Stimulus transmission by tonic and burst responses in a minimal model of thalamic circuit

Baktash Babadi

baktash@ipm.ir

School of Cognitive Sciences (SCS), Institute for studies in theoretical Physics and Mathematics (IPM), Tehran, Iran

Abstract

Burst and tonic responses are studied in a minimal model of thalamic circuit composed of a retinal spike train, a relay neuron and a reticular neuron. The integrate-and-fire-or-burst model is used to simulate the neurons. Cross-correlograms show that burst events are more reliable than tonic firings in stimulus transmission to the cortex, and may be capable of scanning the sensory spike train for certain temporal correlations. The effect of brainstem projections on thalamic bursts during wakefulness and the possible role of bursts in attention mechanisms are discussed.

Keywords

Thalamus, Burst, Tonic, Reticular nucleus, Integrate-and-Fire-or-Burst model

Introduction

The thalamic relay cells respond to the sensory stimulus in two distinct modes, known as tonic and burst. When in tonic mode, the relay cell responds to the incoming stimulus by one or more individual action potentials. In the burst mode, the response of the cell to the stimulus is in the form of dense, stereotyped packets of action potentials, called burst events. Until recently, it was believed that thalamic bursts are only present during certain pathological states and slow wave sleep. However, recent evidences indicate that bursts are also present during normal awake states in Lateral Geniculate Nucleus (LGN: the visual nucleus of thalamus), and may play an important role in the transmission of sensory stimulus to the cortex (see [10] for a review). Nevertheless, the nature of information carried by bursts in comparison with tonic responses is still a mater of question. This study aims to approach this question by means of numerical simulations of a biologically realistic minimal LGN circuit.

The neurons in the thalamic reticular nucleus densely innervate the thalamic relay neurons with GABAergic inhibitory synapses and provide the major inhibitory input to them [1]. On the other hand, in LGN, as the prototypical thalamic nucleus, individual relay neurons receive very strong excitatory input from a single retinal ganglion cell, which constitutes the main excitatory drive of the relay cell [5]. Thus, a minimal thalamic (LGN) circuit, which will be studied here, consists of 1) a thalamic relay neuron, 2) a thalamic reticular neuron, and 3) an input spike train from the retinal ganglion cell. Note that a similar minimal circuit was subject of dynamical clamp experiments in the studies of Le Masson and colleagues [6].

Methods

The retinal spike train is modeled as a renewal process with *g* distributed intervals. The mean rate of the modeled spike train is *30 Hz* and the order of *g* is *8* [14]

For the thalamic relay cells (TC) and reticular neurons (RN) the integrate-and-fire-or-burst (IFB) model has been used. The IFB model is an extension of the simple integrate-and-fire model by adding a slow variable, which represents the gating parameter of the low threshold calcium current. Although quite simple, the IFB model captures most of the biological properties of the thalamic cells and its behavior matches properly with the experimental data (for details see [12]). The only difference between the TC IFB and the RN IFB is that the threshold for the low threshold calcium current is slightly higher in the RN IFB [11].

The TC receives the retinal spike train via an excitatory AMPA synapse and in turn sends its spikes to the RN via another excitatory AMPA synapse. The RN sends its spikes to the TC via inhibitory $GABA_A$ and $GABA_B$ synapses (figure 1). For the AMPA and $GABA_A$ synapses, conductance changes are modeled by exponentially decaying functions. The decay time constants for the AMPA and $GABA_A$ synapses are *5 ms* and *10 ms* respectively. For $GABA_B$ synapse, the conductance changes are modeled by a double exponential function with a rise time constant of *100 ms* and a decay time constant of *200 ms*. The reversal potential for the AMPA synapses is *+55 mV*, for the $GABA_A$ synapse is -*90 mV* and for the $GABA_B$ synapse is -*110 mV*, which correspond to Na, Cl and K ions respectively. The maximal conductance values of the synapses are *0.038 mS* for the retina-TC AMPA, 0.025 *mS* for the TC-RN AMPA, 0.012 *mS* for RN-TC $GABA_A$, and

0.0005 mS for RN-TC $GABA_B$. These values are chosen in pilot simulations so that the response properties of the thalamus in awake animals could be reproduced, namely *60%* efficiency of retinal spikes in generating TC spikes [9], *1%* of total TC spikes in burst [7], parallelism between RN and TC firings with the same firing rate [13], and finally the ratio of *96%* to *4%* between $GABA_A$ and $GABA_B$ maximum conductances [6].

The burst events in the spike train generated by the TC are then identified using the "liberal criteria" proposed by Ramcharan and colleagues [7]. According to this criteria, a burst event is a group of spikes, with first one proceeding a silent period of *>50 ms*, the first inter-spike-interval in the burst being *>6 ms*, and all the following spikes are part of the burst event if their inter-spike-interval increases no more than *2 ms* for each successive spike, up to a maximum allowed inter spike interval of *16 ms*. Thus, from the original spike train of the TC, two additional spike trains are extracted: 1) the tonic spike train, containing the spikes that do not contribute in bursts, and 2) the burst event train, containing the first spike of each burst event (figure 2). As bursts are highly stereotyped events [8], only the first spike of each burst is chosen as a representative for the event.

Results

All the results are obtained by simulating the model thalamic circuit for *1000s* (in neuron time). Figure 3 shows the cross-correlograms of the tonic spike train (3.a) and the burst event train (3.b) of the model TC with the retinal spike trains, normalized by the rate of the corresponding TC events (tonic spikes or burst events respectively). The peaks of these normalized cross-correlograms are indices of reliability of the TC activity for transmitting the retinal information [6]. As can be seen, the peak is considerably higher for the burst event train than the tonic spike train. This suggests that burst events are more reliable in transmitting retinal information. Moreover, the cross-correlogram for the burst events (3.a) has two distinct peaks: a lower peak about *80 ms* after retinal spikes, and a higher peak near zero. This may suggest that burst events scan the retinal spike train for certain temporal correlations.

It is believed that the noradrenergic projections from the brain stem during wakefulness decreases the gain of RN-TC inhibition [3]. In order to investigate the effect of RN-TC inhibition on the reliability of tonic and burst spikes of the TC, the model is simulated with different values of GABAergic inhibition. Figure 4 shows the reliability index for tonic and burst firings as a function of maximal $GABA_A$ conductance. Note that the 96% to 4% ratio of $GABA_A$ to $GABA_B$ is maintained in each case. As can be seen, the reliability of burst events has a peak at the maximal $GABA_A$ conductance of *0.012 ms*, while the reliability of tonic spikes is monotonous (increasing) as a function of the maximal GABAergic conductance. Increasing the maximal GABAergic conductance, will also increase the ratio of spikes participating in bursts (data not shown). Interestingly, the maximum reliability of burst events occurs when 1% of all TC spikes are in burst, which is in agreement with the observed burst frequency in awake animals [4,7].

Discussion

The results indicate that burst events are indeed reliable transmitters of information to the cortex, at least in a minimal circuit of thalamus. Although bursts are rare in the spike train of the TC in wakefulness, their reliability is considerably higher compared to tonic spikes. In wakefulness, the noradrenergic projections from the brainstem to the thalamus decrease the inhibitory gain of the RC-RN synapse [3], which in turn decreases the incidence of thalamic burst events and non-monotonically modulates their reliability. The results show that the maximum reliability of the burst events coincides with a low probability of bursting. Thus, it turns out that the high reliability of the thalamic bursts is achieved in the expense of their scarcity in awake state.

The two-peaked cross-correlogram of the burst events may suggest that they are capable of scanning the retinal spike train for some spike-silence-spike temporal sequences. As proposed earlier by Crick [2], this in turn may be suggested as a possible mechanism for bottom-up attention, in which a cue preceding a target stimulus can evoke the bottom-up attentional processes.

Although the studied thalamic circuit is highly simplified, it is possible to use the similar methods for more realistic and complex models, and also for simultaneous in vivo recordings of retinal ganglion cells and thalamic relay cells [5].

References

[1] C.L. Cox, J.R. Huguenard, D.A. Prince, Nucleus reticularis neurons mediate diverse inhibitory effects in thalamus, Proc. Natl. Acad. Sci. USA 94 (1997) 8854-8859.

[2] F. Crick, Function of the thalamic reticular complex: the searchlight hypothesis, Proc. Natl Acad. Sci. U. S. A. 81 (1984) 4586-4590

[3] K. Funke, H. C. Pape, U. T. Eysel, Noradrenergic modulation of retinogeniculate transmission in the cat, J Physiol. 463 (1993) 169-191.

[4] W. Guido, S.M. Lu, J.W. Vaughan, D.W. Godwin, S.M. Sherman, Receiver operatingcharacteristic (ROC) analysis of neurons in the cat's lateral geniculate nucleus during tonic and burst response mode, Vis. Neurosci. 12 (1995) 723-741.

[5] J.E. Hamos, S.C. Van Horn, D. Raczkowski, D.J. Uhlrich, S.M.Sherman, Synaptic connectivity of a local circuit in lateral geniculate nucleus of the cat, Nature 317 (1985) 618-621.

[6] G. Le Masson, S. Renaud-Le Masson, D. Debay, T. Bal, Feedback inhibition controls spike transfer in hybrid thalamic circuits, Nature 417 (2002) 854-858.

[7] E.J. Ramcharan, J.W. Gnadt, S.M. Sherman, Burst and tonic firing in thalamic cells of unanesthetized, behaving monkeys, Vis. Neurosci. 17 (2000) 55-62.

[8] P. Reinagel, D. Godwin, S.M. Sherman, C. Koch, Encoding of visual information by LGN bursts, J. Neurophysiol. 81 (1999) 2558-2569.

[9] M.H. Rowe, Q. Fischer, Dynamic properties of retino-geniculate synapses in the cat, Vis Neurosci. 18 (2001) 219-231.

[10] S.M. Sherman, Tonic and burst firing: dual modes of thalamocortical relay, Trends in Neurosciences 24 (2001) 122-126.

[11] G.D. Smith, S.M. Sherman, Detectability of Excitatory versus Inhibitory Drive in an Integrate-and-Fire-or-Burst Thalamocortical Relay Neuron Model, The Journal of Neuroscience 22 (2002) 10242-10250.

[12] G.D. Smith, C.L. Cox, S.M. Sherman, J. Rinzel, Fourier analysis of sinusoidally driven thalamocortical relay neurons and a minimal integrate-and-fire-or-burst model, J Neurophysiol 83 (2000) 588-610.

[13] M. Steriade, L. Domich, G. Oakson, Reticularis thalami neurons revisited: activity changes during shifts in states of vigilance, J Neurosci. 6 (1986) 68-81.

[14] JB. Troy, JG. Robson, Steady discharges of X and Y retinal ganglion cells of cat under photopic illuminance, Vis. Neurosci. 9 (1992) 535-553.

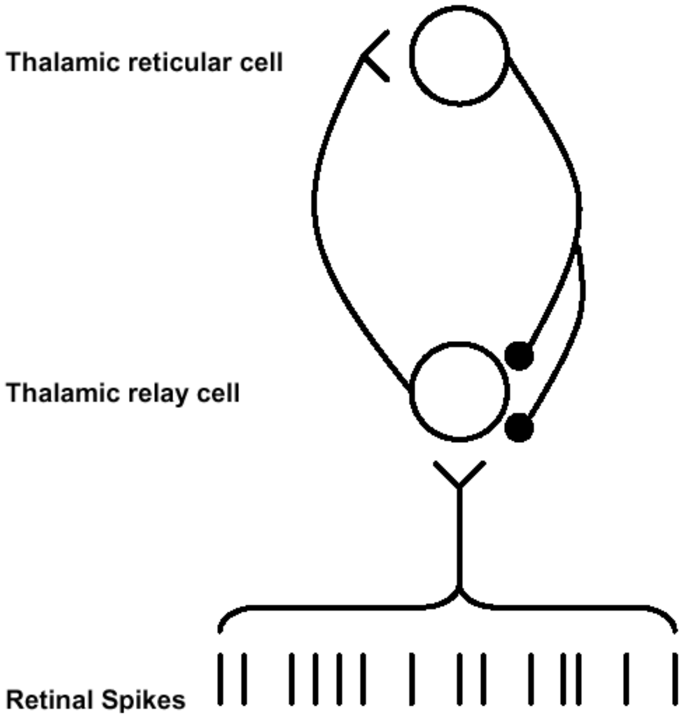

Figure 1.

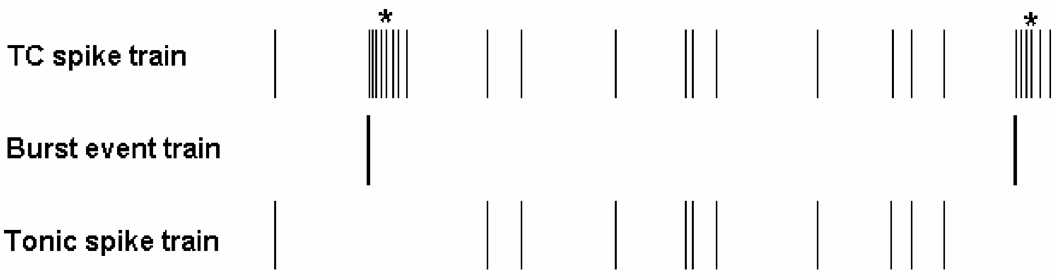

Figure 2

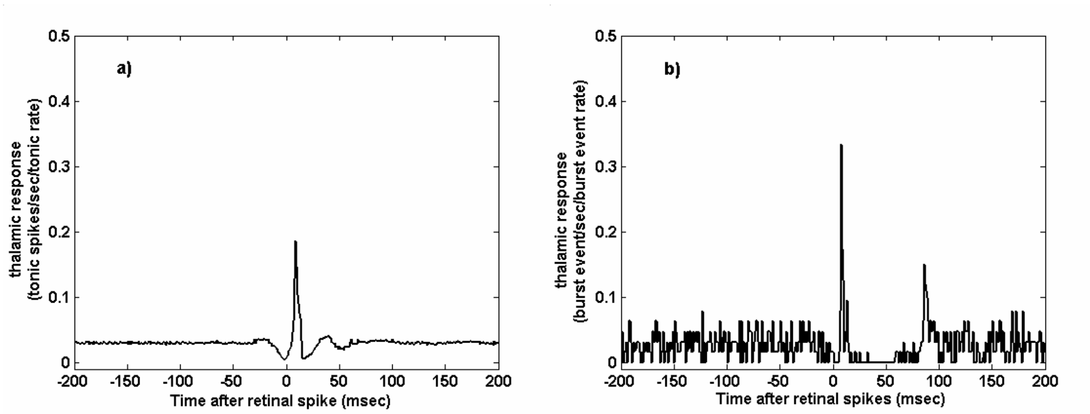

Figure 3

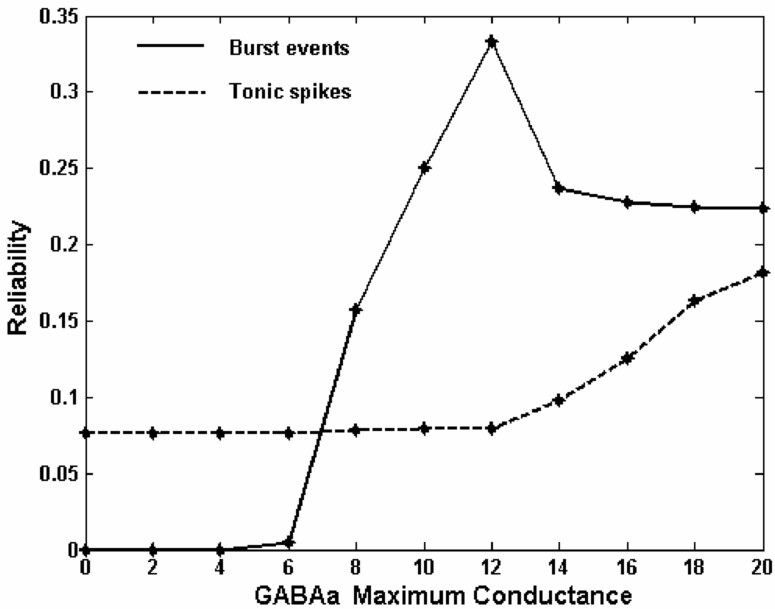

Figure 4

Figure captions

Figure 1. The minimal thalamic (LGN) circuit. The retinal spike train excites the thalamic relay cell. The thalamic relay cell excites the reticular cell, and the reticular cell inhibits the relay cell via $GABA_A$ and $GABA_B$ synapses.

Figure 2. Discriminating burst and tonic responses. Both burst and tonic responses are present in the original spike train of TC (top). Bursts (marked with asterisks) are identified by the “liberal criteria” (see text). From the original spike train, the burst event train (middle) and the tonic spike train (bottom) are then extracted.

Figure 3. a) Cross-correlogram of tonic spike train and the retinal spike train, normalized by the rate of tonic spikes. b) Cross-correlogram of burst event train and the retinal spike train, normalized by the rate of burst events. Note that the peak is higher for burst events, and also of two peaks exist for the bursts.

Figure 4. The reliability index of burst events (solid line) and tonic spikes (dashed line) as a function of $GABA_A$ maximum conductance. The reliability of bursts has a peak at maximal $GABA_A$ conductance of *0.012 ms*, while the reliability of tonic spikes is monotonous .