Using Tones in Wideband Noise to Investigate Effects of Neural Fluctuations and Local Off-CF Inhibition in the Inferior Colliculus: Models and Physiology

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Summary

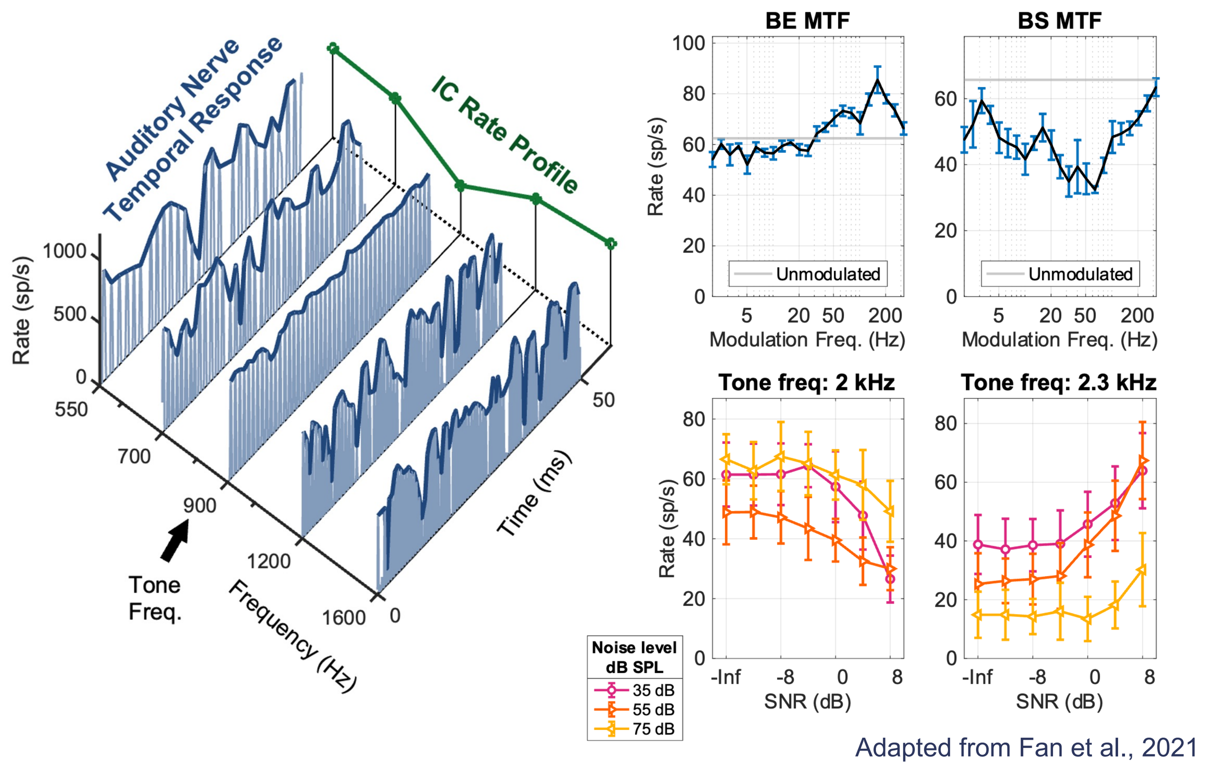
1. We tested the hypothesis that off-CF inhibition, in combination with fluctuation sensitivity, could account for responses in the inferior colliculus (IC) to narrowband and wideband tone-in-noise (WBTIN) stimuli.
2. Extracellular single-units were recorded in awake rabbit IC to WBTIN. Tones were varied with respect to CF. Noise spectrum level and SNR were varied.
3. Previous results showed that IC cells had responses to narrowband TIN that varied depending on modulation-transfer-function (MTF) type.
4. In response to WBTIN most IC neurons, regardless of MTF type, were excited by tones near CF and inhibited by tones over frequency regions flanking CF.
5. WBTIN response profiles across tone frequencies were fit with a Difference of Gaussians (DOG) function.
6. Expanding a computational IC model to include off-CF inhibition more accurately matched physiological results. Other models are being explored.

Introduction

Many mechanisms in the auditory periphery and midbrain impact the representation of complex sounds in the IC. Here we focus on two mechanisms:

Mechanism 1: Neural Fluctuations

- Neural fluctuations are low-frequency variations in auditory-nerve (AN) responses that are shaped by peripheral nonlinearities, such as inner-hair-cell transduction and cochlear compression.
- Most IC cells are excited (band-enhanced, BE), suppressed (band-suppressed, BS), or both (Hybrid, H), by fluctuations (Kim et al., 2020).
- For tone-in-noise (TIN) stimuli, fluctuation amplitudes are reduced for AN fibers tuned near the tone frequency (below, left).
- A narrowband Gaussian TIN study found that BE IC rates decreased and BS IC rates increased when tone levels increased (Fan et al., 2021, below right).
- These results are consistent with neural fluctuation sensitivity and could be explained by IC models featuring same-frequency inhibition and excitation (SFIE) (Carney & McDonough, 2019).



Adapted from Fan et al., 2021

Mechanism 2: Off-CF Inhibition

- In this study, a different pattern of responses was observed for wideband TIN. These results suggest a role for off-CF inhibition, previously proposed to explain response properties such as sensitivity to frequency modulation.

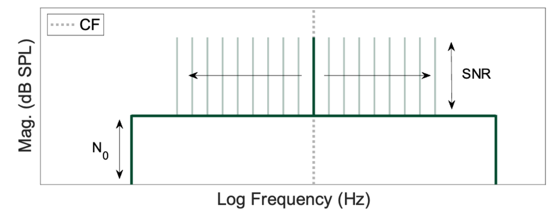
Methods

Physiology

- Single-unit extracellular recordings made in awake rabbit IC using four tetrodes.
- Characteristic frequency (CF) was determined with a response map.
- Modulation transfer functions (MTFs) were categorized as BE, BS, or Hybrid based on increased or decreased rates with respect to unmodulated stimuli (Kim et al., 2020)

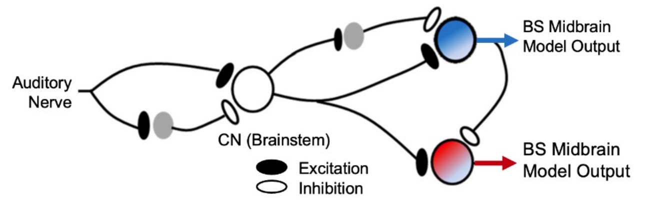
Wideband Tone-in-Noise (WBTIN) Stimuli

- 4-octave wideband Gaussian noise centered on CF of the target neuron
- Tone varied in frequency across 3 octaves centered on CF of the target neuron
- Spectrum level (N_0) = 3, 23, 43 dB SPL
- Signal-to-noise ratio (SNR) = 20, 30, 40 dB SPL w.r.t. N_0, at and above detection threshold for rabbit (Zheng et al., 2002)
- Stimuli were diotic or contralateral

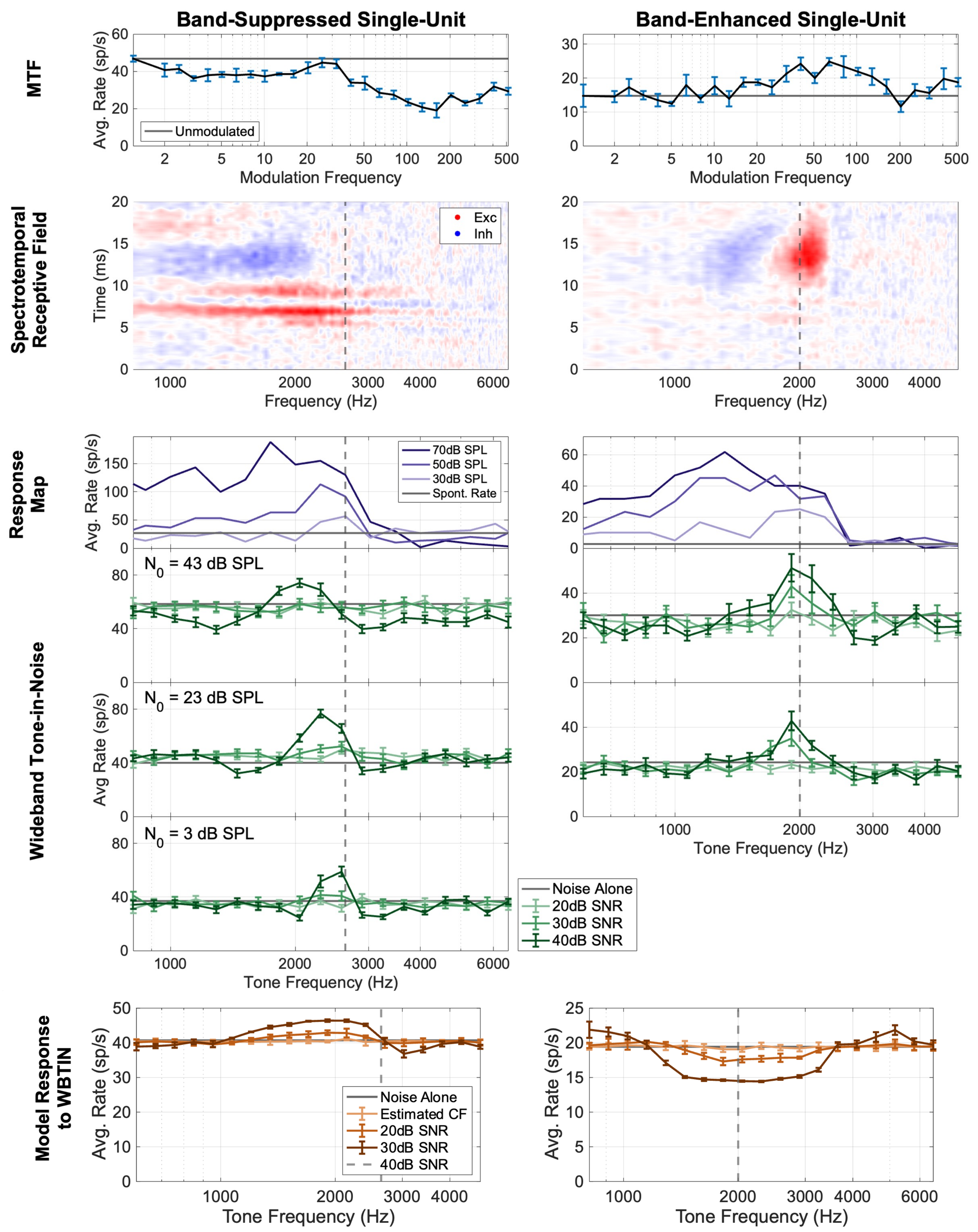


Models

- Auditory-nerve model: Zilany et al., 2014.
- IC same-frequency inhibition-excitation (SFIE) model: Carney & McDonough, 2019.
- Off-CF inputs were added to the IC model to test the hypothesis that off-CF inhibition could account for wideband TIN responses.



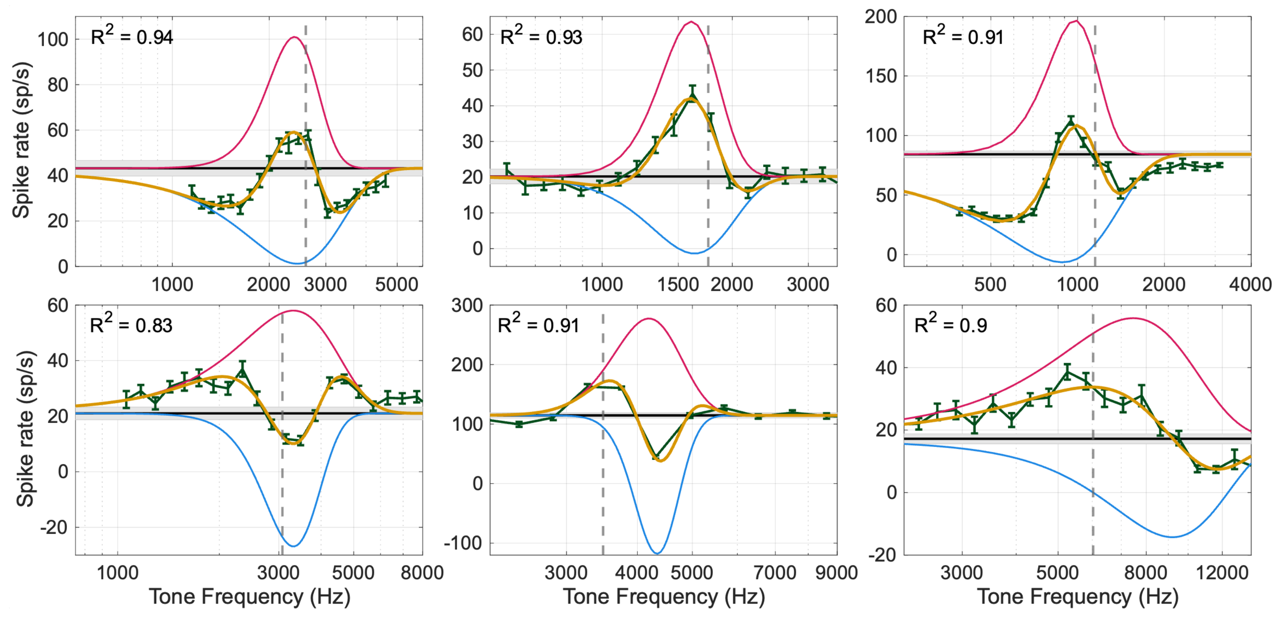
1. BE and BS IC responses to WBTIN have excitatory regions with inhibitory sidebands



Example responses for two IC neurons: BS (left) and BE (right). MTFs, spectro-temporal receptive fields based on wideband noise responses, response maps for pure tones, and responses to WBTIN. Bottom: Predictions of SFIE IC models do not match IC profiles.

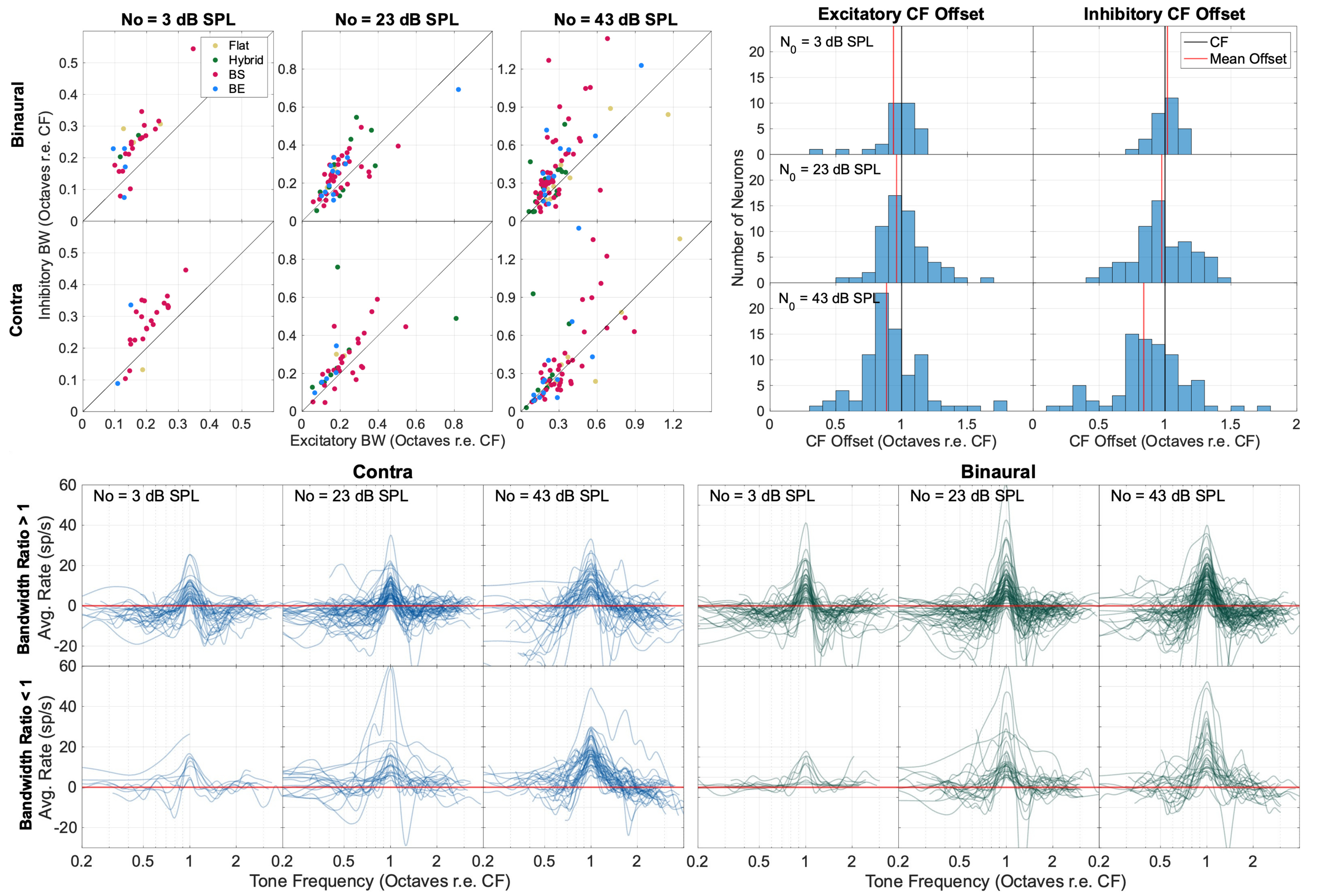
2. Responses to the 40-dB SNR WBTIN were quantified by fitting a difference of Gaussians (DoG) function

$$W_{DoG}(f) = e^{\frac{-(f+f_e-f_c)^2}{2\sigma_e^2}} - g * e^{\frac{-(f+f_i-f_c)^2}{2\sigma_i^2}} \qquad g = \frac{g_i}{g_e}$$



Examples of six IC responses to suprathreshold (40-dB SNR) WBTIN were characterized by fitting a DoG curve. DoG equation was modified from Su & Delgutte 2020 to include a parameter for frequency offset, because peak responses often do not match CF. The fit was evaluated using the coefficient of determination (R^2). DoG fits are described by the excitatory and inhibitory bandwidths (σ, Hz), the center-frequency offset, and a strength term.

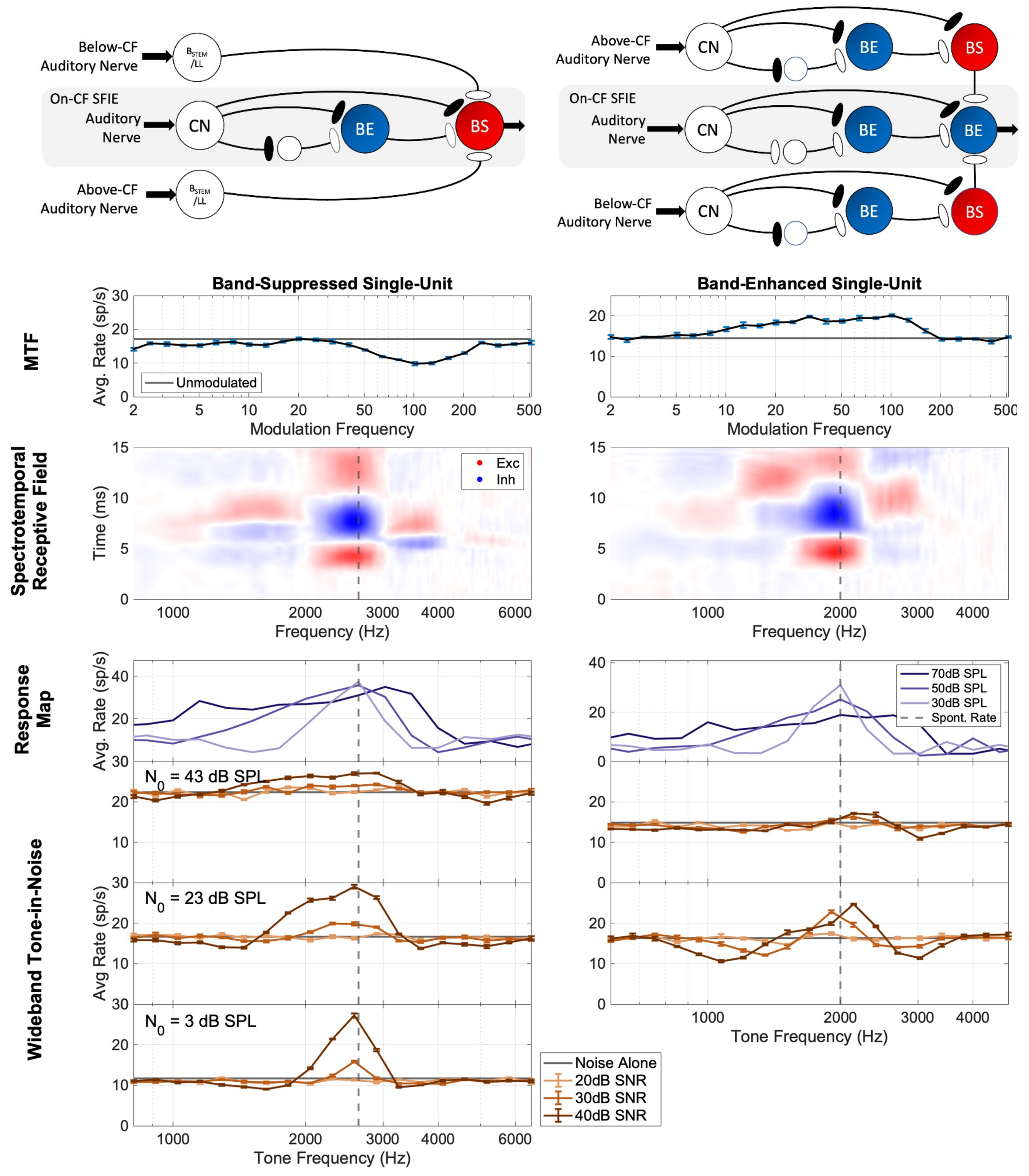
3. DoG fits for population of IC neurons allow quantification of inhibitory and excitatory aspects of the WBTIN response



MTF	Binaural (n=119)	Contra (n=59)
BE	20	15
BS	66	18
H	20	9
Flat	13	14

DoG curves were fit to 40-dB SNR WBTIN datasets for a population of neurons (n = 119). Top left: Scatter plots of inhibitory vs. excitatory bandwidth (σ_i, σ_e) values in octaves w.r.t. CF. Top right: Binaural DoG excitatory and inhibitory peak offsets, in octaves with respect to CF. Binaural and contralateral (not shown) responses had same trends. Bottom: WBTIN single-unit responses smoothed and overlayed, centered on peak. Contralateral (blue, left) and Binaural (green, right) responses. Responses are plotted separately for different N_0 values and based on the ratio of the inhibitory and excitatory bandwidths, $\sigma_{ratio} = \sigma_i/\sigma_e$.

4. Adding off-CF inhibitory inputs to the IC model improves predictions



Examples of a model BE and BS unit, each with off-CF inhibitory inputs. In both models, off-CF inputs are added to the original SFIE configuration.

BS Model (left): BS circuit diagram. To create a BS cell with off-CF inhibition, the on-CF BS cell is inhibited by a brainstem neuron with off-CF inputs. This configuration results in a model with a BS MTF and weak inhibition flanking excitation.

BE Model (right): BE circuit diagram. The output BE cell is created by taking an on-CF BS cell and adding two off-CF inhibitions from neighboring BS cells. This model has responses appropriate for a BE cell, including responses to narrowband TIN (not shown). The WBTIN responses feature excitation near CF and inhibitory regions (compared to noise alone) off-CF, similar to the single-unit responses shown in Results 1.

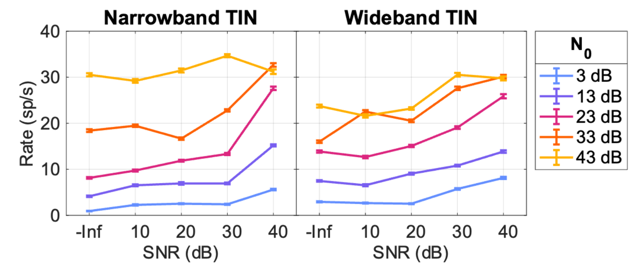
Conclusions

- Responses to WBTIN as a function of tone frequency differ from previous on-CF responses to narrowband TIN. Where narrowband TIN responses were dependent on MTF type, response profiles for WBTIN were similar, regardless of MTF type.
- Responses to WBTIN as a function of tone frequency revealed inhibitory sidebands (compared to the noise-alone response) not seen in the response map or noise STRF.
- Inhibitory and excitatory components of the response to WBTIN can be quantified with a DoG fit.
- The DoG fit allowed investigation of inhibitory and excitatory aspects of WBTIN responses. No differences between MTF types were seen.
- An SFIE model with added local off-CF inhibitory inputs better predicted BE cell responses than the SFIE model alone. Similarly, adding off-CF inhibitory inputs from the brainstem to a BS model cell better predicted WBTIN responses of BS neurons.

Future Directions

Physiology

- We are recording responses to a shifting narrowband TIN stimulus to compare how the responses to narrowband and wideband noise differ in the same neuron. Below is a BS neuron response to on-CF narrowband and wideband TIN.



Modeling

- We will explore the impact of efferent gain control on responses to WBTIN using a model that includes efferent feedback (Farhadi et al., 2022).

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Supported by: NIH R01-DC010813, NIH F31-DC020630