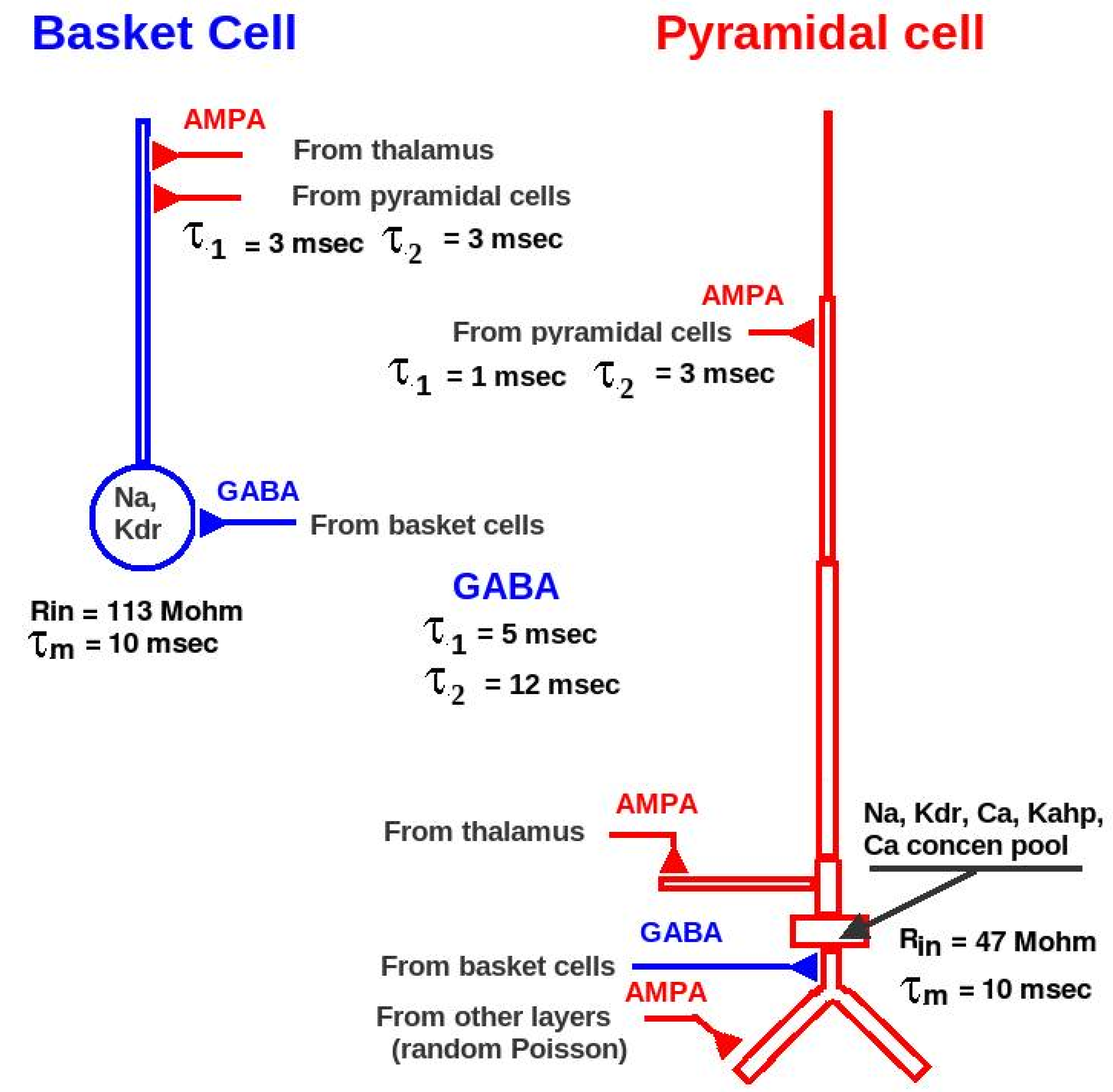
To reduce unknown parameters, ACnet2 omits:

- A detailed model of interlaminar connections
- Other inhibitory channels (GABA B, NMDA) or cells
- Gap junctions between inhibitory cells
- Synaptic plasticity (e.g. facilitation, depression, STDP)

The goal: Find a set of parameters that allow the propagation of waves of excitation with neither undamped oscillation nor excessive inhibition of response to input stimuli.

Major unknown parameters: The weighted synaptic conductances for the four types of connections.



ACnet2 cells and connections

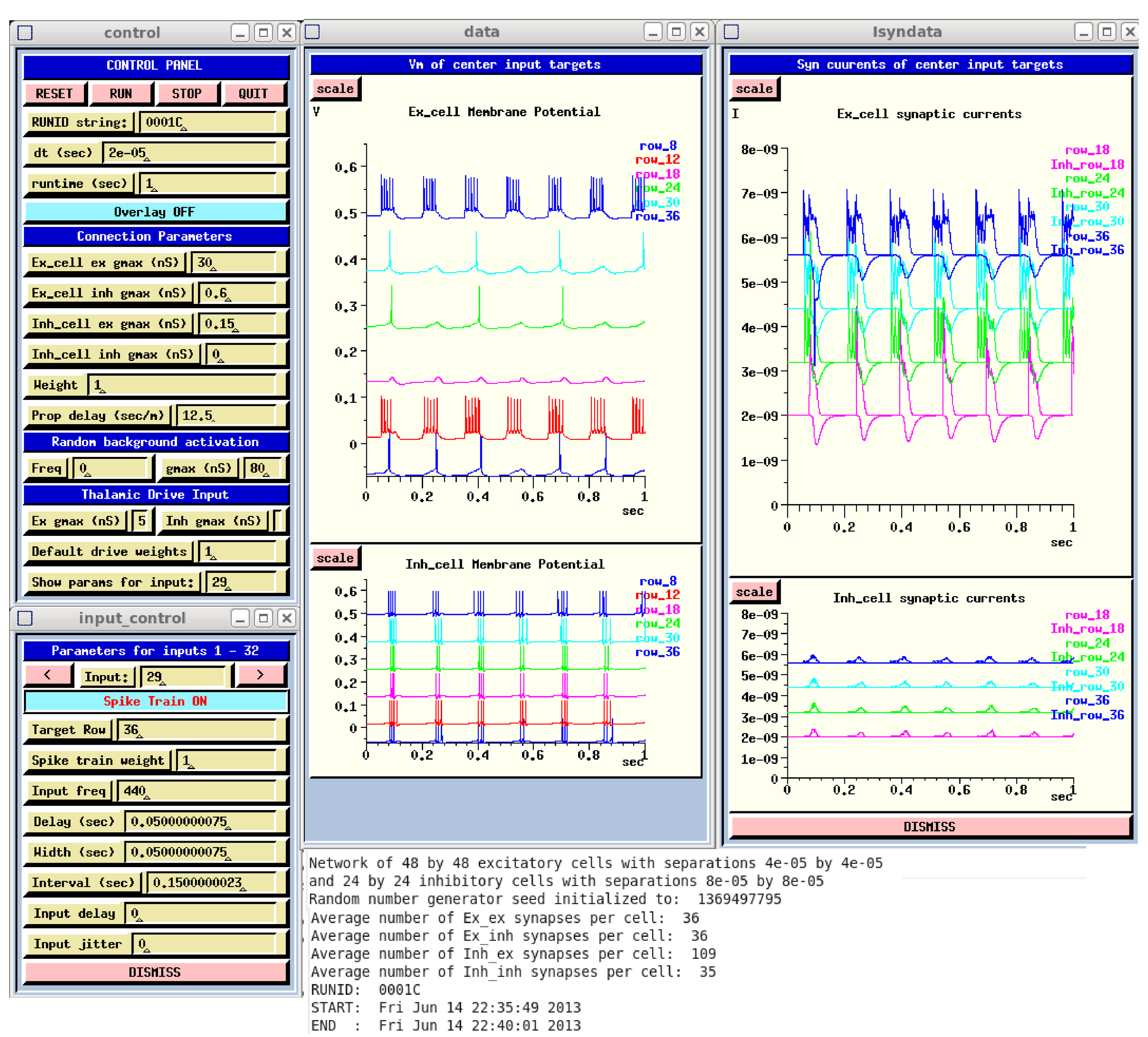
Model Details

- Pyramidal cell morphology and passive parameters from Bush and Sejnowski [4] reduced neocortical cell
- Ball and stick basket cell – 40 um soma, 2 x 200 um dendrite
- Excitatory cells on a grid with SEP_X = SEP_Y = 40 um; inhibitory cells at twice the spacing
- Probability of all connections given by $P(r) = P_0 \exp(-(r/s)^2)$; s = 10*SEP_X = 0.4 mm

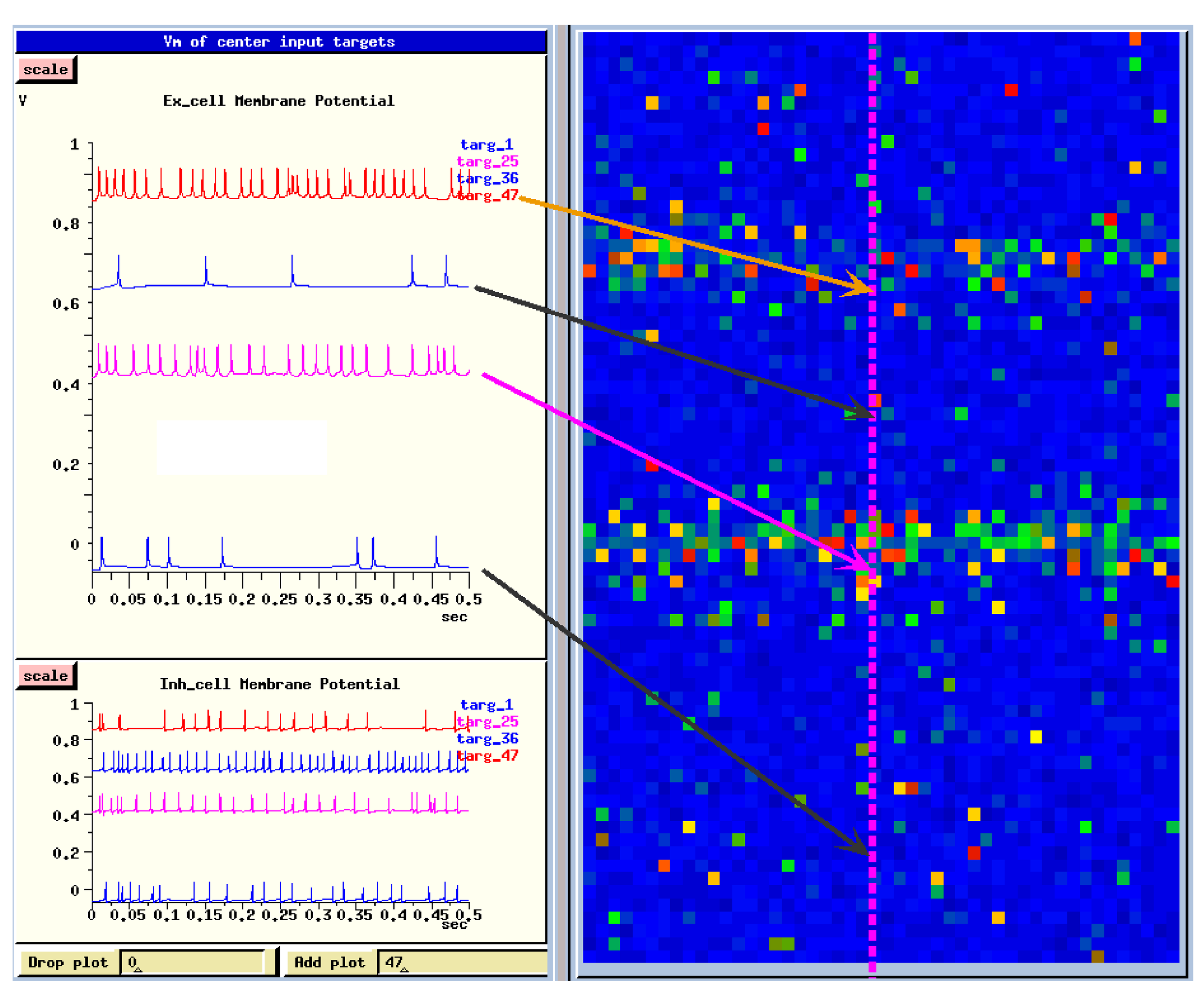
  Fit from references [5,6] with all weights = 1.0
- $P_0(Ex\text{->}Ex) = 0.15$, $P_0(Ex\text{->}Inh) = 0.45$, $P_0(Inh\text{->}Ex) = P_0(Inh\text{->}Inh) = 0.6$

The choices for the four synaptic conductance values used were more arbitrary than other parameters shown in the Run Time GUI. These reflected a balance of excitation and inhibition that resulted in an appropriate average background firing rate for the inhibitory cells (about 22 Hz.) The GABA conductance of basket cells, and their mutual connection probability are poorly known. This set, the "M series" has a maximal basket cell AMPA conductance of 0.15 nS, and zero GABA conductance, in accordance with the model proposed in reference [6]. The "N series" parameters increased the basket cell AMPA conductances to 0.3 nS and provided mutual inhibition with a 0.1 nS basket cell GABA conductance, These resulted in similar background firing rates, but less robust wave propagation.

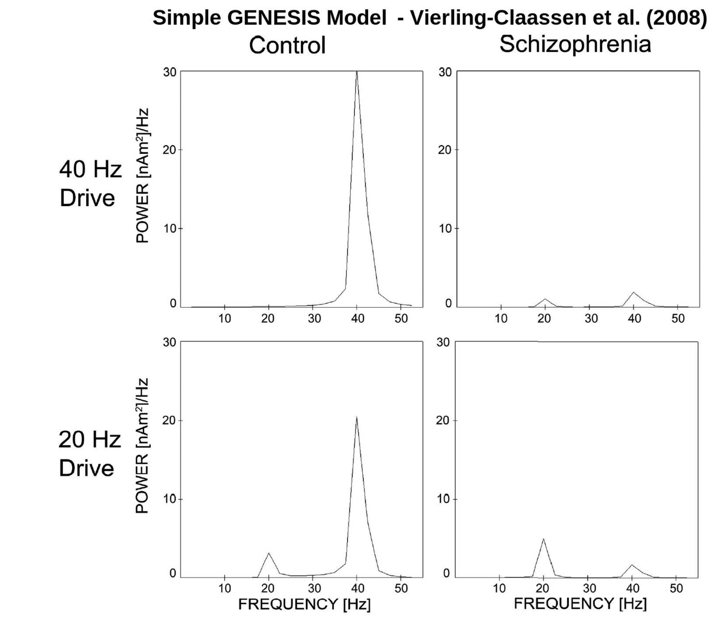
Run Time GUI with default parameters



Visualizing activity during a simulation replay



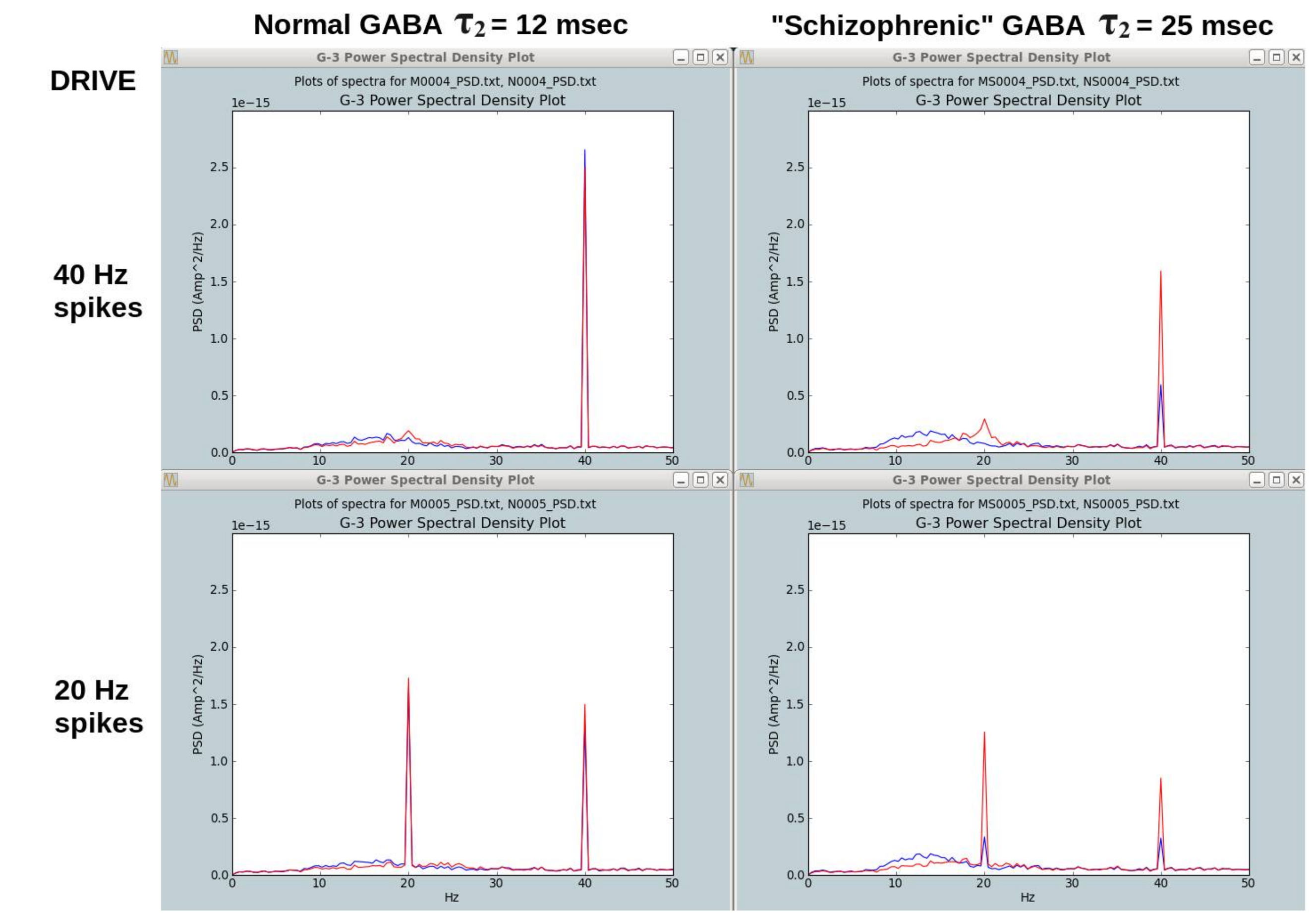
o Simple GENESIS Model (P. Siekmeier) - small populations of excitatory and inhibitory fast spiking cells based on Sharon Crook's CPG model [1]
o Simple coupled oscillator model with realistic synaptic conductances (N. Koppel)



For each model, an increase in the decay resulted in stronger 20 Hz peaks, but no components other than 20 and 40 Hz.

Question: Can the more realistic ACnet2 model explain the other frequency components? Can a comparison of the "M" and "N" series spectra refine the model?

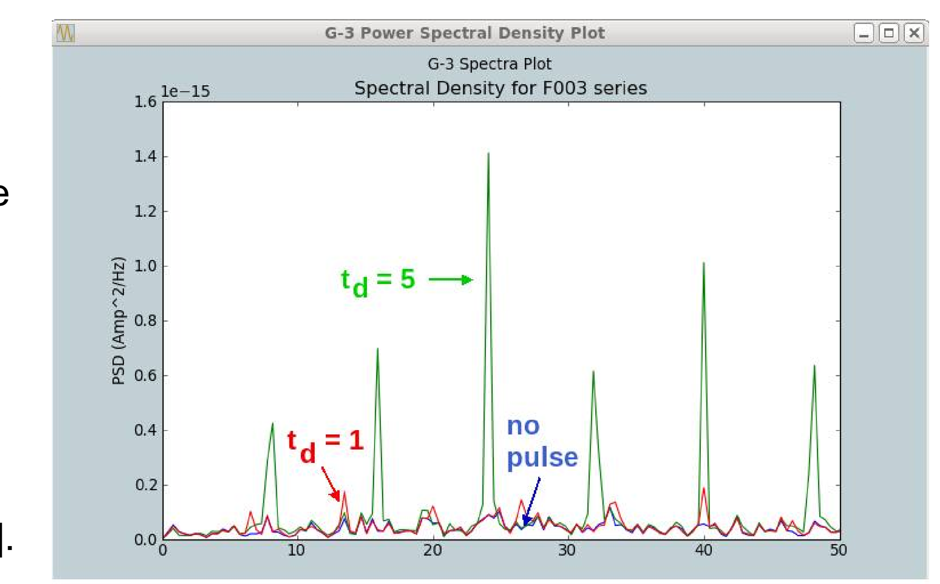
Answer: The results comparing the M and N series show that the search for an optimal balance between excitation and inhibition of the basket cells is not over, and is "left as an exercise for the reader", or for those who would like to experiment with the model. For example, the PSD for the normal subjects listening to 40 Hz clicks shows a notch, rather than a peak at 20 Hz, and none of the models reproduce this effect. The time course of the GABA conductance is also poorly known with some authors reporting much slower decay than others. Fits to other experiments such as the suppression of closely spaced tones by lateral inhibition may further narrow the range of parameters.



Effects of fMRI gradient fields on cortical activity

Rapidly pulsed magnetic (B) gradient fields used in fMRI studies generate electric (E) fields in the body. The trapezoidal B pulses produce pairs of positive and negative E pulses with a width t_r equal to the rise and fall times of the trapezoid pulses and separated by a delay t_d arising from the plateau. Depending on whether the depolarizing E field precedes or follows the hyperpolarizing one, this has the potential to accelerate or delay the generation of action potentials.

The figure shows the EPSC PSD plots obtained from simulated effects of the E fields on the ACnet2 model undergoing normal background activity in the absence of auditory stimuli (blue), and with additional simulated fMRI pulses applied every 12.5 msec, t_r = 0.2 msec, t_d = 1 msec (red), and t_d = 5 msec (green), illustrating the effect of increasing t_d. Further details are given in [8].



Obtaining the scripts: The simulation scripts, analysis tools, and documentation will be available from a link on the **Documentation** page at ***http://genesis-sim.org***.

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References

1. Bower JM, Beeman D (1998, 2003) The Book of GENESIS: Exploring Realistic Neural Models with the General NEural SImulation System, second edn. Springer-Verlag, New York. Free internet edition available at: http://www.genesis-sim.org/GENESIS/iBoG/iBoGpdf
2. Cornelis H, Coop AD, Bower JM (2012) A Federated Design for a Neurobiological Simulation Engine: The CBI Federated Software Architecture. PLoS ONE, 7(1): e28956. doi:10.1371/journal.pone.0028956
3. Rodriguez AL, Cornelis H, Beeman D, Bower, JM (2012) **Multiscale modeling with GENESIS 3, using the G-shell and Python.** *BMC Neuroscience*, 13(Suppl 1):P176. doi:10.1186/1471-2202-13-S1-P176.
4. Bush PC, Sejnowski TJ (1993) Reduced compartmental models of neocortical pyramidal cells, J Neurosci Methods 46:159-166
5. Yuan K, Shih JY, Schreiner CE, Winer JA (2008) GABAergic network differences between auditory cortex areas, Soc Neurosci Abstr poster 67.12
6. Levy RB, Reyes AD (2012) Spatial profile of excitatory and inhibitory synaptic connectivity in mouse primary auditory cortex, J Neurosci 32:5609-5619
7. Vierling-Claassen D, Siekmeier P, Stufflebeam S, Kopell N (2008) Modeling GABA alterations in schizophrenia: a link between impaired inhibition and altered gamma and beta range auditory entrainment. J Neurophysiol 2008
8. Beeman D, Wachtel H (2013) Disruptive effects on neocortical processing by pulsed fMRI gradients: A modeling study in the auditory cortex (to be presented at Society for Neuroscience Session 636, November 2013)