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Synchrony measure for a neuron driven by excitatory and inhibitory inputs and its adaptation to experimentally-recorded data

Christina Zavou, Antria Kkoushi, Achilleas Koutsou, Chris Christodoulou*

Department of Computer Science, University of Cyprus, P.O. Box 20537, 1678 Nicosia, Cyprus

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ABSTRACT

The aim of the current work is twofold: firstly to adapt an existing method measuring the input synchrony of a neuron driven only by excitatory inputs in such a way so as to account for inhibitory inputs as well and secondly to further appropriately adapt this measure so as to be correctly utilised on experimentally-recorded data. The existing method uses the normalized pre-spike slope (NPSS) of the membrane potential, resulting from observing the slope of depolarization of the membrane potential of a neuron prior to the moment of crossing the threshold within a short period of time, to identify the response-relevant input synchrony and through it to infer the operational mode of a neuron. The first adaptation of NPSS is made such that its upper bound calculation accommodates for the higher possible slope values caused by the lower average and minimum membrane potential values due to inhibitory inputs. Results indicate that when the input spike trains arrive randomly, the modified NPSS works as expected inferring that the neuron is operating as a temporal integrator. When the input spike trains arrive in perfect synchrony though, the modified NPSS works as expected only when the level of inhibition is much higher than the level of excitation. This suggests that calculation of the upper bound of the NPSS should be a function of the ratio between excitatory and inhibitory inputs in order to be able to correctly capture perfect synchrony at a neuron's input. In addition, we effectively demonstrate a process which has to be followed when aiming to use the NPSS on real neuron recordings. This process, which relies on empirical observations of the slope of depolarisation for estimating the bounds for the range of observed interspike interval lengths, is successfully applied to experimentally-recorded data showing that through it both a real neuron's operational mode and the amount of input synchrony that caused its firing can be inferred.

1. Introduction

The neural code refers to the mechanisms with which a single neuron and networks of neurons exchange sequences of spike trains. Discovering and understanding these mechanisms and in particular, figuring out how cells encode, decode and process information is very important in our quest of deciphering the neural code. A key aspect of solving the neural encoding problem is to determine the operational mode of a neuron. Generally, a neuron is considered to be operating in one of two modes, either temporal integration or coincidence detection. Temporal integration implies that neurons operate as integrate-and-fire devices, i.e., firing reflects integration of excitatory and inhibitory postsynaptic potentials (EPSPs and IPSPs) in a time-dependent manner as some evidence suggests, e.g., Bernander et al. (1991), Shadlen and Newsome (1998) where the firing rate is mainly a function of the input rate. Under this assumption, variations in the timing of individual spikes and more importantly coincident arrival of multiple spikes at the input of the cell, have little effect on the firing rate or the spike timing of the post-synaptic neuron. Coincidence detection however implies that coincidences and the precise timings between input spikes affect the neuron's response times. This is supported by some other evidence indicating that firing times are strongly influenced by synchronous excitation (see for example Softky and Koch, 1993; Stevens and Zador, 1998). In this mode, the neuron is more likely to fire when multiple input spikes arrive, making the output rate and timings more sensitive to the temporal nature of the pre-synaptic activity. Coincidence detection has functional implications in Hebbian learning (Hebb, 1949; Brown et al., 1990; Seeburg et al., 1995), synaptic plasticity (Markram et al.,

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* Corresponding author.
E-mail addresses: czavou01@gmail.com (C. Zavou), antriakkoushi13@gmail.com (A. Kkoushi), achilleas.k@cs.ucy.ac.cy (A. Koutsou), cchrist@cs.ucy.ac.cy (C. Christodoulou).

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1997), binaural localisation (Peña et al., 1996) and visual attention (Kreiter and Singer, 1996; Singer and Gray, 1995), while temporal integration (or graded neuronal activity) is important for a number of cognitive processes like decision making (Mazurek et al., 2003), interval timing perception (Durstewitz, 2003), as well as for motion perception (Fredericksen et al., 1994).

Identifying the operational mode of a given neuron based on the cell's activity is an open problem. Several methods have been proposed to solve this problem like, the coincidence advantage (Abeles, 1982), the integration time window measure (König et al., 1996) and the neural mode and drive (Kanev et al., 2016) (for a review of these methods, see Kanev et al., 2016). One other method is the normalised pre-spike slope (NPSS) of the membrane potential measure of Koutsou et al. (2012). This method aimed to measure the relative contribution of coincidence detection and temporal integration to the firing of spikes of a simple neuron model. The degree of presynaptic synchrony has been linked to the continuum between the two operational modes of a neuron (König et al., 1996; Aertsen et al., 1996; Kisley and Gerstein, 1999; Rudolph and Destexhe, 2003), and many studies have linked the degree of presynaptic synchrony to the derivative of the postsynaptic membrane potential (Kisley and Gerstein, 1999; DeWeese and Zador, 2006; Kobayashi et al., 2011; Goedeke and Diesmann, 2008). Koutsou et al. (2012) developed a method (NPSS) which correlates the membrane potential derivative prior to firing to the degree of presynaptic synchrony, and by extension, a method which determines the neuron's operational mode by inferring the degree of response-relevant input synchrony through the membrane potential slope. The NPSS measure calculates the two bounds for the slope of the membrane potential: the upper bound, which represents the slope of the membrane potential in the case where the neuron was firing as a result of purely synchronised inputs (coincidence detector), and the lower bound, which represents the slope of the membrane potential in the case where the neuron was firing as a result of many, randomly distributed input spikes (temporal integrator). The final value is determined by linearly normalising the measured slope of the membrane potential prior to each spike fired by the neuron between the two calculated bounds.

When developing the method, Koutsou et al. (2012) used the leaky integrate and fire (LIF) neuron model (Tuckwell, 1988) driven only by excitatory inputs. The method itself relied on the assumption that there were no inhibitory inputs driving the neuron and this was stated as one of the limitations of the NPSS. Given this limitation, in the first part of this paper we adapt the NPSS of Koutsou et al. (2012) so that it can be applied to models which are driven by both excitatory and inhibitory inputs. In the second part of this paper we present a procedure for adapting the NPSS to experimentally-recorded data, where we assume as in the theoretical NPSS that the intracellular membrane potential and the related stimuli are available, but as the underlying neuron model is not available we rely on empirical observations of the slope of depolarisation, in order to estimate the bounds for the range of inter-spike interval (ISI) lengths observed.

2. Method

2.1. Original normalised pre-spike slope measure

The NPSS measure developed by Koutsou et al. (2012, 2016) studies the relationship between the slope of depolarisation of the membrane potential prior to firing and the amount of synchrony that exists in the input spike trains which causes the firing. More specifically, these authors demonstrated that the level of their developed NPSS of the membrane potential is equivalent to the degree of the response-relevant input synchrony. The NPSS can estimate the operational mode of a neuron as a value in the continuum between the two known candidates - coincidence detection and temporal integration. For their study, they used a simple LIF neuron model and by simulating various cases with different input synchrony ranges, they demonstrated that there is a strong relationship between the pre-spike potential slope and the presynaptic synchrony.

The measure requires the definition of a coincidence window, w, which defines the maximum difference in timing between a set of spikes that is considered coincident (synchronous). The value of this window was set to 2 ms in the original study (Koutsou et al., 2012). By measuring the normalized pre-spike slopes in that window, they could infer presynaptic synchrony responsible for firing (response-relevant input synchrony). A dramatic mean potential change within w implies coincidence detection of highly synchronized inputs, while a smooth mean potential change within w implies temporal integration of random inputs (EPSPs and IPSPs). Alternatively, firing could be caused by a varying degree of contributions from both modes which would be signified by an intermediate rate of change in the potential and would indicate a moderate degree of synchronization in the neuron's inputs.

Normalizing the pre-spike slopes and defining the continuum between the two modes, required the definition of the slopes for the two extreme cases: completely synchronous inputs and completely random inputs, i.e., the bounds of the operational mode continuum (see Fig. 2 in Koutsou et al., 2012). The upper bound (U_i, Eq. (1)) reflects the case where the membrane potential reaches the threshold potential (V_{th}) solely within the coincidence window. This is done by calculating the membrane potential at the start of the coincidence window under the assumption that there were no input spikes arriving in the period since the last spike. The equations also assume that the reset potential V_{reset} and the resting potential V_{rest} are not equivalent (if they are equivalent, the equations are substantially simplified) in order to account for the LIF neuron model with partial reset (Bugmann et al., 1997; Koutsou et al., 2012). Once we know the theoretical membrane potential at the start of the window, the upper bound is calculated as the rate of change in membrane potential required to reach threshold (Eq. (1)).

The lower bound (L_i) reflects the case where the membrane potential reaches V_{th} from V_{reset} in the whole ISI (Δt_i), by slowly integrating (random) inputs (Eq. (2)). The bound is taken to be the rate of change in the membrane potential during the coincidence window before the end of the ISI ($\Delta t_i - w$). Note that V_{rest} is considered the lowest possible potential in the case of Koutsou et al. (2012), where they consider no inhibition.

$$U_i = [V_{th} - (V_{rest} + (V_{reset} - V_{rest})E)]\, w^{-1} \tag{1}$$

$$L_i = [V_{th} - (V_{reset} + I_V(1 - E))]\, w^{-1} \tag{2}$$

$$E = e^{-\frac{\Delta t_i - w}{\tau_m}} \tag{3}$$

$$I_V = \frac{V_{th} - V_{reset}}{1 - e^{-\frac{\Delta t_i}{\tau_m}}} \tag{4}$$

Here, Δt_i is the duration of the ISI preceding the *ith* output spike ($\Delta t_i = t_i - t_{i-1}$), I_V is the constant input required to fire at the end of the ISI starting from V_{reset}, τ_m is the neuron's membrane leak time constant and E is a common term that is used to calculate the effect of the membrane leak from the start of the ISI up to the start of the coincidence window, $\Delta t_i - w$.

The two bounds are used to linearly normalise the measured membrane potential slope (m_i) for the period within the coincidence window (Eq. (5)).

$$M_i = \frac{m_i - L_i}{U_i - L_i} \tag{5}$$