Change of Synaptic Strength by Spike Timing

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Abstract

Experiments [Markram et al., 1997] have shown that the coincidence of postsynaptic back propagating action potentials (bAPs) and unitary excitatory postsynaptic potentials (EPSPs) can induce changes in synaptic strength. The strength is up- or down-regulated depending on the precise timing of the postsynaptic AP relative to the EPSP. In this project, we propose a calcium dynamic model that could explain the experimental results.

1 Introduction

Early studies [Stuart and Sakmann, 1994] have revealed that dendrites are active conductance that could relay action potentials propagating back to the ending of the dendritic tree. Further studies [Markram et al., 1997, Magee and Johnston, 1997] discovered that APs propagating back into the dendritic tree could modify the synaptic connections. And the key is the calcium dynamics which depend on the relative timing of the back-propagating APs and the subthreshold EPSPs [Koester and Sakmann, 1998].

2 The Model

A three states vesicle pool model is first established as presented by [Tsodyks and Markram, 1997] .

$\frac{dR}{dt} = \frac{I}{\tau_{rec}} - U_{SE} \cdot E \cdot \delta(t - t_{EPSP})$,

$\frac{dE}{dt} = -\frac{E}{\tau_{inact}} + U_{SE} \cdot E \cdot \delta(t - t_{EPSP})$,

$I = 1 - R - E$,

where $\delta(x)$ is the Dirac Delta function and t_{EPSP} is the time of the EPSP.

We further enrolled Ca^{2+} dynamics that has a constant rate of decay and a calcium influx term at each EPSP and back-propagating AP.

$\frac{dCa}{dt} = Ca_{decay} + Ca_{influx,EPSP} \cdot \delta(t - t_{EPSP}) + Ca_{influx,AP} \cdot \delta(t - t_{AP})$,

Studies [Koester and Sakmann, 1998] have shown that the post-APs propagating back into the dendritic arbor can open voltage-dependent calcium channels (VDCCs) and mediate a calcium inflow. The EPSPs, caused by pre-APs, can transiently open the NMDA receptors and mediate a calcium influx. However, local rise in the calcium level, for example from the post-APs, can cause inhibition of the NMDA receptors.

To be consistent with the experimental results, we suppose the $Ca_{influx,AP}$ to be a constant term in this simple model, but $Ca_{influx,EPSP}$ is inversely proportional to the intracellular calcium level.

$Ca_{pre-AP,influx} = Ca_{influx} \cdot (1 - \frac{Ca}{Ca_{max}})$,

As determined by [Dodge Jr and Rahamimoff, 1967] , the EPSC is proportional to about the fourth power of the calcium level.

$EPSC = A_{SE} \cdot E \cdot U_{SE} \cdot Ca^4$,

Lastly, the postsynaptic potential is modeled by a passive membrane mechanism.

$\frac{dEPSP}{dt} = -EPSP + \frac{R_{in} \cdot EPSC}{\tau_{membrane}}$.

3 Results

We will demonstrate two properties of our model in this section. Both of them are in consistent with experimental results. Firstly, we will show that the relative timing between the EPSP and the post-AP is critical for the changes of synaptic strength and it is confirmed by experiments shown in Fig. 1.

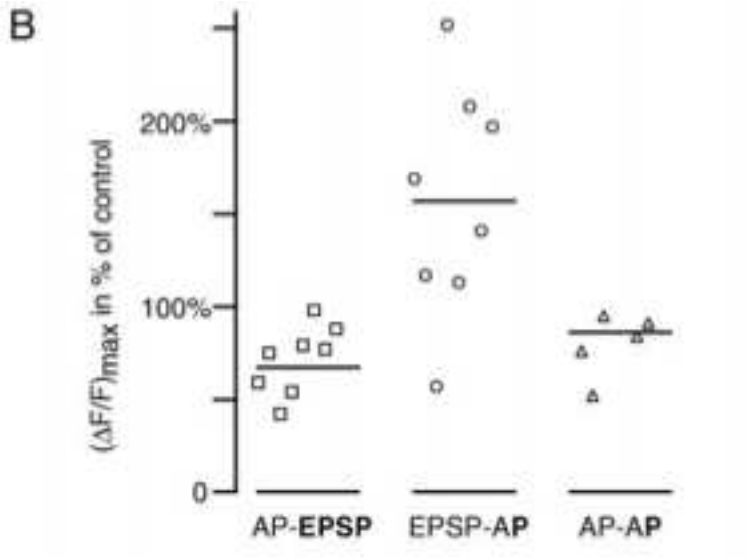

Fig.1 Relative timing of the EPSP and the post-AP [Koester and Sakmann, 1998] .

We will also demonstrate that the synaptic strength depends on the stimulus frequency which is consistent with experiments shown in Fig. 2.

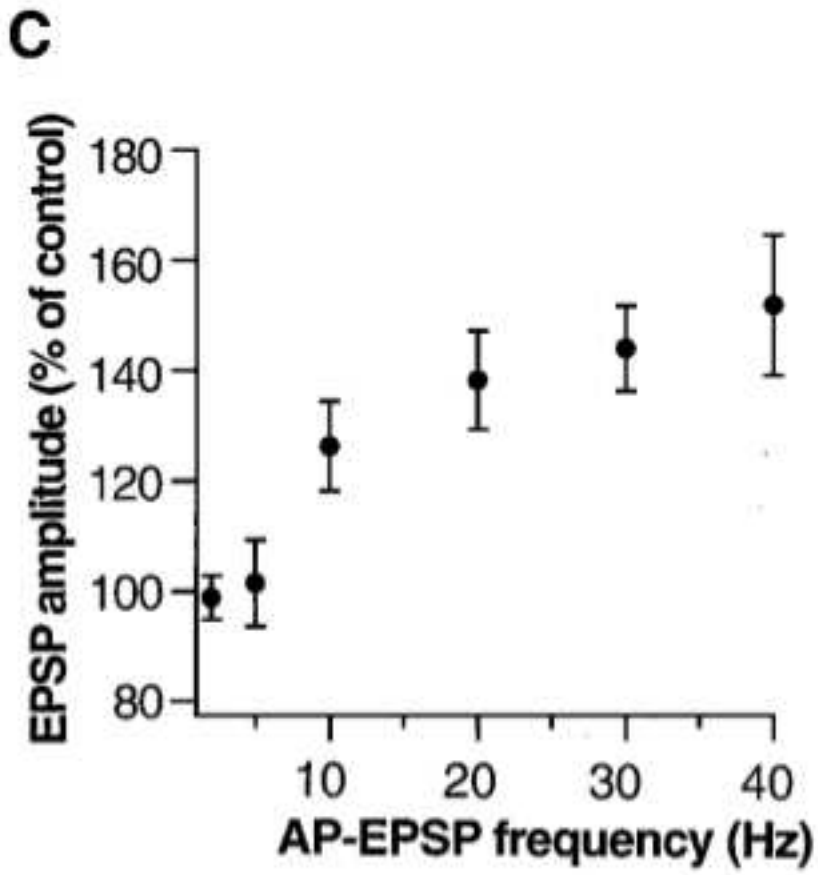

Fig.2 Stimulus frequency dependent synaptic change [Markram et al., 1997] .

3.1 Spike Timing Dependent Synaptic Change

In order to show that the synaptic strength depends on the timing of the EPSP and the back-propagating AP, we first show a set of control simulations to rule out the possibilities that the EPSP or the post-AP alone could enhance the synaptic strength.

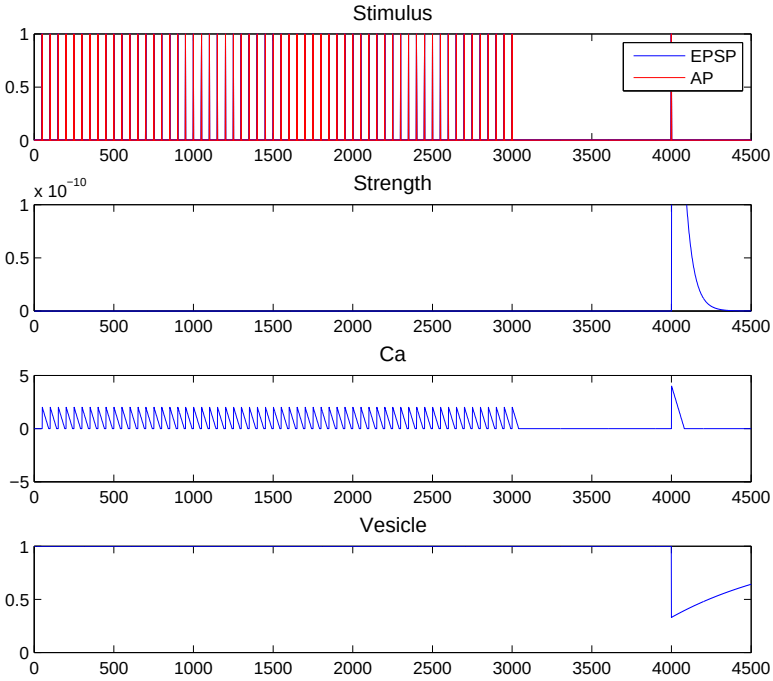

Fig.3 The post-AP only

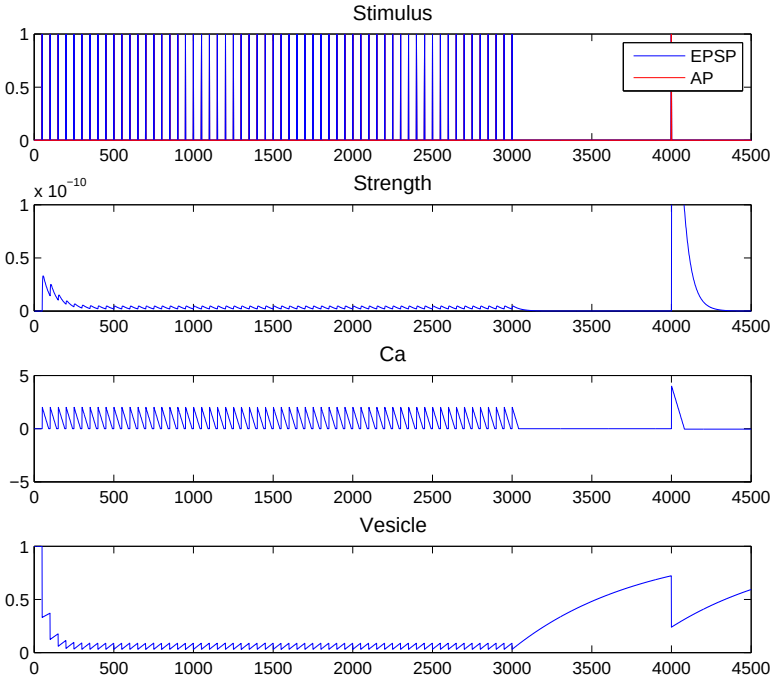

Fig.4 The EPSP only

As shown above in Fig.3 and Fig.4. Without the pre-APs, the post-APs alone in the model can not generate the EPSPs. Also the EPSPs alone could only provide a transient increase in the calcium level which goes back to the baseline without the help of the back-propagating APs.

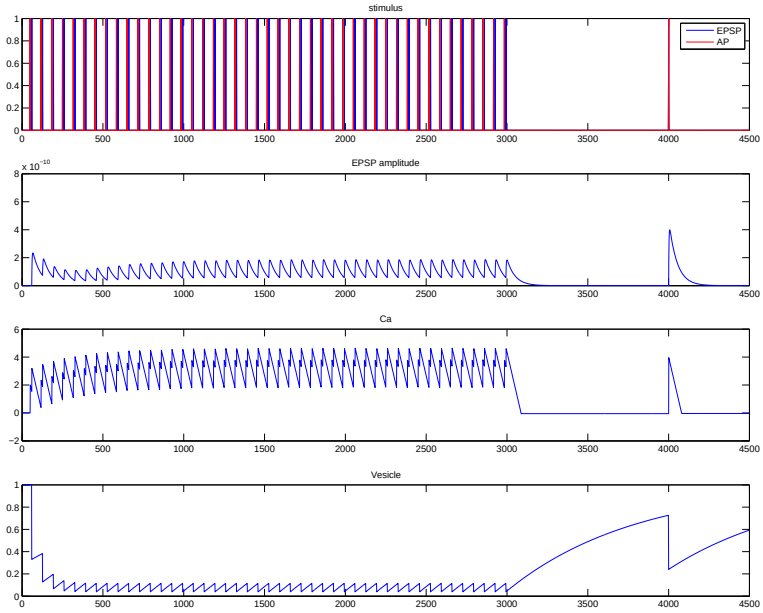

Fig.5 The post-AP comes 10ms before the EPSP

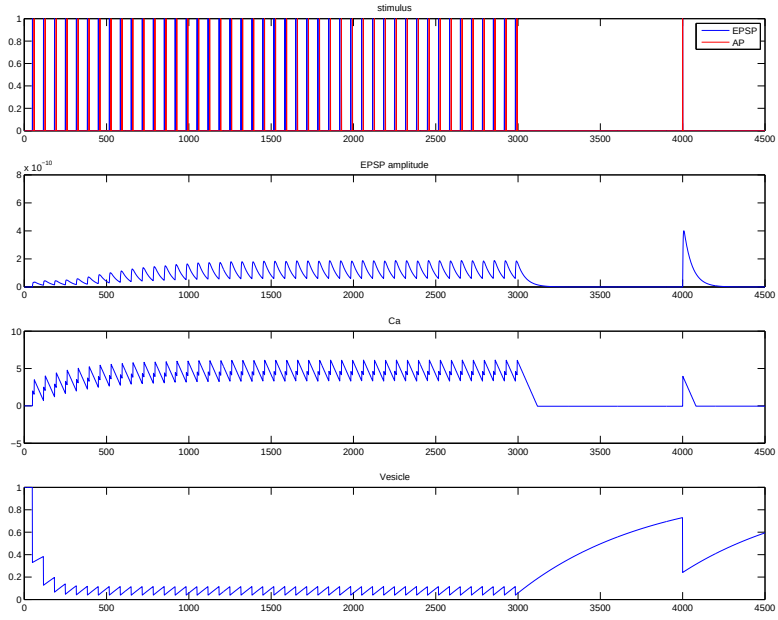

Fig.6 The EPSP comes 10ms before the post-AP

The timing difference between the EPSP and the post-AP plays a key role in modulating the synaptic strength. Shown in the third panel of Fig. 6, If the EPSP comes first, it will transiently elevate the

calcium level which could be significantly accumulated if the back propagating AP also comes in a timely manner. However, if the post-AP comes first, the NMDA receptors will be inhibited by the elevated calcium level from VDCC inflow. This reduces the peak calcium concentration even if the EPSP comes immediately after the post-AP (Fig.5).

3.2 Frequency Dependent Synaptic Change

We also investigated the dependence of synaptic strength to stimulus frequency. As shown in Fig.7, low frequency stimulus give the intracellular calcium enough time to relax back to its background level but because of the vesicle pool depletion, the synapse is depressed. However, for high frequency stimulus (Fig.8), the calcium have no time to decay back to the baseline and will accumulate to a higher steady level. This will increase the synaptic connection.

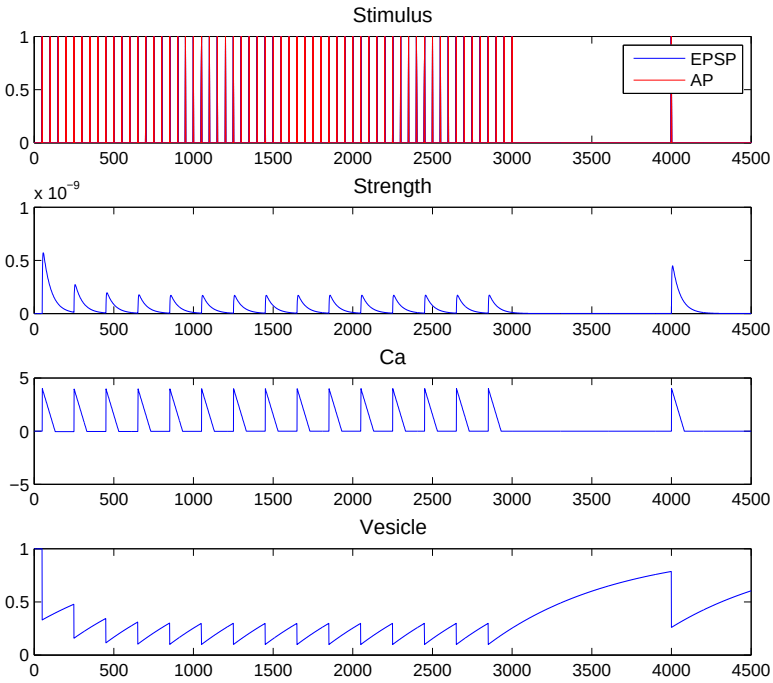

Fig.7 5Hz

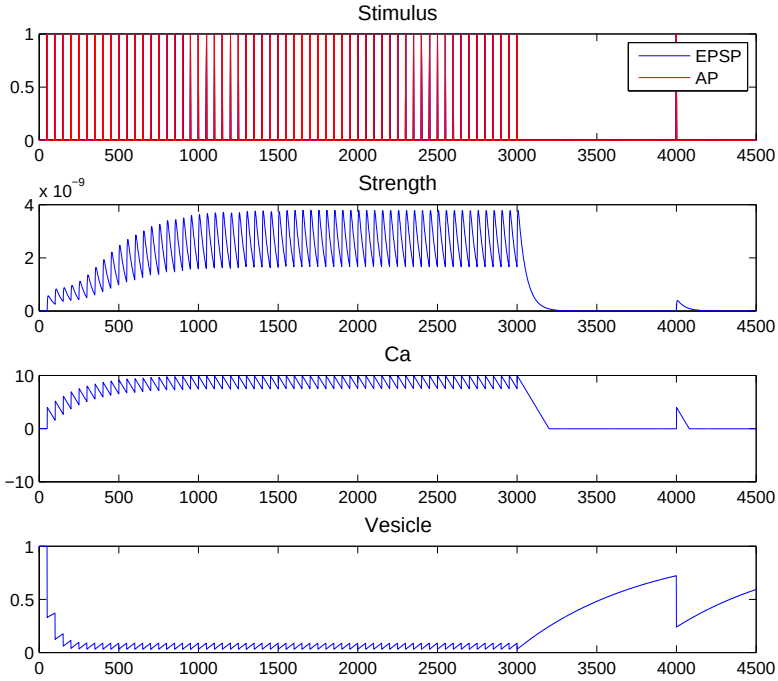

Fig.8 20Hz

4 Conclusion

In this project, we build up a model to explain the time dependence of synaptic change. Our model simulates the calcium dynamics by taking into account the calcium uptake from both the EPSPs and the back propagating APs. This mechanism also revealed the time relationship between the two parts which is consistent with experimental results.

References

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