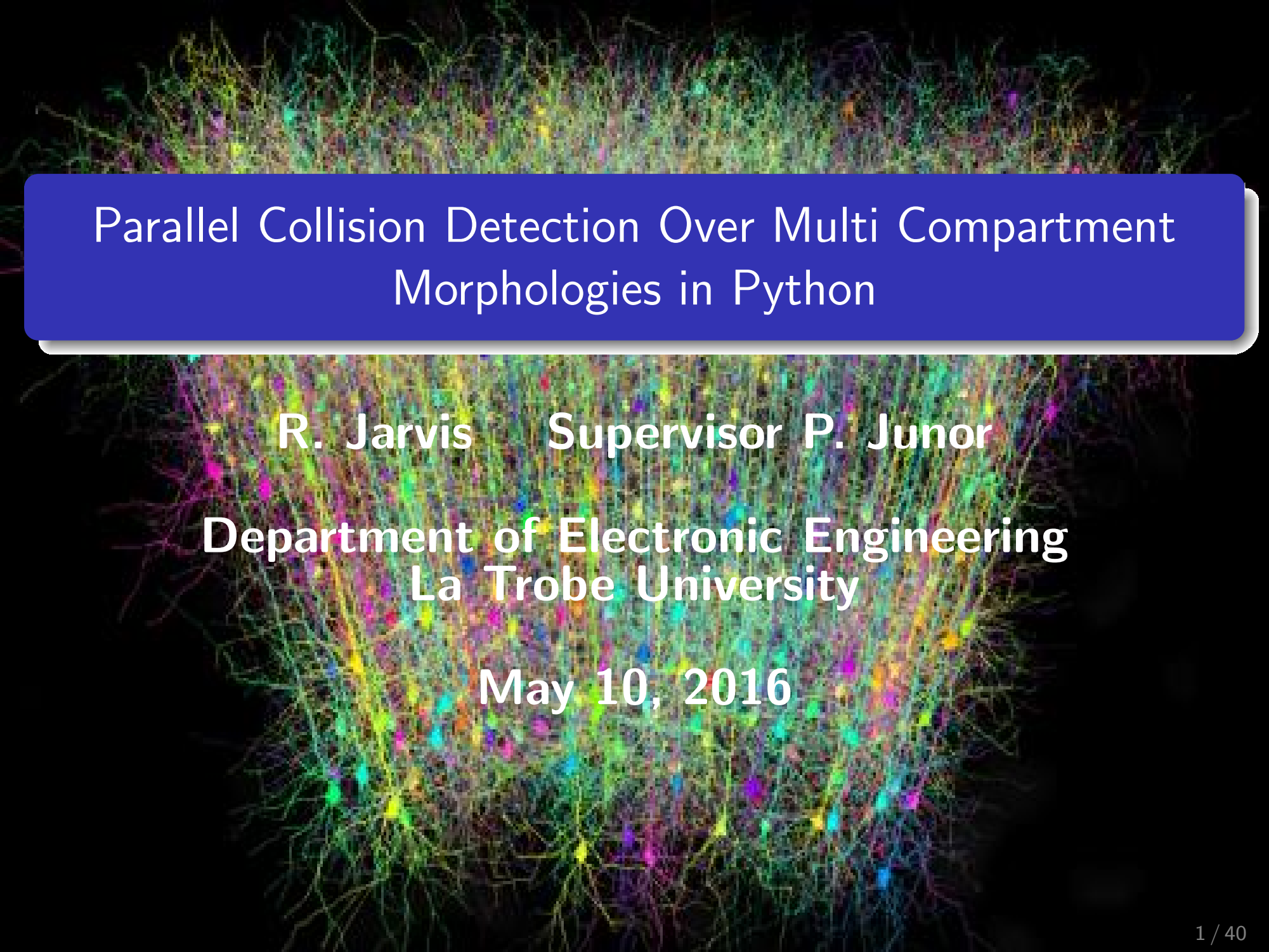


Parallel Collision Detection Over Multi Compartment Morphologies in Python

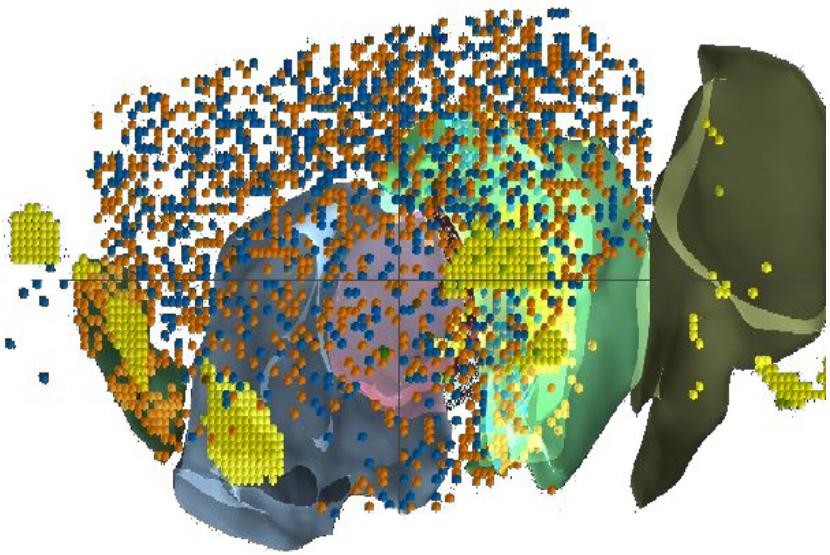
R. Jarvis Supervisor P. Junor

Department of Electronic Engineering
La Trobe University

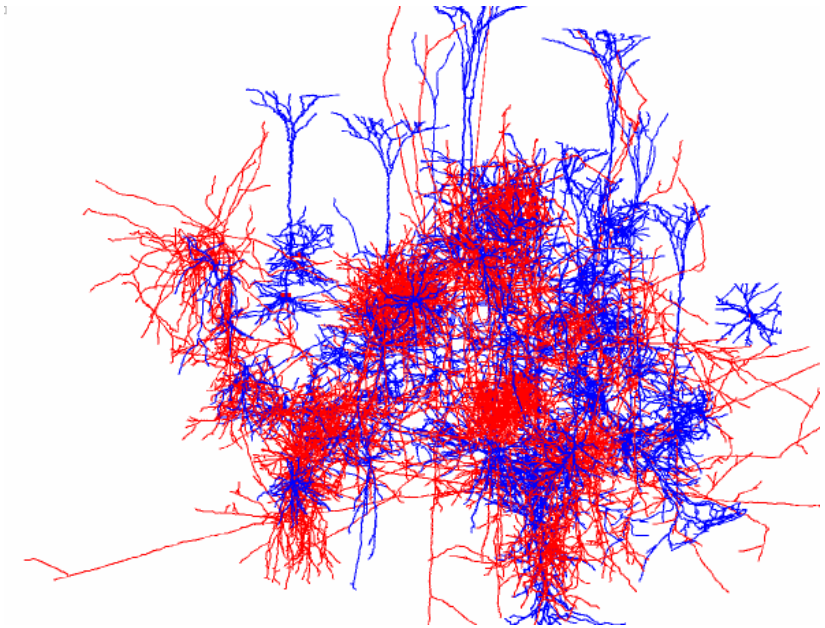
May 10, 2016

Introduction

- Made with NEURON-7.4 as a Python module.
- Why did I do this, given the difficulty in staining many adjacent neurons
- Neuromorpho data largely comes from different rodents in different labs.
- Many of the atlas ontologies (neurons) are normalised onto one brain atlas (Allen Brain Atlas)



$100mm^3$



μm^3

http : //neuromorpho.org/neuroMorpho/LSVideo.jsp

Motivation: Looking to a Future including Network Reconstuction

- Why did I do this? I was inspired by the Blue Brain Project to find out more about real neural networks. Although this is maybe premature.
- Light Sheet microscopy, brainbow, and STED may make it possible to digitally reconstruct neural forest structure as opposed to singular trees.
- The Neuromorpho derived morphologies where acting as place holders NeuroMAC is currently able to grow realistic 3D neuron forests in silico, using a forest shapes the trees approach to neural dev.
- The Human Brain Project has recently been open sourced, The Open Brain Project uses a mix and match to creating neuron morphologies

```
1 https://bbp.epfl.ch/nmc-portal/microcircuit
```

Motivation: What we could understand with network reconstruction

- Reduced neuropil hypothesis. Atrophy of neural forests is observed in hippocampus and cortex.
- Does reduced electrotonic distance change firing dynamics more than reduced connectivity of networks caused by the atrophy of synapse locations.
- Allen Brain has recently acquired gene expression based connectivity maps that may map to selected to the coordinates comprised by SWC files.

From Reconstructed Cells to Reconstructed Networks.

- In order to move from reconstructed Cells to reconstructed networks, one must connect neurons in a biologically informed way. Spatial and anatomical data from the Allen Rodent Brain Atlas, is used to inform cell centre position and synapse polarity.

- Neurons are connected by conducting an exhaustive search in the neural volume for near contact points and allocating a network connection to the intervening synapse cleft.

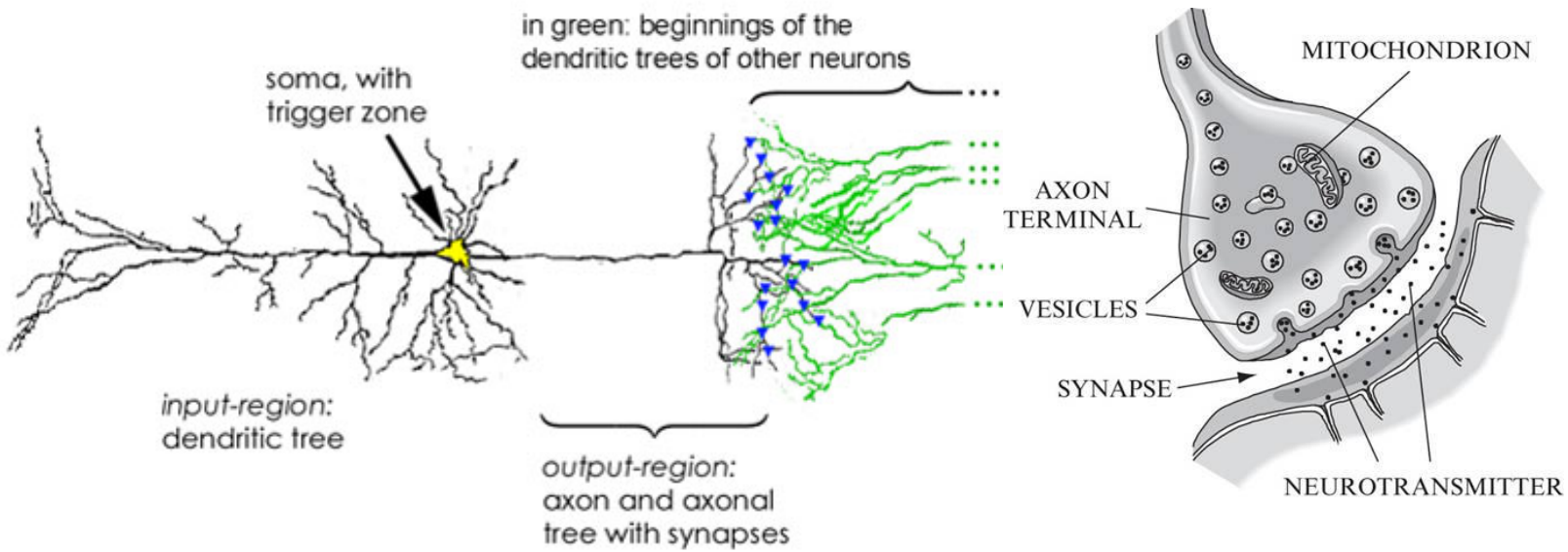
Types of Data

- 3D structure SWC files.
- Spike times for cell indexs -¿ raster plots.
- From Raster Plots you can move to Spike Distance
- Transfer Entropy.
- Ajacency matrices, sometimes population specific.
  - Ajacency matrices, Indexs are sorted before
  - Displaying as a chord diagram
- Membrane potential traces.

(sources:) http://www.igi.tugraz.at/maass/129/129a.htm

Pre and Post Synapses

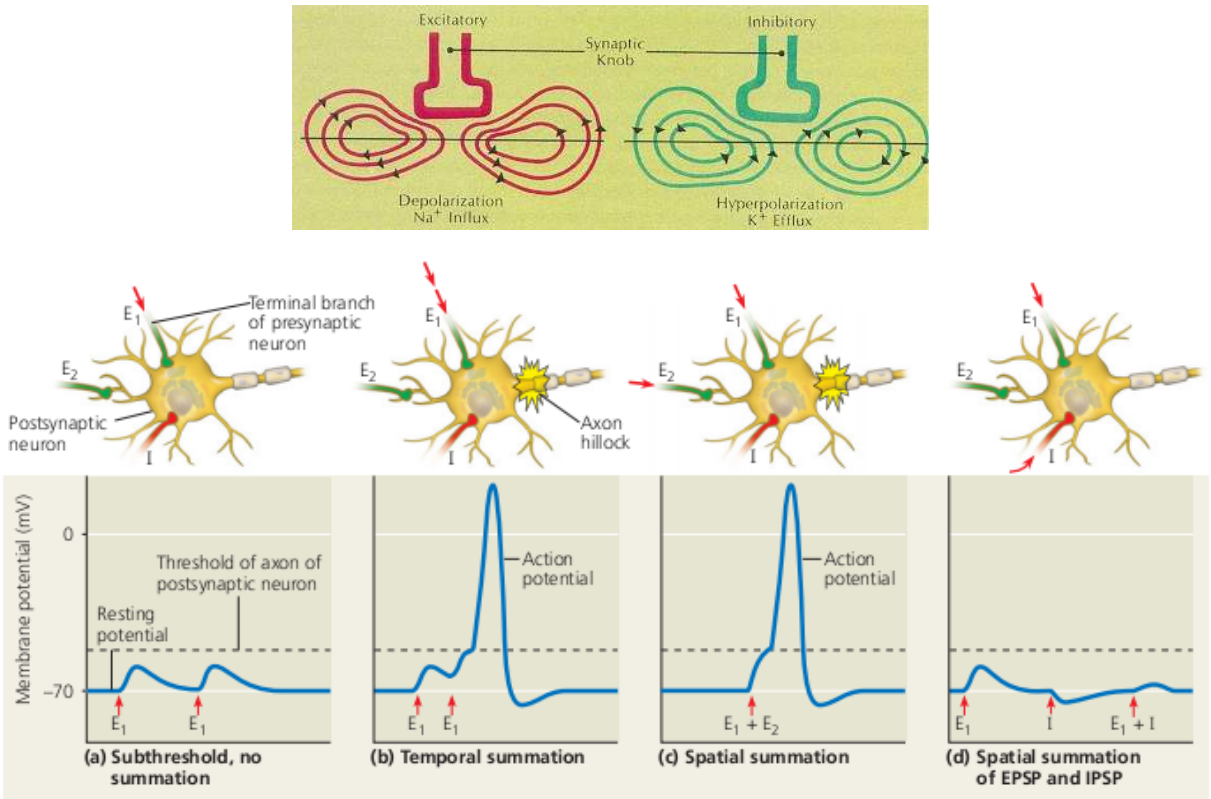
- In most what follows I will be referring to pre synaptic locations and post synaptic locations.



(sources:) http://www.igi.tugraz.at/maass/129/129a.htm

EPSP and IPSP

- Some people think of neurons as analog input digital output.
- One or more IPSPs can prevent a spike from occurring, by depressing the membrane potential.

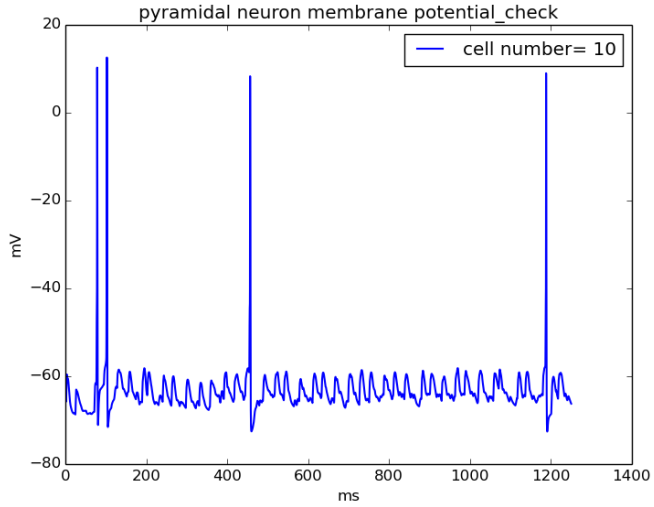


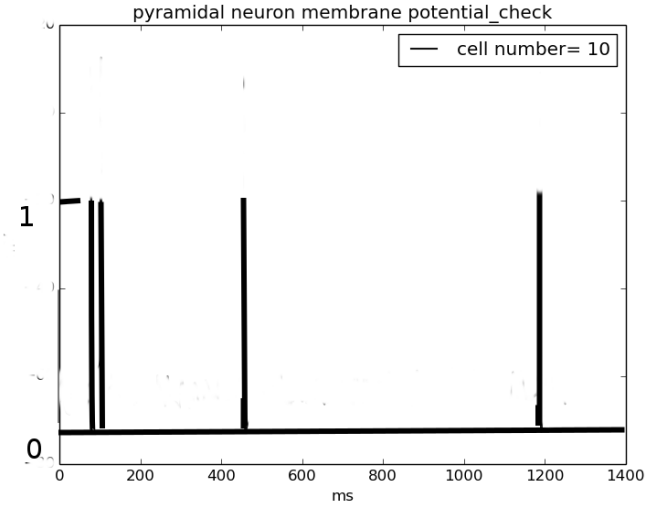
▲ **Figure 48.17 Summation of postsynaptic potentials.** These graphs trace changes in the membrane potential at a postsynaptic neuron's axon hillock. The arrows indicate times when postsynaptic potentials occur at two excitatory synapses (E_1 and E_2, green in the diagrams above the graphs) and at one inhibitory synapse (I, red). Like most EPSPs, those produced at E_1 or E_2 do not reach the threshold at the axon hillock without summation.

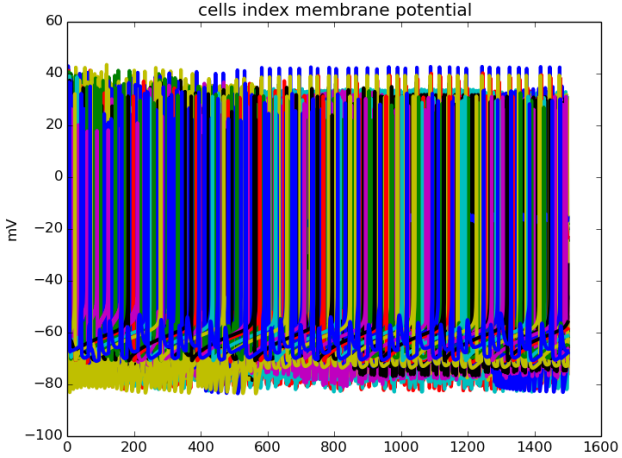
(sources:) http://www.cerebromente.org.br/n12/fundamentos/neurotransmissores/neurotransmitters2.html
http://www.studyblue.com/notes/note/n/chapter-48-nervous-system/deck/4169450

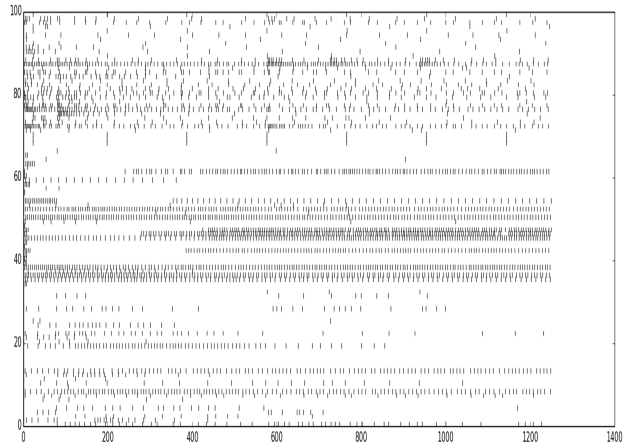
Pre Processing Signals: Spike Trains

- Continuous membrane potential thresholded, the times each neuron fires is stored. Time binning makes signal coarse grained.

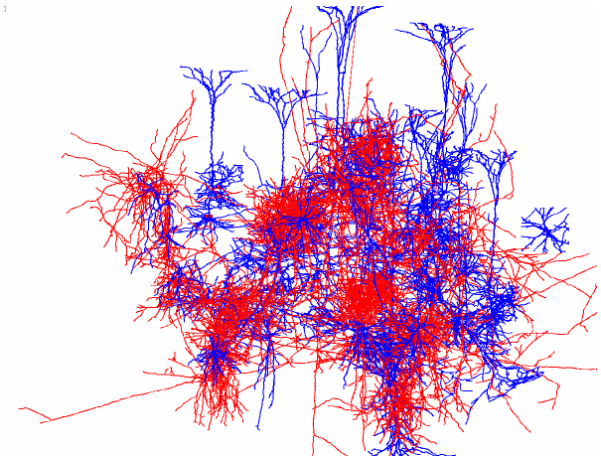








Connectivity and the Adjacency Matrix.



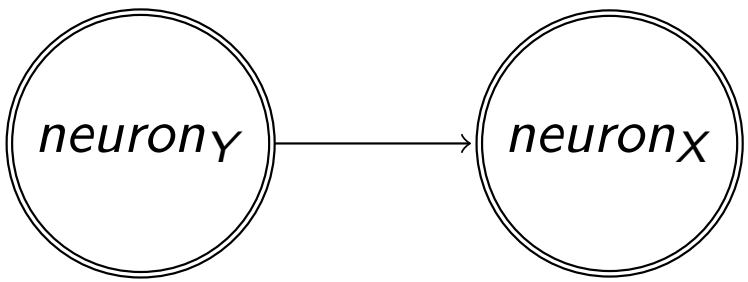
I$\rightarrow$E=2073, $fb_1 - = 1081$

Information In the Spike Train

- The number of spikes per bin: Δt is the source of uncertainty in the spike train.
- There are two major sources of information:
- 1st the external input (sensory).
- 2nd sources of variability that are intrinsic to the brains dynamics.

An Interpretation of Information Flow:Prediction

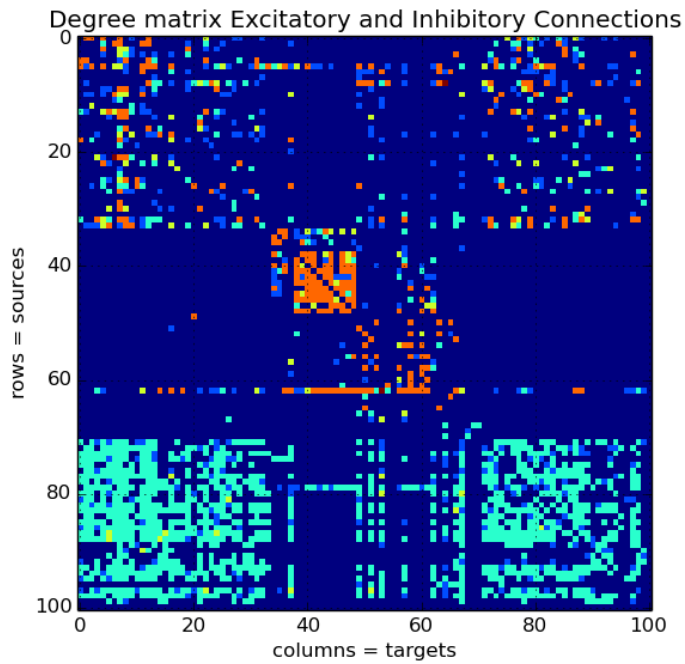
- Using Transfer Entropy we can say that $neuron_Y$ influences $neuron_X$ if $neuron_Y$'s past activity reduces the uncertainty about $neuron_X$'s future activity.



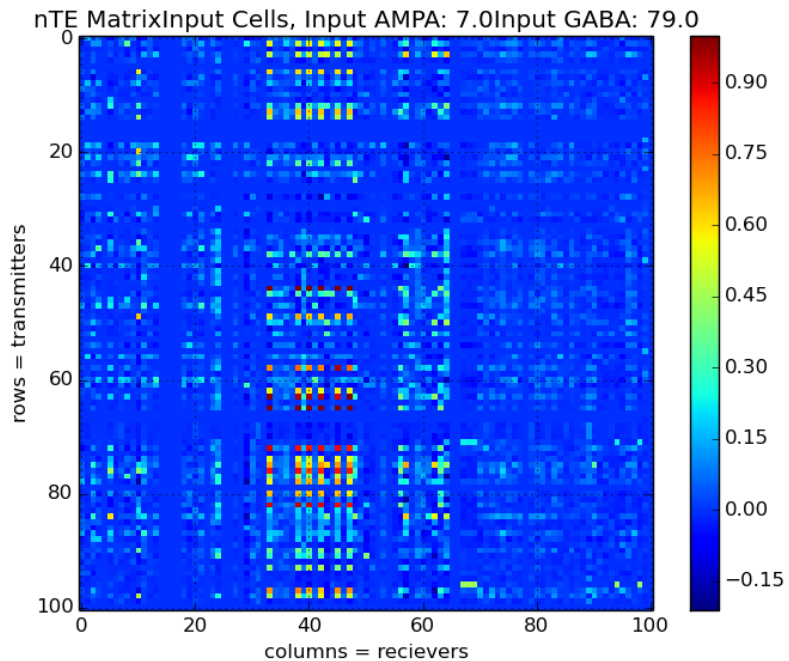
- When a particular type of entropy (uncertaintity) is reduced prediction is increased.

Resulting Information Flow

- One cell can predict another cells activity acting through intermediate neurons
- A reduction in firing probability still represents an information transmission influence.



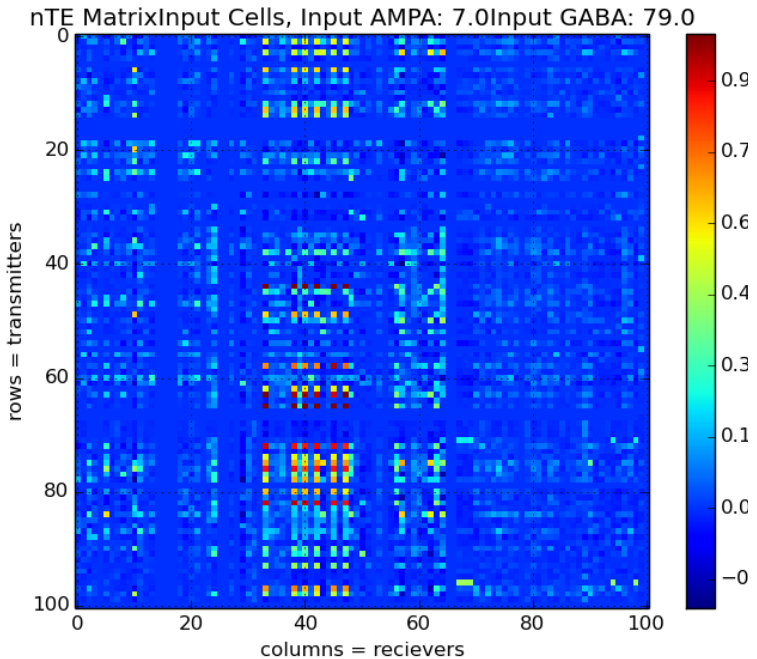
Connectivity



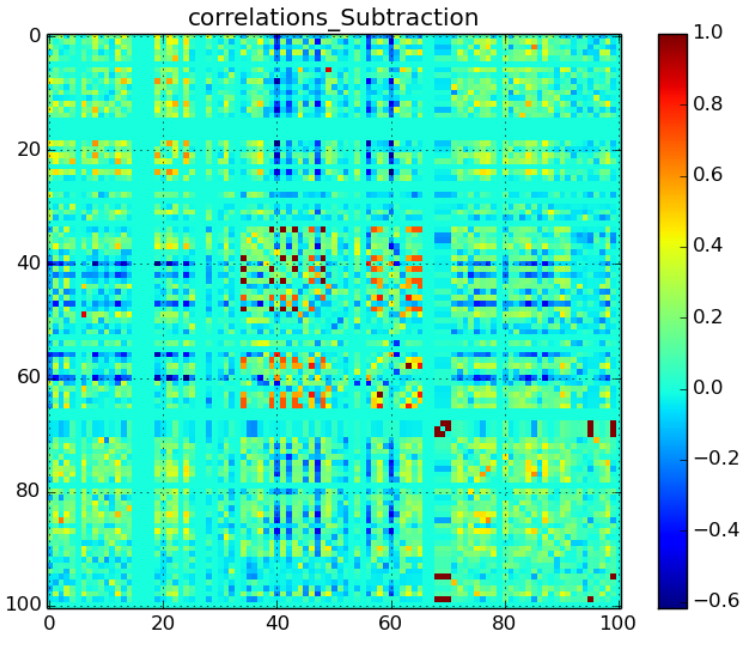
nTE

Information Flow Between Neurons

- Degree matrix shows the quantity and direction of information transmitted between each pair of neurons.



nTE

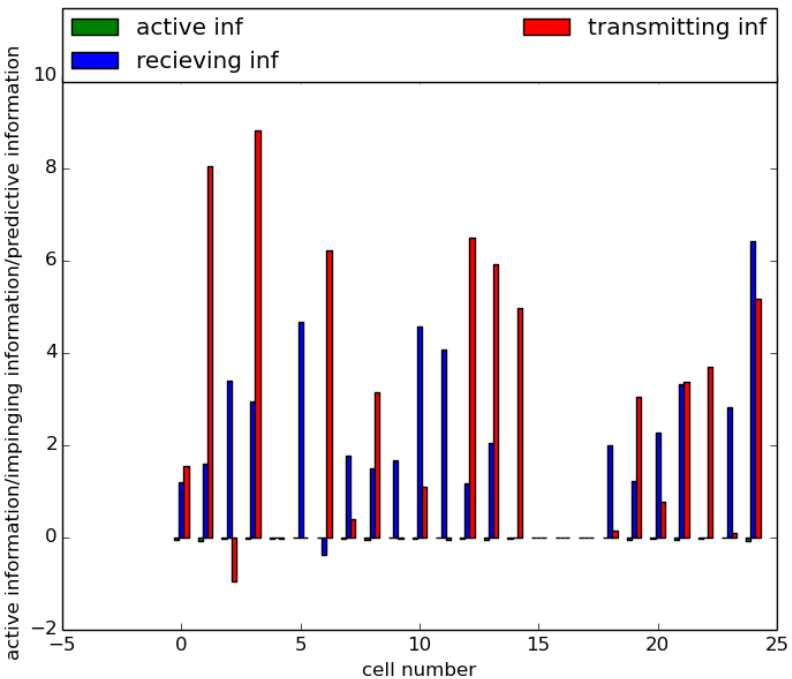


Correlation Matrix

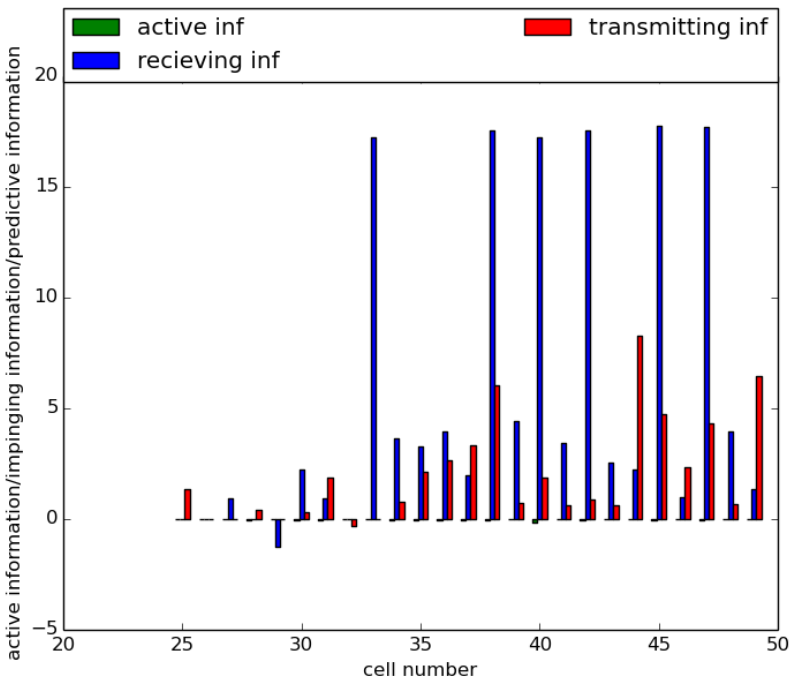
- Presence of information flow contributes validation of reconstruction because when information does flow, it suggests information is not randomly created and destroyed at every node.

Information Flow

- In Von Neuman architecture no conflict between transmitting, translating, and storing information. Respective tasks performed by the bus, the CPU, RAM. One entire neuron simultaneously engages in information transfer, information alteration and information storage.



Sums, Cells[0,24]



Sums, Cells[25,49]

Drawbacks and Future Work

- Predictive changes in spike train information may occur for reasons other than direct connectivity (effective connectivity). Such as when some cells are synchronised to another cell that has a direct connection.

  Future work:

- Within cell transfer entropy. The model I implemented contains within cell and between cell feedback. Working memory function of neurons can be inferred from within cell transfer entropy.
- Completely parallelising the network. As well as a partial parallelisation (communication between CPUs), the implementation was performed by formulating the simulation as an embarrassingly parallel problem.
- Inputing a signal into the normalised transfer entropy algorithm that has been qauntised into more than two levels, because neural network outputs are amplitude modulated signals.

Summary

- Discussed how TE identified functions. TE distinguished information sending neurons from information receiving neurons.
- Transfer Entropy was used to quantify **Information Flow** within and between neurons.
- I described how information flow in IPSPs can be detected.
- I have discussed how the presence of information flow contributed to the validation of model.
- Generally I have described the analysis of Information flow in a cortical neural network, and why it is of interest.

References

Kerr, Cliff C et al (2012)

Electrostimulation as a prosthesis for repair of information flow in a computer model of neocortex

IEEE 20(2), 153 – 160.

Neymotin, Samuel A et al (2011)

Synaptic information transfer in computer models of neocortical columns

Journal of computational neuroscience 30(1), 69 – 84.

Gourévitch, Boris and Eggermont, Jos J (2007)

Evaluating information transfer between auditory cortical neurons.

Journal of Neurophysiology 97(3), 2533 – 2543

Lizier, Joseph T et al (2012)

Local measures of information storage in complex distributed computation

Information Sciences 208, 39–54

The End

made with LaTeX

Questions?

Trifid

- Trifid is a large Intel system and is VPAC's sixth and largest cluster. Trifid has 180 compute nodes, with a total of 2,880 cores. It has a HPL (high performance Linpack) rating is 45.9 TFLOPS. It obviously runs HPC Linux.
- 180 nodes 2,880 cores of Intel $E5-2670$
- 4 GB PC1600 memory per core (64 GB per node),
- In practice could access (99GB on one node)with 6 nodes having 16 GB per core (256 GB per node)
- This computer 4000mbRAM
- 4 nodes will be GPU/MIC capable FDR Infiniband.
- CentOS 6 Linux
- VPAC NFS for home
- VPAC 165TB DDN S2A high performance array for work/scratch/projects (using Lustre).

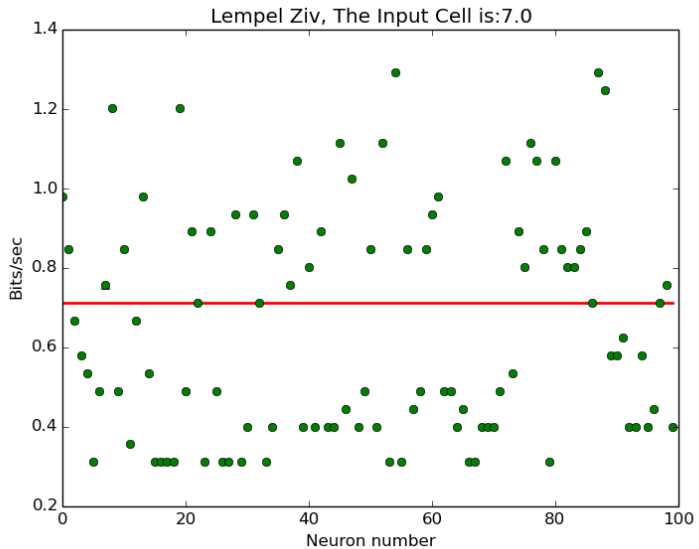
Trifid

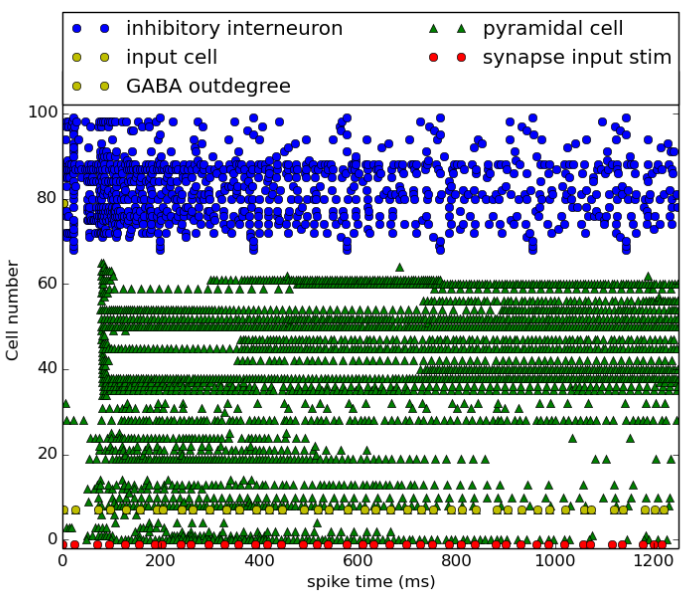
- I succesfully made an algorithm which could distribute the cells over over the hosts, in NEURON, I did this again in Python.

- Parallelising the wiring diagram was non trivial. It was more complex than necessary using NEURON and MPI alone. Mpi4py has many nice features for easy point to point communication of Numpy Vectors.

Stored Information

- stored information





Applications

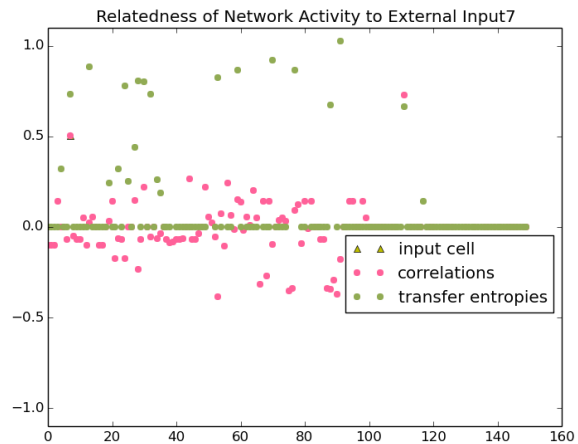
- Reverse engineering principles of brain function.
- The dynamic clamp Closed loop, real-time NEURON. Models a missing network, and Substites in the missing network behavior with electrode arrays.
- Cogntive neuro prosthesis. If we understand what neurons are doing in the hippocampus and prefrontal cortex it is more likely that we will be able to replace their functions in the future.

Applications

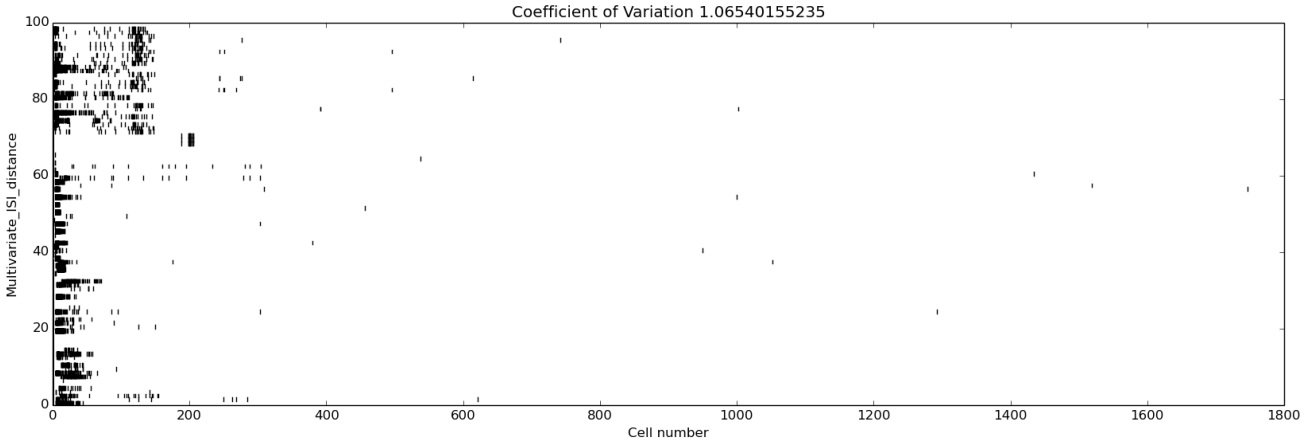
- The motivation of neuron simulations is to try to reverse engineering principles of brain function.

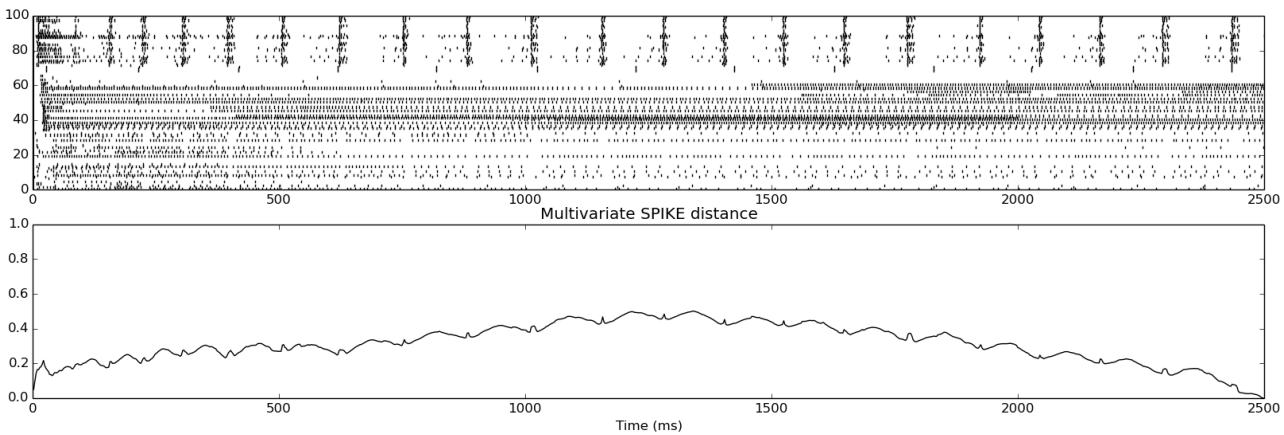
- The dynamic clamp Closed loop, real-time NEURON. Models a missing network, and Substites in the missing network behavior with electrode arrays.

- The information in the network was also related to the synaptic events that were used to stimulate the network (at two cells only). However information in the network was more strongly related to the altered information found across the network.



Information Translation





Wiring Algorithm: Searching the volume of spike sources

HOC

```
proc wire_distances(){
    forsec $o1.spk_trig_ls{
    for (x){
        if((x>0)&&(x<1)){
            if(ismembrane("xtra"){
                find_distances(x_xtra(x), y_xtra(x),
    z_xtra(x), secname(), x, $o2)
            }
        }
    }
}
```

Self Reflection

HOC

```
1 //String processing performed elsewhere enabled
    execution of Strings performed here.
    Facilitates network connections.

3   sprint(synapse_post, "%s%s%g%s", sec_string2, "
    syn_ =  new AMPA(",storex,")")

5     execute(synapse_post) //put a post synapse at
    the target

7     sprint(synapse_pre, "%s%s%g%s", sec_string1,"
    nc = new NetCon (&v(",num_seg,"),syn_)")

9     execute(synapse_pre)
```

Find Contact Points Algorithm

HOC

```
forsec $o7.spk_rx_ls{
  sec_string1=$s4
  num_seg=$5
  if(strcmp(str_src,str_target)==0){ break }
    if(Cell[py.int(tail_src)].div.x[py.int(
tail_target)]>3){ break }
      if (ismembrane("xtra")) {
        for(x){
          if((x>0)&&(x<1)){
            r = (sqrt((x_xtra(x) - $1)^2 + (
y_xtra(x) - $2)^2 + (z_xtra(x) - $3)^2))
            if(r<10){//units of um.
              if(Cell[py.int(tail_src)].div.x
[py.int(tail_target)]<3){
```

Transfer Entropy

The transfer entropy was used to analyse connectivity and to find neurons which were sources of stored information: Then the transfer Entropy (TE) from neuron/process X_1 to neuron/process X_2 is then the amount of reduction of uncertainty between the past of X_1 and the future of X_2
$TE_{X_1 \to X_2} = I\left(X_2^F; X_1^P | X_2^P\right) = H\left(X_1^F | X_2^P\right) - H\left(X_2^F | X_1^P, X_2^P\right)$
By expanding out the equations for entropy H we get:

$$TE_{X_1 \to X_2} = \sum_k \sum_l \sum_m P(X_2^F = k, X_2^P = l, X_1^P = m) \times log_2 \left(\frac{P(X_2^F = k | X_2^P = l, X_1^P = m)}{P(X_2^F = k | X_2^P = l} \right) \tag{1}$$

Transfer Entropy

The input stimulus should be a more stronger predictor of the activity of the neuron projected onto.
Related to mutual information (the reduction of uncertaintity, when conditional probabilities are considered), except that it involves the difference in entropy between the future state of X and the current state of Y.
By expanding out the equations for entropy H we get:

$$h_2 - h1 = -\sum_{x_{n+1},x_n,y_n} p(x_{n+1}, x_n, y_n) log_2 p(x_{n+1}|x_n)$$

$$+\sum_{x_{n+1},x_n,y_n} p(x_{n+1}, x_n, y_n) log_2 p(x_{n+1}|x_n, y_n)$$

$$= -\sum_{x_{n+1},x_n,y_n} p(x_{n+1}, x_n, y_n) log_2 p(\frac{x_{n+1}|x_n,y_n}{x_{n+1}|x_n})$$

$$h_2 - h_1$$

gives the amount of information that is gained by considering the probability of Y firing and X firing too.

Within Cell Feedback

Within cell feedback

- Self projecting synapses
- Back Propagating dendrite action potentials, that can teach post synapses on the dendrite.

Hodgkin Huxley Equations with Synaptic Current

- The Hodgkin Huxley model is a model of spike generation in response to an electrode. The Hodgkin Huxley equation in analytic form is given by the following equation:
- A deterministic equation that first described quiescent conditions.

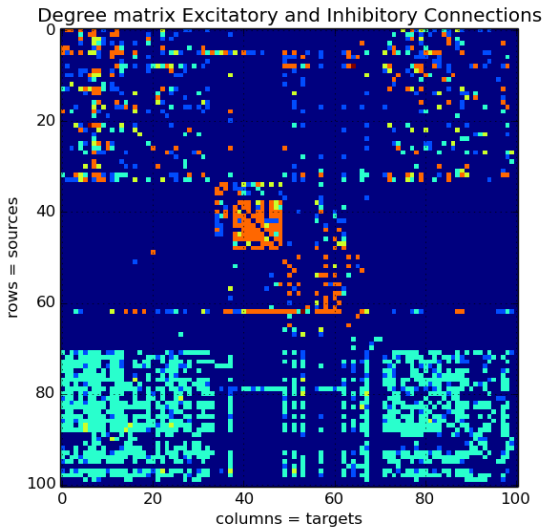
$$\frac{1}{2\pi a r_i}\frac{\delta^2 V_m}{\delta x^2} =$$

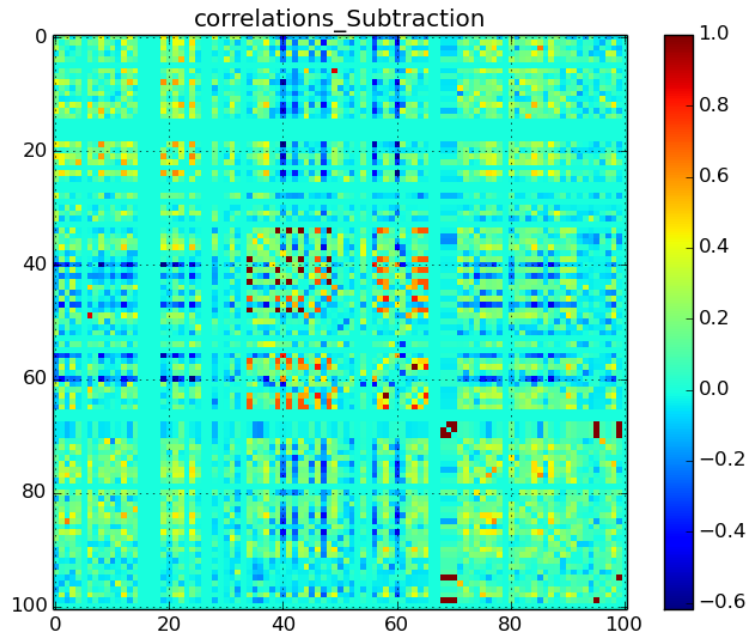
$$C_m\frac{\delta V_m}{\delta t} + (V_m - E_K)G_K(V_m,t) + (V_m - E_{Na})G_{Na}(V_m,t) + (V_m - E_L)G_L(V_m,t) + I_{syn} \quad (2)$$

There are separate equations for the conductance's and that is where the non linearity's emerge from.

- Using a similar approach, but with a cubic grid rather than cylinders results in an equation is iterable in discrete temporal steps Δt and spatial steps Δx

$$v_i^{n+1} = v_i^n + \frac{d\Delta t}{4R_i C_m \Delta x^2}(v_{i-1}^n - 2v_i^n + v_{i+1}^n) - \frac{\Delta t G_m}{C_m v_i^n - J_i^n} \quad (3)$$


Degree matrix Excitatory and Inhibitory Connections
rows = sources
columns = targets
0
20
40
60
80
100


correlations_Subtraction
0
20
40
60
80
100
1.0
0.8
0.6
0.4
0.2
0.0
−0.2
−0.4
−0.6

Spectral Granger Causality

Spectral Granger Causality was also used.

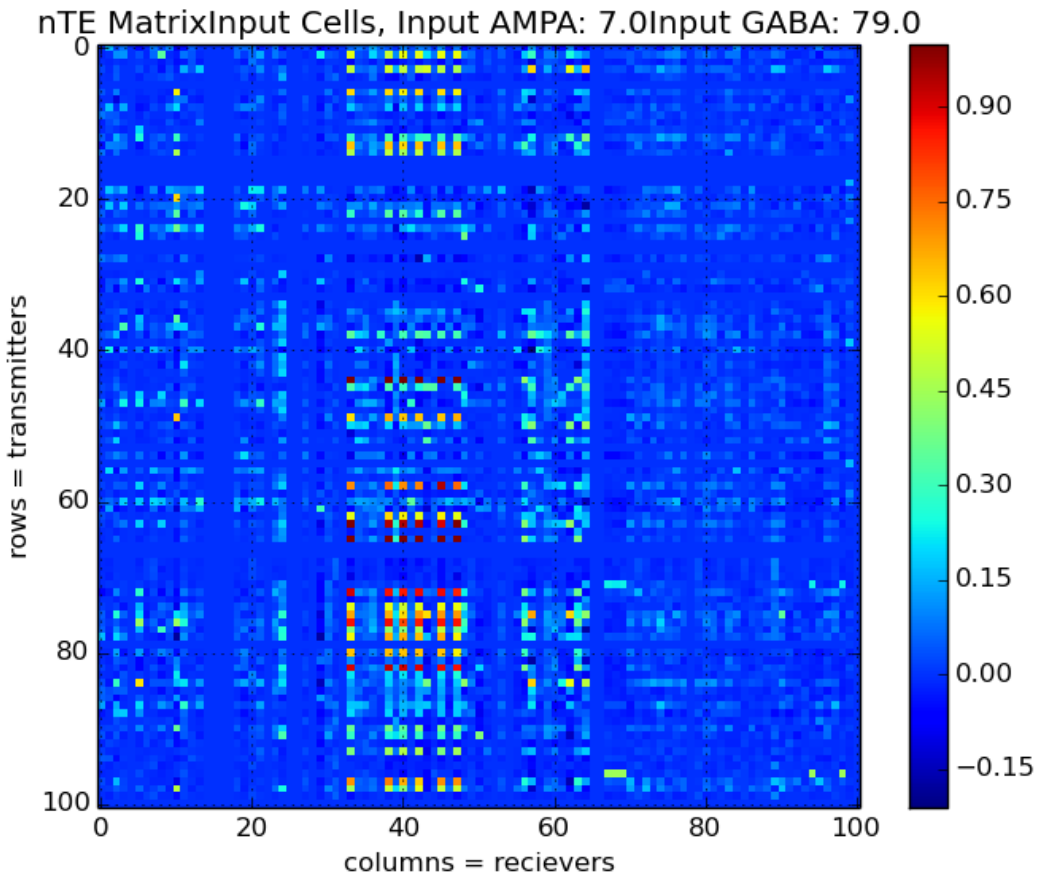
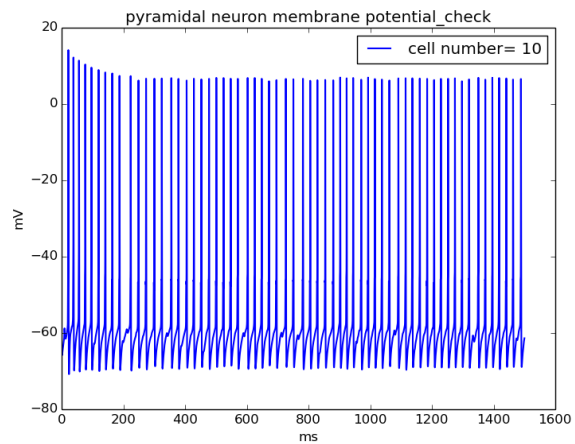
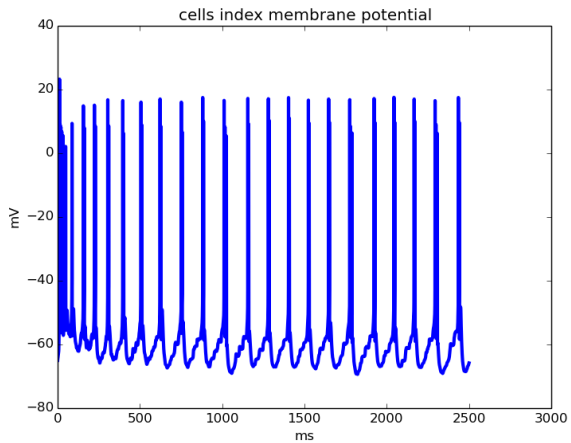


Figure : nTE

Example
$X_1$1: 1110110100110011101101 X_2: 1010101011011011001

Traditionally in neuroscience the membrane potential has been quantised into two levels, and the time at which a neuron fires is recorded. The motivation codes employed by sensory and motor pathways, are understood to operate on the level of these discrete events.
There is reason to be agnostic about the way information is represented in the brain. One reason is because Action Potentials in many different cortical neurons actually are amplitude modulated.
To counteract this problem there is no reason why the amplitude could not be quantized into ten or more voltage levels. The algorithms which perform entropy calculations are able to accommodate greater than a two symbol alphabet, such that all ten voltage levels could be used to represent different neuron states (different information).




cells index membrane potential
40
20
0
−20
−40
−60
−80
mV
0
500
1000
1500
2000
2500
3000
ms