Gain modulation and balanced synaptic input in a conductance-based neural model

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Abstract

Gain modulation of neural responses by the balanced component of the synaptic input is analyzed in the gaussian approximation using a single compartment conductance-based neural model. The model is analyzed in the "normal operating regime", in which the output spiking-rate of the neuron is equal to the spontaneous spiking-rate in the absence of any stimulus. The gain in response to both additional excitatory synaptic input and injected current is found to be modulated in a non-linear way by the level of balanced synaptic input.

Key words: Gain modulation, integrate-and-fire neurons, gaussian approximation, synaptic input, conductance-based neural model

1 Introduction

Neural gain modulation is a measure of how a modulatory input (that is independent of the stimulus) affects the amplitude of the response that a neuron generates due to the stimulus (the unmodulated input). It is a non-linear mechanism by which information is combined (or integrated) from within a single pathway or between different pathways of neural processing, which may be of sensory, motor or cognitive origin. Gain modulation provides a computational means by which neural systems may transform, combine or compare the representations that they carry of the physical world and by which they more accurately control (i.e. modulate) their output. Gain modulation plays an important role in sensory-motor integration, such as eye and reaching movements, and in spatial perception, as well as in auditory masking, attentional processing, object recognition and navigation. Gain modulation is one of the

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few neural computational principles that pervades neural processing, since it plays an important role in a number of different modalities (sensory, motor and cognitive), different brain areas (cortical and sub-cortical), and different neural functions [12].

Gain modulation has been observed experimentally to play an important role in neural processing. However we lack an understanding of the underlying biophysical mechanisms by which gain modulation is implemented in neural systems. The central question is: "How do neurons achieve the non-linear, multiplicative behavior characteristic of gain modulation when their input-output relationship is basically integrative?". A number of possible mechanisms have been proposed [12], although they are not necessarily exclusive. One suggested mechanism involves the effect of non-linear interactions in the dendritic processing of neurons [9]. Another approach involves the effect of recurrent connections between neurons, which may give rise to non-linear interactions [11,6]. A third approach is through correlations in the synaptic input [13]. A fourth approach is that addressed in this paper, namely the effect of the balanced component of the synaptic input in providing the non-linear gain modulation of the neural response [5]. The various mechanisms are, of course, by no means mutually exclusive, e.g., the balanced component of the input could partly arise via feedback from recurrent connections.

This paper examines how balanced synaptic input can modulate neuronal gain. This modulation is a result of the effect of the balanced synaptic input upon the variance of the synaptic current, which can be varied independently of the mean synaptic current (which is determined by the difference of the excitatory and inhibitory inputs). The possible role of balanced input in neuronal gain modulation was highlighted by a recent *in vitro* study in which a variable current (with zero mean) was injected into a rat cortical pyramidal neuron and the gain associated with the injection of an additional constant current was measured [5]. The results indicated that the variability of the injected current affected the neuronal gain multiplicatively. In this paper we examine gain modulation as a result of balanced synaptic inputs in a conductance-based model. The analysis will be carried out in the gaussian approximation [3,4,1], which is most accurate for neurons with a large number of small-amplitude synaptic inputs. The effect of synaptic input over a range of input conditions (input rates, numbers of synapses and EPSP/IPSP amplitudes) is analyzed. The gain is measured as the rate of increase of the output spiking-rate of the neuron in response to increased input. Two different forms of input are examined: excitatory synaptic input (i.e., in excess of the balanced component of the synaptic input) and injected current.

2 Methods

A conductance-based leaky integrate-and-fire neuron (with reversal potentials) is used in which the membrane potential $V(t)$ receives from its presynaptic inputs both excitatory and inhibitory contributions and decays in time with a characteristic time constant (the membrane time constant τ) [16]:

$$dV(t) = -\frac{(V(t) - v_0)}{\tau} dt + g_E(V_E - V(t))\, dP_E(t) + g_I(V_I - V(t))\, dP_I, \quad (1)$$

where v_0 is the reset potential, V_E and V_I are the (constant) reversal potentials ($V_I \leq v_0 \leq V(t) \leq V_{\rm th} < V_E$). $dP_E(t)$ and $dP_I(t)$ are independent temporally homogeneous Poisson processes with constant intensities $N_E\lambda_E$ and $N_I\lambda_I$, respectively, i.e., each of the N_E excitatory input fibers (and N_I inhibitory input fibers) has a rate λ_E (resp. λ_I). In the balanced neuron considered here we choose $N = N_E = N_I$. The postsynaptic current amplitudes g_E and g_I are chosen to be nonnegative (and are identical for all excitatory and inhibitory inputs respectively). The values of g_E and g_I are chosen so that the average excitatory and inhibitory inputs are balanced at the potential V_B ($V_I < V_B < V_E$), denoted the *balance-potential*,

$$g_E \frac{(V_E - V_B)}{\theta} = g_I \frac{(V_B - V_I)}{\theta} \equiv b = b_0/\sqrt{N} \qquad , \qquad \theta = V_{\rm th} - v_0. \quad (2)$$

When the membrane potential reaches a threshold, an output spike is generated and the membrane potential is reset to its resting value v_0. In the absence of spike generation, the membrane potential reaches an equilibrium value, V_Q, about which it fluctuates with variance σ_Q. The membrane potential approaches V_Q with a time constant given by τ_Q. The values of V_Q, σ_Q, τ_Q are [7,1]

$$V_Q = \frac{v_0/\tau + r_{11}}{1/\tau_Q} \qquad , \qquad \sigma_Q^2 = \frac{\mu^2 r_{20} - 2\mu r_{21} + r_{22}}{2/\tau_Q - r_{20}} \quad (3)$$
$$\frac{1}{\tau_Q} = \frac{1}{\tau} + r_{10} \qquad , \qquad r_{mn} = N_E\lambda_E g_E^m V_E^n + N_I\lambda_I g_I^m V_I^n.$$

The analysis is carried out in the Gaussian approximation [3], in which the probability density of the membrane potential $p(v, t \,|\, v', 0)$ is parameterized as

$$p(v, t \,|\, v', 0) = \frac{1}{\sqrt{2\,\pi\,\Gamma(t; v')}} \, \exp\left\{ -\frac{(v - \Upsilon(t; v'))^2}{2\,\Gamma(t; v')} \right\}, \quad (4)$$

where $\Upsilon(t;v)$ and $\Gamma(t;v)$ are the (time-dependent) mean and variance of the membrane potential. The Gaussian approximation is accurate in the limit of a large number of input synapses, N, which allows the probability density of the membrane potential to be evaluated using a self-consistent analysis [1]. The output spike distribution $f_\theta(t)$ obeys the renewal equation [10,2]

$$p(V_{\rm th}, t \,|\, v_0, 0) = \int_0^t dt' \; f_\theta(t') \; p(V_{\rm th}, t \,|\, V_{\rm th}, t'), \tag{5}$$

where $p(v, t \,|\, v', t')$ is the conditional probability density of the membrane potential having the value v at time t, given that it had the value v' at an earlier time t'. The effect of reversal potentials is to impose a lower bound to the membrane potential, and consequently it is necessary to consider their effect when inhibition plays an important role. In the model where reversal potentials are neglected, the amplitudes of the excitatory and inhibitory post-synaptic potentials (EPSPs and IPSPs, resp.) are constant (i.e., independent of the existing membrane potential). In this case the gaussian approximation gives results that are identical with the diffusion method, in which the membrane potential is modelled as a stochastic process that is characterized by its first two moments. However, the gaussian approximation differs from the diffusion method when reversal potentials are included since it accounts for non-linear summation and allows different time-courses for the mean, $\Upsilon(t;v)$, and variance, $\Gamma(t;v)$, of the membrane potential (these are given explicitly in [1]).

3 Results

An essential part of the analysis is defining the "normal operating regime" of a neuron, to ensure that the chosen parameter values correspond to biologically relevant neural behavior. This is achieved in our model by the condition that the output spiking-rate in the absence of a stimulus corresponds to the spontaneously active spiking-rate. This requires that there be a slight excess of excitation in the spontaneously active neuron (for the values used here, this is satisfied by $\lambda_E = \lambda_I + \lambda_P = \lambda_{\rm spon}$ with $\lambda_P = 1$ spike/sec).

The parameter values chosen are: V_I=-75 mV, v_0=-65 mV, $V_{\rm th}$=-55 mV, V_E=0 mV, so that the ratios of the potential differences are $(v_0 - V_I) : (V_{\rm th} - v_0) : (V_E - V_{\rm th}) = 1 : 1 : 5.5$. The passive membrane time constant is τ=10 ms, the amplitude of the post-synaptic potentials is given by $b_0 = 1$, the spontaneous spiking-rate is $\lambda_{\rm spon} = 5$ spikes/sec, the balance potential is $V_B = V_Q = -58.675$ mV, and the number of excitatory and inhibitory synapses is $N = N_E = N_I = 4000$. The results are not very sensitive to the

choice of $V_B = V_Q$ and $b_0 = 1$ so long as λ_P is chosen appropriately to fulfill the above condition on the spontaneous spiking-rate.

Figure 1 shows the output spiking-rate (plot **a**) for the parameter values given above: The solid line is for the "1X" case in which the balanced input is just the spontaneous activity, and the dashed line is for the "2X" case in which the balanced input has twice the spiking-rate of the spontaneous activity. Plot **b** shows the gains for the "1X" and "2X" conditions. Plots **c**,**d** show the equivalent results for injected current.

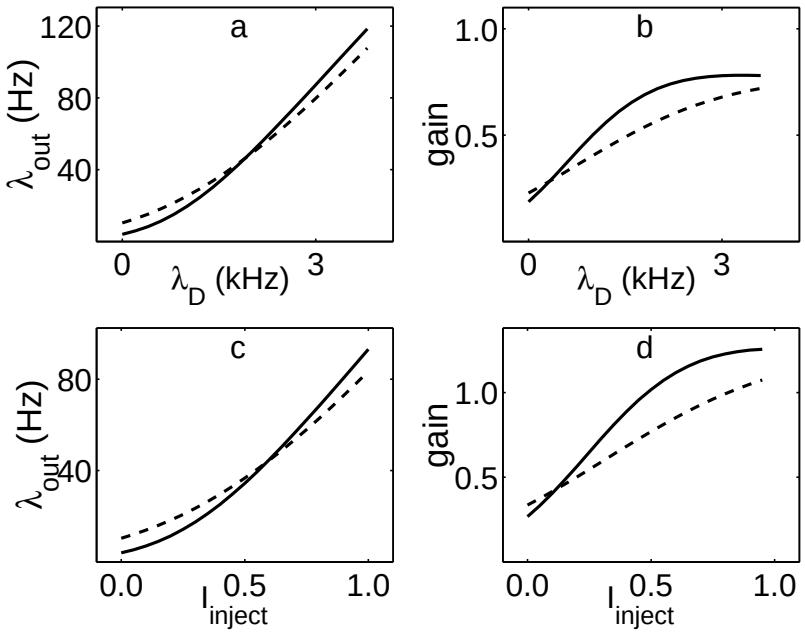

Fig. 1. Plot of results showing the output spiking rate λ_{out} and neuronal gain: (**a**),(**b**) for excitatory synaptic input with total driving input spiking-rate of λ_{D} (the spiking-rate in excess of the balanced input spiking-rate, summed over all N inputs), for the "1X" (solid line) and "2X" (dashed line) cases, and (**c**),(**d**) for injected current input showing the results for the "1X" (solid line) and "2X" (dashed line) conditions.

4 Discussion and Conclusions

There has been considerable interest in the role of balanced synaptic inputs recently, since neurons receiving balanced input produce a variability of spike times (usually measured by the coefficient of variation of the interspike interval distribution) that agrees with values observed in cortical neurons [14]. Neurons that receive predominately excitatory input, on the other hand, would be expected to have a membrane potential that is relatively smooth, resulting in regular firing and a small value of the coefficient of variation [15].

The results of this study indicate that, in the normal operating regime for the neuron, the effect upon the neuronal gain of balanced synaptic input is not simply multiplicative. However, the balanced inputs do give rise to a non-linear gain modulation effect, when the gain is measured both with respect to synaptic input and to injected current. Although the results presented here represent only one set of parameters, they are representative of the results over a large part of the normal operating regime of a typical cortical neuron. We are currently studying gain modulation over the entire range of biologically plausible neural parameters. We are examining particularly the dependence of gain modulation upon the parameters V_Q, τ_Q, σ_Q, and details of these studies will be published elsewhere.

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