Hippocampal mossy fiber boutons as dynamical synapses

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1 Summary ($\sim$ 1000 words)

1.1 Introduction

Usually models assume that the synaptic efficacy is static, or at least change only at a very low time scale with learning. Biologically, this is not correct, and a good amount of studying is being dedicated to identify the roles of these short time scale adaptations.

In the present paper, the consequences of dynamic properties, namely facilitation and depression, associated to hippocampal mossy fiber boutons are explored: specifically a study is carried on the dependence of the pyramidal cell activity with the input stimulus frequency to the mossy fiber boutons as well as the influence of single vesicle post-synaptic response magnitude on this dependence.

Hippocampal mossy fibers have their origin in dentate granule cells and terminate on the proximal dendrites of CA3 pyramidal cells where its activity produces fast glutamergic excitatory post-synaptic potentials (EPSPs). They have a strong influence in CA3 pyramidal neurons activity not only due to the proximal location but also because of the multiple release sites, up to 37 (Chicurel and Harris, 1992), which generate large EPSPs.

In this study we used a realistic topology of a CA3 pyramidal neuron with calcium dynamics and plausible ionic currents and a model of mossy fiber synapses that incorporates facilitation and depression with a probabilistic interpretation.

1.2 Methods

All simulations were performed with *NEURON* (Hines and Moore, 1997).

The CA3 pyramidal neuron model used (Migliore et al, 1995), with realistic topology, included the following currents: INa (transient), ICa, IT low threshold, IK, IA, IK, Ca; and calcium dynamics. All the parameters used were based in

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experimental results. The temperature was set to 30 Celsius. Using *NMODL* (Neuron Model Description Language) a model was created for the mossy fiber synapse based in Fuhrmann et al. (2002) probabilistic model for dynamic synapses which accounts for facilitation and depression processes. According to this model, P_r, the probability of release for every release site at time of a spike, t_{sp}, is given by $P_r(t_{sp}) = P_{vr} \cdot P_{va}$ where P_{vr} is the probability of vesicle release for a release site with an available vesicle (affected directly by facilitation) and P_{va} is the probability of a vesicle to be available for release at time t (directly affected by depression). The dynamics are:

$$\frac{dP_{vr}}{dt} = \frac{1 - P_{vr}}{\tau_{rec}} - P_{va} \cdot P_{vr} \cdot \delta(t - t_{sp}) \tag{1}$$

$$\frac{dP_{va}}{dt} = -\frac{P_{va}}{\tau_{facil}} + P_{vainc} \cdot (1 - P_{va}) \cdot \delta(t - t_{sp}) \tag{2}$$

where P_{vainc} is the step increment in the P_{va}, τ_{facil} is the relaxation time constant of facilitation and τ_{rec} the relaxation time constant of depression.

The post-synaptic response is then calculated according to the classical quantal model of release: $PSR = q \cdot n \cdot P_r$, where q is the the post-synaptic response to the release of each vesicle and n is the number of vesicle release sites. The values used for τ_{rec} and τ_{facil} were 300 and 1000 respectively which are in close contact with biological measured values (Markram et al. 1998). The post-synaptic conductance was modeled as a two state kinetic scheme synapse described by rise time of 0.5 ms and decay time constant of 5 ms (Jonas et al. 1993).

On this model a small number of mossy fiber synapses ($\sim$5) were connected to the CA3 pyramidal neuron with a increased associated conductance: instead of the typical 1 nS unitary conductance (Jonas et al. 1993), values ranging from 5 to 20 nS were used. The synapses were placed in the proximal region and all received the same stimulus characterized by a specific constant frequency (no variability was added to the interspike time intervals).

The dependency of the activity of the pyramidal neuron with the frequency and the post-synaptic conductance was measured as the number of spikes generated in a time window of 600 ms. The reason why a longer time window, which would put in evidence the steady-state conditions, was not used was because we were analyzing fast adaptations in a system that changes its state continuously. For a study in steady-state EPSP amplitude as a function of pre-synaptic frequency in dynamical synapses please see Markram el al. 1998.

1.3 Results

We began by analyzing the pyramidal neuron response, measured as the number of spikes in a 600 ms time windows, to constant frequency stimulation from the mossy fiber synapses. Figure 3 (in the *Graphics* section) shows the tuning curve for a single vesicle post-synaptic response, q, of 15 nS.

Since no noise was added, and associated with each bouton there was 25 release sites, no averaging was needed and each point in the graphic corresponds to a single trial. Due to the facilitation and depression properties, the dynamic synapses act

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as a band filter where input frequencies higher than 30 Hz or below 10 Hz have less impact in the neuron's activity. The peak frequency, associated with the highest activity, is 16 Hz. Dendritic filtering also affects the response to the high frequencies.

Changing the post-synaptic response trough the variable q, has the interesting effect of moving the peak frequency. Figures 1, 2 and 4 show the peak frequencies obtained with different values of q.

The associated peak frequencies are 12Hz (q=5nS), 16Hz (q=10nS) and 18-20Hz (q=20nS). A peak frequency of 8Hz was obtained with a single vesicle post-synaptic response of 2.5nS (graphic not shown). Beyond this values this relation saturates.

1.4 Discussion

A subtle point in this study is the size of the time window. Although for times superior to 600ms the tuning curves would show a even more defined band filter shape, it is important to keep in mind that we are dealing with fast adaptation processes. Another aspect that should be taken into account is that the first burst associated with the initiation of the stimulus (corresponding to synaptic dynamical properties transient) was not eliminated in the construction of the tuning curves.

The dependence of the peak frequency with the single vesicle post-synaptic response leaves space for speculation about the role of this dependence in information processing. Although experimental data (Richmond et al. 1990) suggests that temporal information is even present in responses to static and steady state stimuli, a strong debate exist around the hypothesis that the brain uses, or not, in a generalised way this temporal codes for processing information. Nevertheless, taking into account that average frequency is the main property when dealing with temporal pattern analysis, this dependence of the peak frequency with the single vesicle post-synaptic response shows that there is a simple mechanism available to, in a rough way and with an appropriate learning mechanism, tune the neuron to specific classes of input temporal patterns. This idea about specific classes of temporal patterns to which a synapse, with well defined parameters, gives its maximum response is explored in Natschläger and Maass, 2002.
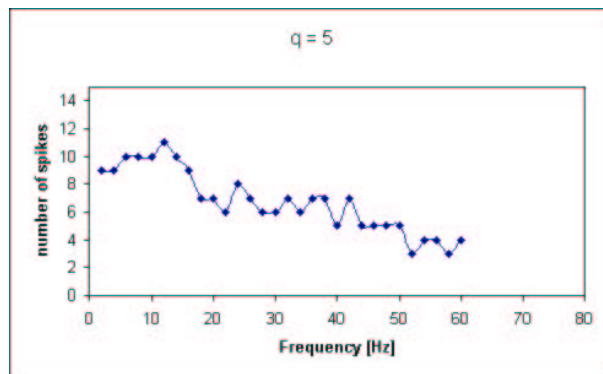
1.5 Graphics

Figure 1: Single Vesicle Post-Synaptic Responses of 5 nS
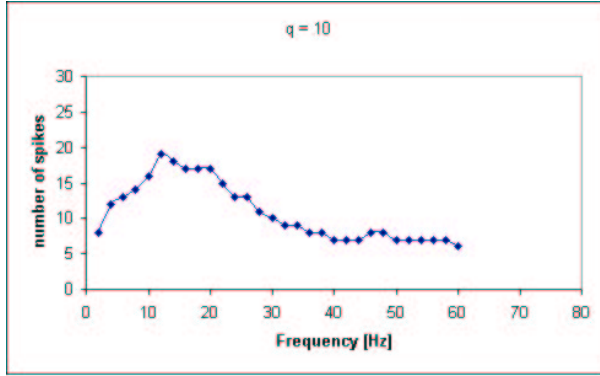
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Figure 2: Single Vesicle Post-Synaptic Responses of 10 nS
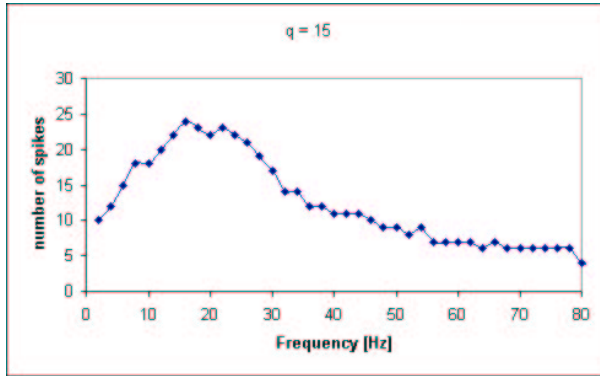

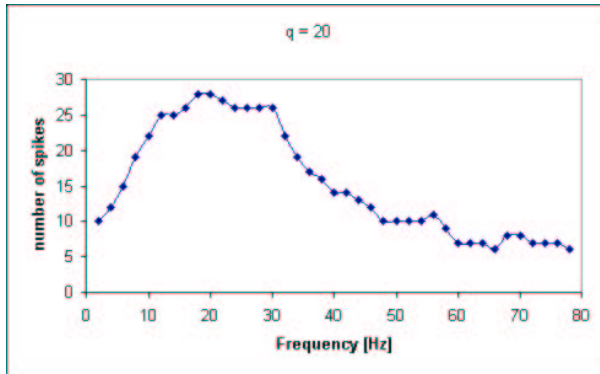Figure 3: Single Vesicle Post-Synaptic Responses of 15 nS

Figure 4: Single Vesicle Post-Synaptic Responses of 20 nS

1.6 References

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