Flysim User Guide

Version 0.8.11

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1. Overview

Computer simulation plays an important role in examining hypotheses and dynamics as well as in the analysis of neural networks. We developed a neural network simulator named Flysim to fulfil these purposes. Our simulator supports several synapse and neuron models, and most parameters, including membrane properties, synapse properties, network structures and stimulation protocols, can be flexibly programmed by the users. Using the simulator, users can easily and intuitively simulate neural networks and find desirable dynamics in their simulations.

1.1 Biological models and program models definition

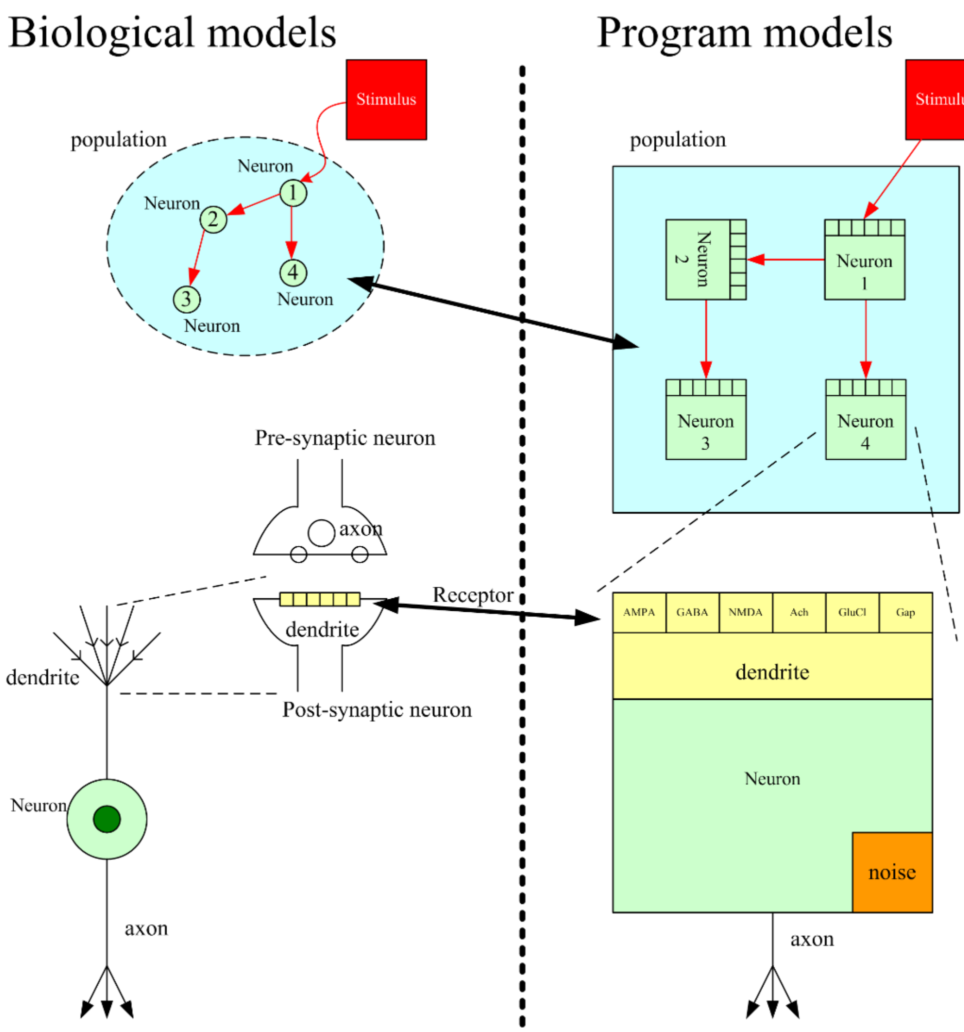

Figure 1 The mapping between the biological models and the program models

In the simulator, every parameter in the biological models is mapped one to one onto the program model definition (Fig 1). Hence, we can describe parameters in one time of all neurons in the same population of the same membrane and synapse models. Flysim supports the leaky integrate and fire (LIF) model and Hodgkin-Huxley model for membrane potential dynamics, and synapse models with exponential decay for six different receptor types: AMPA, GABA, NMDA, Ach, GluCL and gap junctions. The action potential transmission on the axon is modeled with a simple time delay, which can be tuned by the users.

1.2 Flysim command options

Table 1 shows command options, which can be displayed by executing “Flysim –h”. These commands are most commonly used. The option “–pro” assign an experiment protocol file, “-conf” assigns a network definition file, “-rp” defines the number of trials the experiment should repeat, “-t” activates the multi-thread model and also sets the number of threads, “-dt” defines the fundamental time step in ms, “-nmodel” specifies the neuron and synapse models to be used in the simulation. The output data type and their file names can be specified by -om, –os, and –or, which are very handy when the simulations are performed in a batch. “–daemon” is an experimental daemon model for the low-level communication operation. Running the command “./flysim” without any other option will by default read the example network.pro and network.conf in the same directory and display the simulation results.

Table 1 Flysim command options

1	-pro network.pro	# read protocol file: default=network.pro
2	-conf network.conf	# read configuration file: default=network.conf
3	-om my_membrane.dat	# for batch operation: output membrane potential file
4	-os my_spike.dat	# for batch operation: output spikes file
5	-or my_rate.dat	# for batch operation: output firing rate: default rate window=50ms, print out=100ms
6	-rp 1	# set repeat times: default=1
7	-t 4	# set multithreading: default=1
8	-dt 0.1	# time step (default=0.1ms)
9	-STP	# use short term plasticity synapse

10	-STD	# use short term depression synapse and this option is disabled when -STP used
11	-LTP	# use long term plasticity synapse (STDP)
12	-nmodel GNL2	# neuron model: classical leaky integrate and fire model

2. Network definition file and description

Fysim reads .conf and .pro files for the network definition and experimental protocol, respectively. Figure 2 shows a toy example that has two populations: Exc1 and Exc2, the definition description is shown Table 2. Each population has 20 neurons with all to all connections; Exc1 only receives background stimulation and excites Exc2. Exc2 is also stimulated by background stimulation and connects to self-population with auto-connection. In the example in table 2, the code between NeuralPopulation:Exc1 and EndNeuralPopulation defines the membrane and connection parameters for all neurons in Exc1, where N=20 stands for 20 neurons in this population and C=0.5 means each neuron has a membrane capacitance of 0.5nF. Taum=20 sets the membrane time constant to 20 ms, RestPot=-70 sets the resting potential to -70 mV, ResrPot=-55 sets the reset potential to -55 mV and Threshold=-50 sets the action potential threshold to -50 mV. The code between Receptor:AMPA and EndReceptor defines the AMPA receptor dynamic, Tau=2 sets the receptor decay time constant to 2 ms, RevPot=0 sets the reversal potential to 0 mV, FreqExt=0 defines the external background stimulation frequency at 0Hz, MeanExtEff=2.1 sets the external stimulation strength at 2.1nS, received by each neuron in the population. We also need to assign connections between different populations. In figure 3, TargetPopulation: Exc2 defines Exc1 connection to Exc1 with mean efficacy of 4.2 nS (MeanEff=4.2). After defining Exc1 population, Exc2 is defined similarly but with auto-connection (Figure 4) to itself population.

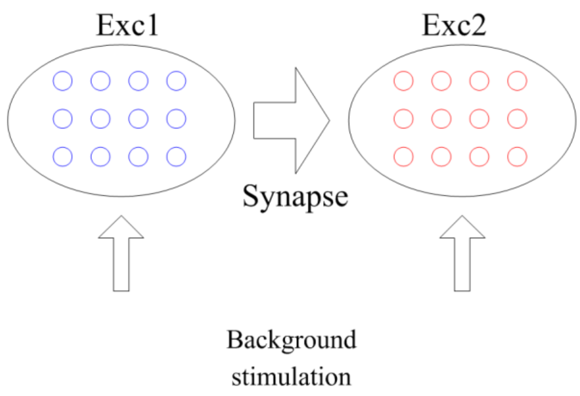

Figure 2. A toy example of a neural network that can be simulated by Flysim.

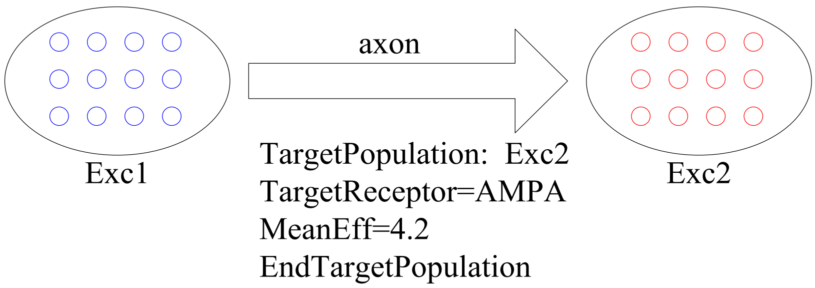

Figure 3 Connections between Exc1 and Exc2.

Figure 4. Absence or presence of post-synaptic population connection to the neuron itself, (a) SelfConnection=true connects neuron in a population to itself, but (b)SelfConnection=false disables auto-connection.

We have previously inspect schematic diagram of our toy example, and we now list all script definitions here. The default neural network definition file is network.conf, the protocol file is network.pro.

Table 2 An example network.conf

1	NeuralPopulation: Exc1	//keyword: neuron population definition from NeuralPopulation to EndNeuralPopulation is named Exc1
2		
3	N=20	//there are 100 neurons in Exc1 population
4	C=0.5	//membrane capacitance is 0.5 nF
5	Taum=20	//membrane leaky time constant is 20 ms
6	Threshold=-50	//action potential threshold voltage is -5 0 mV
7	RestPot=-70	//resting state membrane voltage is -70 mV

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ResetPot=-55               //reversal potential is -55 mV
RefractoryPeriod=1.9       //refractory period is 1.9 ms
SpikeDly=0.3               //spike delay in axon transmission is 0.3 ms
STP_pv=0.6                 //STP parameter: vesicle release ratio pv
STP_tD=300                 //STP parameter: time constant of D factor
STP_aF=1.0                 //STP parameter: scaling of F factor
STP_tF=7000                //STP parameter: time constant of F factor
STP_aCap=2.0               //STP parameter: scaling of peak calcium level
STP_tCap=100               //STP parameter: time constant of peak calcium level
STP_aCar=3.0               //STP parameter: scaling of resting calcium level
STP_tCar=70                //STP parameter: time constant resting calcium level

Receptor:AMPA              // AMPA receptor parameters setting
Tau=5                      //decay time constant=5ms
RevPot=-70                 //reversal potential=-70mV
FreqExt=0.84375            //external stimulation=0.84375Hz
MeanExtEff=2.1             //external connection mean efficacy=2.1nS
EndReceptor                //end of receptor definition

TargetPopulation: Exc2     //post-synaptic population is Exc2
TargetReceptor=AMPA        //and connect to Exc2's AMPA receptor
MeanEff=4.2                //mean efficacy is 4.2nS
Connectivity=0.5           //connection ratio 0.5 between Exc1 and Exc2 means each neuron in Exc1 has 10(20*0.5=10) post-synaptic neurons randomly in the Exc2 population.

EndTargetPopulation        //end of Exc1 to Exc2 connection

EndNeuralPopulation        //this keyword means the end of population Exc1 definition from NeuralPopulation

NeuralPopulation: Exc2

N=20
C=0.5
```

```
Taum=20
Threshold=-50
RestPot=-70
ResetPot=-55
RefractoryPeriod=1.9
SpikeDly=0.3
SelfConnection=true       //auto-connection enable: default is false

Receptor:AMPA
Tau=5
RevPot=-70
FreqExt=0.84375
MeanExtEff=2.1
EndReceptor

TargetPopulation: Exc2
TargetReceptor=AMPA
MeanEff=4.2
EndTargetPopulation

EndNeuralPopulation
```

3. Experiment protocol and description

We now introduce the procedure for writing an experiment protocol file. The protocol is based on the event trigger strategy, with each event representing changes in a population stimulation. In table 3, the code embedded between EventTime 3000.0 and EndEvent defines a stimulation initiated at 3000.0 ms. Type=ChangeExtFreq, Population:Exc1, Receptor:AMPA and FreqExt=240.0 set a 240Hz input to the AMPA receptors for the neurons in the population Exc1. Label=#1#, the keyword “Label” combined with “#1#”, is reserved for future developments. The next event: Type=ChangeMembraneNoise, GaussMean=0.43 and GaussSTD=0.03, defines a current input with a mean=0.43 nA and a Gaussian distributed noise with STD=0.03 nA. Finally, Type=EndTrial ends the description of the experimental process at time 10100ms. We have shown some simple examples previously, and list all keywords below. The absence of –pro assign protocol file means that flysim will run the default settings (network.pro).

Table 3 network.pro example

DefineMacro	//This keyword combines with EndDefineMacro to form a macro block, we can define many macro inside block
GroupName:Sti2	// GroupName, GroupMembers and EndGroupMembers three keywords format a macro block
GroupMembers:Exc2,Exc1	//populations list in sequence
EndGroupMembers	
EndDefineMacro	
EventTime 3000.0	//Event trigger at time 3000.0ms
Type=ChangeExtFreq	//stimulation is receptor type
Label=#1#	//reserved descript
Population: Exc1	//target population is Exc1
Receptor: AMPA	//target receptor is AMPA type
FreqExt=240.0	//stands for 240Hz frequency stimulation to AMPA receptor type

```
EndEvent

EventTime 6500.0
Type=ChangeMembraneNoise    //current injection type stimulation
Label=#1#
Population: Exc1
GaussMean=0.43              //Gaussian mean = 0.43nA
GaussSTD=0.03               //Gaussian STD = 0.03nA
EndEvent

EventTime 10100.00
Type=EndTrial               //EndTrial 10100.00 ms means that the experiment stops at time 10100ms
Label=End_of_the_trial
EndEvent

OutControl                  //OutControl block for dumping neural network variables
FileName:MemPot.dat         //Define FileName is MemPot.dat
Type=MemPot                 //dump membrane potential to file
population:AllPopulation    //keyword AllPopulation print all population into file
EndOutputFile

FileName:Spikes.dat
Type=Spike                  //dump neuron spikes to file
population:Sti2             //output population is Sti2 macro which in Exc2, Exc1 sequence
EndOutputFile

FileName:FRates.dat
Type=FiringRate             //dump population firing rate to file
FiringRateWinodw=50         //average firing rate window is 50ms
PrintStep=10                //every 10ms dump data to file
population:Exc2
EndOutputFile
EndOutControl               //end of control block
```

3.1 File output control

Data output can be defined in the OutControl block at the end of the protocol file (table 3). The users can define three different output data types: membrane potential (MemPot), neuron spike (Spike), and population firing rate (FiringRate). Inside the block, FileName: MemPot.dat, Type=MemPot, population:AllPopulation and EndOutputFile specify that the membrane potential in all populations is stored in MemPot.dat. “AllPopulation” also can be replaced by Exc1 or Exc2, (but not “Exc1,Exc2”) if only the membrane potential of one population needs to be stored. The commands Type=Spike specify the spike train output. If you want examine the firing rate of neurons, use the commands Type=FiringRate. By issuing FiringRateWinodw=50 and PrintStep=10 for the firing rate output, you can print out the average firing rate calculated with 50-ms time windows with a step size of 10ms.

3.2 Macro

Macro defines a group of neural populations which can be used as a target in the input events. Macros should be specified in the beginning of the protocol file, and starts with DefineMacro and ends by EndDefineMacro. Inside the block, GroupName defines the Macro name, GroupMembers lists populations that comprise the group in sequence and EndGroupMembers ends the definition of a group. In table 3, groups Sti1 and Sti2 both consist of Exc1 and Exc2 but in a different order. The order is preserved in the output file when the corresponding group is specified in the OutControl block.

Appendix

A.1 LIF

In the sub-threshold membrane potential regime, Flysim uses the leaky integrated and fire mechanism. The membrane potential eq. (1) has a synapse current term including external stimulation and pre-synaptic neuron stimulation. Pre-synaptic neuron stimulations can come in 5 types of chemical synapse and 1 type of electrical synapse. Equation (3) is a single exponential time constant decay used in fast response receptor type, such as AMPA, GABA, Ach and GCL. These receptors only have different decay time constant and reversal potentials. NMDA receptor dynamics are more complex and given in eq. (3)(4), since the opening of this receptor is also influenced by magnesium ions. Gap junction between neurons are described by the last term in eq. (2).

$$C_m \frac{\mathrm{dV}}{\mathrm{dt}} = -g_L(V - V_L) + I_{\mathrm{syn}} \ldots..(1)$$

$$I_{\mathrm{syn}} = \sum g_{\mathrm{AMPA}} s_{\mathrm{AMPA}} (V - V_E) + \sum g_{\mathrm{GABA}} s_{\mathrm{GABA}} (V - V_E) + \sum \frac{g_{\mathrm{NMDA}} s_{\mathrm{NMDA}} (V - V_E)}{1 + [M_g^{2+}] \frac{e^{-0.062V}}{3.57}} + \sum g_{\mathrm{GAP}} (V - V_{\mathrm{post}}) \ldots.(2)$$

$$\frac{\mathrm{ds}}{\mathrm{dt}} = \sum_k \delta(t - t^k) - \frac{s}{\tau} \ldots.(3)$$

$$\frac{\mathrm{dx}}{\mathrm{dt}} = \sum_k \delta(t - t^k) - \frac{x}{\tau_x} \ldots.(4)$$

$$\frac{\mathrm{ds}}{\mathrm{dt}} = \alpha_s (1 - s) x - \frac{s}{\tau_s} \ldots.(5)$$

We solve eq.(1) to (5) with a first order exponential integrator (EI) approximation as numerical iteration in each time step. Eq. (6) is derived from (1) with EI form, Eq. (7) is derived from (3) with EI form and equation (4)(5) has the EI form (8)(9).

$$V = V * df_V + \frac{ef_V}{C_m}(g_L * V_L + I_{syn}), \tau_V = \frac{g_L}{C_m}, df_V = exp\left(\frac{-dt}{\tau_V}\right), ef_V = \tau_V \left(1 - exp\left(\frac{-dt}{\tau_V}\right)\right) \ldots.(6)$$

$$s = s * df_s + \delta(t - t^k), df_s = exp\left(\frac{-dt}{\tau_s}\right)\text{....(7)}$$

$$x = x * df_x + \delta(t - t^k), df_x = exp\left(\frac{-dt}{\tau_x}\right)\text{....(8)}$$

$$s = s * df_s + ef_s * \alpha_s * x * (1 - s), df_s = exp\left(\frac{-dt}{\tau_s}\right), ef_s = \tau_s * \left(1 - exp\left(\frac{-dt}{\tau_s}\right)\right)\text{....(9)}$$

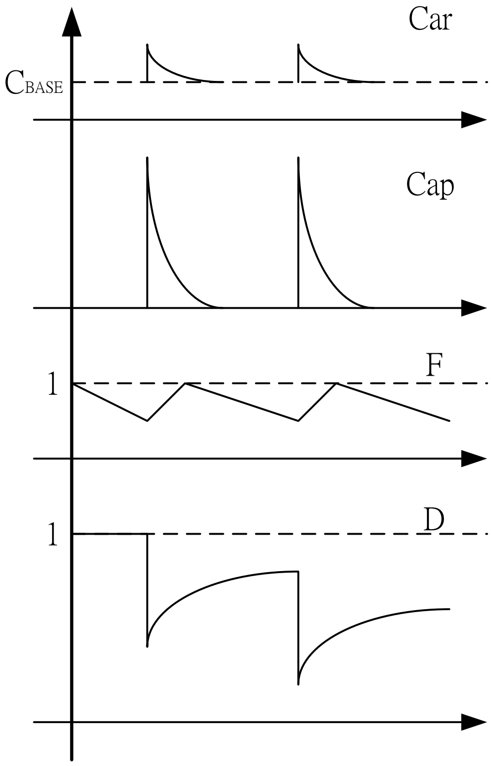
In each time step, simulator will update all gating variable on each neuron by pre-synaptic neuron firing or not:

If (presynaptic neuron firing)
$s = s + 1$ ....(10)
else
$s = s * df_s$...(11)

If (presynaptic neuron firing)
$x = x + 1$.......................................(12)
else
$x = x * df_x$...(13)

A.2 Short term plasticity

Flysim supports short-term facilitation (STF) and short-term depression (STD) as shown in figure 5. This type of plasticity influences the millisecond to hundreds of millisecond time-scale of the dynamics of synapse. Use option –STP to activate this mechanism, which then calculates $\frac{ds}{dt} = D * F * \sum_k \delta(t - t^k) - \frac{s}{\tau_s}$ (instead of Eq. (3) in Appendix A.1) and $\frac{dx}{dt} = D * F * \sum_k \delta(t - t^k) - \frac{x}{\tau_x}$ (instead of Eq. (4) in Appendix A) for synaptic dynamics. The other option –STD is used for only STD, at F is set to 1 all of the time. The variables D and F depend on the calcium dynamics as represented by C_{ar} and C_{ap}. The associated equations are described in Fig 5.



$$\frac{dC_{ar}}{dt} = \frac{(C_{BASE} - C_{ar})}{\tau_{Car}} + \alpha_{Car} \cdot \delta(t)$$

$$\frac{dC_{ap}}{dt} = -\frac{C_{ap}}{\tau_{Cap}} + \alpha_{Cap} \cdot \delta(t)$$

$$\frac{dF}{dt} = -\frac{F}{\tau_F} + (C_{ar} + C_{ap}) \times (1 - F) \times \alpha_F$$

$$\frac{dD}{dt} = \frac{(1 - D)}{\tau_D} + D \times (1 - pv \cdot F) \times \delta(t)$$

Figure 5. Short term plasticity is determined by the facilitation variable F and depression variable D, which depend on the calcium dynamics.

A.3 Long term plasticity

Spike timing dependent plasticity (STDP) is an extensively studied mechanism of long-term synaptic plasticity on a time scale of tens of seconds to tens of minutes, and implemented in Flysim for synapse conductance changes. As shown in figure 6, we use an additive rule for long-term facilitation (LTF) and a multiplicative rule for long-term depression (LTD). This mechanism must open long-term plasticity (–LTP) option in command line.

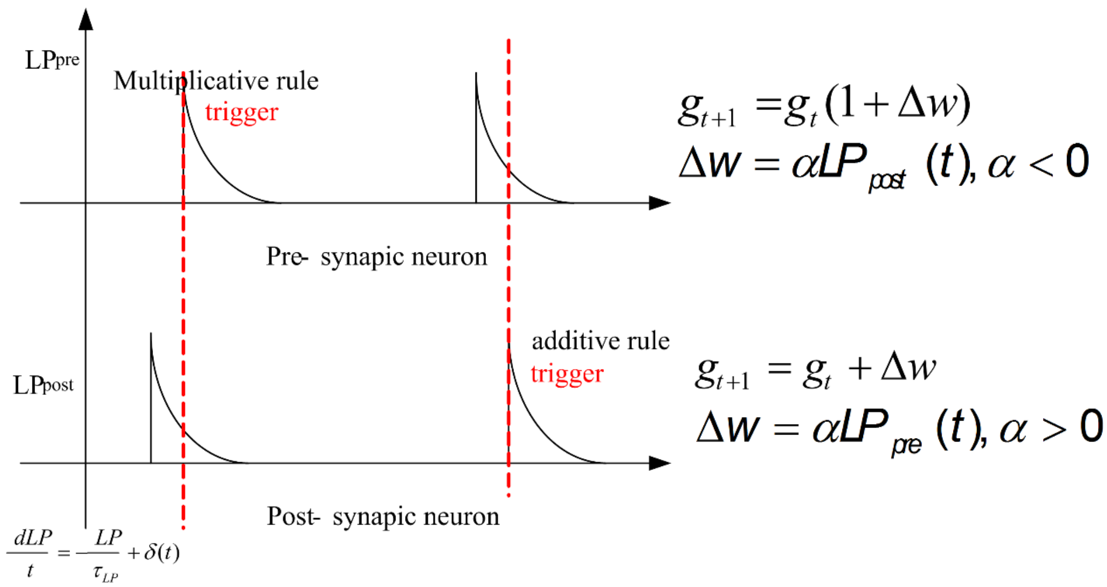


Figure 6. Long-term plasticity is measured between pre- and post-synaptic spike pairs. Each spike is associated with a single exponential decay variable LP. Additive rule is used when α is positive and the post-synaptic neuron firing, multiplicative rule is used when pre-synaptic neuron firing with negative α. Where α is scaling factor. Combine positive or negative α in positive or negative inter spike interval can shape different type STDP.

In an example shown in figure 7, several spike pairs can change the synaptic conductance by over 20%, from 1.5nS increasing to 1.9nS, or decreasing to 1.1nS in the long term.

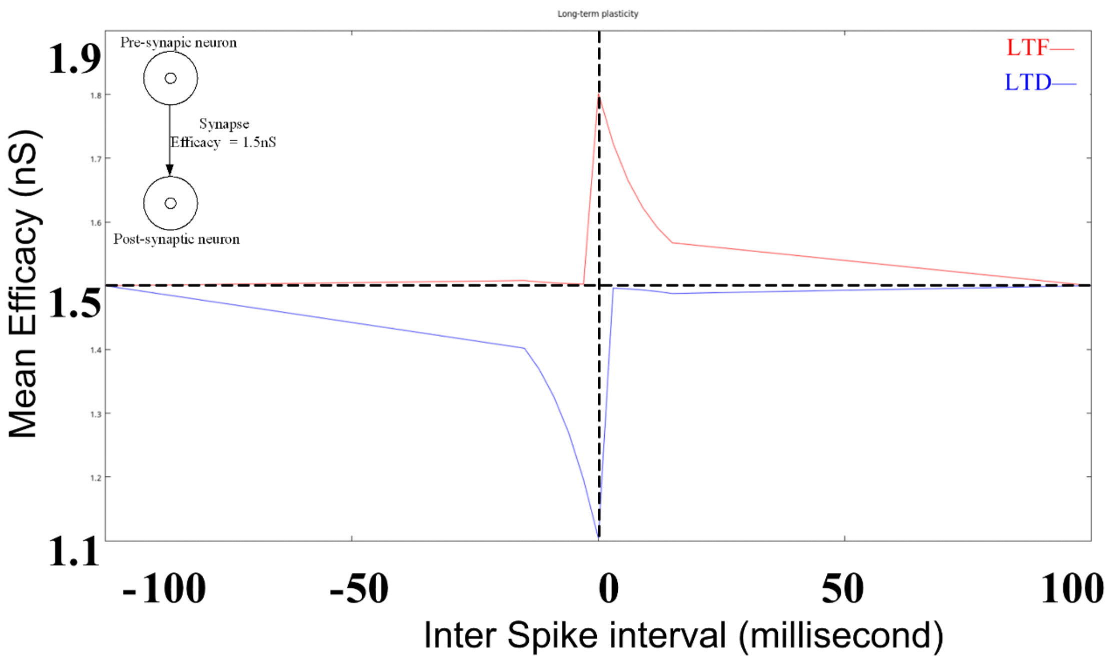


Figure 7: Curve showing conductance changes as a function of spike pair time differences during STDP mechanism. Red line presents LTF as additive rule with positive α in positive inter spike interval, and LTD performs multiplicative rule with negative α drawn in blue line.

A.4 External(background) stimulation

In the protocol definition, each neuron has 2 types of external stimulation, whereby one is the receptor input, and the other is the current input. The receptor input uses Poisson spike trains to stimulate each neuron's receptors. The command Type=ChangeExtFreq sets the input type to be receptor. To set the receptor type to be AMPA, use Receptor:AMPA, where AMPA can be replaced by AMPA, GABA, NMDA, ACH, GCL or Gap for the corresponding receptor types. FreqExt=240 sets the input spike rate to be 240 Hz. This rate value is limited between 0 and 10,000 Hz.

The second input type, the current input, is simulated by a direct current injection to the membrane with a Gaussian noise, and the mean and the standard deviation of the current can be specified by the users (Fig 8).

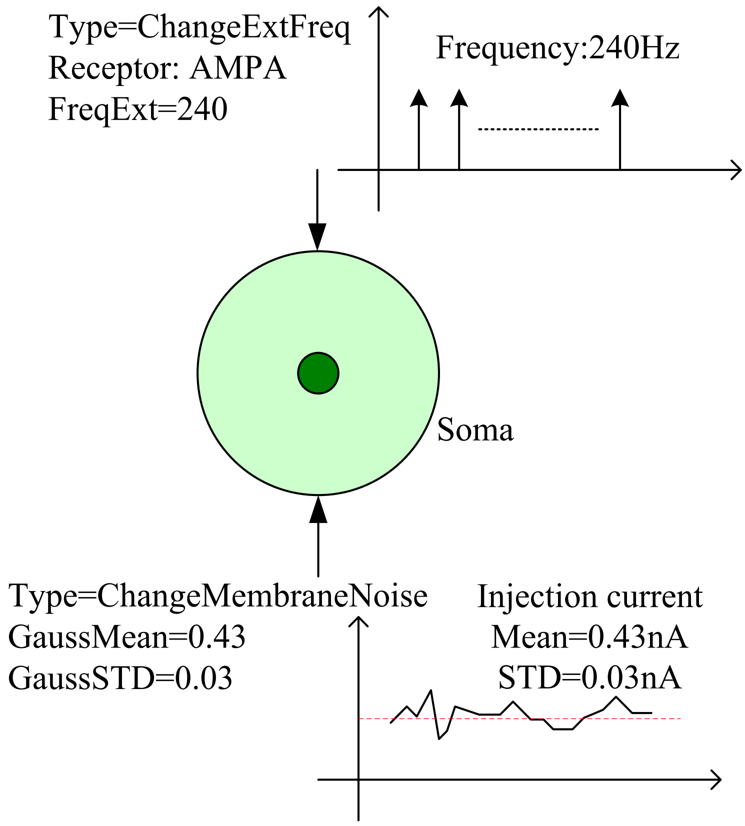


Figure 8. In Flysim, each neuron can receive two types of input: the receptor input and the current input.

The current input can be activated by using the command Type=ChangeMembraneNoise. In Figure 8, GuassMean=0.43 sets the injected current to 0.43 nA (negative values hyperpolarize the neuron), and GaussSTD=0.03 generates a standard deviation= 0.03 nA.

Reference

Hempel CM, Hartman KH, Wang XJ, Turrigiano GG, Nelson SB, Multiple forms of short-term plasticity at excitatory synapses in rat medial prefrontal cortex. J Neurophysiol 83:3031–3041.

Wang, X.-J. Synaptic basis of cortical persistent activity: the importance of NMDA receptors to working memory. J. Neurosci. 19: 9587–9603.