Reproducing LGN cells behavior using a simple mathematical model

Pierre Fortier and George Wahba

Department of Cellular and Molecular Medicine, University of Ottawa, Ottawa ,ON , Canada K1H 8M5

uOttawa

Introduction

The study of detailed neural networks has been an important innovation to be able to study, otherwise hard to observe, neural behavior. Simulation software such as NEURON is capable of using complex conductance equations during simulations but they become a problem in simulations of large networks and often researchers must cut down the number of cells they simulate. This project aimed to create a mathematical model that would reproduce the spike patterns of the cells of the Lateral Geniculate Nucleus (LGN) in the NEURON simulation software. Instead of using conductance equations, as has already been done [2], we created a new model as an expansion of the Izhikevich equation [1] which has been previously made to reproduce general spiking patterns with a simple mathematical equation. We also introduced noise to our model. In addition, we used the model to create a network of LGN cells. We tested the efficiency of the simplified mathematical model by testing the execution time of simulations for diverse quantities of neurons. We also tested for compatibility between the spiking frequency and the stimulation amplitude of the conductance and the mathematical model. Adjustments were made to the original Izhikevich code to derive the quickest possible model.

Methods

For the project we used the Izhikevich mathematical model (NEURON accession no.39948) [1]. This package includes a general equation that can generate specific spiking patterns by plugging in different parameter values. We cut down the code to include only the patterns we needed in our project. As a reference, we used the LGN neuron model (which runs on the conductance equations) found in the NEURON model database under accession no.279 [2]. We added noise to the Izhikevich model using the equation found in Poliakov and al., 1996 [3]. We edited mainly the Izhikevich annex "*.mod" file to generate the LGN cell behaviour by introducing a code that monitored the time spent under a specific voltage and could switch modes when the time exceeded a certain time threshold (100ms). We measured execution times using the same computer to allow consistency. We adjusted as best we can the time step size for each model for consistency but the Izhikevich model runs with a variable time step. To quantify the spiking frequency we used a code that tracked whenever the voltage passed 30mV.

Results

Figure 1 demonstrates the similarity between the conductance model and the mathematical model we produced, both simulating an LGN cell.

1

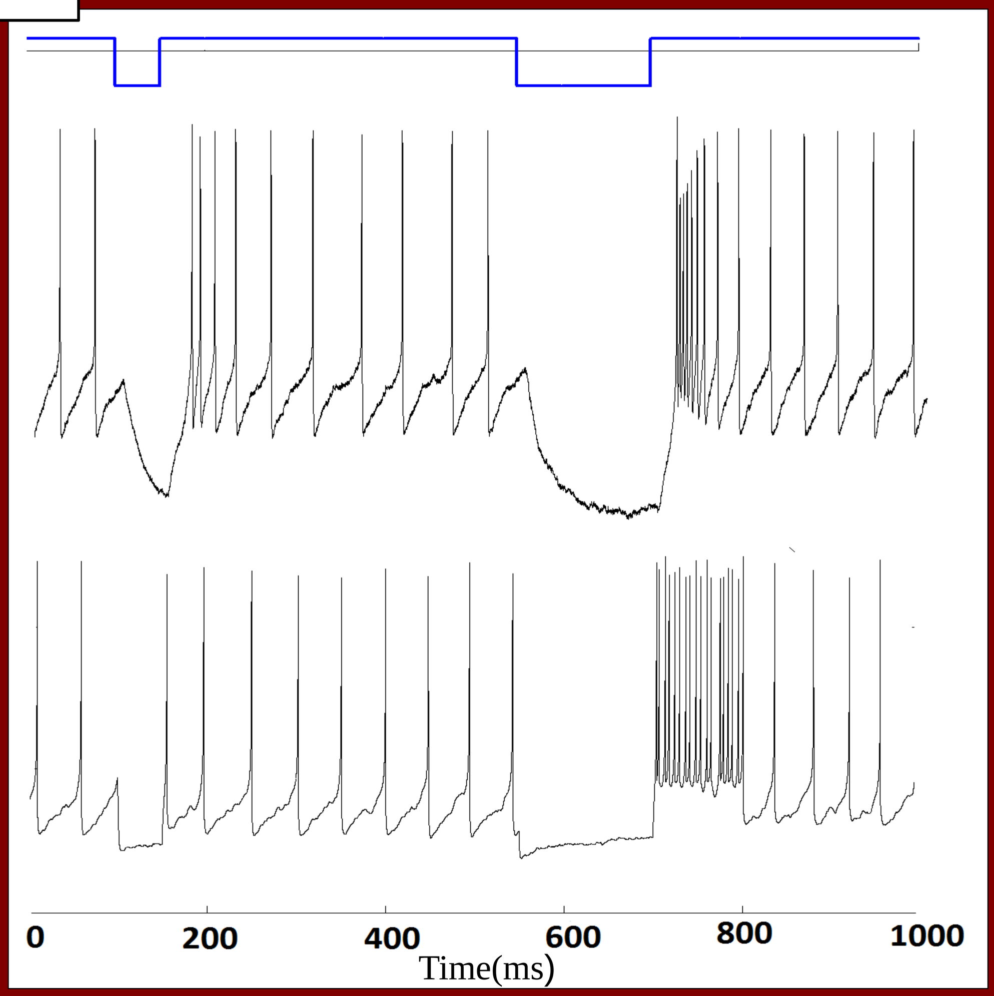

Figure 1. Comparison of spiking pattern of the normal conductance model (on top) and the pattern generated using the simplified model (bottom). Both simulations ran with similar stimulation amplitudes shown in blue on top.

The following pseudocode explains how we recreated the LGN cell behavior in our model:

```
if (mode=tonic)
      if (below -70mV for more than 100ms) {
            switch to bursting mode }
      else {stay in tonic mode}
if (mode=bursting)
      if (above -70mV for more than 100ms) {
            switch to tonic mode}
      else {stay in bursting mode}
```

As seen, in Figure 1, the model we generated is very similar to the conductance model. The pseudocode above is the outline of the code used to generate the simplified mathematical model. We see that the conductance model which is actually based on specific chemical and electric properties of LGN cells, also closely follows this outline. For example, we specify that 100ms must be spent under -70mV for there to be a switch to bursting mode if we are in the tonic mode. Both models start off in tonic mode and receive a short 50ms hyperpolarization. Because 100ms must be spent under -70mV for the mode to change, there is no change in the spiking mode. However at 550ms, we introduce a long hyperpolarization that forces the cell potential to drop under -70mV for 100ms and in both cases we see a change towards bursting firing. The bursting firing in both cases also only lasts about 100ms before returning to tonic firing which also is specified in the pseudocode above.

2

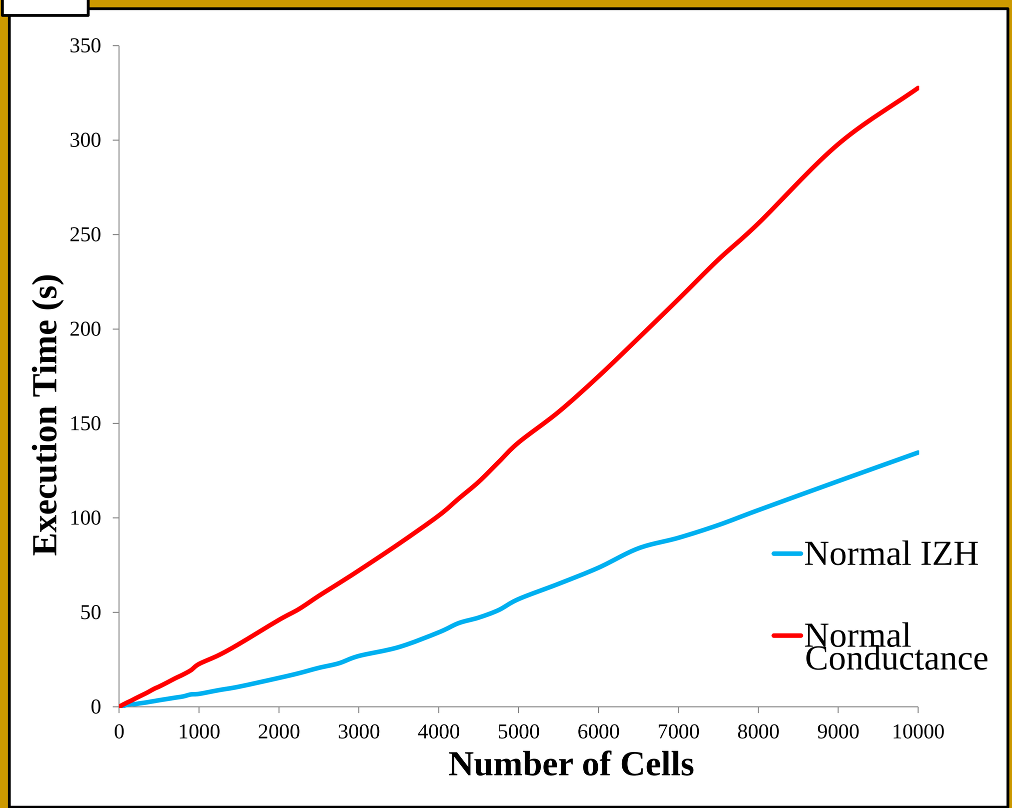

Figure 2. Execution time of simulation as a function of the number cells used in each simulation. The red curve gives the simulations made with the normal conductance model and the blue curve gives the simulations made with the simplified mathematical model. Both ran comparable simulations.

As seen in Figure 2, the mathematical spiking model was much quicker than its conductance-based counterpart. As we increase the number of cells, the time difference becomes more important. In fact, by the time we reach 10,000 cells which is a plausible number of cells to use in the simulation of a full system, the simple mathematical model is 2.5 times faster than the traditional model.

3

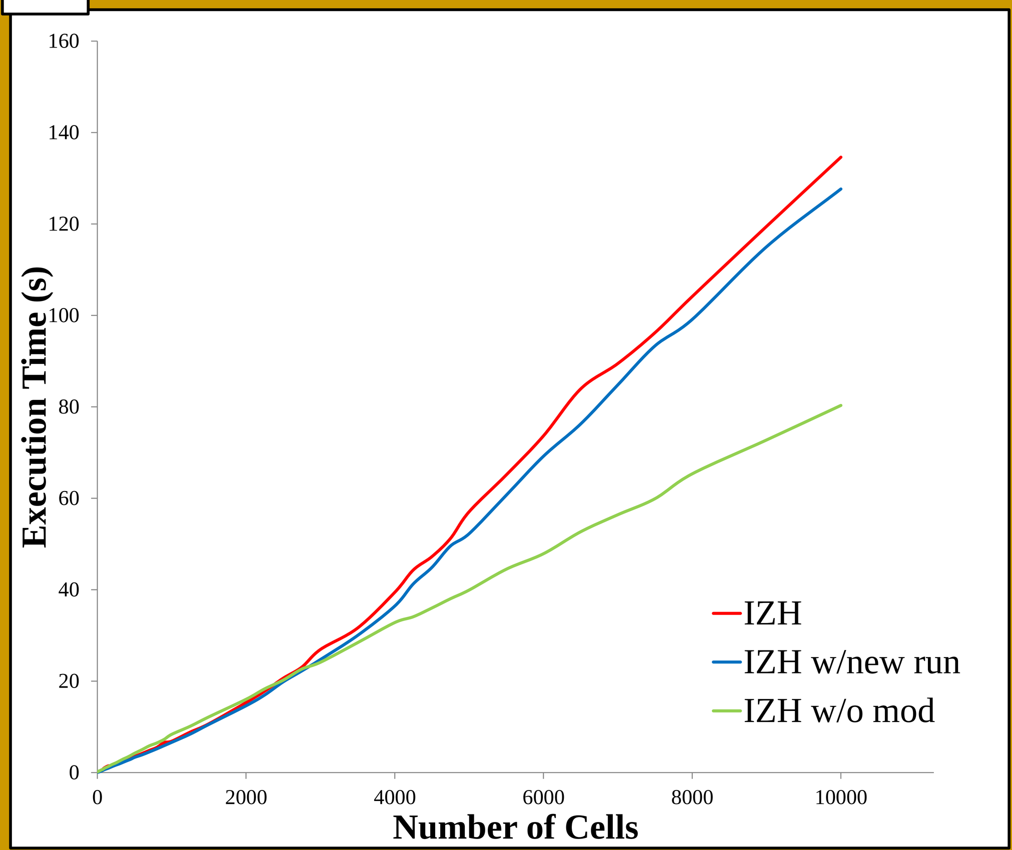

Figure 3. Execution time of simulation as a function of the number cells used in each simulation. The red curve gives the simulations made with the normal mathematical model. The model with the slightly modified "run" procedure is given in blue while the model we created without using the normally used annex "*.mod" file is given in green.

The standard "run" procedure in NEURON, which runs the simulation, encloses a "steprun" function, which advances time, but also constantly plots. As a result, to improve efficiency, we changed the run procedure to plot only at the end. In addition, the standard Izhikevich model uses an annex ".mod" file to make its calculations. Instead, we merged the normal file and its annex into one file. As seen in Fig.3, both changes improved the speed of execution of the model.

4

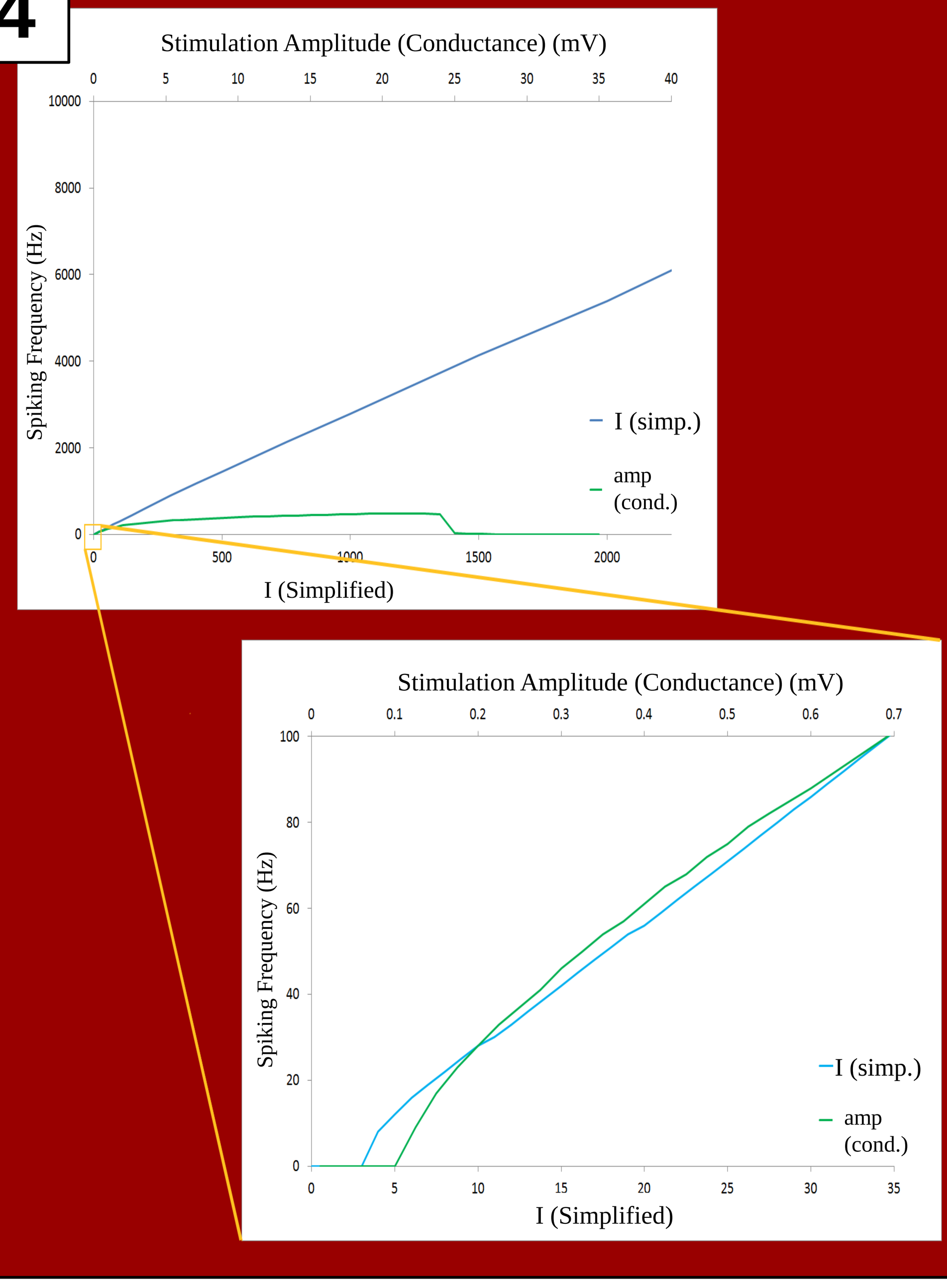

Figure 4. The spiking frequency as a function of either the spiking amplitude in the normal conductance model (top x-axis) or the "I" parameter in the simplified mathematical model (bottom x-axis). The blue curve follows the bottom x-axis while the green curve follows the top x-axis. A zoom-in of an area of interest (spiking till 100Hz of spiking) is given.

In the Izhikevich equation we used for the simplified mathematical model, the parameter "I" serves as the measure of the amplitude being delivered to the cell. As shown in Figure 4, there seems, at first, very little compatibility between the magnitude of the amplitude of the stimulation used in the normal conductance model (given by "amp") and the magnitude of "I." In fact, we see that in the conductance model, the frequency eventually reaches a plateau while in the Izhikevich simplified mathematical model, the spiking frequency increases linearly with "I" without limit. That said, in real neurons of the visual system, spiking rarely crosses 80Hz [4]. As result, if we zoom in on the area below 100Hz, the area under which we would expect real cells of the visual system to spike, we see that there is, in fact, very much compatibility between "I" and the amplitude of the stimulation in the normal conductance model.

5

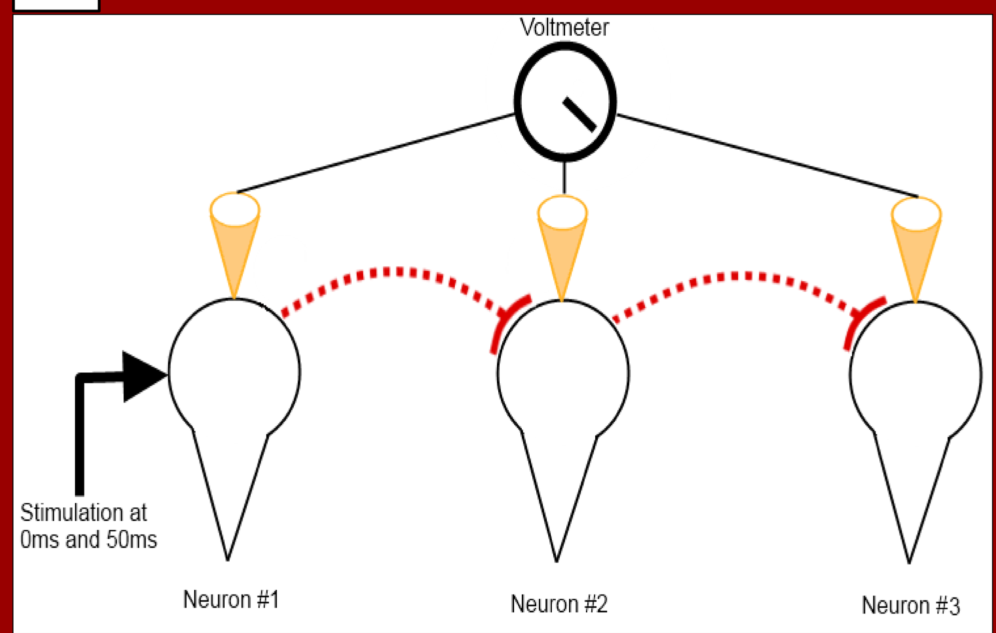

Figure 5. A diagram showing a sample network we designed with the cells running on the mathematical model. As shown, two stimulations are given to the first neuron. The first stimulation is given immediately and the second is given 50ms later. The three neurons are synaptically connected and pass the signal from one to another. Figure 6 shows the recorded voltage in each cell.

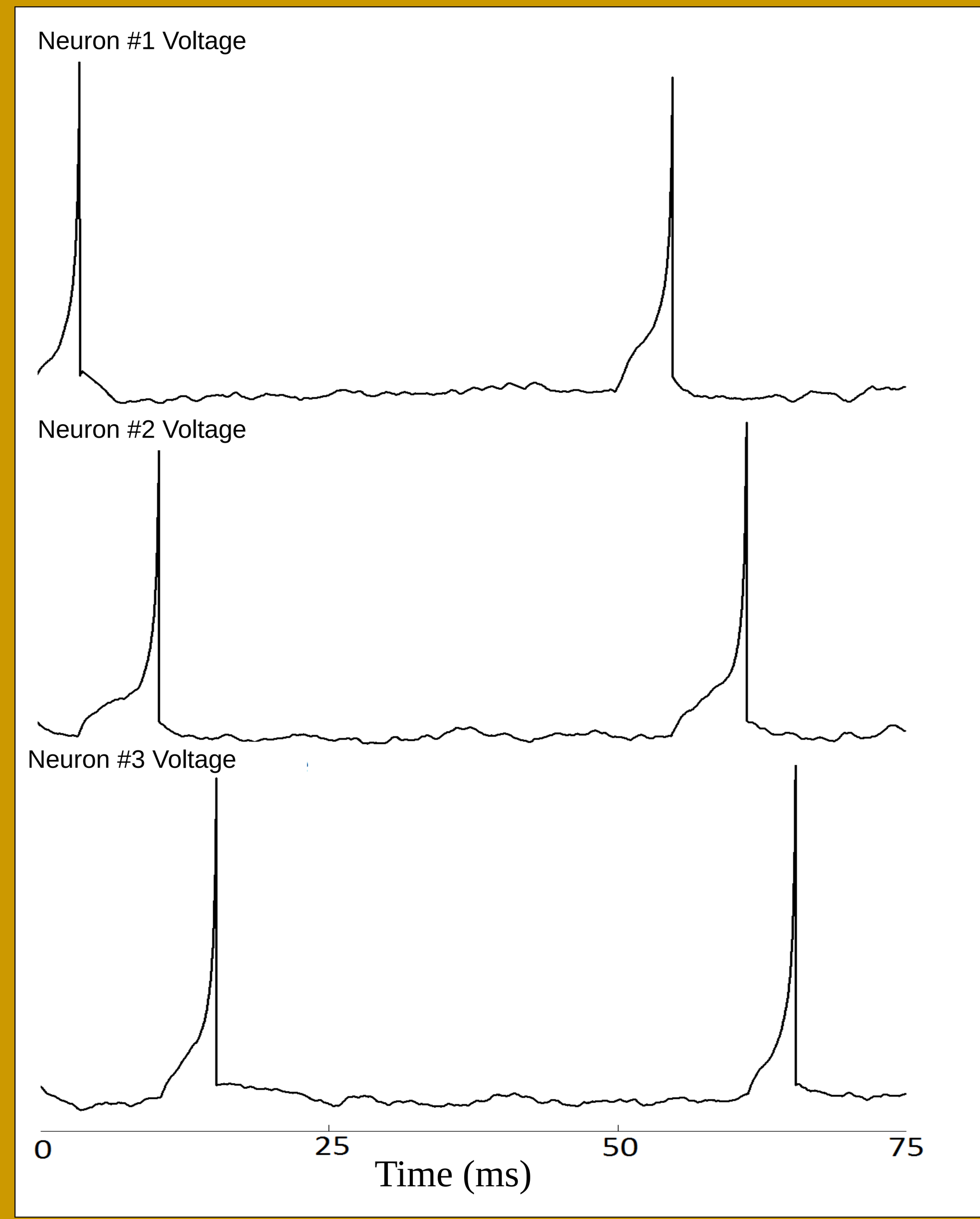

Figure 6. The voltage of three synaptically connected neurons running on the mathematical model. The connectivity of the neurons is shown in Fig.5.

This shows that the simple mathematical model we used is not only useful to stimulate large number of unconnected cells but can be used to design models and produce very realistic results such as seen in Fig.6 . As seen the first cell fires first, transmits to the second which transmits to the third. As a result, we see staggered spikes after each stimulation on each neuron.

Conclusions

In conclusion, we have found in our study that using a simple mathematical model can be much faster than the traditional conductance model. We were able to use simple mathematical equations to model LGN cells effectively and we were also able to use it to create networks. Small tunings to the mathematical model's code can, as shown here, also greatly improve performance. Future studies can continue to expand the Izhikevich equation to model other complex cells in the nervous system.

References

[1] Izhikevich, E. 2003. Simple model of spiking neurons. IEEE Transactions on neural networks. 14:1569-1572

[2] Destexhe, A., Neubig, M., Ulrich, D., Huguenard, J. 1998 Dendritic low-threshold calcium currents in thalamic relay cells. The Journal of Neuroscience. 15;18(10):3574-3588

[3] Poliakov, A., Powers, R. , Sawczuk, A. and Binder, M. 1996. Effects of background noise on the response of rat and cat motoneurons to excitatory current transients. The Journal of Physiology. 495.1: 143-157

[4] Ohzawa, I., Sclar, G. and Freeman, RD. 1985. Contrast gain control in the cat's visual system. The Journal of Neuroscience. 54: 651-667

Contacts

Dr. Pierre Fortier; pfortier@uottawa.ca
also see Lab website at;
http://head.med.uottawa.ca/public/webpages/ResPage/

George Wahba; gwahb103@uottawa.ca

Many thanks to Dr. Fortier for his kindness and patience during this project.

Research Support: University of Ottawa Undergraduate Research Scholarship (UROP)