

# Network-Level Control of Frequency Tuning in Auditory Cortex

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Lateral inhibition is a fundamental circuit operation that sharpens the tuning properties of cortical neurons. This operation is classically attributed to an increase in GABAergic synaptic input triggered by non-preferred stimuli. Here we use *in vivo* whole-cell recording and two-photon  $\text{Ca}^{2+}$  imaging in awake mice to show that lateral inhibition shapes frequency tuning in primary auditory cortex via an unconventional mechanism: non-preferred tones suppress both excitatory and inhibitory synaptic inputs onto layer 2/3 cells ("network suppression"). Moreover, optogenetic inactivation of inhibitory interneurons elicits a paradoxical increase in inhibitory synaptic input. These results indicate that GABAergic interneurons regulate cortical activity indirectly via the suppression of recurrent excitation (inhibition-stabilized network model), rather than via the direct inhibition. Together with our previous finding that inhibitory SOM cells are regulated by the behavioral relevance attached to sounds, these results demonstrate a dynamic nature of sensory tuning that is enabled by cortical inhibitory circuits.