

A modeling study of cortical waves in primary auditory cortex

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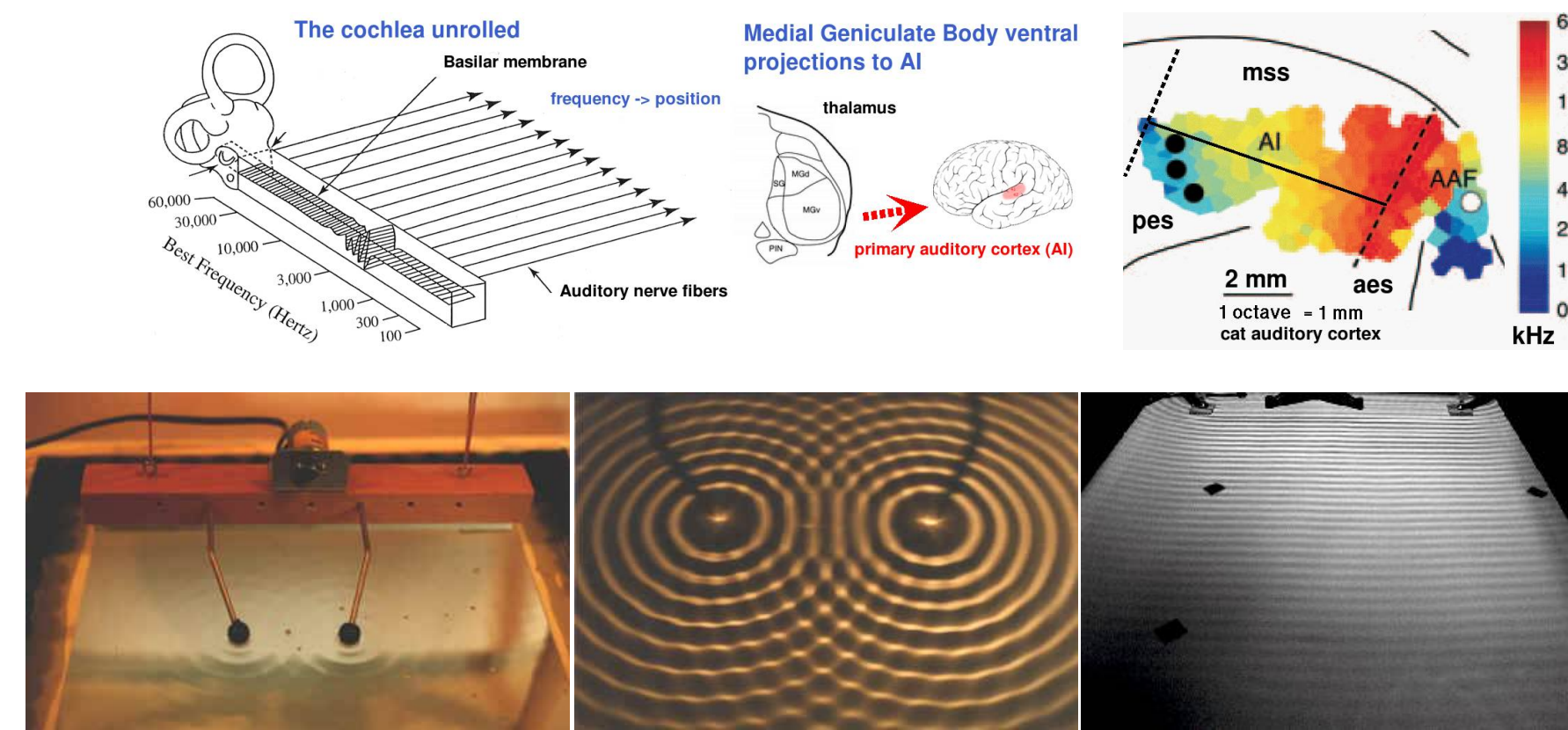
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Purpose of the model

Cortical waves have been observed in many cortical areas, including the primary auditory cortex (AI). The thalamorecipient layer (IV) is an ideal test-bed for the study of cortical waves because the inputs from thalamus are arranged tonotopically along an axis, reflecting the logarithmic mapping of frequency to position generated in the cochlea. Wave propagation along this axis is essentially one-dimensional. Thus, a biologically realistic model of a piece of this region can act like a 'ripple-tank' used for the study of one-dimensional wave motion and interference in physics.



Can this spatial distribution of thalamic inputs to a model of AI layer IV produce: Cortical waves? Wave interference from two-tone stimuli? Consequences for perception ?

The ACnet2 simulations were implemented with the GENESIS simulator [1,2]. They were also designed as tutorial examples on the construction of cortical networks with well-documented simulation scripts designed for extension to more detailed models. The simulation scripts for GENESIS 2.3 are available for download and are (slowly) being converted to GENESIS 3 (G-3). They, and the G-3 visualization tools used in the analysis of these results [3], will become the basis for Python-based examples and tutorials on network construction with G-3.

Biologically detailed and realistic models: Can hope to explain mechanisms causing the system's behavior. **BUT** a very large space of poorly-defined or poorly-quantified parameters to be explored. Analysis of results is difficult.

vs. Simple models: Few parameters to vary and easier analysis of results. **BUT** important details that affect behavior may be left out. Parameters fit to account for responses to one type of stimulus may not apply to another.

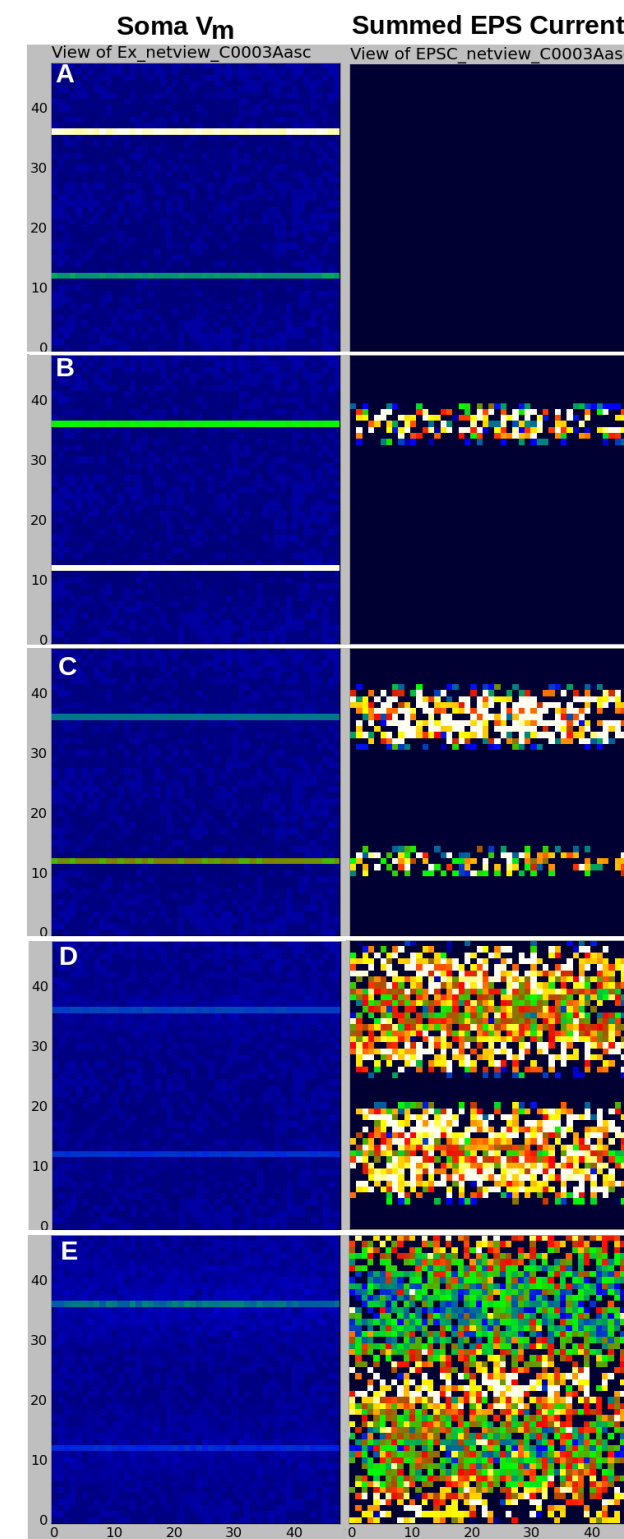
The compromise - ACnet2 provides Biological realism, costumizability, and extensibility with:

- A population of $N_X \times N_Y$ (typically 48×72) nine-compartment pyramidal cells
- A smaller population of two-compartment inhibitory basket cells
- Firing patterns under current clamp representative of pyramidal and basket cells in the auditory cortex
- Choice of connection algorithms for the four types of connections (Ex-->Ex, Ex-->Inh, Inh-->Ex, Inh-->Inh)
 - Decay of connection probability with radial distance
 - Decay of connection weight with radial distance
 - Constant probability or weight
- Choice of axonal conduction velocities
- Can specify synaptic inputs at appropriate dendritic locations on the cell for the type of input
- Customizable scripts for providing various stimuli to the network, including:
 - Stimuli may provided to a single row, or to a block of cells
 - For realistic thalamic connections to AI, to adjacent rows with an an exponentially decaying probability.
 - Choice of pulsed single frequency spike trains, Poisson-distributed random spike trains, or MBGv thalamic cell model that produces interspike intervals (ISIs) corresponding to experiment
- Inputs from other cortical layers are approximated by a random Poisson-distributed activation of the cells
- May be run in 'batch' mode without graphics, or with a GUI to explore parameter changes and input parameters

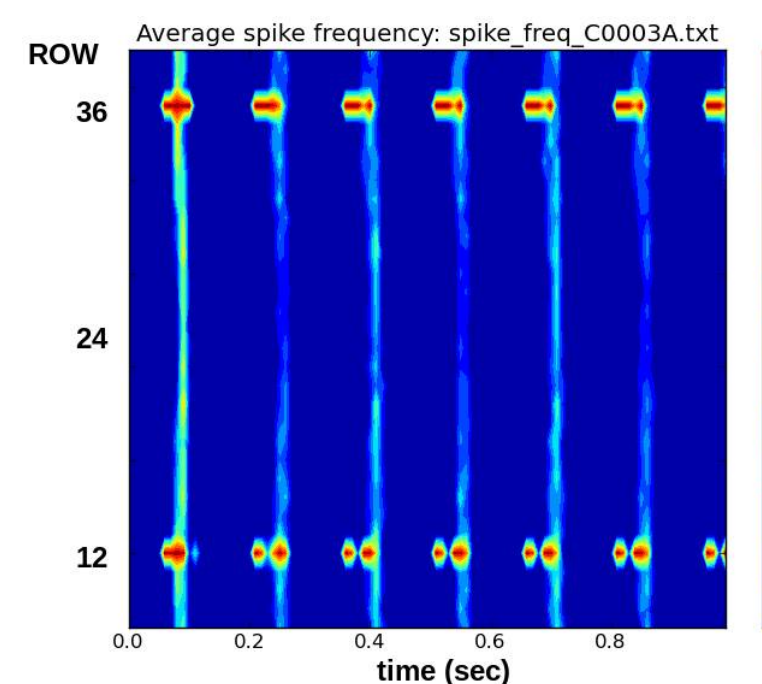
Results

Propagation and Interference of Cortical Waves from Two-tone Inputs

50 msec spike train pulses of 220 Hz and 440 Hz were applied to rows 12 and 36 (a one octave separation of 24 rows = 0.96 mm) to the oblique apical dendrites of the pyramidal cells of the target row, and to the dendrites of 65% of the basket cells corresponding to the target row. The figure at the right shows a sequence of frames from a replay of data generated from the simulation, using the G-3 Python Netview tool. From top to bottom, frames A-E show how the initial responses to the two tone input produce a growing wave of excitation past the initial responses of the input rows, culminating in constructive interference in the middle shown in E. The frames on the left represent the soma membrane potential of the pyramidal cells, and are an indication of firing or changes in the subthreshold potential. Those on the right give their post-synaptic currents due to excitatory connections (EPSCs) from other pyramidal cells, and are indicative of spreading activation of the network that may have a more subtle effect on firing rate. Although the input model provides for a realistic spread of thalamic inputs that have typically observed spike time distributions at a given characteristic frequency, this example used single row excitations from the spike trains, in the absence of background input. The default parameters for the "M series" runs shown in the **Run Time GUI** were used to generate these results. The most important requirement for the generation of cortical waves was that there be as sufficient delay in the onset and decay of inhibition after excitation. This was achieved by assuming a combination of realistic values of synaptic time constants and axonal conduction delays.



Although there is little evidence of increased firing in the left frames, a plot of the average firing rate of cells on a given row can provide some information on the influence of the input on network firing. The contour plot produced by the G-3 "rowrateplot" utility shows vertical bands, indicating the spread of increased firing from the input rows to other rows.



Other applications of the Acnet2 model – MEG responses to click trains

Vierling-Claassen et al. [7] have studied the MEG responses of normal and schizophrenic subjects to auditory click trains of 20, 30, and 40 Hz.

Experiment: MEG spectra show an alteration in gamma band power spectra for schizophrenic subjects, with increased 20 Hz components.

Hypothesis: The increased decay of GABA conductances that has been observed in schizophrenic subjects extends inhibition and favors 20 Hz components in the spectra over 40 Hz.

The models: Simulated MEG power spectral density (PSD) was calculated from the summed EPSCs of the pyramidal cells for two simple network models:

