

Introduction to NEURON(90 Mins):

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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 compartment 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 Ca^{2+} dependant K channels
 - Incorporation 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.

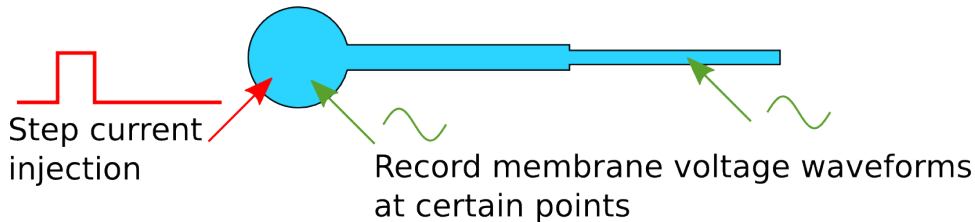
HOC Interpreter

- 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

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.

Neuron with Soma & Axon
(Hodgkin-Huxley channels)



HOC - Graphical User Interface

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

```
$ nrnoc  
oc>
```

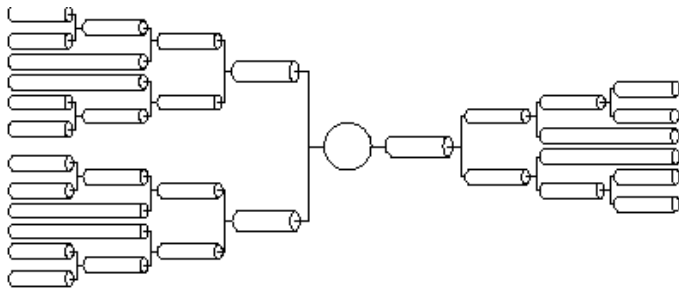
NEURON also has a graphical user interface:

```
$ 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.
- **Length** and **diameter** 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_proximal diam = 0.5
```

```
oc> axon_proximal L = 20
```

```
// Setup the connections:
```

```
oc> connect soma(1.0), axon_proximal(0.0)
```

```
oc> connect axon_proximal(1.0), axon_distal(0.0)
```

Morphologies III (Segmentation)

- NEURON separates the description of the overall morphology from the amount of discretisation of the simulation.
- To solve simulations more accurately, 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_proximal nseg = 3
```

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.

Channels II (Examples)



Channels III (Using channels)

- Channels are *inserted* 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> create soma
oc> soma insert hh

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

Summarising Cells:

```
oc> soma psection()  
    // displays details about 'soma'  
  
oc> forall psection()  
    // displays details about all sections
```

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:

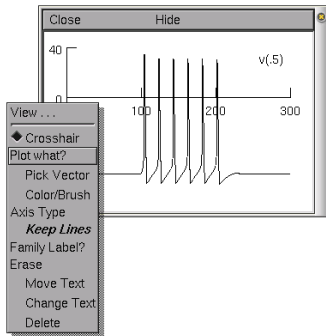
```
oc> objvar stim
oc> soma stim = new IClamp(0.5)
oc> stim.del = 100
oc> stim.dur = 100
oc> stim.amp = 0.1
```


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 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
- More things with NEURON: *nrnivmodl*, *cvode*,
- Interfacing with Python (limitations)
- other simulators - GENESIS, MOOSE
- other options; *morphforge*, *neuroml*, *nineml*, *neuronvisio*, *pynn*;
- Links to other tools