# Neural Networks and Biological Modeling

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## Mini-Project: Single-Neuron Models

This project explores single-neuron models using NEURON. Make sure you have correctly installed NEURON, see the Yale repository[1] or Andrew Davidson's instructions[2] for installing NEURON for python. For using NEURON within python, you need to install the source code of NEURON If you choose not to use python, you will have to write a *.hoc* file and ask neuron to run this file. It is also possible not to write any code and use the Graphical User Interface (GUI) provided with NEURON but this is not recommended due to lack of versatility of the GUI. The aim of the project is for you to grasp the basic capabilities of NEURON. You will have to build different detailed models and study the synaptic integration of these models.

Along with the course notes you can use the following references:Carnavale, Hines, *The NEURON Book*, (2006); Koch, *Biophysics of Computation* (1999); Gerstner, Kistler, *Spiking Neuron Models* (2002).

## Exercise 1: Single Compartment Model: HH, $HH_x$ and $HH_{xx}$

### 1.1 The importance of additional ion channels on the integration of synaptic inputs

Create three different somatic compartment models:

- A standard HH model, with sodium, potassium and leak current. Note that instead using the traditional 'hh' mechanism of NEURON, we use $hh2$, which defines the sodium, potassium dynamics for cortical neurons. [3] This neuron will be refer as $HH$.
- A $HH$ model augmented with an additional ion channel $Ix$. As for the 'hh2 mechanism', you have to add the mechanism 'Ix' stored in the file 'Ix.mod'. Then you can simply use the command 'insert Ix'. This model will be refer as $HH_x$.
- A $HH$ model augmented with the mechanism $Ixx$ (Ixx.mod): $HH_{xx}$.

For all these models, create a soma with a length of 67 $\mu m$ and a diameter of 67 $\mu m$, an intracellular resistivity $R_a = 100\ \Omega \cdot cm$ and a specific membrane capacitance $C_m = 1\ \mu F/cm^2$. Insert passive mechanisms with $g_{pas} = 0.00015\ S/cm^2$ and a reverse potential $E_{pas} = -70$ mV. Insert Hodgkin-Huxley sodium current $I_{Na}$ and potassium current $I_K$ (do not forget to use the 'hh2' mechanism in the file "HH_traub.mod"). Set $e_k$ to 100 mV, $e_{na}$ to 50 mV and $vtraub_{hh2}$ = -55 mV. Then fix the maximum sodium and potassium conductance to 0.05 $\mu S$ and 0.005 $\mu S$, respectivelly. Finally set the temperature (variable *celsius*) to 36 celsius degrees. Then on each neurons add 40 $\alpha$-synapses with time constant $\tau = 2$ ms, reverse potential $E = 0$ mV, and $g_{max} = 0.005\mu S$ for $HH$, $g_{max} = 0.01\mu S$ for $HH_x$ and $g_{max} = 0.001\mu S$ for $HH_{xx}$.

### 1.2 Neuron Types

[1] http://www.neuron.yale.edu
[2] http://www.davison.webfactional.com/notes/installation-neuron-python/
[3] To install a new mechanism in NEURON, first compile the file '.mod' that defines the mechanism with the command mknrndll of NEURON. Then you can simply use the command 'insert *name_of_the_mechanisms*'.

Using multiple injections of step currents, find the type of each model (i.e. Type I or Type II).

### 1.3 Spike!

For each model, find the minimum number of simultaneously-activated synapses needed to evoke a single spike.

### 1.4 Synaptic integration

To define the type of synaptic integration of each model, one have to study how the single synaptic inputs are summed to form the final somatic voltage. For each model, measure the peak amplitude of the somatic EPSP as a function of the number of simultaneously-activated synapses (in subthreshold regime).
What type of synaptic integration these neurons perform (i.e. how the individual EPSP are combined to form the final EPSP)? Try to explain the differences between these three models.

### 1.5 The additional ion channels

Using NEURON, show the dynamics of the two additional currents $Ix$ and $Ixx$ and explain their effects on the subthreshold voltage. Hint: In neuron you have access to all the state variables. For instance you can plot the dynamics of the Ix-current.

## Exercise 2: Dendritic Integration of Synaptic Inputs

Make a soma of 353 $\mu m^2$ connected with a cylindric passive dendrite of 0.5 $mm$ length and a diameter of 3 $\mu m$, called 'dendrite 1'. For the soma add the Hodgkin-Huxley mechanism (use *insert hh*). For the Hodgkin-Huxley mechanism, use $\bar{g}_{na} = 0.2\ S/cm^2$, $gl_{hh} = .0001\ S/cm^2$ and $el_{hh} = -70.0$ mV and default values for the others parameters.
For dendrite 1 add passive mechanism (use *insert pas*) with, at least 50 segments, a passive reverse potential of $-70.0$ mV and a passive conductance of $0.0001\ S/cm^2$. Set the intracellular resistivity $R_a = 123\ \Omega \cdot cm$ and a specific membrane capacitance $C_m = 2\ \mu F/cm^2$.
Connect two extra cylindric dendrites at the end of the first dendrite, so that it form a 'Y' (dendrite 2 and 3). Use exactly the same parameters for the three dendritic branches. Then add on dendrite 2 a new ion channels $Ix$ (i.e. 'Ix.mod') and set $\bar{g}k_{ix}$ to 2e-5 $\mu S$. Similarly add on dendrite 3 the current $Ixx$. Then distribute 50 excitatory $\alpha$-synapses at the middle of dendrite 2 and 3, with parameters $\tau = 2$ ms, $E = 0$ mV and $g_{max} = 0.002\mu S$.

### 2.1 Spike again!

How many synapses $N_{min}$ do you need to activate in order to evoke a single somatic spike? Answer this question for the three different cases: (i) all the co-activated synapses are on dendritic branch 2, (ii) all the co-activated synapses are on dendrite 3 and (iii) half of the activated synapses are on dendrite 2 and half on dendrite 3. Always use synchronous activation of the synapses.

### 2.2 Spatial summation of synaptic inputs

Show that this neurons can perform linear and supra-linear summation of synaptic inputs depending on the location of the inputs. Here again use only synchronous activation of the synapses.

### 2.3 Veto-Inhibition

Add a new inhibitory $\alpha$-synapse on the middle of the first dendritic branch. For this synapse assume a time constant $\tau = 5$ ms and a reverse potential $E = -70$ mV. For $1.5N_{min}$ activated synpases find the maximal conductance $g_{max}$ and the onset $\Delta T$ for a single inhibitory stimulation that will veto the spike.