Introduction to NEURON(90 Mins):

Contents

(Thanks to David Sterratt for the use of some images from his set of NEURON tutorials)

Introduction

Who am I

- I am not a NEURON guru
- 3rd year Ph.D student (4 years using NEURON for modelling work)
- Teaching-Assistant for Neural-Computation course at Edinburgh Uni
- One of the developers of NineML (incl. NEURON interface)
- Author of *morphforge* - a high-level interface to NEURON in python

Why use NEURON (5-10 mins)

From the NEURON website (my bold type):

- is a flexible and powerful **simulator of neurons and networks**
- has important advantages over general-purpose simulators helps users **focus on important biological issues** rather than purely computational concerns
- has a convenient user interface
- has a **user-extendable** library of biophysical mechanisms
- has many enhancements for **efficient network modeling**
- offers customizable initialization and simulation flow control
- is widely used in neuroscience research by experimentalists and theoreticians
- is well-documented and **actively supported**
- is **free, open source**, and runs on (almost) everything

Use-cases - What does it do? I

- Modelling of multicompartmental neurons in which membrane voltage is calculated from ion flows across the membranes
- Connections between cells through synapses (chemical & electrical)
- Defining your own channels & synapses
- If you are interested in large networks of 'simple', single compartement neurons, there are other options.

Use-cases - What does it do? II

- For a single compartment cell with simple HH dynamics, you can probably write your own solver using ODE solvers in matlab/python.
- As your models develop more complexity:
  - Current dependancies e.g. intracellular Ca2+ dependant K channels
  - Incoorperation of the cable equations for multicompartmental neurons
  - Connections via synapses & gap junctions (synaptic delays)
- You may find that you are reimplementing lots of mathematical solving, which has been already been done efficiently in NEURON.
- MOD files provide a standard for exchanging channel descriptions (e.g. modeldb)
- NEURON is highly parallelisable (e.g. BBP) for large networks
- There is a python interface

What do i need to use it?

- It runs on most operating systems (Windows/Linux/Mac). On the NEURON website: - Windows installer - Mac package - Linux .deb, .rpm package
- Eilif Muller has precompiled binaries including Python support http://neuralensemble.org/people/eilifmuller/software.html

Resources

- Active questions board
- ModelDB
- The NEURON Book

Basics of NEURON (20-25 mins)

Overview

- NEURON is complex (I will cover a lot of material in the next slides, don't worry if you don't remember all the details - its the concepts that are important)
- NEURON is old (& built on even older software)

2 Parts: HOC and NMODL files

- Two main types of language:
  - Interpreted languages (Python/matlab) are interactive, but slow
  - Compiled languages (Fortran/C/C++/...) are fast, but not interactive
- NEURON uses both:
  - 'HOC' - which controls the 'structure' of the simulation
  - 'NMODL' - a compiled language for specifying the dynamics of channels/synapses (e.g. Hodgkin-Huxley type channels). We will not cover NMODL in this tutorial.

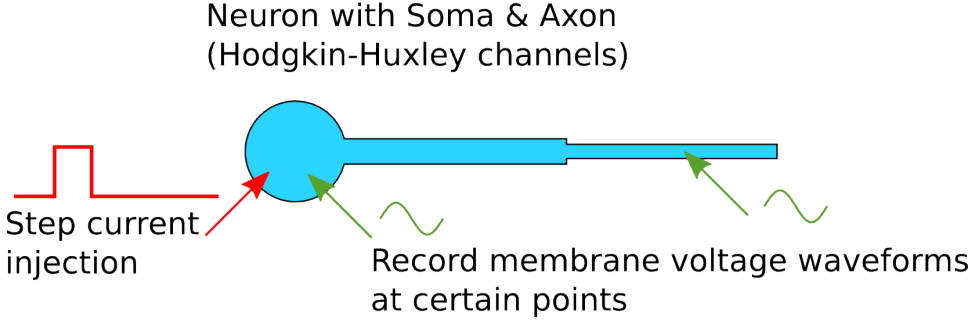
HOC Interpreter

- HOC is an interactive interpreter which controls the 'structure' of the simulation:
  - creating morphologies
  - defining which channels to apply and changing certain parameters (channel densities)
  - creating stimuli: current clamps, voltage clamps
  - defining what you want to record: voltages, internal states
  - setting simulation parameters: stimulation time-steps,
  - running the simulation

```
oc> /*type commands here*/
```

Example Simple simulation: Soma + Axon, HH Channels, with current injection

- We will walk through the steps required to simulate a neuron, which has as soma and an axon, stimulate it with a current clamp, and visualise the somatic membrane voltage.



HOC - Graphical User Interface

NEURON can be used entirely from the commandline and with 'scripts':

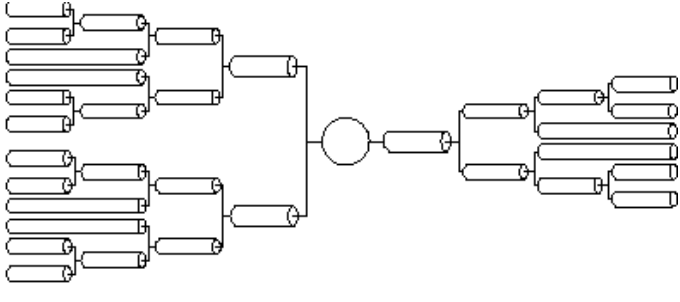
```
$ nrnoc
oc>
```

NEURON also has a graphical user interface:

```
$ nrngui
oc>
```

Morphologies I (Overview)

- Neuron morphologies are represented as a tree of 'unbranched cylinders' called 'Sections' which describe the 'gross' morphology of the neuron.
- E.g.



Morphology II (Building & Connecting Sections)

- 'Sections' are created with the *create <name>* command
- Section are connected together with the *connect* function.
- '0' defines one end of the Section, '1' defines the other.
- **L**ength and **diam**eter of the sections are set as properties for each section.

```
// Create 3 Sections:
oc> create soma
oc> create axon_proximal
oc> create axon_distal

// Setup the sizes of each Section:
oc> soma L = 12.3
oc> soma diam = 12.3

oc> axon_proximal diam = 1.0
oc> axon_proximal L = 50
```

```
oc> axon_distal diam = 0.5
oc> axon_distal L = 20

// Setup the connections:
oc> connect soma(1.0), axon_proximal(0.0)
oc> connect axon_proximal(1.0), axon_distal(0.0)

// (Mysterious line explained later)
oc> access soma
```

Morphologies III (Segmentation)

- NEURON separates the description of the overall morphology from the amount of discretisation of the simulation.
- To solve simulations more accuratly, Sections can be subdivided into 'segments'.
- Each segment has its own voltage and state variables
- (Hines & Carnevale recommend using an odd number of segments)

```
oc> axon_proximal nseg = 11
oc> axon_distal nseg = 3
```

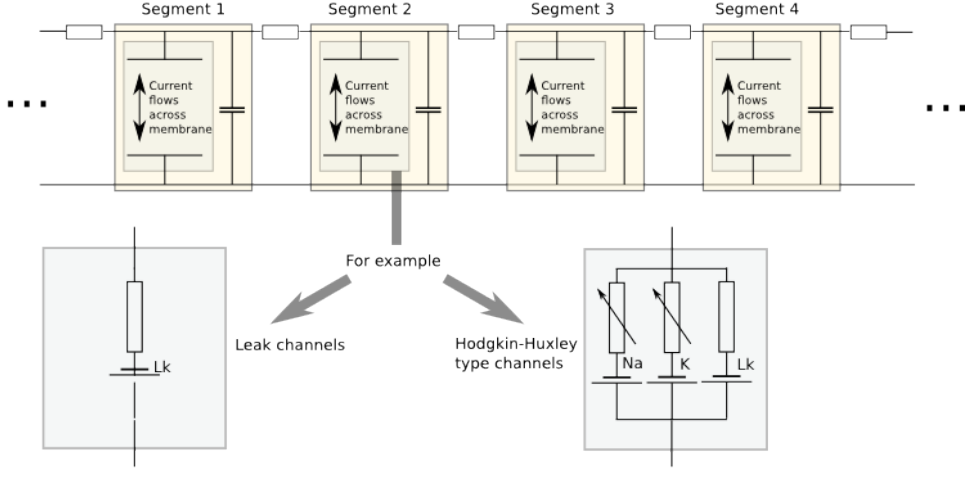
HOC: *psection()*

```
oc>forall psection()
soma { nseg=1  L=12.3  Ra=35.4
    axon_proximal connect soma (1), 0
    /* First segment only */
    insert morphology { diam=12.3}
    insert capacitance { cm=1}
}
axon_proximal { nseg=11  L=50  Ra=35.4
    axon_distal connect axon_proximal (1), 0
    /* First segment only */
    insert morphology { diam=1.0}
    insert capacitance { cm=1}
}
axon_distal { nseg=3  L=20  Ra=35.4
    /*location 0 attached to cell 0*/
    /* First segment only */
    insert morphology { diam=0.5}
    insert capacitance { cm=1}
```

Channels I (Overview)

- Neurons are interesting because of their active membrane channels
- Channels define the currents flowing across the membrane (e.g. sodium, potassium, leak)
- NEURON covers common use-cases:
    - it is possible to define your own using NMODL files (not covered here)
    - it comes with some predefined channel definitions.
- NEURON automatically inserts a membrane capacitance and an axial resistance

Channels II (Segments)



Channels III (Using channels)

- Channels are *insert*ed into each Section
- Channels can have parameters that can be changed in HOC, (e.g. conduction density)
- E.g.

```
// Insert the channel into the soma Section
oc> soma insert hh

// View and change some properties:
oc> soma.gnabar_hh
    0.12
oc>soma.gnabar_hh = 0.2
```

Channels IV (Summary):

```
oc> soma psection()
soma { nseg=1  L=12.3  Ra=35.4
    axon_proximal connect soma (1), 0
    /* First segment only */
    insert morphology { diam=12.3}
    insert capacitance { cm=1}
    insert hh { gnabar_hh=0.2 gkbar_hh=0.036 gl_hh=0.0003 el_hh=-54.3}
    insert na_ion { ena=50}
    insert k_ion { ek=-77}
}
```

Stimuli (Overview)

- NEURON is very flexible in the stimulation protocols that can be used
- Most commonly used are:
    - Current Clamp (*IClamp*)
    - Voltage Clamp (*SEClamp*, *VClamp*)

Stimuli (Current Clamp)

- For example, a current clamp called 'stim' at the centre of the soma:

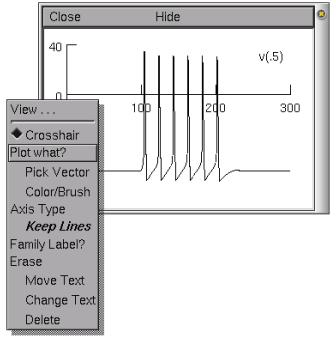
```
oc> objref stim
oc> soma stim = new IClamp(0.5)
oc> stim.del = 100
oc> stim.dur = 100
oc> stim.amp = 0.1
```

Running the simulation

- NEURON simulations are run:
  - with the 'run()' command from *.hoc*
  - clicking 'Init & Run' from the GUI
- By default, running the simulation will not plot anything....

Plotting the results

- We want to plot the internal states of the simulation (e.g. membrane voltage, current flows, state variables)
- This is easiest done by using the NEURON GUI
- (It is also possible to save results to file using code)



Exercises (45 mins)

- We will work through the tutorial from David Sterratt and Andrew Gillies.
- Section **A:** investigates a single compartment neuron containing HH channels, stimulated with a current clamp
- Section **B:** extending this to a multicompartmental neuron
- These can be found at: *http://www.anc.ed.ac.uk/school/neuron/*

Wrap Up (10 mins)

Useful things to know about NEURON

- *nrnivmodl* is a tool that is used to compile all the .mod files in your local directory, so they can be used in HOC.
- NEURON is contains an 'adaptive-timestep' integrator, which can dramatically improve simulation time in some circumstances. This is enabled simply by adding *cvode_active(1)* before calling *run()*
- NEURON has a python interface. This allows you to use the hoc Interpreter from within Python, and access stored data as numpy-arrays.

Competitors to NEURON

- other simulators - GENESIS, MOOSE

Other Tools in the ecosystem

- other options; morphforge, neuroml, nineml, neuronvisio, pynn;
- Links to other tools