Problem set #1, Part 2. Oscillations

In class we discussed different modes of oscillation in neural networks, some dependent on intrinsic voltage-dependent signaling, some on network interactions, and some on a combination of the two. Thalamic relay neurons express high levels of T-type calcium channels that promote "burst" firing, in which action potentials will be produced in high frequency clusters. T-channels are silent at rest (~ -65 mV) as a result of a process of termed voltage-dependent inactivation. The channels can be primed (de-inactivated) by membrane hyperpolarization , i.e. bringing their membrane potentials to values more negative than rest. Such hyperpolarization can occur through slow, steady-state changes in membrane potential, as occur through neuromodulatory mechanisms that open resting potassium channels, or through transient hyperpolarization, as through inhibitory post-synaptic potentials mediated by GABA receptors.

We will use the modeling software provided in class to examine the relationship between synaptic inhibition and burst firing in thalamic relay neurons.

Problem set 1, part 2. Launch the program SimCC, and load the parameter file ps1_pt2_exp1.cc5, provided. Start the simulation via the menu Run->Begin, or command B (mac) or alt B (PC). Note that changes in Vm that occur at the onset, within the first 100ms of the simulation. For the purposes of this problem set, you can largely ignore these as they mainly reflect the system coming into equilibrium from the initial conditions (numbers and types of leak and voltage gated ion channels) set in the model.

This simulation mimics an IPSP at 300 ms that transiently hyperpolarizes the membrane potential due to an underlying synaptic current (IPSC) that has fast kinetics, as can be seen in the bottom trace (gGABA).

- You can export the simulation to a text file for importing to MATLAB, etc, through the export menu
- Note that upon termination of the IPSC the membrane potential overshoots (positive to -60 mV) from its initial stable state of around -68 mV. This coincides with activation of the transient calcium current, I_T, which produces an inward, depolarizing current.
- Now take this simulation and modify it to alter the kinetics of the IPSC, via the menu tree Parameters->Synaptic Currents->IPSC kinetics. Note that the initial value is 4, which is scaling the decay kinetics of the IPSC to be 4-fold faster than normal. $GABA_A$ receptors are modified in their gating by drugs such as alcohol, anesthetics, hypnotics, muscle relaxants, etc, to produce changes in decay rates and enhance inhibition. To explore the parameter space of IPSC kinetics and the effects on neuronal excitability, use log steps to modify this value (e.g. by two-fold at each trial). For example, you might try a new value of 2. Hit OK, and the command Run, Overlay (or Alt Y) to generate an overlaid trace.

Q1) What difference in response do you see between these two situations? As the IPSP decays what is the subsequent membrane potential response? How is it different with a kinetic factor of 4 vs 2? Do you see quantitative or qualitative changes? For examples, do you see presence or absence of action potentials, or just changes in the post-inhibitory response such as amplitude or duration? Now continue to modify the IPSC kinetics parameter in log steps (values between 0.03125 and 4), while overlaying more simulations with command Y.
Q2) What is the relationship between IPSC kinetics and output of this neuron? Output could be measured by the presence or absence of a rebound membrane potential response and/or the generation of fast action potentials. Be sure to explore the complete range of kinetics until you have reached the limit of neural output at each extreme of slow and fast kinetics.
Q3) Plot the relationships between IPSC kinetics and responses (i.e., IT response, rebound overshoot response, number of action potentials generated), and explain the result. Is there a monotonic relationship between IPSC duration (as governed by decay rate), and post-inhibitory response? If not, what are some potential explanations for these findings, especially regarding the decreased rebound responses observed with the longest IPSC durations?
Q4) Instead of modifying kinetics, instead modify the number of IPSCs, and compare and contrast results with those obtained in Q3.