations show a ***narrow*** peak at 0-lag (of the order of few milliseconds)

Population statistics

* The distribution of timing jitter (σ) indicates that 50% the overall population exhibits high locking to the stimulus fine structure (σ<10ms). The statistics indicate that this property may be independent of the recording condition (40% in anesthetized animals, 60% in awake).

* About 10% of our population does not fit our correlation mathematical model (not included in the population statistics plots).

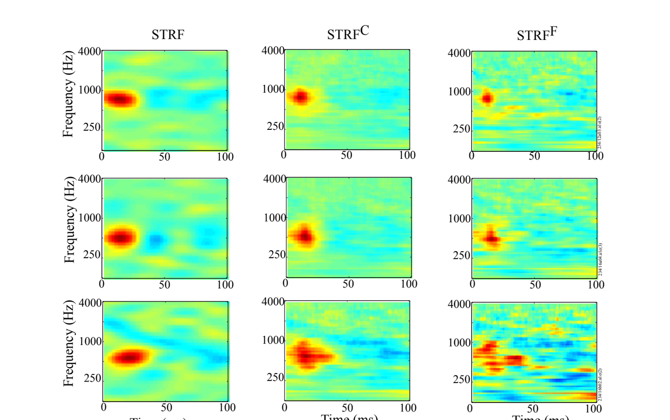
* The skewness towards 0 of the distribution of spike deletion (α) suggests that spike deletion is a common property among most units.



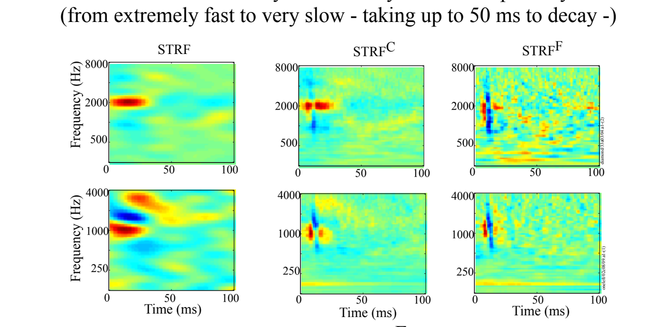
⇨ Overall, 50% of the recorded cells show a very precise locking to the fine structure (σ < 10 ms).

Examples of STRFs

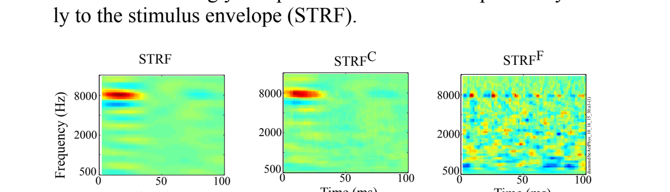
⇨ STRFs, $STRF^F$s, $STRF^C$s display a wide variety of shapes and response characteristics



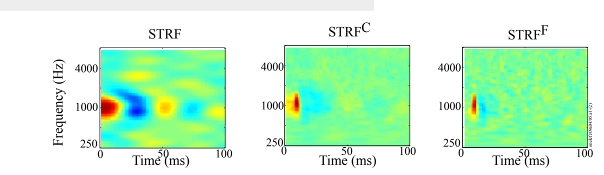
⇨ Many units with apparently similar STRFs display very different $STRF^F$s. These later vary considerably in their temporal dynamics (from extremely fast to very slow - taking up to 50 ms to decay -)



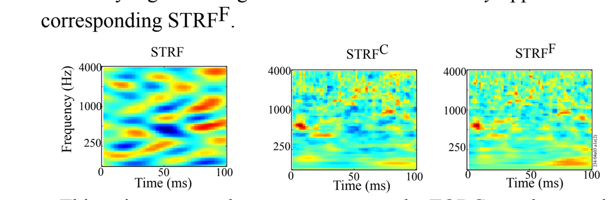
⇨ Units with seemingly comparable $STRF^F$s can respond very differently to the stimulus envelope (STRF).



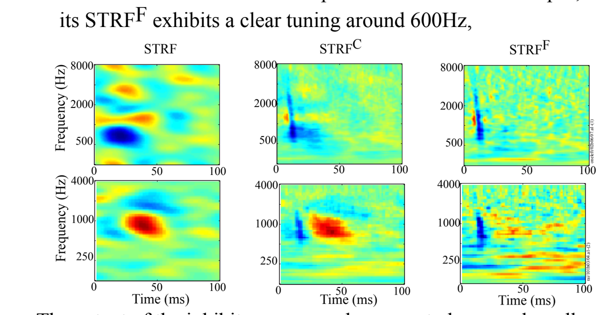
⇨ Due to strong interaction between carrier tones for high BF cells, some units show multiple peaks in their $STRF^F$s.



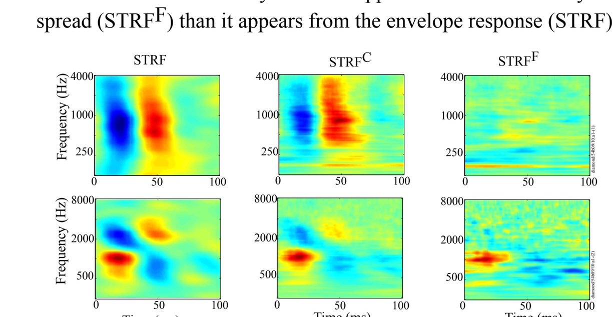
⇨ Inhibitory regions in regular STRFs don't *necessarily* appear in the corresponding $STRF^F$.



⇨ This unit seems to show no response to the TORC envelopes, while its $STRF^F$ exhibits a clear tuning around 600Hz,



⇨ The extent of the inhibitory surround appears to be more broadly spread ($STRF^F$) than it appears from the envelope response (STRF)

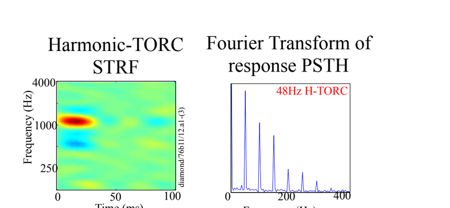


⇨ Some STRF pairs (recorded from adjacent cells) exhibit interesting variability in their STRFs as well as their $STRF^F$s. (The fact that the first unit is broadly tuned could explain the absence of a $STRF^F$ for this unit).

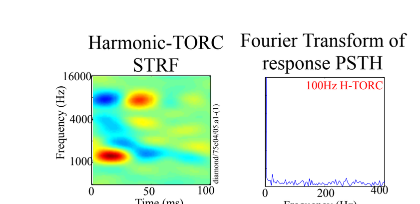
Harmonic vs. regular TORCs

Cells vary in their responses to harmonic vs. regular TORCs. While some units show a clear locking to the harmonic carriers of TORCs, other are not locked at all

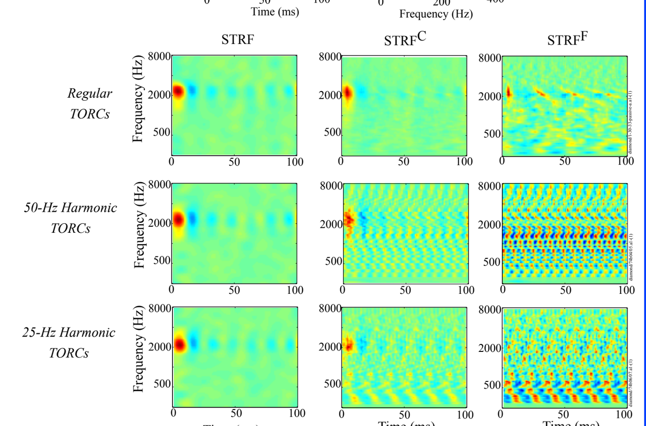
Response locked to harmonic carrier



No locking to the stimulus carrier



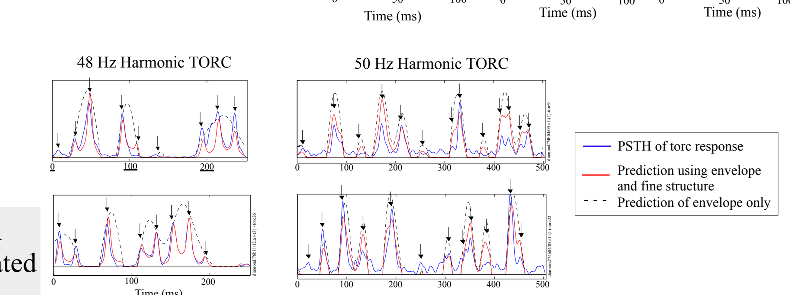
For the units which appear to show locking to the harmonic carrier tones (about 50% of our tested units), the cell's STRF is exactly the same whether obtained with regular or harmonic TORCs. On the other hand, the $STRF^F$ and $STRF^C$ of the units exhibit different properties for the regular vs. harmonic TORCs.



⇨ The striped nature of the $STRF^F$ indicates the locking of the cell to the carrier tones of the harmonic TORCs.

Response predictions

The little arrows in the graphs show the peaks of harmonic sinusoid with period corresponding to the stimulus carrier.



⇨ Prediction of cell's responses show that cortical neurons respond to the fine-structure as modulated by the stimulus envelope.

Discussion

Summary of previous and current results

❑ Temporal dynamics in sub-cortical stages have been shown to exhibit time constants lower than those observed in the cortex. The locking to cochlear envelopes of stimuli is well-preserved in responses in the inferior colliculus (Escabi and Schreiner 2002) as well as the auditory thalamus (Miller et al. 2002).

❑ Research has shown that AI cells can respond very precisely with jitter as low as 1 millisecond to transient sounds and stimuli onsets (Heil 1997).

❑ It has been generally accepted that cortical neurons exhibit slow dynamics, which are reflected in their Spectro-Temporal Receptive Fields (STRFs). These dynamics have commonly been attributed to synaptic depression (Carandini et al. 2001), NMDA receptors (Krukowski and Miller 2001), and other physiological mechanisms.

However,

❑ We show that AI neurons, when driven by appropriately designed stimuli, are capable of exhibiting: **(a)** fine temporal resolution, **(b)** which persists over extended periods of time (more than 2.5 seconds). These precise cortical responses are a manifestation of the stimulus envelopes at the level of the cochlea.

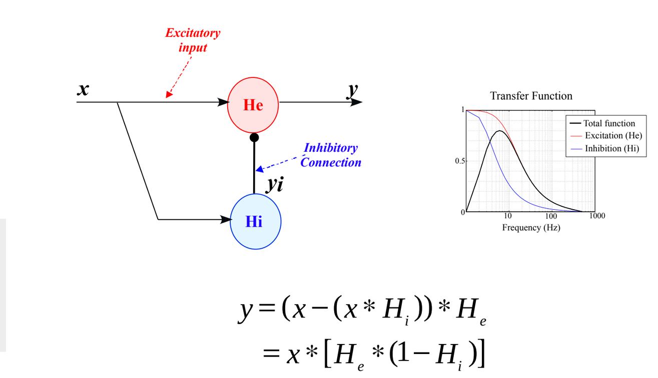
We present a simple model which addresses mechanisms that could explain this timing paradox. The model suggests that cortical responses are indeed responses to fast temporal envelopes, modulated by slow envelopes.

A model of cortical interactions

* The model consists of interactions of a fast excitatory function with a slower inhibitory function.

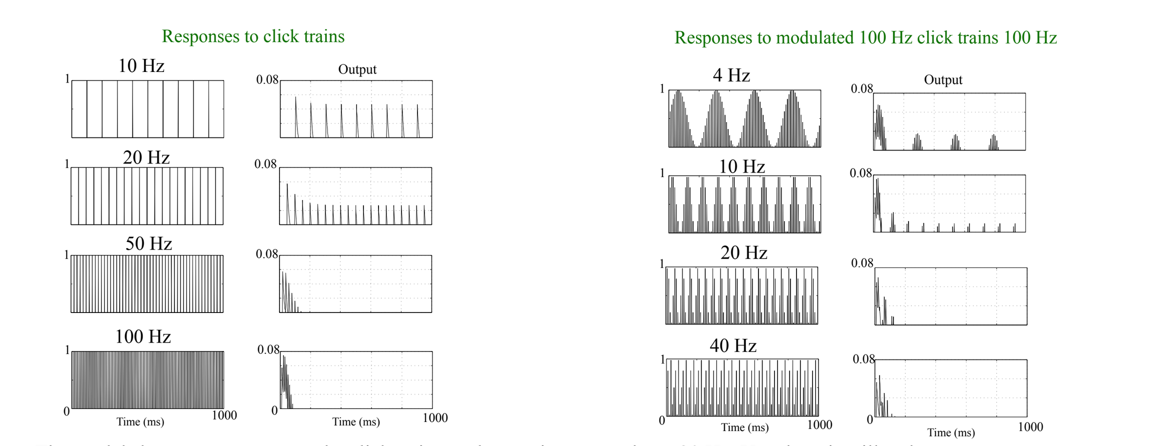
* The weights of the synaptic connections, as well as the cutoffs of the different functions, can be changed to model various aspects of cortical responses.

⇨ The overall response shows a tuning around 5-15 Hz. The model transfer function exhibits its cutoffs at very low and at very high modulation rates.



$$y = (x - (x * H_i)) * H_e$$
$$= x * [H_e * (1 - H_i)]$$

Simulations of model responses



⇨ The model shows no response to the click trains as the rate increases above 20 Hz. Yet, there is still a clear response to the input onset. On the other hand, fast click trains (100 Hz) can elicit a response if they are modulated at rates that are within the dynamic range of the overall system's transfer function.

Summary

❑ Temporal responses in the auditory cortex are not limited to slow dynamics. Our data show that cortical neurons are capable of precisely locking to the stimulus fast envelopes (which we refer to as "fine-structure).

❑ Fine temporal discharge patterns in cortical neurons are not limited to sound onsets and transients. Precise spiking is also observed in steady-state cortical responses.

❑ In this study, we presented a technique for analyzing the cells' responses to stimulus "fine-structure . With this technique, we show that these fast responses reflect the interactions of the stimulus carrier tones at the level of the auditory nerve.

❑ The response properties of AI units to fast envelopes are captured by the $STRF^F$. These responses reflect the activity at the thalamic inputs to the cortical units. On the other hand, the slow dynamics of AI responses are captured by the STRF. The STRF is a reflection of the temporal integration taking place at the level of the auditory cortex.

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