Week 5: Modeling Non-Linear NMDA Channels

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July 27, 2015

1 The complexity of NMDA channels

I did it, I got the NMDA synapses to work!
NMDA channels are much trickier to model than AMPA receptors. NMDA channels have a much longer time constant than AMPA channels, by a factor of about 50. They also posess a non-linear property– at high pre-synaptic firing rates their conductance saturates and they no longer pass through any ions. This property implies that the spike trains do not obey the superposition property like they do for AMPA channels, the input spike trains coming from different neurons cannot be summed up linearly at the same gating variable. Also, NMDA synapses are influenced by membrane voltage and Magnesium concentration.
The property that the NMDA synapses are voltage and Magenesium concetration dependent implies that their conductance has to be multiplied by a non-linear voltage dependendent factor in the following fashion

$$g_{NMDA}/(1 + b * exp(-a * v)$$

The dynamics of channel is modeled with the following differential equation:

$$\frac{ds}{dt} = -\frac{1}{\tau_s} + \alpha_s x(1 - s))$$

and the dynamics of the auxiliary gating variable x is given by:

$$\frac{dx}{dt} = -\frac{1}{\tau_x} x$$

In code the solution to the problem takes the form:

```
eqs_exc='''
dv/dt=(-Gee*s_tot*(v-E_nmda)/(1+b*exp(-1/a*v)))/Cm_e : volt
ds_ext/dt=-s_ext/t_ampa : 1
ds_nmda/dt=-s_nmda/t_nmda+alpha*x*(1-s_nmda): 1
dx/dt=-x/t_x : 1
s_tot : 1
'''
```

The technical solution to the superposition principle at the gating variable comes from the Stanford assignment notes “Persistent activity in a spatial working memory model”- The NMDA gating variable is integrated presynaptically

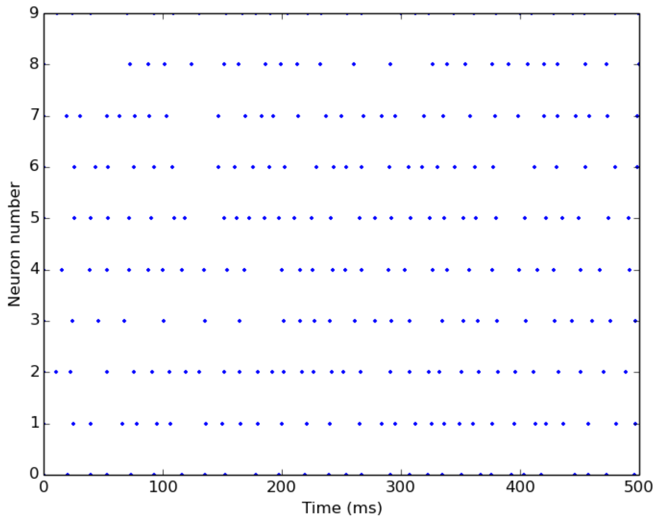

Figure 1: AMPA connected network with Poisson stimulation

for each neuron projecting NMDA synapses. The product of this computation is then used to compute the input currents to postsynaptic neurons.

In code this solution takes the following form:

```
 @network_operation(clock=simulation_clock, when='start')
def update_nmda(clock=simulation_clock):
    s_NMDA=exc_neurons.s_nmda.sum()
    exc_neurons.s_tot=s_NMDA
```

2 The Experiment

We made a group of neurons with AMPA and NMDA synapses. The AMPA synapses were used to deliver Poisson input to the cells, as this could not be done through the NMDA channels. We connected the neurons within this network through the NMDA channels in the following manner:

```
inter_connectivity = Connection(exc_neurons,exc_neurons,'s_tot',weight=1.0,spar
```

The spiking patterns of the network of the previously simulated neurons with AMPA interconnections receiving identical Poisson input are illustrated in Figure 1. The network of NMDA connected channels with Poisson input is illustrated in Figure 2.

We sought to formally quantify the differences between these spike trains and once again used PyEntropy package for mutual information calculations. The similarity matrix computed thus is shown below. The mutual informations were extremely low, indicating that the NMDA channels significantly change the response of the network to stimuli (Figure 3).

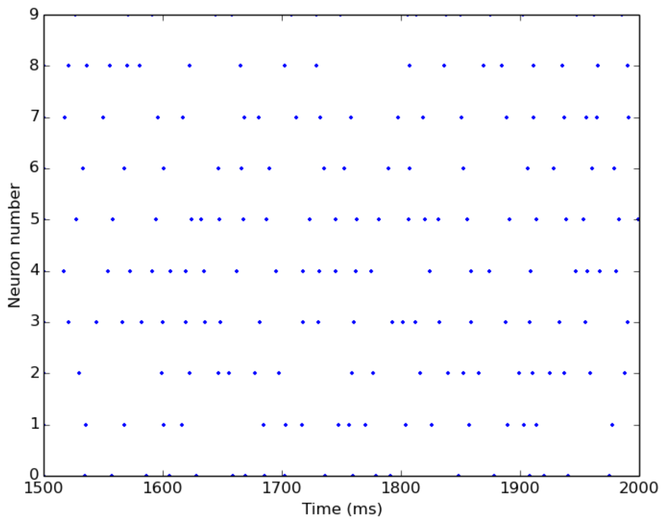

Figure 2: NMDA connected network with Poisson stimulation

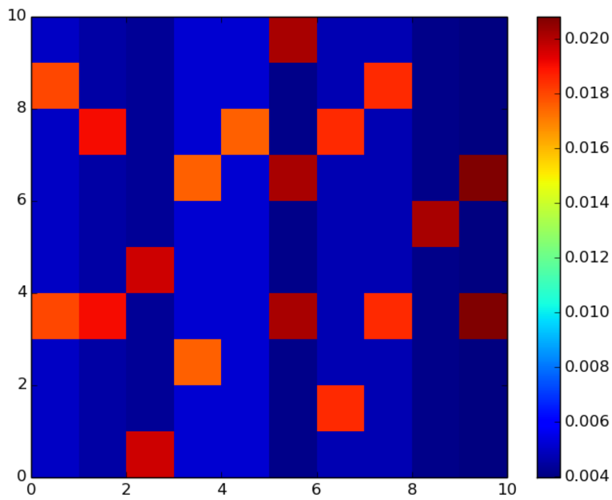

Figure 3: Excitatory neurons without inhibition (frequency 1.8 kHz)

3 Code

The code for this simulation is available on www.github.com/mariakesa under the title NMDA$_{F}inal.py$.

4 References

(1)Compte, A., Brunel, N., Goldman-Rakic, P., Wang, X-J. “Synaptic Mechanisms and Network Dynamics Underlying Spatial Working Memory in Cortical Network Model”, Cerebral Cortex, 2000