Correlations modulate the non-monotonic response of a neuron with short-term plasticity

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Abstract

The impact of synchronous inputs onto a simple neuron model with synapses showing short-term plasticity (STP) is studied. The synaptic model includes depression, stochastic release and facilitation. The mean and second order statistics of the current are computed. The combination of synchrony and STP produces a non-monotonic behavior of the current variance σ, while the mean μ saturates monotonically. Provided that μ saturates under threshold, the output rate inherits the resonant behavior of σ, making the neuron respond maximally to a specific rate. Information about the input rate is therefore transmitted beyond the saturation of μ by means of σ.

Keywords: Short-term plasticity; synchrony; stochastic transmission; neural response

1 Introduction

Although short-term synaptic plasticity was first observed more than sixty years ago [3], its computational implications are still not fully explored. It has been suggested [**?**] that short-term depression (STD) provides a gain control mechanism which prevents a neuron from firing with increasingly higher rates, because, in the stationary regime, the mean synaptic current eventually saturates. This imposes an important constraint in the type of input messages that a neuron is sensitive to. More exactly, synaptic depression prevents the neuron from distinguishing the input rate beyond a certain saturation frequency ν_{sat} [9, 1].

On the other hand there has been an increasing interest in analyzing the impact of input correlations in the neural response [2, 7, 5] and to study whether they provide plausible coding strategies. In the present work we analyze the effect of cross-correlated inputs impinging on a target cell across dynamical stochastic synapses. We find that considering the all-or-none stochastic nature of synaptic transmission is important because the fluctuations of the synaptic current play a crucial role in driving the neuron response. We will show that when the mean current has saturated, a neuron can still be sensitive to its inputs because the current variance can be modulated either by the input rate ν, or by the input correlations.

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It will be shown that the presence of synchrony in the stimulus makes the response of a leaky integrate-and-fire neuron (LIF) exhibit a non-monotonic behavior, where the cell responds maximally to a preferred ν. While the amount of synchrony increases the gain of the resonance, the values of the synaptic parameters determine the position of the maximum.

Some of these results were previously presented in abstract form [6].

2 The model

The input stimulus consists of the afferent spike trains coming from C pre-synaptic neurons: $S_i(t) = \sum_l \delta(t - t_i^l)$ $(i = 1, 2, \ldots C)$. The activity of each afferent fiber is a modeled by stationary Poisson process with identical rate ν. The correlation among pre-synaptic neurons is positive and instantaneous, which means that there exist zero-lag cross-correlations or perfect synchrony. The second order statistics of the stimulus are completely defined by the correlation function of two spike trains which is

$$C_{ij}(t, t') \equiv \quad < S_i(t)\, S_j(t') >= \quad \nu\, \rho\, \delta(t - t') + \nu^2$$

The coefficient of correlation of the afferent spikes, ρ, equals the probability that given a spike at the fiber i at time t, there is another one at the fiber j at the *same* time.

The C presynaptic neurons connect onto a target cell. Each connection is composed of an arbitrary number of functional contacts, M, where transmitter release takes place. At each of these contacts a stochastic model of vesicle depletion, which incorporates a facilitating mechanism, is implemented: we model the dynamics of the vesicles by setting a primed pool (PP) of vesicles which can hold at most one of them. When a spike arrives the primed vesicle fuses the membrane, releasing its transmitter content, with a probability u. When this occurs, the PP is depleted and the time it takes to be replenished is a random variable following an exponential distribution with mean τ_v. During the recovery time no vesicle can undergo exocytosis upon arrival of a spike. This model was previously used in [8].

We model the facilitation of the transmission following the model proposed in [9]. The variable $u(t)$ represents the probability of release given that there is a vesicle ready. Upon arrival of a spike, it increases by an amount $U(1-u(t))$ and decreases exponentially towards the resting value U with a time constant τ_f.

The total synaptic current generated by a sequence of releases occurring at different contacts is assumed to be a sum of instant pulses:

$$I_{syn}(t) = \sum_{i}^{C} \sum_{n}^{M_i} J_{i,n} \sum_{k}^{rel} \delta(t - t_{i,n}^k) \tag{1}$$

where i is the index of the pre-synaptic neuron, n indicates the functional contact, and the last sum in k refers to the sequence of releases in the contact (i, n), that is, the subset of the incoming spikes which succeeded in triggering a synaptic response. The number of functional contacts that a neuron establishes, M_i, varies across neurons with a certain distribution with mean $\bar{M}$ and variance $\bar{M}^2\Delta_M^2$.

The current is numerically integrated with a leaky integrate-and-fire (LIF) neuron whose potential $V(t)$ follows:

$$\frac{dV(t)}{dt} = -\frac{V(t)}{\tau_m} + I_{syn}(t) \qquad \text{if } V(t) < \theta \tag{2}$$

When $V(t)$ reaches the threshold, θ, a spike is emitted and the potential is reset to H where it remains during a refractory period τ_{ref}. The synaptic efficacies, $J_{i,n}$ (introduced in eq. 1) measure, in voltage units, the amplitude of the PSP produced by the release of one vesicle. They are distributed with mean $\bar{J}$ and variance $\Delta^2\bar{J}^2$.

Averaging the stochastic response over trials with the same spike train pattern, this model becomes the phenomenological models of references [9, 1], which reproduce the experimental data. However, the resulting deterministic model leads to a neuron response different from that of the stochastic model. This occurs because the fluctuations due to the stochasticity of the synapse are wiped out in an *averaged* model, so that the synaptic current variance generated is severely reduced.

3 Statistics of the synaptic current

We will start considering synapses which do not show facilitation or equivalently $\tau_f = 0$. In this case, given that a vesicle is ready, the release probability is always $u(t) = U$. The mean and connected correlation function of the synaptic current (eq.1) read:

$$\mu = C\bar{M}\bar{J}\nu_r = C\bar{M}\bar{J}\frac{U\nu}{1+U\nu\tau_v} \tag{3}$$

$$C_I(t,t') = \sigma^2\delta(t'-t) - \frac{\Sigma_2}{2\tau_c}e^{-\frac{|t'-t|}{\tau_c}} \tag{4}$$

where ν_r is the rate of release at a single functional contact. The time constant is $\tau_c \equiv \frac{\tau_v}{1+U\nu\tau_v}$. The coefficients σ^2, which we shall call the current variance, and Σ_2 are

$$\sigma^2 = C\bar{M}\bar{J}^2\nu_r\left[(1+\Delta_J^2) + \frac{U(\bar{M}(1+\Delta_M^2)-1)}{1+U\nu\tau_v(1-U/2)} + \frac{U(C-1)\bar{M}\rho}{1+U\nu\tau_v(1-U\rho/2)}\right] \tag{5}$$

$$\Sigma_2 = 2C\bar{M}\bar{J}^2\nu_r^2\tau_c\left[(1+\Delta_J^2) + \frac{U(\bar{M}(1+\Delta_M^2)-1)(1+U\nu\tau_v/2)}{1+U\nu\tau_v(1-U/2)} + \frac{U(C-1)\bar{M}\rho(1+U\nu\tau_v/2)}{1+U\nu\tau_v(1-U\rho/2)}\right]$$

Several observations must be made here: i) μ rapidly saturates as ν increases (see middle plot in fig.1). Making an expansion of μ around its asymptotic value up to first order in $\frac{1}{\nu}$, the saturation frequency, ν_{sat}, is defined as the frequency at which the first order correction equals the zero order term. It equals $\nu_{sat} = \frac{1}{U\tau_v}$ and sets the point beyond which the *stationary* value of μ is insensitive to the value of ν [1]. ii) The negative exponential correlations are due to the refractoriness arising from vesicle recovery. iii) The releases at different contacts are synchronized by means of two sources: the synchrony present in the pre-synaptic activity (last term within the squared brackets of eq. (5) when $\rho > 0$) and the fact that each pre-synaptic neuron stimulates M different contacts with exactly the same train (second term within the brackets of (5) when $M > 1$). The striking feature about this release synchrony is that it is modulated by the input rate, and eventually vanishes when ν goes to infinity. More precisely, making $M = 1$, the coefficient of correlation of the releases takes the form:

$$\rho_r = \frac{U\rho}{1+U\nu\tau_v(1-U\rho/2)} \tag{6}$$

This expression shows the impact of unreliability and depression on the synchronization of the responses: the first, i.e. $U < 1$, attenuates the effect of $\rho > 0$, while the second

makes the releases desynchronize when ν becomes large, i.e. $\lim_{\nu\to\infty}\rho_r = 0$. Computing the saturation frequency for σ^2, as it was done before for μ, it yields

$$\nu'_{sat} = \frac{1}{U\tau_v}\left(1+\frac{U(M-1)}{1-U/2}+\frac{U\rho(C-1)M}{1-U\rho/2}\right) \quad (7)$$

Therefore, beyond ν'_{sat}, the current variance saturates to the value $\sigma^2 \simeq \frac{C\bar{M}\bar{J}^2(1+\Delta_J^2)}{\tau_v}$. This expression equals the fluctuations produced by $C\bar{M}$ independent Poisson trains with rate $\frac{1}{\tau_v}$. But that is exactly the vesicle recovery rate, which explains that, in saturation, the release statistics are essentially governed by the vesicle recovery process. Because recovery occurs *independently* at each contact, in saturation, there are no correlations across contacts. Therefore, in this regime, the trace of the input synchrony cannot be detected.

When $\rho > 0$, or $M > 1$, we obtain that $\nu'_{sat} > \nu_{sat}$. This implies that after the mean current has saturated, the second order statistics still conveys information about ν. This information can be read out by the neuron if its output is sensitive to the fluctuations of the current. Recent works [7, 5] have shown that this is the case when the neuron works in a sub-threshold regime. This regime is defined by the condition that the mean depolarization, which in our case equals $< V(t) > \simeq \mu\tau_m$, falls below threshold. We find that for a wide range of plausible values of the parameters, $\mu\tau_m$ saturates below threshold, leading naturally to the regime where the modulation of the current variance is maximally expressed in the output.

What happens when facilitation is included? As a first approximation, we can substitute U in the previous expressions of σ^2 and ρ_r by its mean value $< u(t) >= \frac{U+U\nu\tau_f}{1+U\nu\tau_f}$. This is a monotonic increasing function of ν which saturates to one. In consequence, at low rates $\rho_r \sim U\rho$ and, since U in facilitating synapses takes very low values (as low as 0.02), synchrony is strongly attenuated. As ν increases, the synapse facilitates and unreliability due to low $u(t)$ no longer weakens the impact of the synchrony. However, as ν becomes higher, depression starts to play a predominant role, and ρ_r decreases because of saturation. Therefore depression and facilitation tend to diminish the magnitude of the release cross-correlations at high and low rates, respectively. Thus, there exists a resonance in the synaptic responses synchrony. As in the case with only depression, the variance σ^2 also displays a non-monotonic behavior as a function of ν (see middle plot in fig. 1).

4 Response of a LIF neuron

To test whether this resonance present in the current fluctuations could be readout by a neuron, we simulated a LIF spike generator integrating $I_{syn}(t)$ plus a balanced background current (see caption of fig. 1). The output rate, ν_{out}, is illustrated in fig. 1 (top and bottom plots) for three different amounts of synchrony ($\rho = 0.06, 0.12, 0.2$). The middle plot shows the numerical and theoretical prediction of the mean and standard deviation of the current received in a time window τ_m. These magnitudes read $\mu\tau_m$ and $\sigma^2\tau_m + \Sigma_2(\tau_m - \tau_c(1-e^{-\tau_m/\tau_c}))$, respectively. The mean saturates monotonically below the threshold value, $\theta = 20$ mV, and it is independent of ρ. The deviation shows a resonant behavior which becomes more prominent as ρ increases. Thus ν_{out} inherits the non-monotonic behavior from the input fluctuations and its overall magnitude scales with the input synchrony. When $\rho = 0$, the fluctuations, which are not resonant anymore, are too small to make the neuron fire. The position of the maximum depends crucially on the synaptic parameters U and

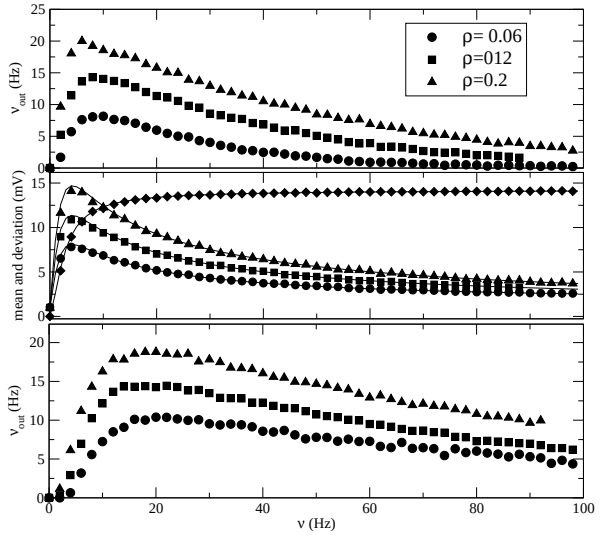

Figure 1: **Non-monotonic response function to a correlated input with STP. Top**: numerical output rate vs. input ν for three different grades of input synchrony (see inset). **Middle**: Mean (diamonds) and variance (symbols as in top) of the synaptic current received in a time window τ_m, for the three same examples as top plot. Solid lines represents the theoretical prediction derived from the expressions (3-5) and shown in the text. **Bottom:** Response function as in top but with a slight change of the parameters U and τ_v. We see that ν_{out} inherits the non-monotonic behavior from the current fluctuations because the mean depolarization $\mu\tau_m < \theta$. While ρ determines the amplitude of the resonant function the parameters U and τ_v set the position of the maximum. Top inset applies for both plots. Error bars are smaller than symbols size. Current parameters: $C = 3750$, $\bar{M} = 1$, $\Delta_M = 0$, $\bar{J} = 0.19$ mV, $\Delta_J = 0$, $\tau_v = 1$ s (top) and 0.9 s (bottom), $\tau_f = 1.5$ s, $U = 0.1$ (top) and 0.028 (bottom). Neuron parameters: $\theta = 20$ mV, $\tau_m = 20$ ms, $H = 10$ mV and $\tau_{ref} = 2$ ms. Background: $J_e = 0.05$ mV, $J_i = -0.2$ mV, $C_e = 2000$, $C_i = 500$, $\nu_e = \nu_i = 2$ Hz and static reliable synapses

τ_v. By coherently changing both, the maximum is boosted with little change in magnitude (compare top and bottom plots).

Moreover, the figure shows that ν_{out} can be modulated for input rates beyond ν_{sat}, i.e. the saturation value for μ. This means that input correlations provide a mechanism by which a neuron with STD can encode information about high input rates by means of the variation of the fluctuations of its afferent current.

5 Conclusions

Short-term depression prevents an individual synapse from releasing transmitter with increasingly higher rates. This constraint may lead to scenarios in which a fixed number of afferent fibers cannot make a target neuron reach threshold unless they *cooperate*, that is,

there exist cross-correlations. But synchronous firing does not necessary produce transmitter discharge with the same grade of synchrony because vesicle release is stochastic. Not only correlations are therefore needed but also reliable transmission. STP makes this unreliability be a function of ν and as a result it shapes in a non-monotonic way the response function. Moreover, our results show (fig. 1) that ρ, besides making the neuron respond in a tuned manner to ν, acts as a gating variable which switches the output on and off.

The parameters U and τ_v, are subject to long term changes by pairing the pre and postsynaptic activities [4]. This could be a plausible way to adjust the selectivity of neurons, since we showed that it depends finely in the values of these two parameters.

Our results stress the importance of the synaptic fluctuations driving the neuronal response. For this reason, taking an averaged synaptic response model, would have leaded to a different result than the one obtained here considering the stochastic nature of release.

To conclude, we showed that neurons can convey information about the input ν by means of the current variance, so that information can be transmitted, contrary to what is generally thought, beyond the saturation of μ.

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