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 rapidly saturates. Provided that μ saturates under threshold, the response 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.

1 Introduction

Although short-term synaptic plasticity was first observed more than sixty years ago [1], its computational implications are still not fully explored. A few years ago [2] and [3] showed 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 a big constraint in the type of input messages that a neuron is sensitive to. More exactly, synaptic depression seems to prevent the neuron from distinguishing the input rate beyond a certain saturation frequency ν_{sat} [2, 4].

On the other hand there has been an increasing interest in analyzing the impact of input correlations in the response of a neuron [5, 6, 7] and to study whether they could provide plausible coding strategies.

In the present work we analyze the effect of cross-correlated inputs impinging a target cell across dynamical stochastic synapses. We find that considering the all-or-none stochastic nature of synaptic transmission turns out to be essential 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. This last case seems to be the underlying mechanism by which neurons in the nucleus laminaris, preserve their interaural time-delay tuning at input rates well beyond the point, where the mean current, produced by their depressing synapses, have saturated [8].

It will be shown that the presence of synchrony in the stimulus makes the response of a leaky integrate-and-fire neuron (LIF) show a resonant 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.

An analytical prediction of the output rate ν_{out} of a LIF neuron is presented, following the formalism described in [7], where the impact of spike cross and auto-correlations is considered.

2 Model of synaptic connection

There are in the literature several models which describe the plastic mechanisms of short term depression and facilitation. Typically a collection of deterministic models have considered the *averaged* synaptic response and inter-trial differences due to the stochastic nature

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of the synaptic transmission are not accounted for. We start by considering the fact that neurons rarely establish a single synapse between them, and that synapses usually have more than one synaptic specialization, or active zone, which is a the particular area where release takes place. Neglecting the spatial dimension of the post-synaptic cell, we use the term *functional contact* to account for any specializations regardless the synapse they belong to. A connection is composed therefore of an arbitrary number of functional contacts, M. 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 pool of primed vesicles (PP) 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 replenish is a random variable following a distribution $f(t)$ with mean τ_v. During this recovery time no vesicle can undergo exocytosis upon arrival of any spike.

We model the facilitation of the transmission following the model proposed in [2]. Thus, the release probability u is a dynamical variable which increases upon arrival of a spike and decreases towards a resting value in an exponential way 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:

$$I_{syn}(t) = \sum_{i}^{N} \sum_{\alpha}^{M} C_m \, J_{i,\alpha} \sum_{l} \delta(t - t_{i,\alpha}^{k}) \tag{1}$$

where i is the index of the pre-synaptic neuron, α of the functional contact, and the last sum in k refers to the sequence of releases and not to the train of arriving spikes. C_m is the membrane capacitance so that $J_{i,\alpha}$ measures in voltage units the amplitude of the PSP produced by the release of one vesicle at the contact (i, α). These synaptic efficacies $J_{i,\alpha}$ are distributed according with a certain distribution with mean $\bar{J}$ and variance $\Delta^2 \bar{J}^2$. The mean of the current will be denoted by $\mu \equiv < I_{syn}(t) >$.

Taking $f(t) = \exp(-t/\tau)_v/\tau_v$, and averaging the stochastic response over trials, the model yields the same depressing behavior as the phenomenological models of refs. [2, 3], which in turn reproduce the experimental results. This deterministic model can also be obtained by taking the limit of infinite contacts per connection while the product $M\bar{J}$ is held constant. In other words, many contacts per connection self-average the synaptic response and the fluctuations due to the stochasticity of the synapse are wiped out.

3 Statistics of the input stimulus

The input stimulus consists of the composition of all the afferent spike trains and it is modeled as: $S(t) = \sum_i^N \sum_k \delta(t - t^k)$ The activity of each afferent fiber is a stationary Poisson process with identical rate ν. The correlation among pre-synaptic neurons is positive and instantaneous, which means zero-lag cross-correlations or synchrony. The second order statistics of the stimulus are completely defined by the two point connected correlation function which reads

$$\begin{aligned} C(t,t') &\equiv < (S(t) - < S(t) >) \, (S(t') - < S(t') >) > \\ &= N \, \nu \, [1 + \rho \, (N-1)] \, \delta(t - t') \end{aligned} \tag{2}$$

The parameter ρ stands for the probability that given a spike at t at fiber the i, there is another one at the *same* time at fiber the j. Thus, it grades the strength of the cross-correlations: if $\rho = 0$ all pre-synaptic neurons fire independently, while if $\rho = 1$ the spikes from different neurons are all aligned in time.

4 Statistics of the synaptic responses

Considering the synaptic responses as point events, we can analytically compute the statistics of the responses when there is no facilitation or equivalently $\tau_f = 0$. In this case the release probability is always $u(t) = U$. Defining the compound train of releases as $R(t) = \sum_i^N \sum_\alpha^M \sum_l \delta(t - t_{i,\alpha}^k)$, its mean and connected two-point correlation function read:

$$< R(t) >= NM\nu_r = NM\frac{U\nu}{1 + U\nu\tau_v} \tag{3}$$

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

where ν_r is the rate of release at a single functional contact. The time constant $\tau_c \equiv \frac{\tau_v}{1+U\nu\tau_v}$ and the coefficient of the delta is

$$\sigma_w^2 \quad = \quad NM\nu_r\left[1 + \frac{U(M-1)}{1 + U\nu\tau_v(1 - U/2)} + \frac{U\rho(N-1)M}{1 + U\nu\tau_v(1 - U\rho/2)}\right] \tag{5}$$

Several things must be noticed here: i) $< R(t) >$ rapidly saturates as ν increases. We can define[2] the saturation frequency[3] $\nu_{sat} = \frac{1}{U\tau_v}$ beyond which the stationary value of $< R(t) >$ is insensitive to the value of ν. ii) The negative exponential correlations in the release process are due to the refractoriness arising from vesicle recovery. iii) The releases at different contacts appear to be 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 afferent train stimulates M different contacts (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 vanishing when ν goes to infinity (see eq. (5)). In particular, if we take for instance $M = 1$, by comparing eqs. (4-5) with eq. (2) an effective release correlation parameter can be defined as

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

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 de-synchronize when ν becomes large. Computing the saturation frequency for σ_w^2, as done with the mean number of releases, it yields to

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

Therefore, beyond ν'_{sat}, the release process tends to be the composition of NM de-synchronized processes with rate $\nu_r(\nu \simeq \infty) = \frac{1}{\tau_v}$. But that is exactly the vesicle recovery rate indicating that, in saturation, the release statistics are governed by the vesicle recovery process, which occurs *independently* at each contact. Therefore, in this regime, neither the trace of the input synchrony, nor the effect of multiple contacts per connection, can be detected. It is important to remark that this de-synchronization occurring because of saturation, will be lost if we neglect the *all-or-none* nature of the synaptic response by considering an averaged response deterministic model.

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 convey information about ν. This information can be read out by the neuron, if its output is sensitive to the fluctuations of

[2] Making an expansion of $< R(t) >$ around its asymptotic value up to first order in $\frac{1}{\nu}$, ν_{sat} is defined as the frequency at which the first order correction equals the zero order term.

the current. Recent works[6, 7] have shown that this is the case specially if the neuron works in a sub-threshold regime, defined by the condition that the mean current lies always below threshold. This condition can be achieved by imposing a balance between excitation and inhibition[9]. Here, no balance is needed because of the saturation of the mean current. We find that for a wide range of plausible values of the parameters, μ saturates under threshold so that the modulation of the current variance is maximally expressed.

What happens when facilitation is included? As a first approximation, we can substitute U in previous expressions of σ_w^2 and ρ_r by the 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. As a consequence, at low rates $\rho_r \sim U\rho$ and, since U in facilitating synapses can be as low as 0.02, synchrony is strongly attenuated. As ν increases, the synapse facilitates and unreliability no longer "dilutes" 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 eliminate the effect of the synchrony at high and low rates, respectively, leaving an intermediate regime in which there exists a resonance in the synaptic responses synchrony. This, in turn, makes the variance σ_w^2 (eq. 5) display a non-monotonic behavior as a function of ν.

5 Response of LIF neuron

To test whether this resonance present in the current fluctuations could be readout by a neuron, we simulated a leaky integrate-and-fire spike generator integrating $I_{syn}(t)$ (eq. 1). Its output rate ν_{out} is illustrated in fig. 1 (top plot) for three different amounts of synchrony present in the input. Along with the numerical results a theoretical prediction is shown. It has been computed following the technique explained in [7], and its full analysis will be carried out elsewhere. The input synchrony was implemented in the simulations by establishing a large number of contacts per connection, while keeping the total number $NM = 3750$ fixed. However, the same results would be obtained by making 3750 monosynaptic connections (i.e. $N = 3750$ and $M = 1$) with the values of ρ supplied in the inset. The bottom plot shows the theoretical prediction of μ and σ. While μ shows a monotonic saturation and it is independent of ρ (or changes in M with NM fixed), σ shows a resonant tuning which scales up with ρ. Thus ν_{out} inherits the non-monotonic behavior of σ and it decreases as the input synchrony becomes smaller. When $\rho = 0$, the fluctuations are not resonant anymore and they are too small to make the neuron respond. The theoretical prediction gives a good a approximation except at the maximum ν_{out} for large values of ρ.

Figure 2 shows the theoretical prediction for ν_{out} for different values of U and τ_v. The position of the maxima and their height change while the tuning shape remains invariant. This shows that the resonant response is a robust effect (provided that μ saturates under threshold) but at the same time the particular shape is sensitive to changes in U and τ_v.

6 Conclusions and discussion

Short-term depression prevents an individual synapse from releasing transmitter repeatedly in a fast manner. Thus, it provides a constraint mechanism by which a neuron has to integrate spatially across synapses in order to reach threshold. Therefore, cross-correlations have a tremendous impact in the output. Moreover, in the example shown in fig. 1, synchrony acts as a gating variable which switches the output on and off, enabling the neuron to respond in a tuned manner to the input rate. Correlated firing has been related with attention and expectation (see [10] for a review). Our results can be interpreted by saying that the response to attended stimuli would not only have a larger response, but the same

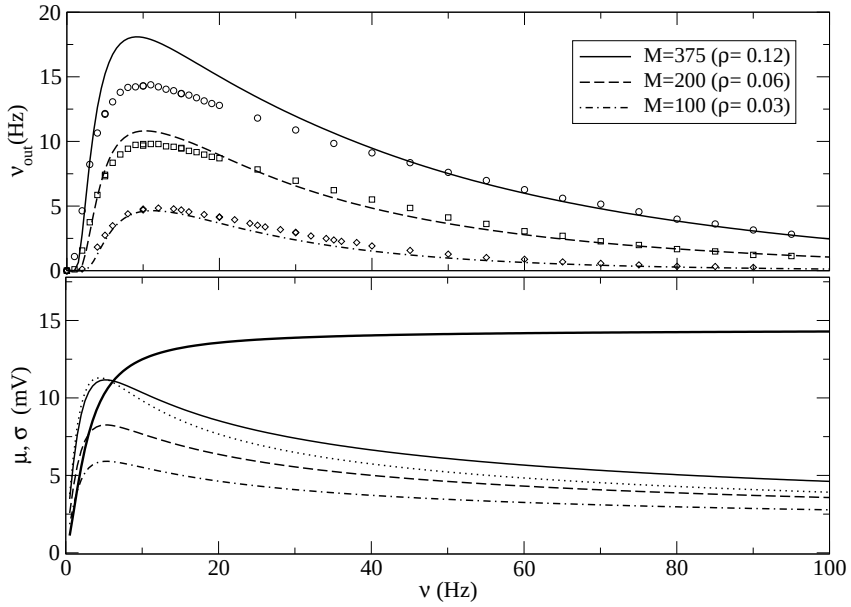

Figure 1: **Top**: analytical and numerical output rate vs. input ν for three different grades of input synchrony. Synchrony was generated by setting $M > 1$ and changing N so that $NM = 3750$ is kept fixed. The values of ρ in the inset would lead to approximately the same ν_{out} with $N = 3750$ and$M = 1$. **Bottom**: Mean current μ (thick solid) and variance σ for the three same examples as top plot. Dotted line representing σ the case $N = 3750$,$M = 1$ and $\rho = 0.12$ illustrates the equivalence between $M > 1$ and $\rho > 0$. Top inset applies for both plots. Other parameters: $J = 0.19$ mV, $\tau_v = 1$ s, $\tau_f = 1.5$ s, $U = 0.1$. LIF neuron parameters: threshold= 20 mV, membrane time constant= 20 ms, reset potential= 10 mV.

mechanism which controls the gain, that is synchrony, naturally give rise to selectivity to the input rate.

Some of the parameters of short-term plasticity, like U, are subject to long term changes[11]. This could be perhaps a plausible way to adjust the selectivity of neurons, since we showed that it depends finely in the values of U and τ_v. Although we have only considered the case of an homogeneous population of contacts, synapses impinging onto a single neuron display a large heterogeneity in the values of their parameters. Our results suggest that this wide distribution, far from spoiling the resonant behavior, could provide the basis to build more sophisticated non-monotonic response functions (e.g. a function with two maxima in the case that U and τ_v distribution is bimodal).

Our results stress the importance of the synaptic fluctuations due to stochastic release and recovery. Taking an averaged synaptic response model, would have leaded to a different result. Finally, it is important to remark 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 thought, beyond the saturation of μ.

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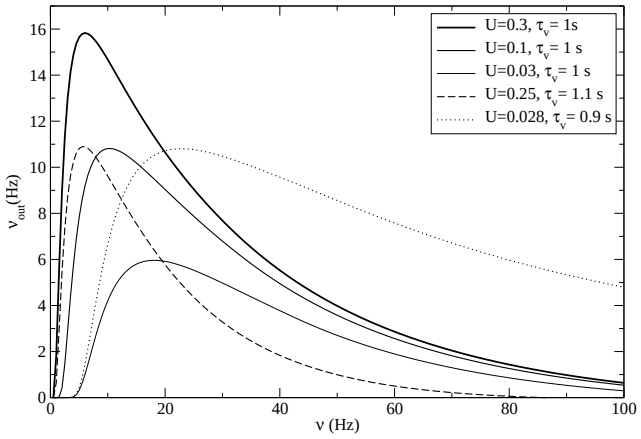

Figure 2: Theoretical ν_{out} vs. input ν for different values of U and τ_v. Other parameters as in figure 1.

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