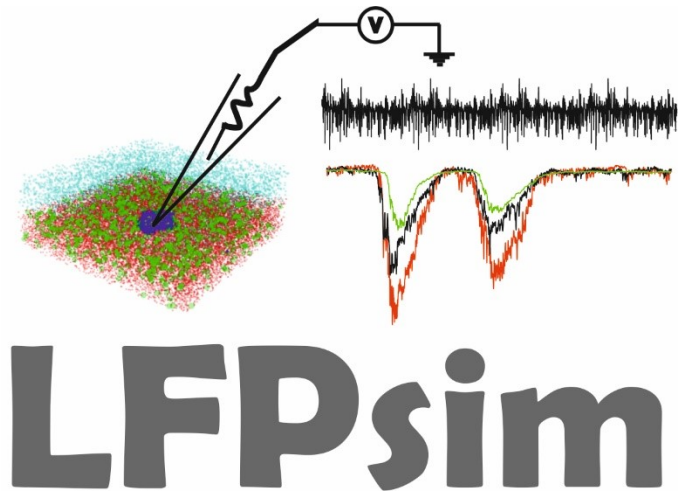

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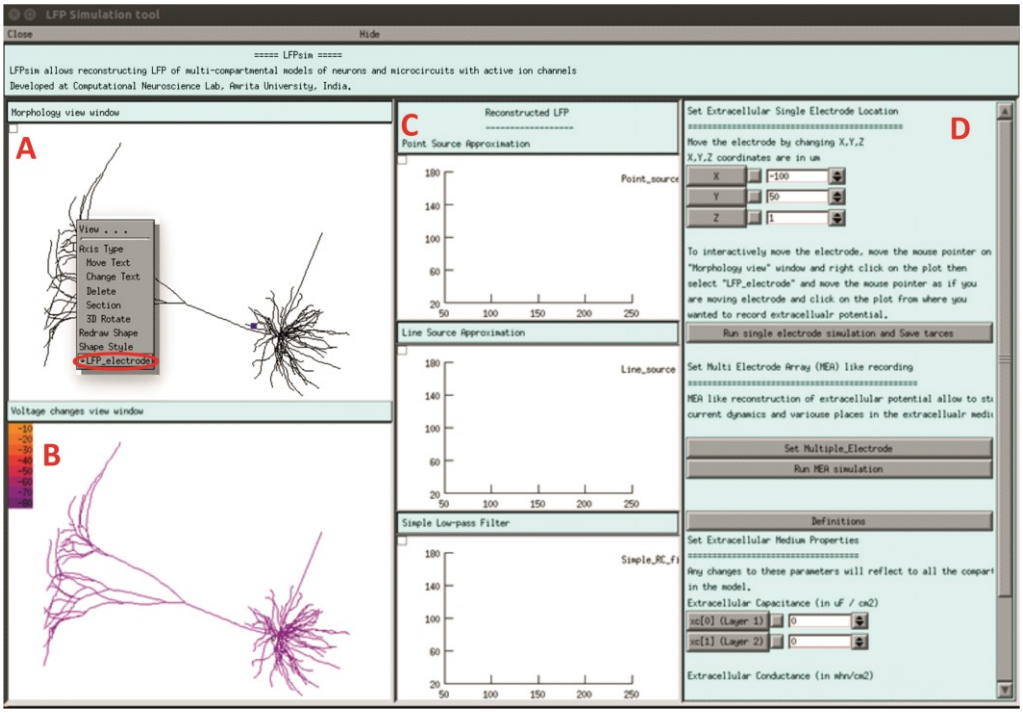
Using LFPsim

LFPsim is a set of scripts for NEURON simulation environment to reconstruct LFP from biophysical models of neurons and networks. LFPsim uses NEURON's extracellular mechanism to calculate total ionic currents from neuronal compartments at each time step (dt). The extracellular potential at a given point (x,y,z) was calculated by setting pointers to "lfp.mod" and for multiple recording points "mea.mod". Point Source Approximation (PSA), Line Source Approximation (LSA) and RC filter techniques were implemented in LFPsim to simulate extracellular potential of a single cell and LFP of network models.

1. Getting familiar with LFPsim Interface

LFP simulation tool GUI was created using NEURON's graphical components. GUI mainly consisted of Morphology view window (A), Voltage changes view window (B), Reconstructed LFP view panel (C), Electrode parameters (D), extracellular medium properties set panel (D).



Supplementary Figure 1. LFPsim GUI. A. ***Morphology view window*** is NEURON's shape plot allowing the visualization of neuron morphology and extracellular electrode location (shown in blue). Right click of mouse on this window allows users to interactively select LFP electrode location by selecting "LFP_electrode" menu (red circle). Right click of mouse on this window will also allow options including viewing the model at different angles. B. ***Voltage changes view window*** is a NEURON's space plot to visualize voltage changes across the neuronal cable during the activity. Voltage range from -70 mV to +40 mV was defined as a colormap. C. ***Reconstructed LFP view panel***, allow users to view reconstructed LFP in three different schema PSA, LSA and RC methods. D. ***Simulation controls*****,** allows setting electrode parameters, extracellular medium properties and running simulation.

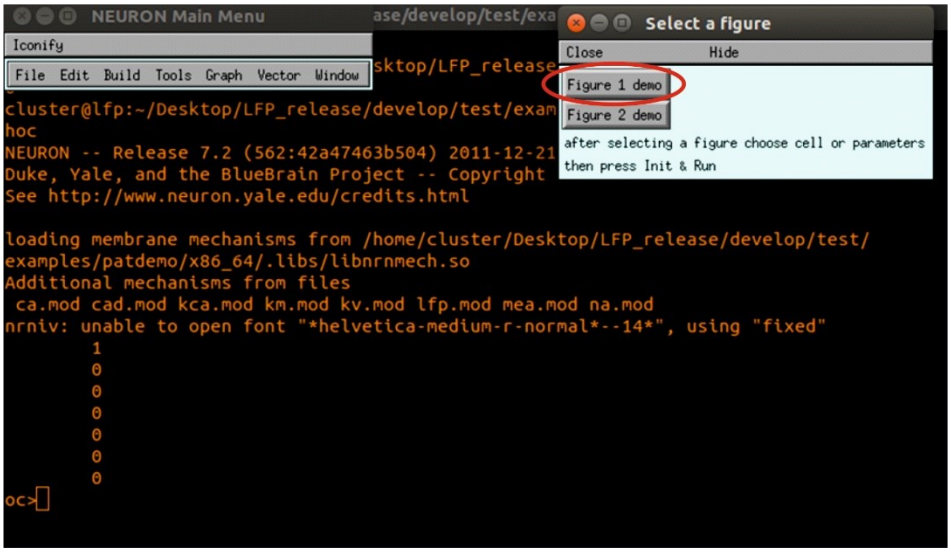
2. Reconstructing LFP of detailed neuron models

To execute LFPsim, stepwise procedure are listed below. Please visit NEURON's website for installing the simulation environment.

Follow steps from 1 to 14 to run single electrode LFP simulation.

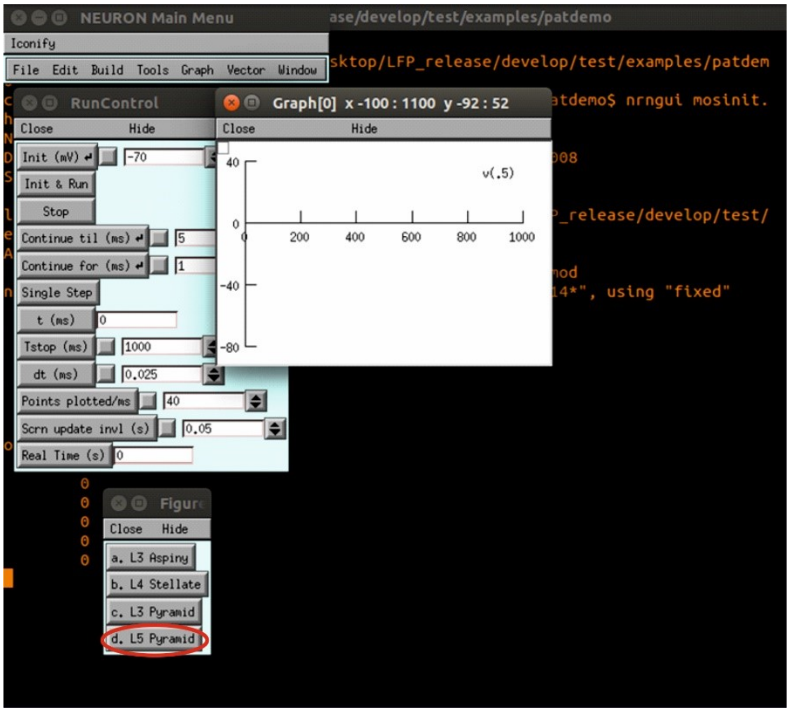
1. Download the LFPsim source code and biophysical model of neuron/network from ModelDB. LFPsim can be downloaded from: <ModelDB link>. In this example, mathematical models of pyramidal neuron (deep, superficial, aspiny, stellate) by (Mainen and Sejnowski 1996) was used (ModelDB Accession ID: 2488).
2. Unzip or extract LFPsim files and model neuron/network.
3. Copy and paste all files and folder in the LFP tool folder to neuron/network model folder. Do note "lfp.mod" and "mea.mod" should be placed along with model's mechanism (mod) files.
4. Please follow the model's "README" file if there are any specific procedures for compiling the model in NEURON.

5. For Linux/Unix users, open a terminal and change present working directory to the neuron model folder, then run *nrnivmodl* to compile the model. If code was pre-compiled before copying "lfp.mod" and "mea.mod" files to the model directory, it is recommended to perform a re-run after including the mod files along with other channels and receptor mod files.
6. For Windows users, double click on "mknrndll" and set the path for where ".mod" files were placed in the model and click on "nrnmech.dll" button for compiling the mechanism files (including the mea and lfp mod files in the same directory).
7. Please follow model's "README" file to load the neuron model in NEURON. In this example, mosinit.hoc file was used to load neuron models. On the Linux terminal, type "nrngui mosinit.hoc" to load the model in Linux. For Windows users, double click on mosinit.hoc file in the model directory. On successful loading, you will see two NEURON windows popping up. As per instructions on the model's README, click on "Figure 1 demo" button to load the neuron.



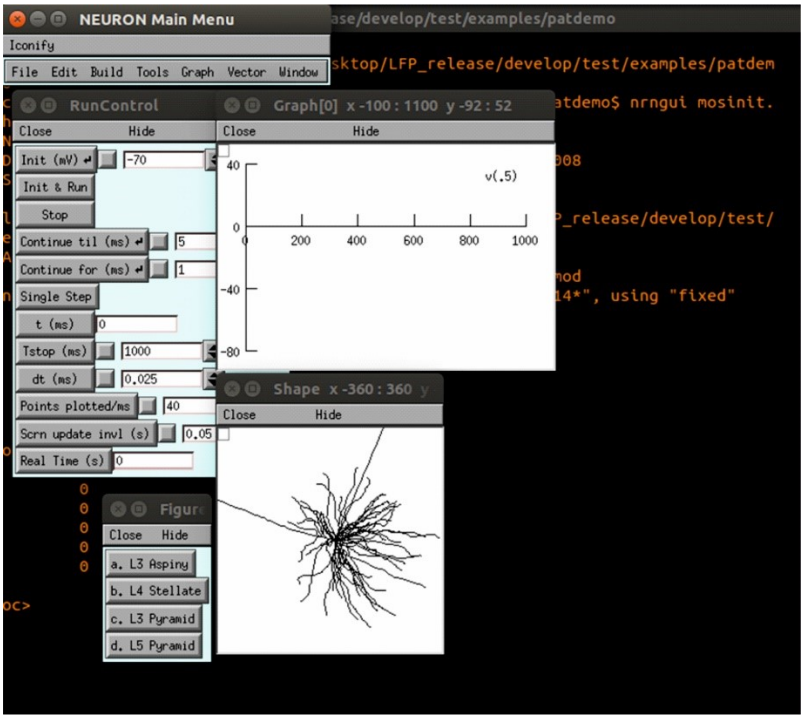
Supplementary Figure 2. Executing pyramidal neuron model.

Click on "L5 Pyramid" button to load the neuron.



Supplementary Figure 3. Executing L5 pyramidal neuron model.

Once the neuron is loaded you can observe a shape plot generated as shown in Supplementary Figure 4.



Supplementary Figure 4. L5 pyramidal neuron space plot.

8. After loading the model into NEURON, call "extracellular_electrode.hoc" from NEURON's "oc>" terminal by typing *xopen("extracellular_electrode.hoc")* to load LFPsim in NEURON.

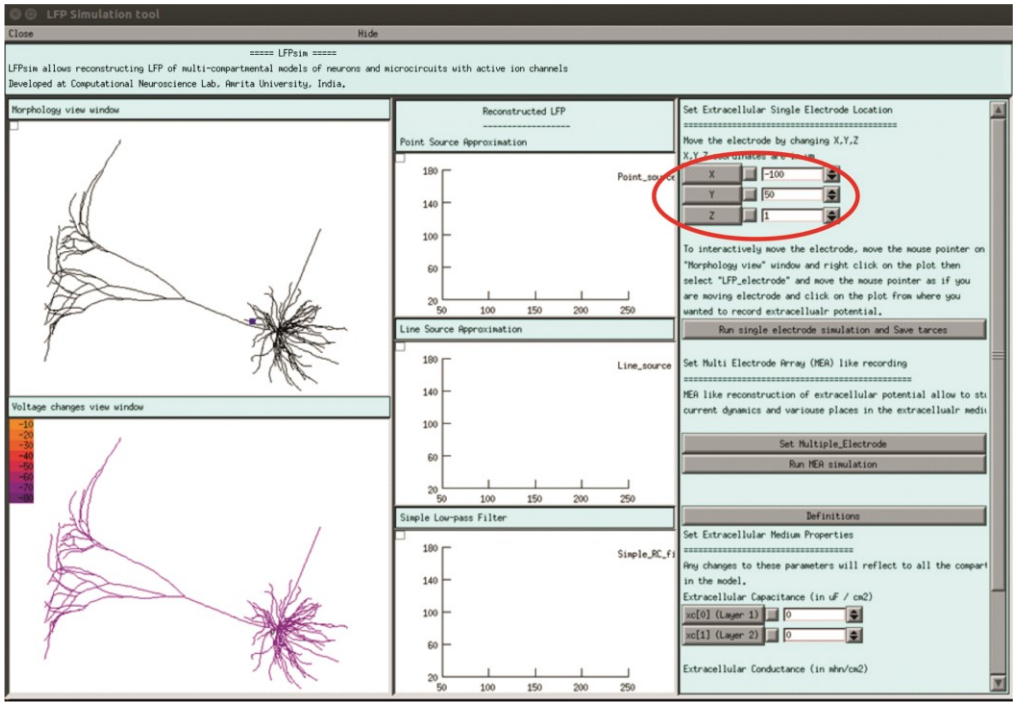
```
cluster@lfp:~/Desktop/LFP_release/develop/test/examples/patdemo$ nrngui mosinit.
hoc
NEURON -- Release 7.2 (562:42a47463b504) 2011-12-21
Duke, Yale, and the BlueBrain Project -- Copyright 1984-2008
See http://www.neuron.yale.edu/credits.html

loading membrane mechanisms from /home/cluster/Desktop/LFP_release/develop/test/
examples/patdemo/x86_64/.libs/libnrnmech.so
Additional mechanisms from files
 ca.mod cad.mod kca.mod km.mod kv.mod lfp.mod mea.mod na.mod
nrniv: unable to open font "*helvetica-medium-r-normal*--14*", using "fixed"
        1
        0
        0
        0
        0
        0
        0
oc>     1
        0
        0
        0
        0
        0
        0

oc>xopen("extracellular_electrode.hoc")
```

Supplementary Figure 5. Loading LFPsim with the NEURON model.

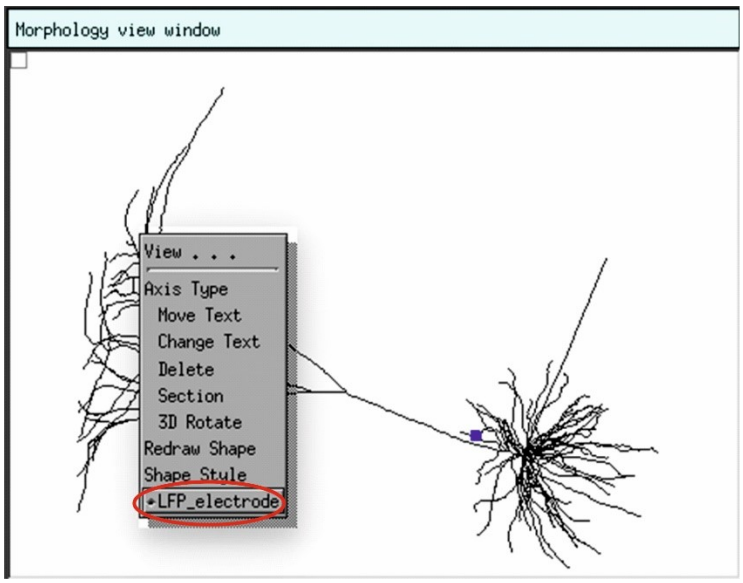
9. One may see the LFPsim GUI on successful execution.



Supplementary Figure 6. LFPsim and pyramidal neuron model.

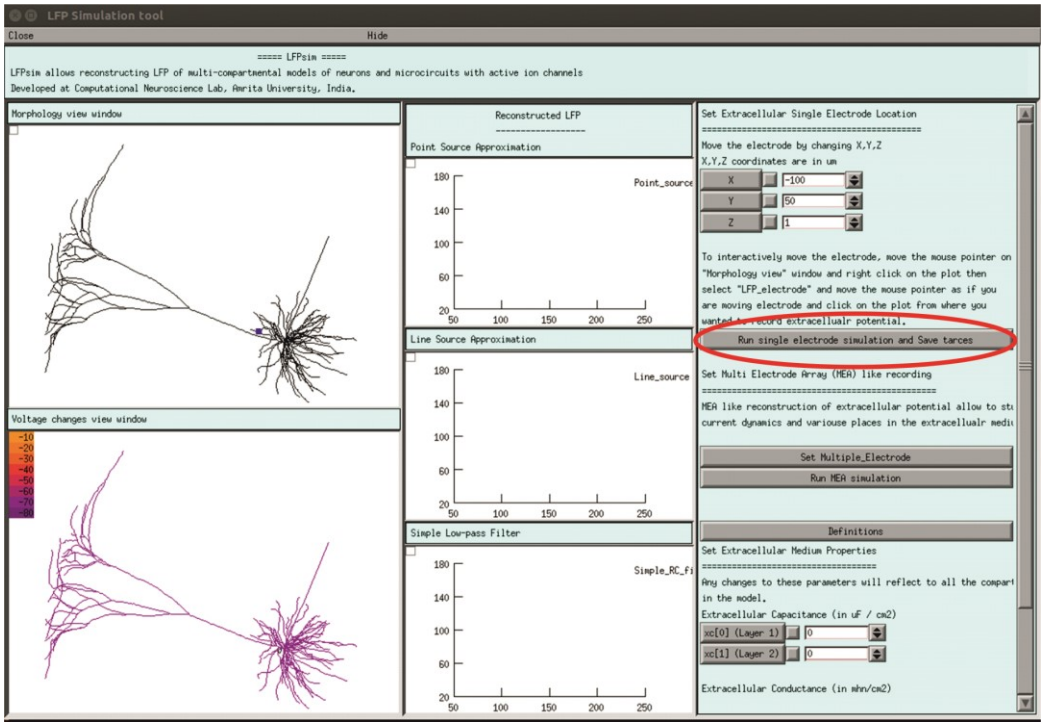
10. Set input stimuli to neuron model.

11. Users can set single electrode location both manually and interactively (see Figure 1D). To set manually, the user need to give values for x,y,z of electrode location in panel D (see Figure 1). To interactively change the electrode position, move the mouse pointer on "Morphology view" window and right click on the plot, then select "LFP_electrode" and move mouse pointer as if you are moving electrode and click on the plot from where you wanted to record the extracellular potential.

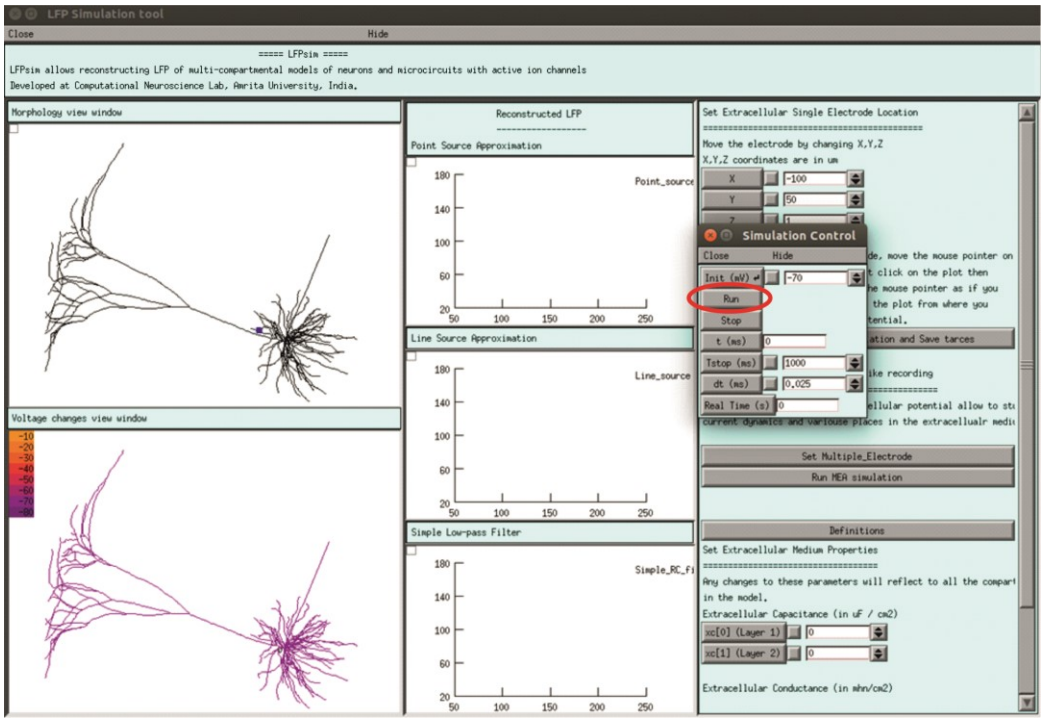


Supplementary Figure 7. Modifying LFP electrode settings.

12. Execute single LFP electrode simulation by clicking on “Run single electrode simulation and save trace” button.

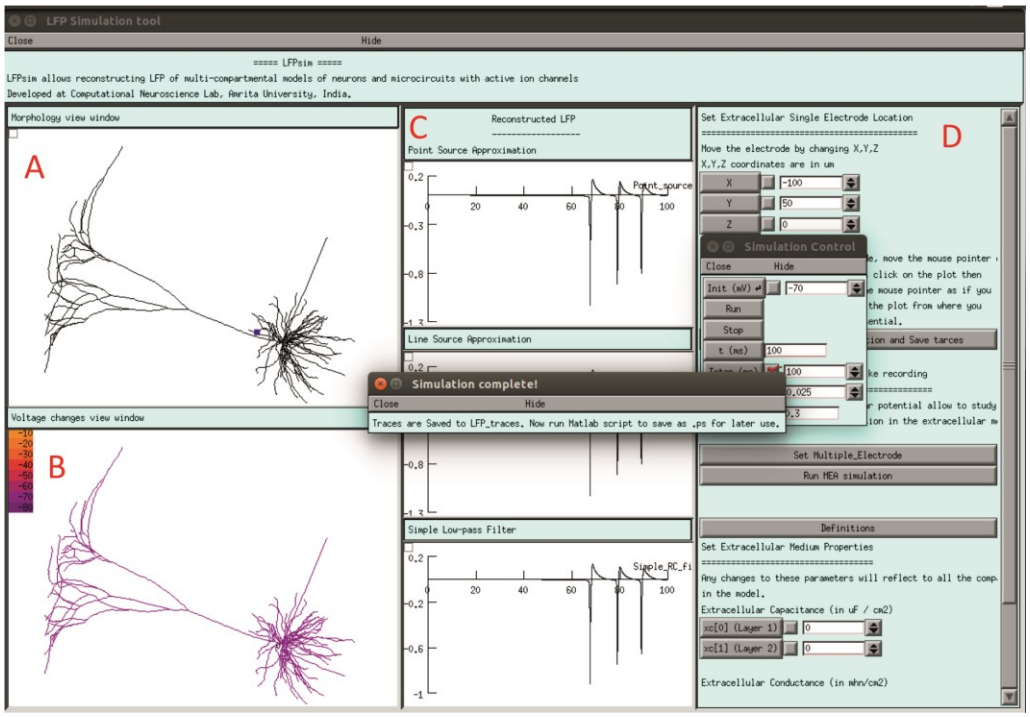


Supplementary Figure 8. Executing LFP simulation on L5 neuron model.



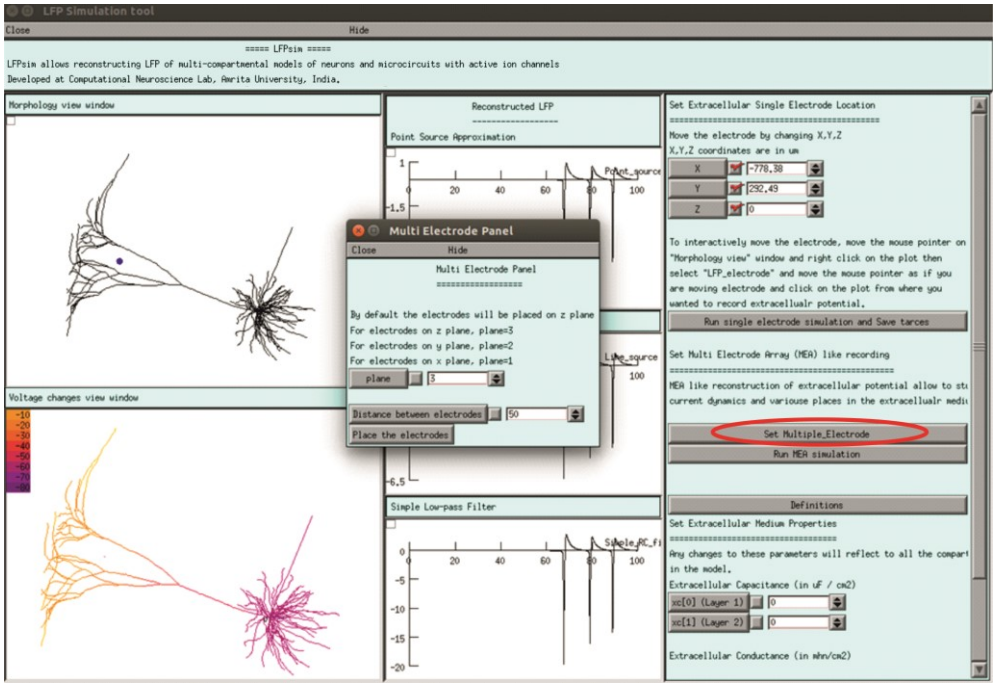
Supplementary Figure 9. Running LFP simulations.

13. When run is completed, a pop up will indicate “Simulations complete” and traces will be saved to “LFP_traces” directory.



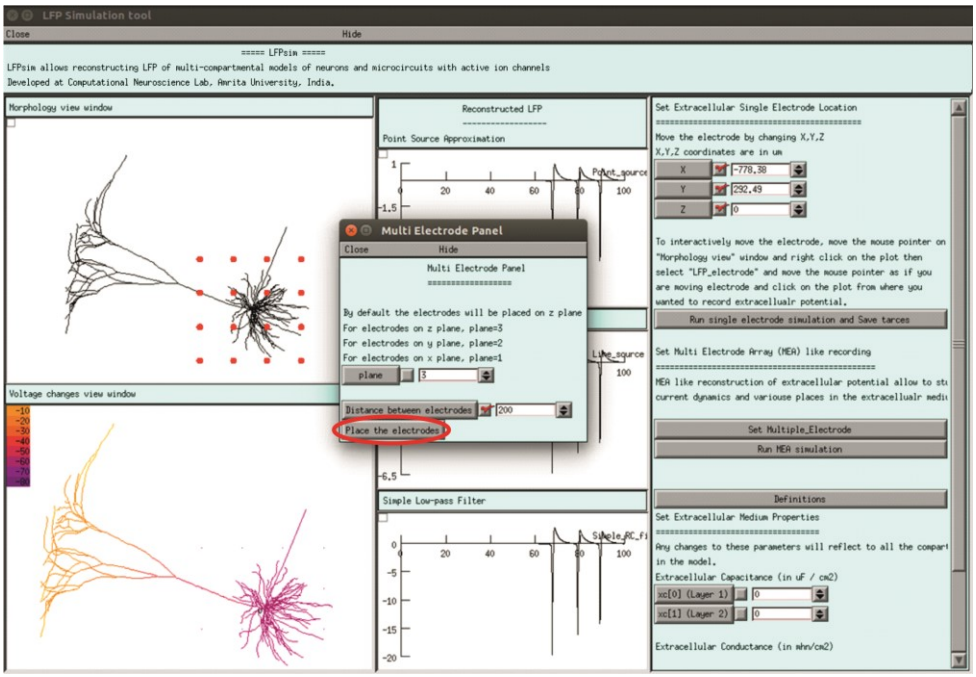
Supplementary Figure 10. Simulation complete indication in LFPsim.

14. Traces may be manipulated plots using GNU Octave, MATLAB or Python; sample scripts are provided in “LFP_traces” directory.
15. **For multiple electrode “MEA” simulation, please follow until step 10,** and Click on “Set Multiple_Electrode” button in simulation control window (see Figure 1D).



Supplementary Figure 11. MEA simulations in LFPsim.

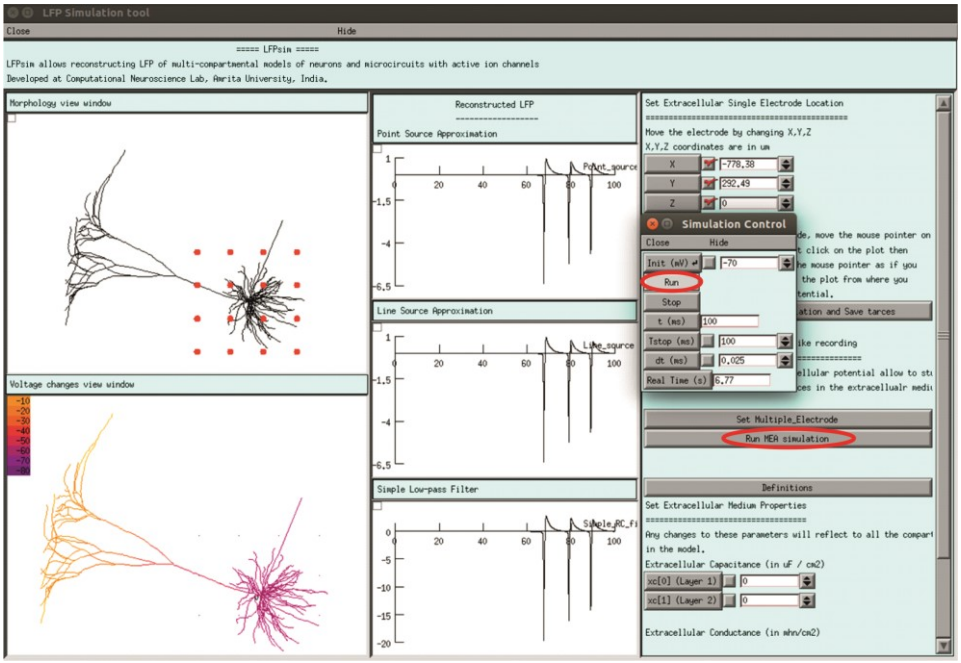
Users can change distance between the virtual electrodes (as an example, 200µm was set). To “set” the electrode location, please click on “Place the electrode” button. Users can see multiple virtual electrodes as red dots in Morphology view window.



Supplementary Figure 12. "Placing" the MEA electrode.

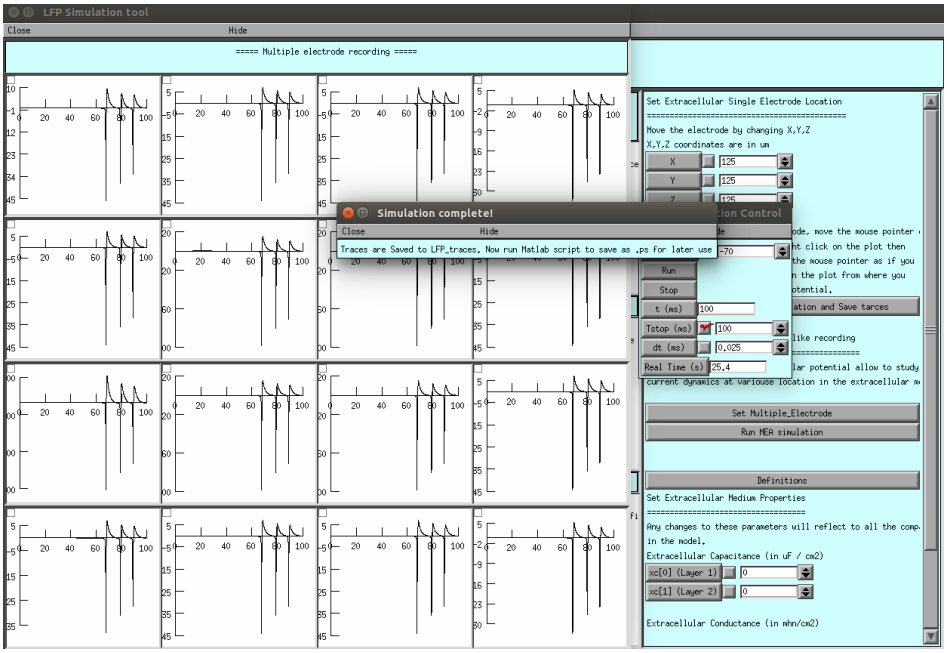
Electrodes can also be relocated on to a different plane by changing plane variable in the panel.

16. After placing the MEA electrodes, user can execute "MEA" simulation by clicking on "Run MEA simulation" button.



Supplementary Figure 13. Simulating "MEA".

17. A pop up "Simulation complete" will indicate run completed and MEA traces will be saved to "LFP_traces".



Supplementary Figure 14. "MEA" GUI in LFPsim.