The effect of feedback inhibition on throughput properties of the dLGN/PGN

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Abstract

The effect of feedback inhibition from thalamic reticular (RE) cells on retinogeniculate transmission by thalamocortical (TC) neurons of the dLGN is analyzed using a minimal integrate-and-fire-or-burst (IFB) network model. The network includes spatially non-local synaptic coupling, alpha-function postsynaptic conductances, and a gamma process representation of spontaneous or visually-driven retinal ganglion cell activity. Potassium leakage conductances control the neuromodulatory state of the network and can eliminate rhythmic bursting in the presence of spontaneous input (i.e., wake the network). During oscillatory full-field stimulation the response of the aroused network depends on average input rate, contrast level, and temporal frequency of modulation.

Key words: Thalamus; vision; dLGN; integrate-and-fire; burst.

1 Introduction

Like other sensory thalamic nuclei, the dorsal lateral geniculate nucleus (dLGN) controls the flow of sensory information to cortex, acting as a state-dependent gateway between the sensory periphery and higher cortical centers [3]. During sleep the principle cells of the dLGN exhibit rhythmic bursts of action potentials (APs) which do not reflect the excitatory glutamatergic drive they receive from spontaneously active retinal ganglion cells (RGCs). Such emergent network properties of the sleeping thalamus require the interaction between excitatory (glutamatergic) TC cells and inhibitory (GABAergic) thalamic reticular (RE) neurons, as well as the low-threshold Ca^{2+} current (I_T) that both TC and RE cells express. During arousal thalamocortical (TC) relay neurons of the dLGN cease rhythmic bursting, enter tonic mode, and respond with conventional APs that faithfully relay EPSPs received from spontaneously active or visually stimulated RGCs.

Computational modeling has played an important role in the dissection of the biophysical basis of thalamus oscillations associated with sleep and certain forms of epilepsy. Here we present and analyze a minimal network model of retinogeniculate transmission, focusing on the throughput properties of the aroused dLGN/PGN when stimulated by a gamma process representation of spontaneous or visually-driven RGC input, the latter corresponding to X-cell responses to oscillatory full-field stimulation.

2 Model

Simulations were performed using a minimal dLGN/PGN network model composed of TC-like and RE-like integrate-and-fire-or-burst (IFB) neuron models [4]. Briefly, an IFB model is constructed by adding a slow variable to a classical integrate-and-fire neuron,

$$C\frac{dV}{dt} = -\underbrace{g_{KL}(V-V_{KL})}_{I_{KL}} - \underbrace{g_{NL}(V-V_{NL})}_{I_{NL}} - \underbrace{g_T\Theta(V-V_h)h(V-V_T)}_{I_T}$$

$$\frac{dh}{dt} = \begin{cases} -h/\tau_h^- & (V > V_h) \\ (1-h)/\tau_h^+ & (V < V_h) \end{cases}$$

where the leakage current $I_L = I_{KL} + I_{NL}$ is the sum of potassium and non-specific components. A spike occurs when V reaches the threshold V_θ, and an absolute refractory period of length t_R is imposed during which $V = V_{reset}$. The slow variable h represents de-inactivation of I_T and the Heaviside function $\Theta(V - V_h)$ is an idealization of I_T activation. The TC-like IFB model originally presented in [4] reproduces the salient response features of TC cells to sinusoidal current injection.

A subtle change in parameters converts the TC-like IFB model into an RE-like version (see Fig. 1A and B). In the TC model, the resting membrane potential (V_L^{TC}, *filled circle*) is more depolarized than V_h^{TC}(vertical branch of h-nullcline, *dotted line*), while in the RE model $V_L^{RE} < V_h^{RE}$. Thus, the TC neuron exhibits tonic spiking when depolarized and post-inhibitory rebound bursts, while the resting RE model is primed to burst because I_T is de-inactivated ($h = 1$) when $V^{RE} = V_L^{RE}$.

The dLGN/PGN network is composed of two one-dimensional arrays of TC-like and RE-like IFB models [4] with connectivity following [2] (see Fig. 1C),

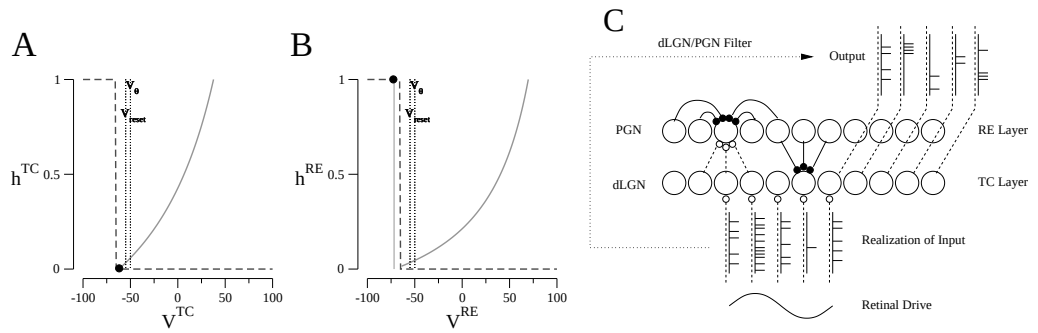

Fig. 1. *A*: and *B*: (V, h)-phase planes for the TC-like and RE-like IFB models (*solid lines*, $\dot{V} = 0$; *dashed lines*, $\dot{h} = 0$). *Filled circles* indicate resting membrane potentials, $V_L^{RE}$and V_L^{TC}. *C*: dLGN/PGN network diagram showing excitatory (*open circles*) and inhibitory (filled circles) synaptic connections. TC parameters in awake state: $C = 1\ \mu\text{F/cm}^2$; in ms: $t_R = 4$, $\tau_h^+ = 100$, $\tau_h^- = 20$; in mV: $V_{KL} = -100$, $V_h = -65$, $V_{reset} = -55$, $V_{NL} = -50$, $V_\theta = -50$, $V_T = 120$; in mS/cm^2: $g_T = 0.08$, $g_{NL} = 0.05$, and $g_{KL} = 0.016$ for V_L^{TC} of -62.1 mV. RE as TC except $g_T = 0.2$, $g_{NL} = 0.04$, and $g_{KL} = 0.031$ mS/cm^2 for V_L^{RE} of -71.8 mV.

$$C\frac{dV_i^{TC}}{dt} = -I_{MEM_i}^{TC} - I_{RETi} - I_{GABAi}$$
$$C\frac{dV_i^{RE}}{dt} = -I_{MEM_i}^{RE} - I_{AMPAi} - I_{GABA_i}^{RE}$$

where $I_{SYN_i} = g_{SYN} \sum_j w_{ji} s_j (V_i - V_{SYN})$ and the exponentially decaying synaptic footprint is given by $w_{ij} = \exp(-|x_i - x_j|/\lambda)/2\lambda$ where $\lambda = 0.1$ (one tenth of the network length). The TC layer receives spontaneous or visually-driven excitatory synaptic conductances (g_{RET}) and feedback inhibition from GABAergic RE cells (g_{GABA}). The RE layer receives excitatory synaptic conductances (g_{AMPA}) from TC cells and GABAergic inhibition from neighboring RE cells (g_{GABA}^{RE}). Postsynaptic conductances of form $s_j(t) = \alpha_j^2 t e^{-\alpha_j t}$ are triggered by spiking of presynaptic neurons ($\alpha_{AMPA} = \alpha_{RET} = 0.1$ and $\alpha_{GABA} = \alpha_{GABA}^{RE} = 0.05\ \text{ms}^{-1}$) [1].

Average X-type RGC responses to oscillatory full-field stimulation were modeled as,

$$\rho(t) = \rho_{DC} + \rho_{AC} \cos(2\pi f t) = \rho_{DC} [1 + c \cos(2\pi f t)],$$

where ρ_{DC} and ρ_{AC} are DC and AC spike rates, $c = \rho_{AC}/\rho_{DC}$ is the stimulus contrast, and f is the temporal frequency of modulation. Event times for spontaneous or visually-driven retinal excitatory postsynaptic conductances are modeled as a modulated gamma process of rate $\rho(t)$ [5].

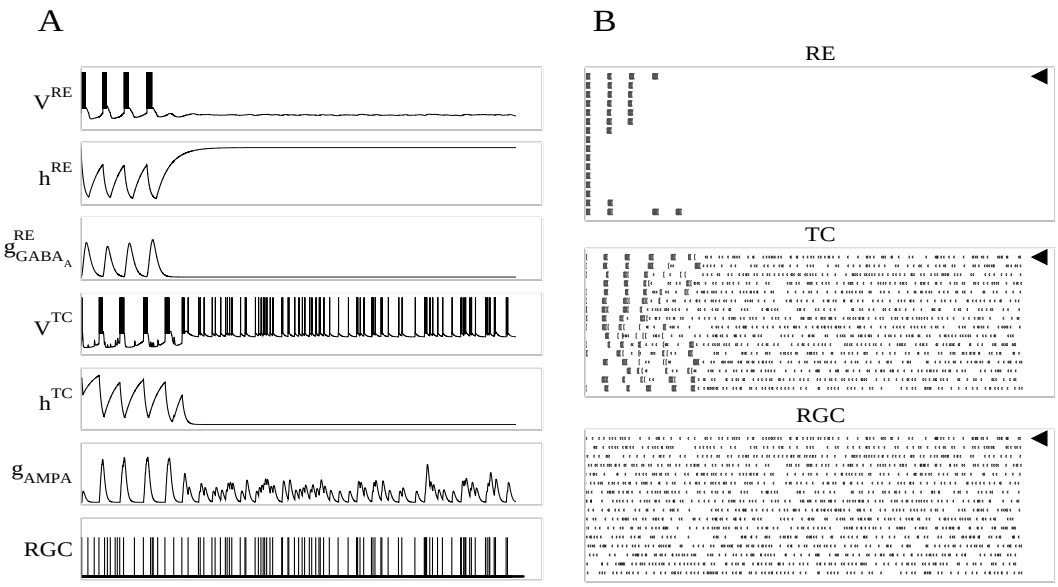

Fig. 2. Aroused network ($g_{KL}^{TC} = 0.016$, $g_{KL}^{RE} = 0.031$ $\mu S/cm^2$) driven by 30 Hz spontaneous input. *A*: Response of neurons in the network (*filled triangle* in B). *B*: Raster plots show network activity under full-field spontaneous stimulation. *Short* and *long vertical lines* indicate burst and tonic spikes, respectively. Network parameters as in Section 2 and in mV: $V_{AMPA} = 0$, $V_{RET} = 0$, $V_{GABA} = -85$, $V_{GABA}^{RE} = -85$; in mS/cm^2: $g_{AMPA} = 0.1$, $g_{RET} = 0.3$, $g_{GABA} = 15$, $g_{GABA}^{RE} = 1$.

3 Simulation results

The neuromodulatory state of the dLGN/PGN network is determined by g_{KL} for each cell type. In the sleep state ($g_{KL}^{TC} = 0.02$, $g_{KL}^{RE} = 0.027$ μS/cm^2) the network exhibits sleep rhythm activity in the presence of a 30 Hz spontaneous retinal input (not shown), while in the awake state ($g_{KL}^{TC} = 0.016$, $g_{KL}^{RE} = 0.031$ $\mu S/cm^2$) rhythmic bursting is not sustained (Fig. 2B). Though some cells exhibit several bursts, ultimately the RE cells are quiescent and TC cells respond in tonic mode faithfully relaying retinal input.

Figure 3 shows the response of the awake network to full-field, sinusoidally modulated input. With cellular and network parameters identical to Fig. 2, modulated stimulation leads to active RE cells and both burst and tonic TC responses.

The awake network responds in three qualitatively distinct manners depending on stimulus parameters (summarized in Fig. 4A): *tonic*, where the RE cells are not active (Fig. 2), *burst-tonic*, RE cells are active (Fig. 3) and *phase-locked bursting*, where TC cell PIR burst are phase-locked to RGC input. Figure 4B shows the three types of responses in simulations identical except for temporal frequency of retinal input (4, 6.25 and 25 Hz, respectively).

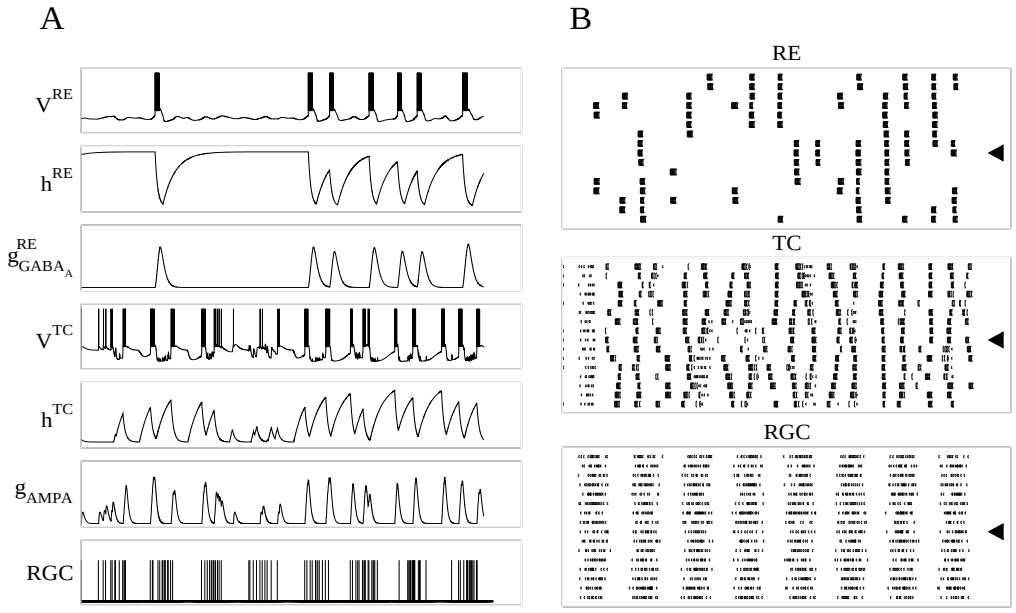

Fig. 3. Aroused network ($g_{KL}^{TC} = 0.016$, $g_{KL}^{RE} = 0.031\ \mu S/cm^2$) stimulated at 2.5 Hz, with $\rho_{DC} = 30$ and $\rho_{AC} = 60$ Hz. *A*: Response of TC and RE neurons in the same retinotopic position (*filled triangle* in B). *B*: Raster plots of network activity under full-field oscillatory stimulation. Though the network is *awake*, RE cells are active and population rhythm is phase-locked to RGC input.

4 Conclusions

The neuromodulatory state of the dLGN/PGN network is determined by g_{KL} for each cell type. In the sleep state, the network exhibits sleep rhythm activity in the presence of a 30 Hz spontaneous retinal input. When g_{KL}^{TC} and g_{KL}^{RE} are chosen to represent the awake state, the network model presented here is unable to sustain sleep rhythm activity: the RE cells are ultimately quiescent and TC cells respond in tonic mode faithfully relaying RGC input. However, in the presence of modulated stimulation with sufficiently high mean firing rate, the RE cells exhibit phase-locked bursts and modify (through feedback inhibition) the response of TC cells and network throughput. Parameter studies indicate three response types depending on mean firing rate, contrast level, and temporal frequency of the stimulus.

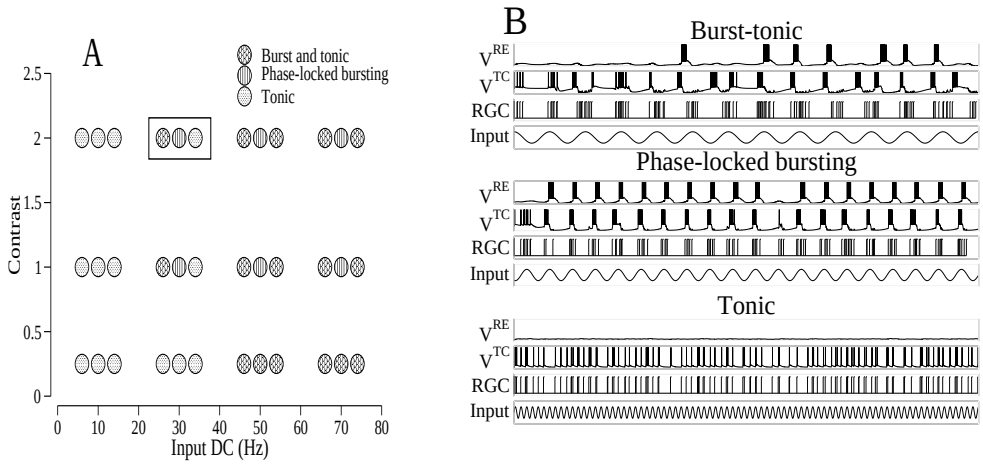

Fig. 4. *A*: Summary plot of network response to stimuli with different mean firing rate and contrast. Circle triplets (◯◯◯) correspond to input frequencies of *4*, *6.25* and *25* Hz. Symbol fill corresponds to *tonic*, *burst-tonic*, and *phase-locked bursting*. *B*: Representative membrane potential and RGC spike times for three network response types in A. Temporal frequency of stimulus is *4* (top), *6.25* (middle) and *25* Hz (bottom).

Acknowledgments

This work was supported by NSF MCB CAREER award #0133132, NSF IBN grant #0228273, and the Jeffress Memorial Trust. The work was performed in part using computational facilities at W&M enabled by grants from the NSF and Sun Microsystems.

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