Spiking Neurons

Computer Exercises using the NEURON Simulator

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Overview

These exercises make use of the **NEURON** simulator (www.neuron.yale.edu). It is not necessary to be familiar with NEURON before attempting these exercises, but previous experience will allow you to progress faster and to try some of the optional, advanced exercises. Prewritten code is available for all of the main exercises, but it is also suggested that you try to write your own **hoc** code for some of them, rather than use the supplied code. For this you will need some familiarity with **hoc**, and a simple text editor eg Notepad. The NEURON documentation available via your NEURON installation will be very useful here.

A number of the exercises are based on examples from the book, "**Principles of Computational Modelling in Neuroscience**" by Sterratt, Graham, Gillies and Willshaw (CUP, 2011). The book will be referred to as **PCNM** in the following text.

The NEURON Model Code

Code files

The code for each of the exercises is stored in an appropriately named folder, as detailed in the instructions for each exercise. In each case there is one or more ".hoc" files containing the code that defines the simulation. These may be accompanied by ".ses" files that contain user interface (GUI) definitions and ".mod" files that define various model components, such as ion channel models.

Running the code

Linux

1. In a Linux terminal window, change to the directory (folder) containing the desired HOC file (command "cd").
2. If the folder contains ".mod" files, first rebuild NEURON to incorporate these model components by typing: "**nrnivmodl**".

3. Run NEURON by typing "**nrngui filename.hoc**" eg "nrngui FIcurve.hoc".

Windows

1. In Windows Explorer, change to the folder containing the desired **hoc** file.
2. If the folder contains ".mod" files, first rebuild NEURON to incorporate these model components by running "**mknrndll**" on this folder (you will find this command in the NEURON Start group).
3. Run NEURON by double-clicking the relevant "**.hoc**" file eg "FIcurve.hoc".

Other Tutorial Material

If you would like more experience with NEURON before trying these exercises, then the following tutorial material is available in the *Documentation* section on the NEURON simulator web site at:

http://www.neuron.yale.edu

NEURON GUI tools

Neuron models and small networks can be constructed in NEURON using in-built GUI tools, with no programming required.

Learning Hoc

To gain basic experience in constructing NEURON simulations by programming them in the scripting language "hoc", try the Neuron tutorial by Gillies and Sterratt.

1. Frequency-Input Current (F-I) Firing Curve of a Neuron

In the following two exercises you will explore how the firing rate of a neuron changes as a function of injected current in the cell body. This corresponds to a typical electrophysiological experiment that is used to in part characterise the properties of a neuron. The code for the exercises is in the **FIcurve** folder.

Exercise 1.1: F-I curve of a simple neuron

A simple compartmental model neuron is stimulated by a constant current injection to the cell body. The cell body is a cylinder 30um in diameter and 30um long, and contains sodium, potassium and leak ion channels, and so can produce action potentials if stimulated to threshold. A 1000um long and 2um thick dendrite is attached to the cell body and is modelled as 11 compartments ("segments" in NEURON terminology), each of which contains only leak ion channels.

Neuron construction:

You can either choose to use the predefined network simulation available in **FIcurve.hoc** in the **FIcurve** folder, or you can try to construct it yourself by writing your own *hoc* file.

If you are constructing your own neuron, then your code should construct a cell of type **SimpCell** using the **SimpCell** template (in **simpcell.hoc**) . Add an IClamp point process to the soma. Give it a delay of 0 msecs, duration of 100 msecs and an amplitude of 0.1 nA.

The exercise is to determine the firing rate response of this neuron to different magnitudes of current injection (which approximates a constant stream of EPSPs due to input from other neurons, which are not modelled). This is the **F-I curve** of our neuron.

Do the following:

1. Run **FIcurve.hoc** or your own **hoc** file in NEURON.
2. Bring up a PointProcessManager window (via Tools->PointProcesses->Managers), click SelectPointProcess and choose an APcount process. Then click Show and select Parameters. This point process will count the number of action potentials the neuron fires.
3. Open up the IClamp in a window (via Tools->PointProcesses->Viewers) and set the amp to 0.1 nA (if necessary).
4. Create a voltage graph for the soma (via Graph->Voltage axis).
5. Open a RunControl window (Tools->RunControl) and set Tstop to 100 msecs.
6. Press Init & Run in RunControl – this will run a simulation of stimulating the cell with the IClamp electrical current for 100msecs. The membrane voltage in the cell body over this time is plotted in the voltage Graph window.
7. Note the action potential count (n) in the PointProcessManager window (it may be zero!).
8. Increase the IClamp current amplitude (amp) by a small amount eg 0.1 nA, and repeat steps 6 and 7. Keep incrementing amp by, say 0.1 each time, then by larger amounts when you get bored! There is no need to go beyond an amp of 3.0.
9. Draw a sketch of amp (x-axis) versus n (y-axis).
10. **ALTERNATIVE** to steps 6-9 is to create a Grapher window in your GUI (Graph->Grapher) with the following settings:
    a. Indep Begin: 0; Indep End: 3; Steps 30
    b. Independent Var: IClamp[0].amp
    c. X-expr: IClamp[0].amp

d. Generator: run()
e. In the plot window, right-click and set “Plot what?” to APCount[0].n

Now you just need to press Plot in the Grapher window to run a number of simulations and automatically plot the complete F-I curve! You can try altering the number of current steps (Steps) and the length of simulation (Tstop in RunControl) to get a smoother curve.

Exercise 1.2: Type I and Type II F-I Curves

The Frequency-Current (F-I) firing curve of a neuron is classified as either Type I, if the frequency of firing increases smoothly from zero, once the firing threshold is reached, or as Type II, if the neuron suddenly starts firing with a finite frequency after the threshold.

Question 1.1: What is the type of the F-I curve of the neuron in exercise 1.1? (Looking at the figure below will help with answering this).

Answer:

In this exercise we will see that the presence or absence of particular ion channels in the membrane can determine the type of the F-I curve of a neuron. The code and GUI are already provided for you using the example code from the PCMN book.

Running the code:

To run the code associated with figure 5.9 in PCNM, open **FItypes.hoc** in NEURON (**after first rebuilding NEURON in the FIcurve folder**). This demonstrates Type I and Type II firing in a neuron, controlled by the presence or absence of the potassium A-type current.

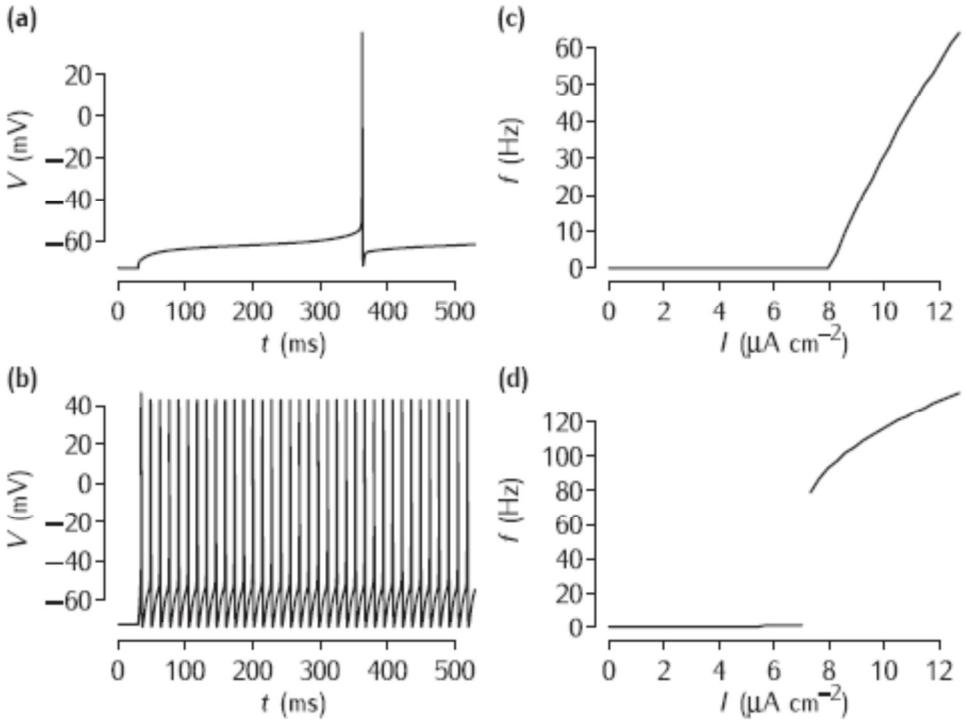


Figure 5.9: (a) First spike in a Type I neuron. (b) Start of spiking in a Type II neuron. (c) f-I curve for Type I. (d) f-I curve for Type II.

Once the simulation file is open, these are the steps to reproduce each panel in the figure above:

Panel (a)

1. In the top **Parameters** window, click on the checkbox next to **Type I parameters**
2. Click on **Set Type I threshold current**
3. Click on **Init & Run** in the **Run Control** window
4. The voltage plot corresponding to Panel (a) above is in Graph[0] in the GUI. The plot windows below this graph show sodium, potassium and leak conductances and current.

Panel (b)

1. In the top **Parameters** window, click on the checkbox next to **Type II parameters**
2. Click on **Set Type II threshold current**
3. Click on **Init & Run** in the **Run Control** window
4. The voltage plot should now look like Panel (b)

Panel (c)

1. In the top **Parameters** window, click on the checkbox next to **Type I parameters**
2. Click on **Plot** in the **Grapher** window
3. Simulations for a number of levels of current injection will be run and the firing frequency will be plotted against current in the **Grapher** window.
4. Once the simulations have run, to make sure you can see these results, right-click in this graph area and select **View... -> View = Plot**

Panel (d)

1. In the top **Parameters** window, click on the checkbox next to **Type II parameters**
2. Click on **Plot** in the **Grapher** window
3. Simulations for a number of levels of current injection will be run and again the firing frequency will be plotted against current in the **Grapher** window.
4. Once the simulations have run, to make sure you can see these results, right-click in this graph area and select **View... -> View = Plot**

Question 1.2: What cell parameters are different between the Type I and Type II examples?

Ans:

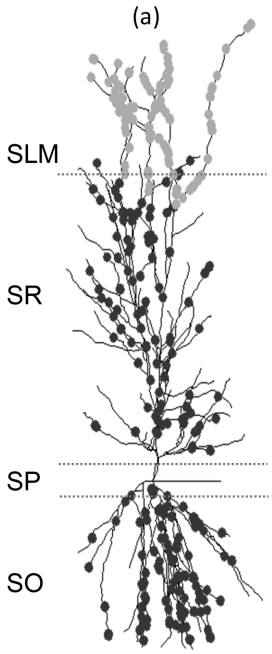
Question 1.3 (supplementary question for later research): Can you explain why the difference in firing characteristics arises?

Ans:

2. Electrical Activity in a Hippocampal CA1 Pyramidal Cell Model

In these exercises you will investigate electrical activity due to current injection and synaptic input in a detailed compartmental model of a hippocampal CA1 pyramidal cell. You will investigate the ability of synaptic input to generate simple spiking, bursting outputs and calcium spikes in the dendrites. You will also study the backpropagation of sodium spikes from the soma into the dendrites, a feature that is important for spike-timing-dependent plasticity (STDP).

The cell model is based on the morphology of an actual PC from a rat (see figure a), with membrane properties extended from the model of *Migliore et al, J Neurophys 94:4145-4155, 2005*. The morphology is divided into 337 electrical compartments (not counting spines). Spatially distributed ion channels consist of the following families: fast sodium (Na), delayed rectifier potassium (K), A-type K, h-current, HVA (putatively R-type) calcium (Ca) and Ca-activated, mAHP K. Na and KDR are distributed throughout the cell, but Na has a higher density in the axon and a lower density in the dendrites; it also has slower recovery from inactivation in the dendrites. K_A and h channels both increase in density with distance from the soma, with a saturating density beyond 350μm (the SLM region). Voltage-gated calcium channels (VGCCs: HVA R-type Ca) are distributed throughout the dendrites and spines with a fixed density. This is a restricted set of all the ion channels identified in CA1 PC membrane, but is sufficient to capture key features of the electrical excitability of the cell. Two distinct features are the ease of spread of signals throughout the dendrites (the electrical compactness) and the ability to generate nonlinear, threshold-gated signals, namely sodium and calcium spikes in the dendrites. Both features can be under the control of inhibition and neuromodulation in a single neuron so that different cell excitability may be obtained in different behavioural conditions. The model has been used in *Graham, Saudargiene & Cobb (2014) Neural Computation 26(10):2194-2222*, to study calcium transients in spine heads due to patterns of synaptic input.



Exercise 2.1: Back-propagating action potentials

In this exercise you will use electrical current injection in the cell body (soma) to initiate an action potential (AP) and then measure the AP amplitude as it travels back into the dendrites (back-propagation; note that a small length of axon is modelled along which the AP forward propagates to potentially reach synapses on other neurons, but we will not look at this).

1. Run the simulation by opening **run_PC.hoc** in the **CA1PC** folder in NEURON (**first rebuild NEURON in this folder**). A multitude of windows will appear. Three are "Shape" windows that display the cell morphology, with one of these showing example synapses with blue, red and yellow coloured dots and another with 3 red dots showing the recording locations of the membrane voltage plots (Graph[0], Graph[1] and Graph[2]). These Shape windows might be hidden by other windows so click on them to bring to the front and then move them to somewhere convenient.
2. We will only use a current injection input, so firstly set "Number" of synapses to 0 (instead of 500) for each dendritic layer (Synapses GUI: SR, SO, SLM; note that you must press the

Return key after setting the number to 0 for this change to be applied) to prevent synaptic input.

3. To generate a somatic AP, find the PointProcessManager window that contains IClamp[0]. If necessary, click Show and select Parameters. Then set IClamp[0] amp to 1.5 nA, to inject a small current into the soma after a delay of 50 msecs.
4. Right-click in the third "Shape plot" window (the one with no coloured dots) and select "Shape plot" (the very last menu option; you may need to move the window to actually see it). This will provide a visualisation of the membrane voltage throughout the entire cell when we run a simulation.
5. Click "Init & Run" in RunControl to run simulation for 200 msecs. Watch the “Shape plot” window to see a colour coding of membrane voltage (you can make this window larger to see it more clearly). Voltage traces will also appear in the three Graph windows.
6. In the Plots GUI, click “Dendrites” under "Max voltage plots" to see the peak membrane voltage in the dendrites as a function of distance from the soma.
7. Reduce the density of K_A channels in the dendrites to 0.01 mS/cm^2 in the "Ion Channels" GUI, rerun the simulation and replot the peak dendritic voltage to see what happens now.

Question 2.1: What was the effect of K_A on the ability of a somatic AP to back-propagate into the dendrites?

Ans:

Exercise 2.2: Synaptic input to SR

CA1 pyramidal cells get excitatory synaptic inputs from hippocampal CA3 pyramidal cells to their apical and basal dendrites in regions stratum radiatum (SR) and stratum oriens (SO). Here we will study the effects of such synaptic input to the SR apical dendrites. Do the following:

1. Set IClamp[0] amp to 0 to remove the somatic current injection; and also return the density of K_A channels in the dendrites to its original value of 0.03 mS/cm^2.
2. Set the number of synaptic inputs to stratum radiatum (SR) to 10. Inputs to these synapses activate postsynaptic AMPA and NMDA receptors which both contribute (with different time courses) to generating an excitatory postsynaptic current (EPSC), which depolarises the pyramidal cell and may lead to postsynaptic spike generation. Initially, the selected number of synapses will all receive one presynaptic stimulus at exactly 50 msecs.
3. Click “Init & Run” to run the simulation. Watch the third Shape window, which you set to be a “Shape plot” in exercise 1, to see the voltage changes throughout the cell. Then study the voltage traces in the three Graph windows: the top trace is from the cell body, the middle trace is from SR, and the bottom trace is from stratum lacunosum-moleculare (SLM).
4. You will see that 10 active synapses do not have a large effect on the pyramidal cell in this simulation. However, measure the amplitude of the EPSP in SR (Graph[1]) and the soma (Graph[0]) and **note these values in the table below**: you can do this by clicking-and-holding with the left mouse button on the voltage traces in these windows; the cursor will change to a cross and will follow the voltage trace as you move the mouse; the x and y coordinates are shown in the top window bar and indicate the time and voltage, respectively; put the cursor on the peak voltage response, read off the y value and subtract the resting value of -65 mV from this to get the amplitude.

Synapses:	10		50		100	
	Soma	SR	Soma	SR	Soma	SR
High K_A (0.03):						
Low K_A (0.01):						

5. Increase the number of activated SR synapses to 50 and rerun the simulation. Again, watch the "Shape plot" and when the simulation has finished, note the voltage traces in the Graph plots and extract and record the EPSC amplitude in the soma and in SR in the table.
6. Repeat this for 100 synapses.

Question 2.2: Approximately, what is the relationship between the number of stimulated synapses and the EPSC amplitude?

Ans:

7. Now run the simulation with 150 activated synapses. This summed input is large enough to generate an action potential in the pyramidal cell.

Question 2.3: Where in the cell is this action potential first generated?

Ans:

8. Repeat with 200 synapses.

Question 2.4: Now where in the cell is this action potential first generated?

Ans:

9. Repeat with 400 synapses.

Question 2.5: What is the cell's response now?

Ans:

10. Set the density of VGCCs (gCa-R) in the dendrites to 0 mS/cm^2 and rerun the simulation with 400 synapses.

Question 2.6: What characteristics of the VGCCs can you deduce from these simulations?

Ans:

11. Return the density of VGCCs (gCa-R) in the dendrites to 0.03 mS/cm^2 and now reduce the density of K_A channels in the dendrites to 0.01 mS/cm^2. Set the number of SR synapses to 10 and run the simulation, noting the EPSC amplitudes in the table.
12. Repeat this with 50 active synapses, again noting the EPSC amplitudes in the table.

Question 2.7: How do these EPSC amplitudes compare with when the K_A density was high?

Ans:

13. Now run with 100 active synapses and note what happens.

Question 2.8: What happens now? Design and run a simulation to test your conclusion.

Ans:

Exercise 2.3 (supplementary): Synaptic input to SLM

The very distal apical dendrites (the SLM region) of this pyramidal cell get excitatory inputs from the entorhinal cortex (EC). Given the distance of these inputs from the cell body, we might suspect that it will be difficult for them to cause a spiking output from this cell. On the basis of what you learnt about the SR inputs in exercise 2.2, design and carry out a set of simulations to determine under what cell configurations (in terms of the cell's membrane ion channel properties) inputs to SLM may cause this cell to fire an output action potential (ie one generated at the soma).

Question 2.9: What are your conclusions?

Ans:

Further exercises (supplementary):

There are many more things about synaptic integration and cell output you can test with this simulation. Feel free to carry out further simulations to explore:

- Inputs from CA3 to stratum oriens (SO)
- Multiple stimuli to each synapse at different frequencies (ie inter-stimulus intervals)
- Asynchronous inputs to groups of synapses

3. Simple Excitation-Inhibition (E-I) Oscillator

A network of two neurons forming an E-I oscillator is modelled.

Each neuron (defined in **simpcell.hoc**) contains a cell body that is a cylinder 30um in diameter and 30um long, and contains sodium, potassium and leak ion channels, and so can produce action potentials if stimulated to threshold. A 1000um long and 2um thick dendrite is attached to the cell body and is modelled as 11 compartments, each of which contains only leak ion channels.

The excitatory cell connects to a synapse on the dendrite of the inhibitory cell, and the inhibitory cell connects back to a synapse on the dendrite of the excitatory cell. There is a connection delay between each cell. The excitatory cell also is stimulated by a constant current injection to the cell body.

Network construction:

You can either choose to use the predefined network simulation available in **EIosc.hoc** in the **EIoscillator** folder, or you can try to construct it yourself by writing your own **hoc** file.

If you are constructing your own network, then your code should construct two cells of type **SimpCell** and connect them together as described above. The **SimpCell** template (in simpcell.hoc) contains suitable synapses to use and a procedure, **connect2target(..)** that can be called to construct network connections. Both connections should have a delay of 2 msecs; the excitatory connection should have a weight of 0.02 and the inhibitory connection a weight of 0.005. Create an **IClamp** current injection object situated in the soma of your excitatory cell. Give it a delay of 0 msecs, duration of 1000 msecs and an amplitude of 0.8 nA. It will also be useful to create a GUI **xpanel()** that allows you to change the connection weights and delays (have a look in **EIosc.hoc** if you need help with this).

The exercise is to determine the firing patterns of these two cells for different current injection amplitudes to the excitatory cell, different connection weights (excitatory and inhibitory) and different connection delays.

Do the following:

1. Use **EIosc.hoc** in the **EIoscillator** folder or your hoc file to run the simulation in NEURON.
2. Open up the IClamp in a window (via Tools->PointProcesses->Viewers) and make sure amp is set to 0.8 nA.
3. Create two separate voltage graphs, one for the excitatory cell soma and one for the inhibitory cell soma ("Graph->Voltage axis"; right-click on plot area and select "Plot what?", then "Show->Object refs" to select the cell somas; use the right-click Delete option to remove the v(.5) plot from your inhibitory cell graph).
4. Open a RunControl window and set Tstop to 1000. Press "Init & Run" – this will run a simulation of stimulating the excitatory cell with the IClamp electrical current for 1000msecs.
5. For this network configuration you should observe a characteristic oscillating firing pattern in both cells. Set the E->I weight to 0 and rerun to see what happens when the cells are not connected. Now reset the E->I weight to 0.02 before continuing to step 6.

6. This network behaviour is actually very sensitive to the current injection amplitude to the excitatory cell. Try changing amp in the IClamp window by small amounts, keeping within a range of between 0.6 and 1.0 nA.

Question 3.1: What different firing patterns emerge?

Ans:

7. Now reset the IClamp amp to 0.8. Try changing the E->I weight in the Weight window in a range between 0.01 and 0.08.

Question 3.2: Again, what different firing patterns emerge?

Ans:

8. Reset the E->I weight to 0.02. Try changing the I->E weight in a range from 0.004 to 0.02.

Question 3.3: What happens now to the firing patterns?

Ans:

9. Reset the I->E weight to 0.005. Try changing the E->I delay between 0 to 4 msecs.

Question 3.4: Again, what happens to the firing patterns?

Ans:

Question 3.5 (summary of results): What is the general behaviour of this circuit and how do the various parameters (weights, delays etc) affect this behaviour?

Ans:

4. Excitation-Inhibition Balance

The balance between excitatory and inhibitory inputs impinging on neurons strongly dictates their firing patterns and can lead to asynchronous firing in networks of neurons. In two exercises we explore the impact of such excitation-inhibition balance. The code is in the **EIbalance** folder.

Exercise 4.1: E-I balance in a single I&F neuron

This exercise runs the code behind figure 8.6 of PCNM that explores the firing characteristics of a single integrate-and-fire neuron being driven by a number of excitatory and inhibitory inputs. This was originally explored by Stein (*Biophysical Journal 5:173-194, 1965*). With a large, balanced number of excitatory and inhibitory inputs (NE=300, NI=150) the cell fires irregularly. With small excitation only (NE=18, NI=0) the cell fires at the same mean rate, but much more regularly.

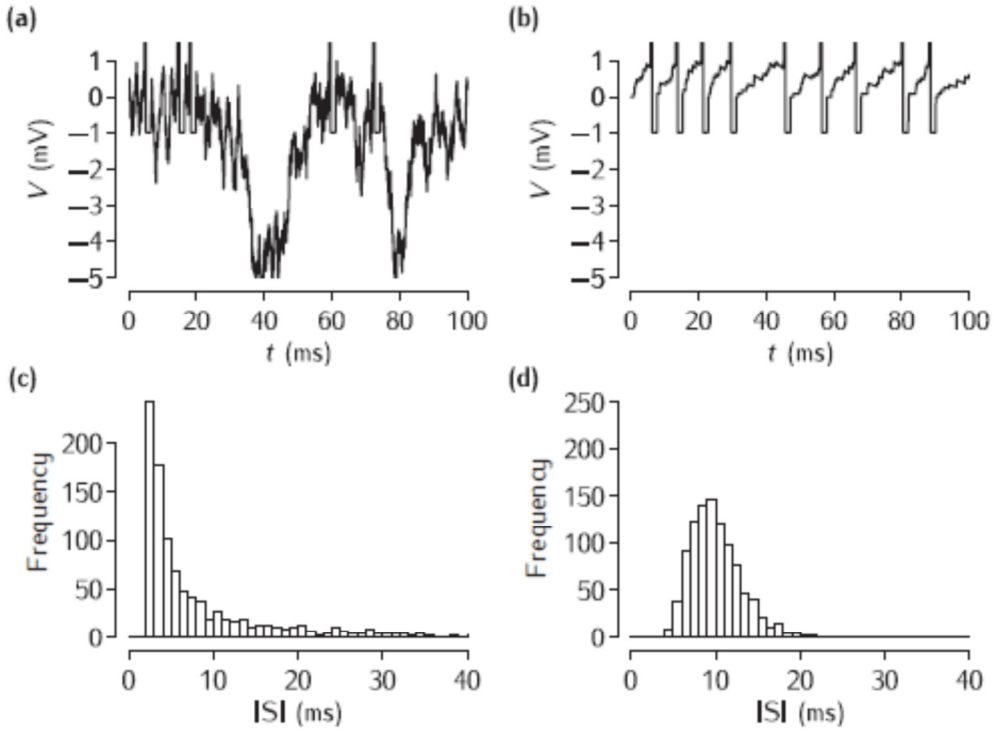


Figure 8.6 (a, c) Large, balanced excitation and inhibition (NE=300, NI=150). (b, d) Small excitation (NE=18, NI=0)

Running the code:

Run the code associated with figure 8.6 in PCNM by opening **EIbalance.hoc** in the **EIbalance** folder, in NEURON.

To reproduce the data behind panel **(a)** and **(c)**:

1. In the **RunControl** window click on **Init&Run**
2. A trace of the membrane potential appears in the top window and at the end of the simulation the histogram appears in the lower window.

To reproduce the data behind panel **(b)** and **(d):**

1. In the **Parameters** window change **NE** to 18 and change **NI** to 0.

2. In the **RunControl** window click on **Init&Run**.

Do the following:

Set the parameters to the large, balanced condition (NE=300, NI=150) and do the following:

1. Explore the effect of changing the strength of the excitatory and inhibitory inputs by changing **JE** and **JI** in the **Parameters** window. Make small changes to one or other input strength and note what effect it has on the regularity of firing. For each value of JE that you try, find a value of JI that results in (a) irregular firing, and a value of JI that results in (b) regular firing.
2. Return the strengths to their original values (JE=0.1, JI=-0.2). Now, in the same way, explore changing the number of excitatory and inhibitory inputs.

Question 4.1: How sensitive is irregular firing to the balance between excitation and inhibition?

Ans:

ADVANCED (supplementary): Examining the NEURON code

The code file corresponding to this simulation is **EIbalance.hoc**. You can load **EIbalance.hoc** into your favourite text editor to examine the code behind these simulations. This code demonstrates constructing I&F neurons as point processes (**IntFire1** in this case), and the use of **NetStim** objects to provide noisy spike trains as inputs. The strange part of this is that the I&F cell has to be inserted into a "dummy" compartmental neuron, but this "dummy" neuron takes no other part in the simulation. This is because NEURON was developed around the concept of simulating compartmental model neurons, and I&F point neurons have been added later to the simulator.

There is other interesting and useful code in this example, showing the use of vectors to collect spike times and calculate statistics, such as the distribution of interspike intervals. You should look up the NEURON documentation to find out more about the different components of this simulation.

Advanced Exercise (supplementary): You might like to explore the different I&F neuron models available with NEURON. The model used (**IntFire1**) contains only a single time constant for the membrane. The other two models available (**IntFire2** and **IntFire4**) introduce further time constants for synaptic inputs. As a further exercise you could try altering the code in **EIbalance.hoc** to use either of these I&F models instead, and explore the effect of synaptic time constants on the cell's firing characteristics. You will need to create a suitable graph to plot the I&F output eg. Plot **ifn.M** on a **state** graph.

Exercise 4.2: E-I Balance in a Network of I&F Neurons

This exercise runs the code behind figure 9.8 of PCNM that explores the firing characteristics of a network of integrate-and-fire neurons, based on the work of Amit & Brunel (*Network: Computation in Neural Systems 8:373-404, 1997*). The network contains randomly connected populations of excitatory and inhibitory neurons, which also receive external excitatory inputs. In an infinitely large network like this, with balanced excitation and inhibition, the cells should fire essentially randomly and uncorrelated with each other. In finite sized networks, as in the simulation, episodes of strong correlations in firing between groups of neurons appear. These become more evident the smaller the network.

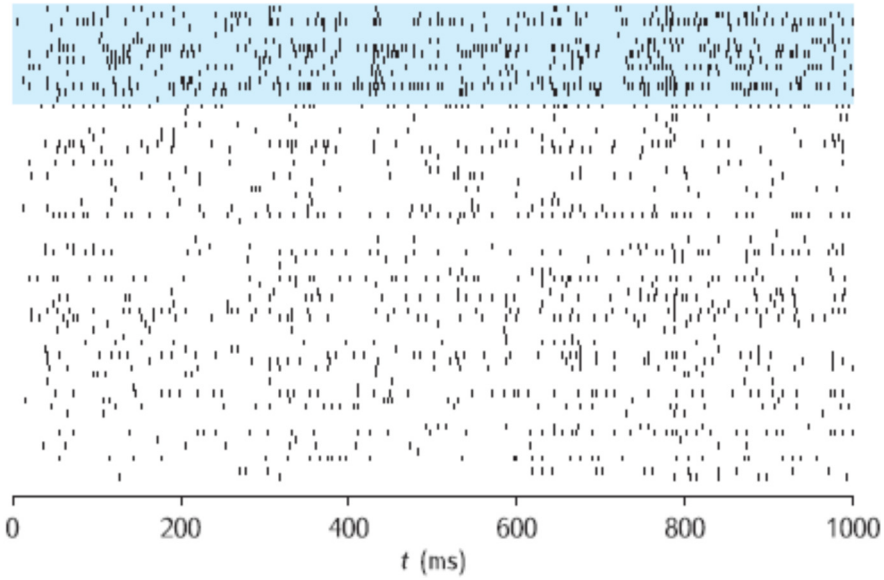


Figure 9.8 Raster plot of activity from 15 inhibitory (shaded at top) and 60 excitatory neurons exhibiting largely irregular firing.

Running the book code:

Run the code associated with figure 9.8 in PCNM by opening **EIbalnet.hoc** in NEURON (**after rebuilding NEURON first**). This simulation is set up to run a network of half the size (scale=0.5) of the network used to produce the results in the figure. It will still take several minutes to set up and run on a decent PC.

Do the following:

Try several smaller networks i.e. reduce the scale parameter below 0.5.

Question 4.2: How do the network firing characteristics change as the size of the network is reduced?

Ans:

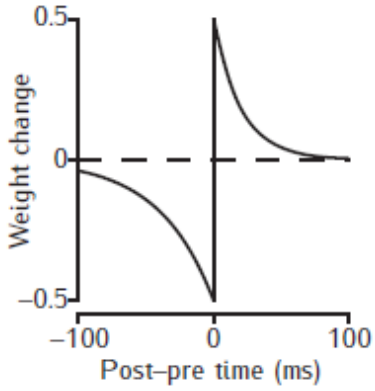
Examining the code:

You can load **EIbalnet.hoc** into your text editor to examine the code behind these simulations. This code provides an example of setting up a randomly connected network of neurons.

5. Spike-Time-Dependent Plasticity (STDP) in Action

There are two exercises to illustrate the effects of **spike-time-dependent plasticity** (STDP). They make use of a simple, saturating version of STDP implemented in **NMODL** in the file **stdpB.mod** in the STDP folder (equation 7.37 in PCNM with leading terms fixed at e_i=e_j=1):

$$\frac{dw_{ij}}{dt} = \epsilon_i \epsilon_j \left[(w^{\mathrm{LTP}} - w_{ij}) \sum_k A^{\mathrm{LTP}} \exp(-(t - \tilde{t}^{\mathrm{pre}})/\tau^{\mathrm{LTP}}) \delta(t - t_k^{\mathrm{post}}) \right.$$
$$\left. - (w_{ij} - w^{\mathrm{LTD}}) \sum_l A^{\mathrm{LTD}} \exp(-(t - \tilde{t}^{\mathrm{post}})/\tau^{\mathrm{LTD}}) \delta(t - t_l^{\mathrm{pre}}) \right].$$



This figure shows schematically the magnitude of the weight change as a function of the time the postsynaptic spike follows a presynaptic input. LTP takes place if the postsynaptic spike occurs after the presynaptic spike, with the magnitude of the weight increase decaying with a time constant of 17 ms. LTD occurs when the presynaptic spike follows the postsynaptic spike, decaying with a time constant of 34 ms.

Exercise 5.1: Phase precession of spike timing

In this exercise, a single neuron receives excitatory input from 10 spike trains through synapses that can undergo STDP. Each spike train consists of regular spikes spaced at 30 msec intervals. However, each spike train is offset by increments of 1 msec, so that the first spike in the 10th spike train occurs 10 msecs after the first spike in the first train. The individual EPSPs from the different spike trains summate, so that initially the cell fires its own action potential near the end of the sequence of spikes from all the inputs. Depending on the STDP parameters, the timing of this postsynaptic spike may evolve over the simulation, relative to the input spike times.

Do the following:

1. Run this simulation using **STDPtiming.hoc** in the **STDP** folder. Open a **Run Control** window and set **Tstop** to 200msecs. Create a voltage plot for the soma of the postsynaptic cell.
2. Press **Init&Run** to see the effect described above (you might want to make the voltage graph as big as possible).

Question 5.1: Do you see any change in the timing of the postsynaptic spike relative to the inputs over the course of the simulation?

Ans:

3. Plot the weights (press the **Plot weights** button in the **Weights & Delays** window) and ***note the pattern of weights across the inputs 0 to 9***. In this simulation, all the weights start at 0.012 and can saturate at a maximum of 0.12 (determined by the weight multiplier) and a

minimum of 0.0012 (determined by the weight divisor). Only LTP, and not LTD, is possible, with a potentiation rate of 0.05.

Question 5.2: What is the pattern of weights across the inputs 0 to 9?

Ans:

4. Try setting the depression rate to 0.2 and rerunning the simulation and replotting the weights.

Question 5.3: What differences can you see in the voltage trace and the weight distribution from previously?

Ans:

5. Try changing both the LTP and LTD rates individually and together to see if the "phase precession" effect on the postsynaptic spike is quicker or slower to emerge. You might need to run the simulation for more than 200msecs.

Question 5.4 (summary): How and why does the timing of the postsynaptic spike change, and why does a pattern emerge of weights across the different inputs?

Ans:

Exercise 5.2: Sequence learning

In this exercise, 10 neurons are connected all-to-all by excitatory synapses that can undergo STDP. Each cell also receives a single external input that is strong enough to make it fire its own AP. These external inputs arrive at an interval of 10 msecs, so that the cells in the network fire in sequence at 10 msec intervals. The connections between cells are set to a weak value (0.001) so that they do not cause the receiving cell to fire. Nonetheless, STDP will change the strength of these synapses depending on the spike times of the cells. The aim of the exercise is to see what pattern of connection weights develops over time as the cells spike in sequence.

Do the following:

1. Run this simulation using **STDPnetseq.hoc**. Open a **Run Control** window and set **Tstop** to 1000 msecs.
2. Create a voltage plot that will plot the voltages from each of the 10 cells (or at least the first few cells) in a different colour on the same plot.
3. Press **Init&Run** to run the simulation for 1000 msecs.
4. The Shape window contains a color matrix representation of all the connection weights. Initially they are all the same. Once your simulation has finished, click the Update plot button, then resize the Shape window a little to get it to actually refresh the colours. Each column shows the weights of the connections a neuron makes to all others in the network, working from the bottom up. The hotter the colour, the stronger the connection.

Question 5.5: Can you see a pattern in the weights that have developed across the neurons?

Ans:

5. The initial simulation contains only LTP. Set the depression rate to 0.2 as well and rerun the simulation. Update the Shape window as above.

Question 5.7: Can you see any difference in the pattern of weights now?

Ans:

6. Try different LTP (Potentiation) and LTD (Depression) rates.
7. Try also changing the delay between successive inputs.

Question 5.8: How do you think this delay might interact with the time windows of LTP and LTD (see the STDP figure above)?

Ans:

Question 5.9 (summary): What patterns of weights emerge? Can you explain why? And how do the patterns vary with different rates of LTP and LTD and with different delays between spikes?

Ans:

Advanced (supplementary) exercise:

Try changing the inputs to each cell so that they are noisy spike trains with no particular phase relationship to each other (change the "start" and "noise" values for each input NetStim object). Also make them such that a few of the cells get high frequency input (around 100 Hz) while the others get much lower frequency input (eg 20 Hz). Run simulations of this with both LTP and LTD rates set at various values, and examine the weight matrix that results. ***Do the faster firing cells become more strongly connected to each other?***

6. Associative Memory in a Network of Spiking Neurons

This exercise runs the code behind figure 9.10 in PCMN that explores autoassociative recall of stored patterns in an associative memory neural network. The network consists of 100 two-compartment Pinsky-Rinzel neurons connected by all-to-all excitatory and inhibitory connections. Stored patterns consist of a random selection of 10 active neurons from the network population of 100 excitatory neurons. Fifty patterns have been stored in the network by binary Hebbian learning.

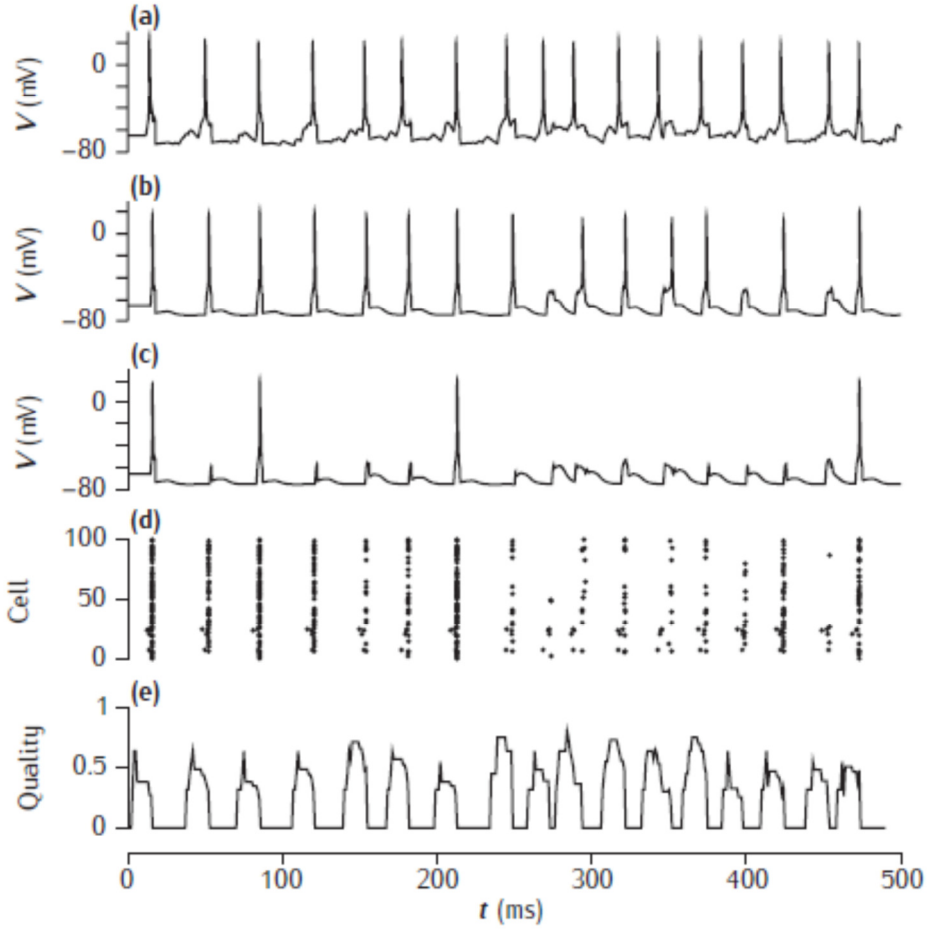


Figure 9.10 (a) Example cue cell. (b) Pattern cell. (c) Non-pattern cell. (d) Raster plot of all cells. (e) Quality of recall.

Running the code:

To run the code associated with figure 9.10 in the book, rebuild NEURON in the **AssocMem** folder and then run **AssocMem.hoc** in NEURON. This runs a simulation in which 4 of the cells in one of the stored patterns are made active by external 500Hz excitatory input. Hopefully the network activity will largely be the recall of the entire stored pattern. Actually, recall is not perfect: all the pattern cells do fire regularly (eg top two voltage plots), but there is also occasional activity of neurons who do not belong to the pattern (eg third voltage plot). Click **Spike Plot** to see a raster plot of the entire network activity.

Do the following:

1. Try reducing the inhibitory weight by small amounts. You should start to see more spurious (non-pattern) cells firing, but they will tend to fire later than the pattern cells. Additionally, the pattern cells will start to fire in bursts.
2. Return the inhibitory weight to its original value, and try changing the inhibitory delay instead. What happens?
3. Try changing the excitatory weights and delays as well.

Question 6.1: How sensitive does pattern recall seem to be to these network parameters?

Ans:

Examining the code:

You can load **AssocMem.hoc** into your text editor to examine the code behind these simulations. Then you can edit **AssocMem.hoc** to make changes to the simulation (suggested exercises below).

Advanced (supplementary) exercise:

Try changing the cue pattern (CPATT) and/or the number of cue cells (CFRAC; the default value of 0.3 results in 4 from 10 cells being selected for the cue) by editing these values in **AssocMem.hoc** and then running the new simulation. The default voltage plots may no longer be for pattern and non-pattern cells as before – you can examine the stored patterns by loading **pattsN100S10P50.dat** into your text editor and trying to find indices of pattern cells to plot in your voltage graphs.

Very advanced exercise:

If you want a real challenge, implement inhibition in this network with an explicit population of inhibitory interneurons (rather than have direct inhibitory connections between the excitatory cells). Any simple model spiking cell eg simpcell.hoc or an I&F model, would be suitable to use for your inhibitory neurons.