“A novel spiking neuron modeling of abnormal hippocampal function in animal model of Down syndrome”

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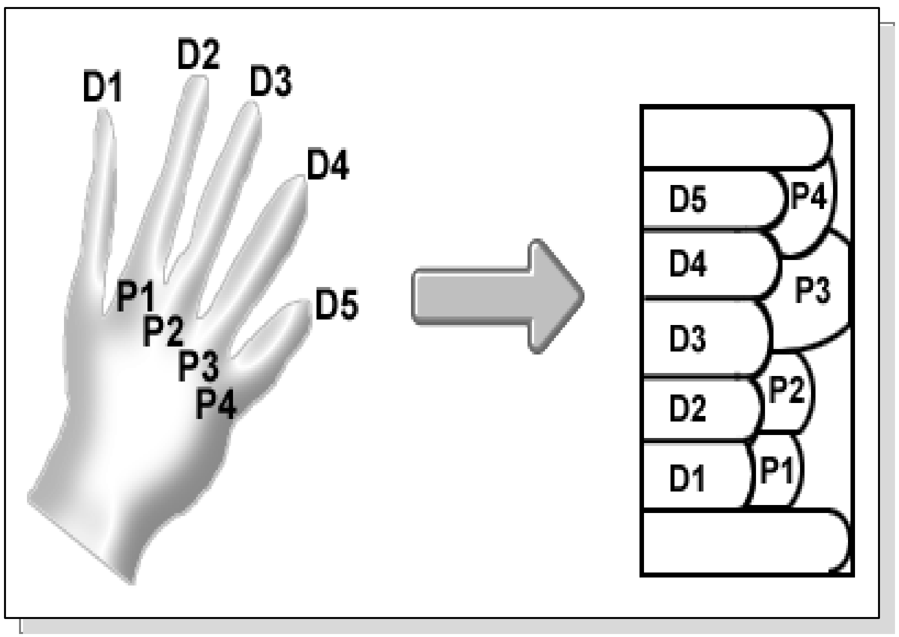
Modeling of the SI Region

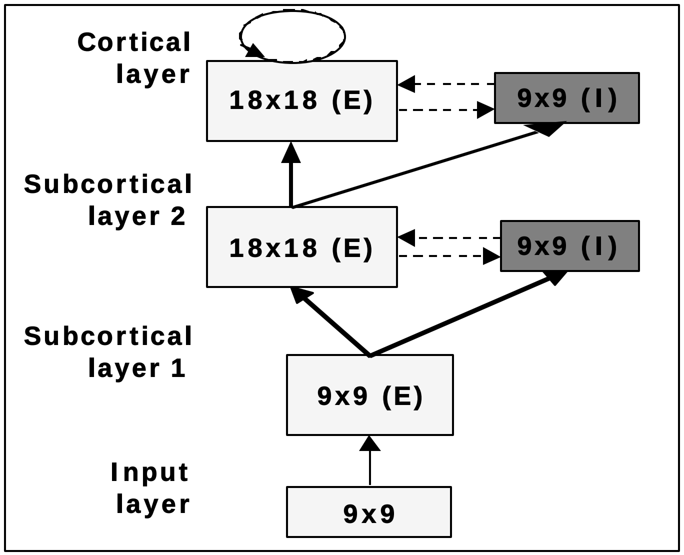
Based on the neuro-physiological descriptions of the ascending somatosensory pathways, and experimental findings, on how the “hand-to-cortex” mapping reorganizes sensory inputs from the hand, we modeled organization and reorganization of the somatosensory cortex.

Sensory inputs from different parts of the hand, *e.g*. the digits and pads on the palm, project into the central nervous system in a topographic manner. As a result a maplike representations of the inputs are present at the spinal, brainstem, thalamic, and cortical levels of the system.



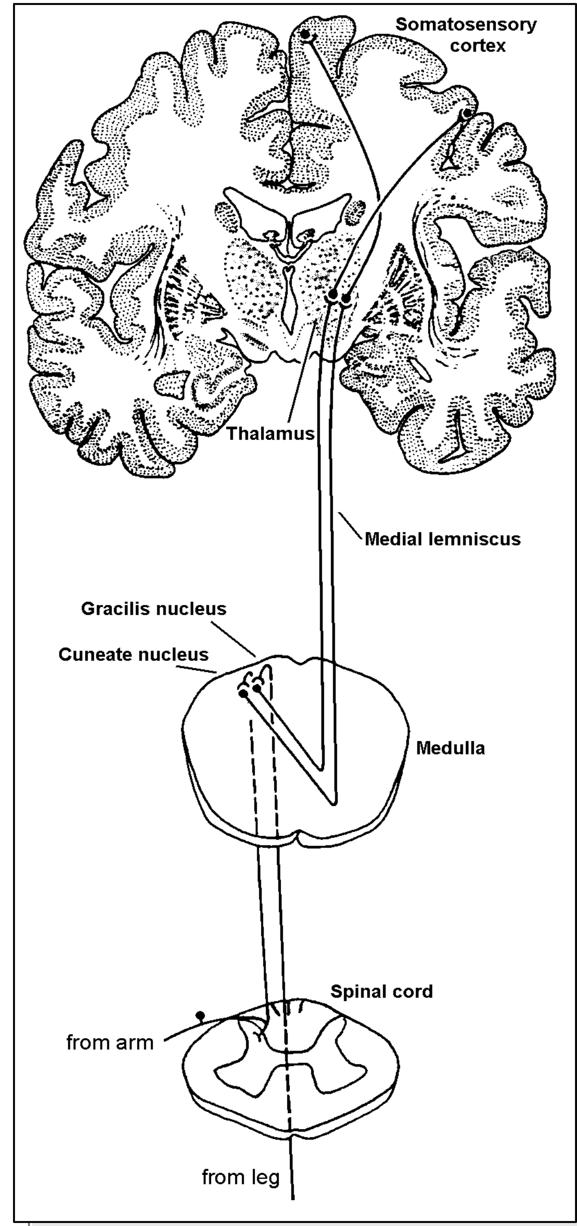
Modeling of the SI Region

The model consisted of over a thousand spiking neurons arranged into four layers corresponding to the four stages of information processing.



The system consisted of these stages of information processing:

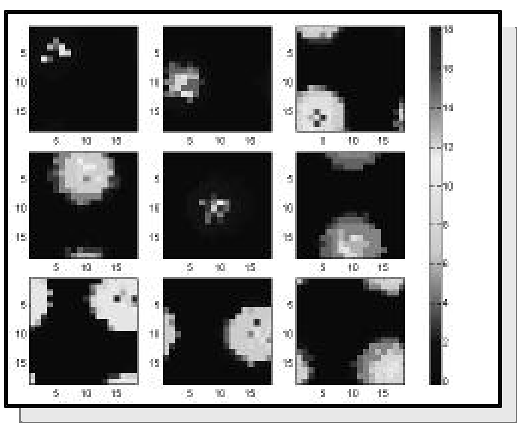
- sensory afferents
- spinal cord-brainstem
- thalamus
- cortex



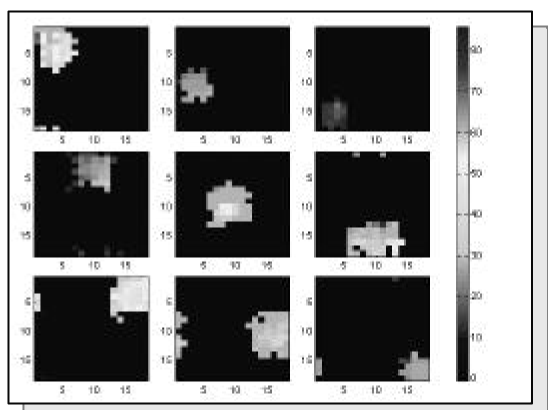
Modeling of the SI Region

Using MacGregor model of a spiking neuron and Temporal Correlation learning rule (TCR) we accurately modeled plasticity occurring in the somatosensory cortex after removal of one or more digits, simultaneous stimulation of two digits, etc. (Sala, Cios and Wall, 1997).

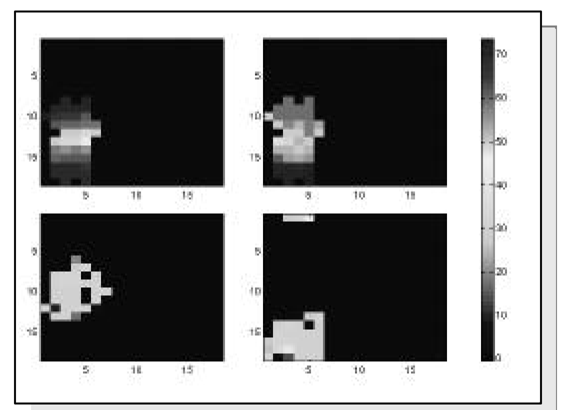
Cortical Response No Learning



Cortical Response Learning Using TCR

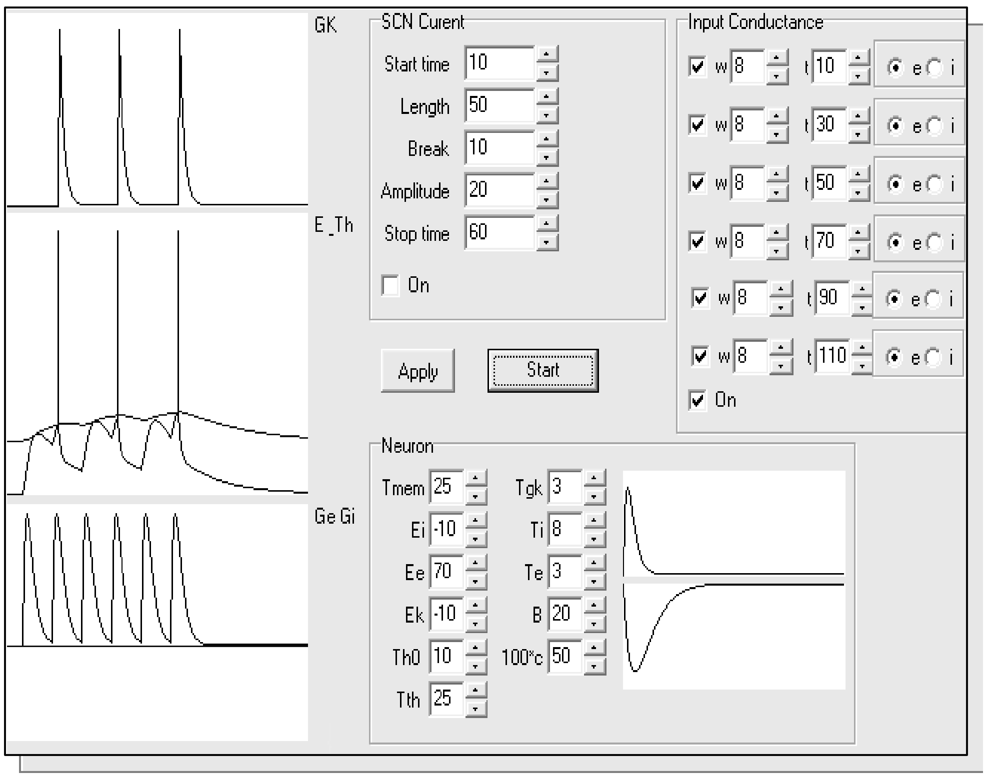


Two Regions Stimulated Together

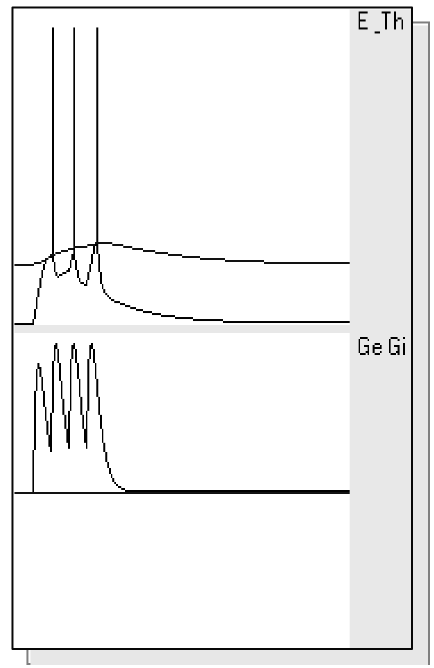


Spiking Neuron Model

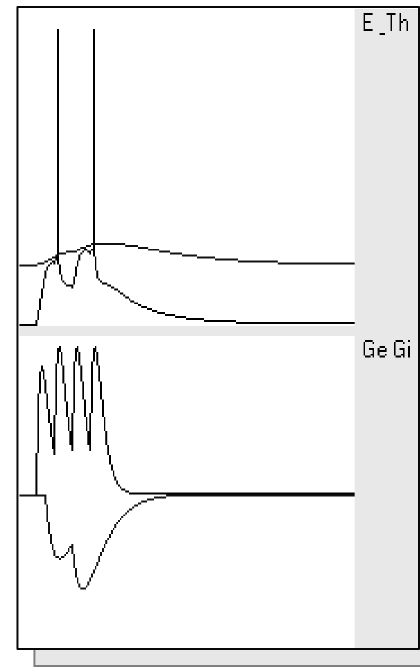
Our spiking neuron model is capable of generating a response to a series of spikes coming from one synapse.



Neuron Model



Excitatory Stimulation



Exc. / Inh. Stimulation

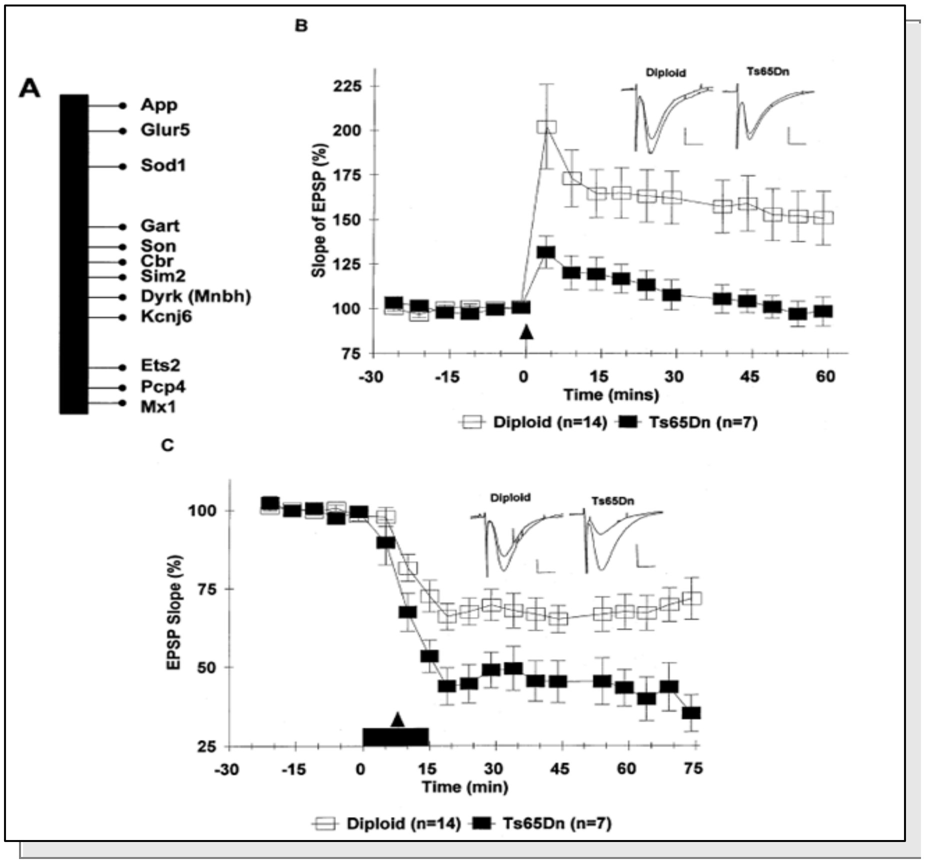
E_Th – black line membrane potential, blue line threshold

$G_e G_i$ – black line excitatory conductance, blue line inhibitory conductance

G_k – potassium conductance

Network Model and Synaptic Plasticity

We are working on implementation of synaptic plasticity rule based on Hebbian rule that effects both excitatory and inhibitory neurons. The plasticity rule will account for both long-term potentiation (LTP) and long-term depression (LTD).



Synaptic Plasticity Rule

The synapse's weights adjustments depend on the correlation between firing of pre- and post-synaptic neurons.

Excitatory synapses will be "rewarded" for influence on firing of postsynaptic neurons and "punished" for lack of this influence, while the inhibitory synapses will be rewarded for blocking of firing of postsynaptic neurons and punished for allowing the neuron to fire.

Hippocampal functions

The hippocampus is thought to contribute to learning and memory, and other higher order cognitive processes. It is said to play a role in declarative memory, recognition of words, faces and spatial coordinates. Abnormal hippocampal function has been implicated in temporal lobe epilepsy and in memory loss in Alzheimer disease. Most of the sensory information enters into the hippocampus through the entorhinal cortex.

Goal

We have already demonstrated that in the CA1 region of the Ts65Dn mouse hippocampus LTP decrease and LTD increase (Siarey et al. 1997 and 1999).

We will apply the network of spiking neurons to emulate abnormal hippocampal function in Down Syndrome (DS, trisomy of human chromosome 21) of the Ts65Dn mouse (a model of DS). This mouse demonstrates abnormal performance in various learning and *behavioral* paradigms implicating impairment of hippocampal function.

Goal

Our model should be capable of dynamic organization changes in response to stimulation history and will involve spatio-temporal processing of thousands of spiking neurons.

The balance of excitation and inhibition will be assured through short-term excitation with long-term inhibition rather than the usual short-range excitation with long-range inhibition.

This research should generate new questions that can be further addressed in both experimental and theoretical manner.