



# A two-dimensional population density approach to modeling the dLGN/PGN network<sup>☆</sup>

Marco A. Huertas, Gregory D. Smith\*

*Department of Applied Science, College of William and Mary, Williamsburg, VA 23187, USA*

## Abstract

The interaction of two populations of integrate-and-fire-or-burst neurons representing thalamocortical cells from the dorsal lateral geniculate nucleus (dLGN) and thalamic reticular cells from the perigeniculate nucleus (PGN) is studied here using a population density approach. A two-dimensional probability density function that evolves according to a time-dependent advection-reaction equation gives the distribution of cells in each population over the membrane potential ( $v$ ) and de-inactivation level ( $h$ ) of the low-threshold  $\text{Ca}^{2+}$  current  $I_T$ . The response of the dLGN/PGN network is studied for optic tract stimulation protocols of different amplitude, duty cycle, and frequency.

© 2006 Elsevier B.V. All rights reserved.

*Keywords:* dLGN; Optic tract stimulation; Burst; Population density

## 1. Introduction

Probability density approaches to network modeling are of interest as computationally efficient methods for large-scale network calculations. However, most prior work exploring the promise of probability density methods have focused on integrate-and-fire models that do not include the low-threshold currents that give rise to post-inhibitory rebound bursting.

Here a probability density approach is used to model two reciprocally connected populations of neurons representing thalamocortical (TC) cells from the dorsal lateral geniculate nucleus (dLGN) and thalamic reticular (RE) neurons from the perigeniculate nucleus (PGN). These two populations of neurons are described by the integrate-and-fire-or-burst (IFB) formalism [5]; neurons in each population are capable of bursting through de-inactivation and/or activation of the low-threshold  $\text{Ca}^{2+}$  current,  $I_T$ . The RE and TC cell populations are described by two-dimensional probability density functions for the distribution of cells over all possible states. The two probability density

functions evolve according to coupled time-dependent advection-reaction equations.

While the dLGN/PGN probability density network is capable of sustaining experimentally observed rhythmic bursting, our primary interest is the network's response to periodic stimuli from retinal ganglion cell axon activity during optic tract stimulation. The calculations presented here are an extension of prior dLGN/PGN modeling of our group [3] and the probability density methods presented in [1,2,4].

## 2. Formulation of model

The population density approach describes the dynamics of a large number of point neurons using a probability density function,  $\rho(v, h, t)$ , over the two state variables of IFB neurons:  $v$ , the membrane potential and  $h$ , the de-inactivation level of the low-threshold  $\text{Ca}^{2+}$  current,  $I_T$ . Each two-dimensional probability density function evolves according to the advection-reaction equation

$$\frac{\partial \rho^k}{\partial t} = -\nabla \cdot \vec{J}^k + \delta(v - v_{\text{reset}}) \vec{J}^k \cdot \hat{e}_v|_{v=v_0}, \quad (1)$$

where  $k$  labels the population (e.g.,  $k = \text{TC}$  or  $\text{RE}$ ),  $\vec{J}^k(v, h, t)$  is the total probability flux for population  $k$ ,

<sup>☆</sup>Supported by NSF Grants IBN 0228273, MCB 0133132, and DMS/BIO/NIGMS 600302.

\*Corresponding author.

*E-mail address:* [greg@as.wm.edu](mailto:greg@as.wm.edu) (G.D. Smith).

and  $\hat{e}_{v,h}$  are the unit vectors in the direction of the  $v$ - and  $h$ -axis, respectively. The total probability flux vanishes at the boundaries ( $\vec{J}^k \cdot \hat{n} = 0$ , where  $\hat{n}$  is a unit vector normal to the boundary) except at  $v = v_\theta$  (the spiking threshold) where  $\vec{J}^k \cdot \hat{e}_v|_{v=v_\theta} \geq 0$  is the probability flux of neurons firing action potentials at each possible value of  $h$ . In Eq. (1) this flux is reinserted at  $v = v_{\text{reset}}$  consistent with the instantaneous voltage resetting of the IFB model. The population firing rate  $r^k$  is obtained by integrating the spiking flux over all values of  $h$ .

The total probability flux  $\vec{J}^k$  is composed of two terms,  $\vec{J}^k = \vec{J}_{\text{int}}^k + \vec{J}_{\text{pop}}^k$  where  $\vec{J}_{\text{int}}^k = (F_v \hat{e}_v + F_h \hat{e}_h) \rho$  and

$$\begin{aligned} \vec{J}_{\text{pop}}^k = & v_{e,c}^k \hat{e}_v \int_{E_c}^v \tilde{F}_{\Gamma_c^*} \left( \frac{v-v'}{E_c-v'} \right) \rho^k(v', h, t) dv' \\ & - v_i^k \hat{e}_v \int_v^{v_\theta} \tilde{F}_{\Gamma_i^*} \left( \frac{v-v'}{E_i-v'} \right) \rho^k(v', h, t) dv'. \end{aligned} \quad (2)$$

In these expressions,  $F_v$  and  $F_h$  are defined by the differential equations  $dv/dt = F_v$  and  $dh/dt = F_h$  of the IFB model (see Ref. [5] for details) and  $\vec{J}_{\text{pop}}^k$  accounts for synaptic changes caused by excitatory (e) and inhibitory (i) currents (with reversal potentials  $E_e$  and  $E_i$ ) triggered by presynaptic spikes arriving at rates  $v_{e,i}$ . Following Ref. [4] these rates are given by

$$v_{e,i}^p(t) = v_{e,i}^{p,0}(t) + \sum_q w_{qp} \int_0^\infty \alpha(t') r^q(t-t') dt', \quad (3)$$

where  $\alpha(t)$  is a temporal kernel that accounts for the finite conduction velocity of action potentials and the quantities  $w_{qp}$  represent the average number of projections to population  $p$  originating from each presynaptic cell in population  $q$ . The quantity  $v_{e,i}^{p,0}(t)$  represents external drive (e.g., from RGC axons). Changes in membrane potential due to the arrival of action potentials are described by the random variable  $\Gamma_{e,i}^*$  whose statistics are included in  $\vec{J}_{\text{pop}}^k$  through the complementary cumulative distribution functions  $\tilde{F}_{\Gamma_{e,i}^*}(x)$  (see Ref. [4]). Fig. 1 shows a schematic representation of the interaction between the RE and TC cell populations in the probability density dLGN/PGN IFB network.

### 3. Results

#### 3.1. Convergence of IFB network Monte Carlo simulations and the population density approach

Figs. 2 and 3 show that as the size of each population increases from 100 to 1000 cells the probability density approach agrees with Monte Carlo results obtained using an equivalent network of IFB neurons.

Fig. 2 compares the population firing rate of both models and demonstrates convergence as  $N$  increases. Fig. 3 compares the probability distributions  $\rho^{\text{TC}}(v, h, t)$

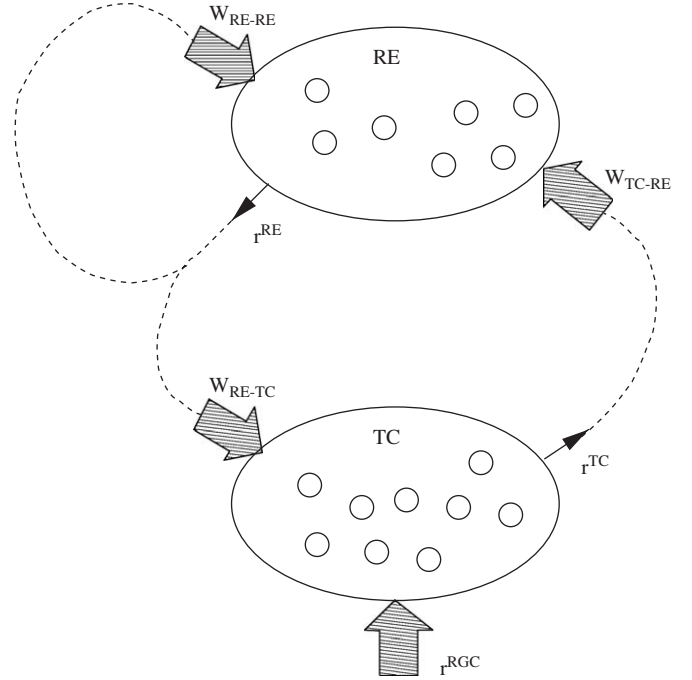


Fig. 1. Schematic diagram showing interacting RE and TC populations (large ellipses) in the probability density dLGN/PGN IFB network. Small arrows pointing outward from the populations represent the probability flux at the spiking threshold  $v_\theta$  (Eq. (1)). Large arrows represent the coupling of the populations scaled by the average number of synaptic connections. Retinal drive to the TC population is also shown.

and  $\rho^{\text{RE}}(v, h, t)$  (filled contour lines) with the  $v$  and  $h$  values of the 500 cell Monte Carlo simulation (scattered points), corresponding to a snapshot of Fig. 2C at 300 ms. Projections of these distributions along the  $v$ - and  $h$ -axes also indicate a good agreement (compare black solid line and histograms).

#### 3.2. Simulation of dLGN/PGN response during optic tract stimulation using the population density approach

Fig. 4 shows the response of the dLGN/PGN network to simulated optic tract stimulation modeled as square pulses of retinal drive ( $v_{e,c}^{\text{TC},0}$  in Eq. (3)). The duration of the active phase was fixed at 1 ms while the period  $T$  and amplitude  $f_{\text{max}}$  were varied. Each panels shows the stimulus (bottom) and TC (middle) and RE (top) population firing rates for the stimulus parameters indicated by the outer axes. The majority of the panels show the steady-state periodic response during two stimulus cycles. Panels I and M show a larger number of stimulus periods and a subharmonic response. The network response to optic tract stimulation is generally periodic and phase-locked to the temporal frequency of the stimulus (see panels A–H, J and N–P in Fig. 4). At high stimulus frequencies ( $T = 5, 10$  ms) the firing rate of the TC population reaches its peak during the stimulus active phase. For lower stimulus frequencies ( $T = 50$  ms) the maximum TC response occurs during a rebound burst caused by the feedback inhibition of RE cells during

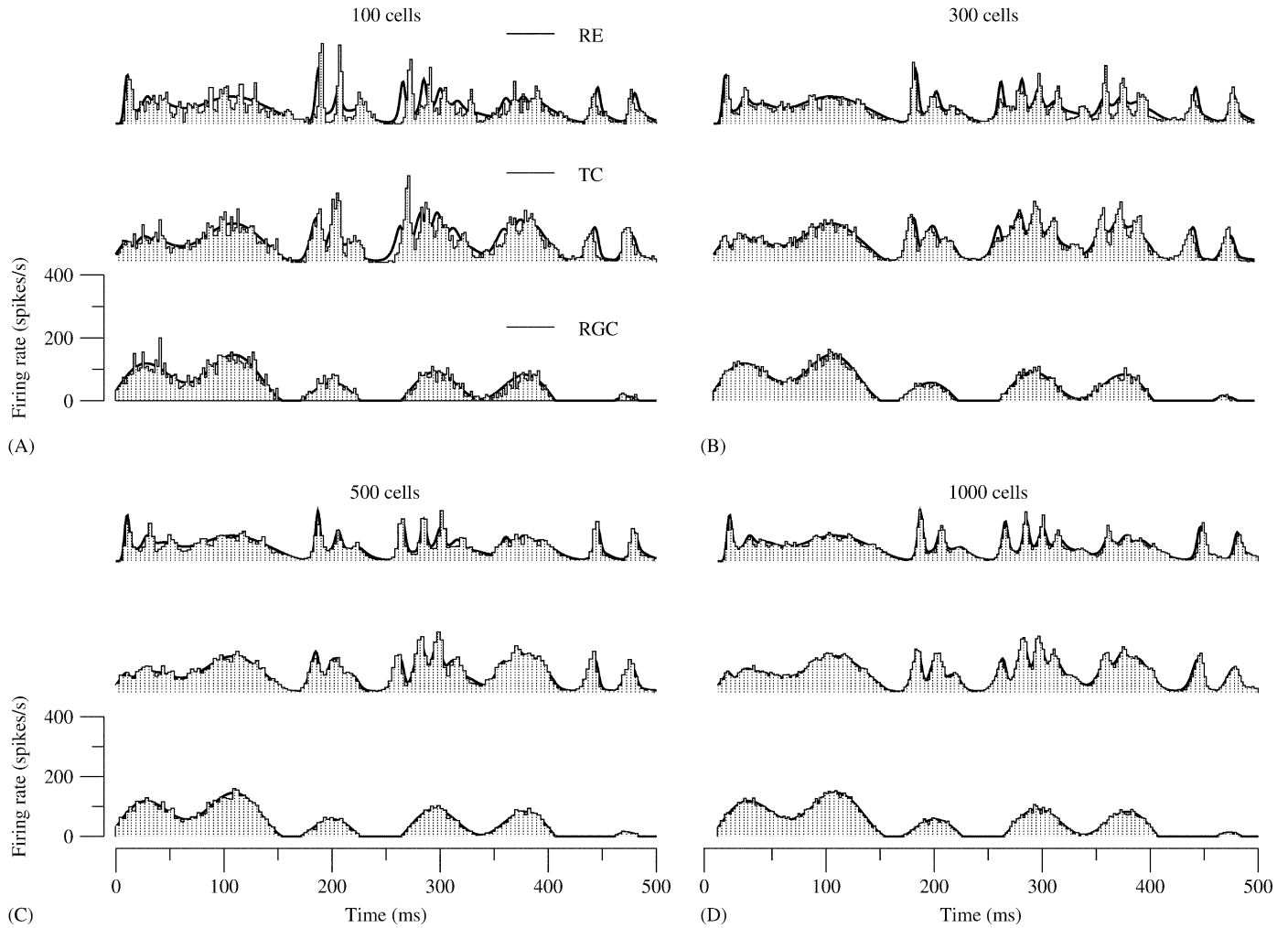


Fig. 2. Convergence of 100–1000 cell Monte Carlo IFB network simulations (*filled histograms*) and the population density approach (*black solid line*). Each panel shows the firing rate of the RE and TC populations (*top* and *middle*, respectively) and the retinal firing rate (*bottom*).

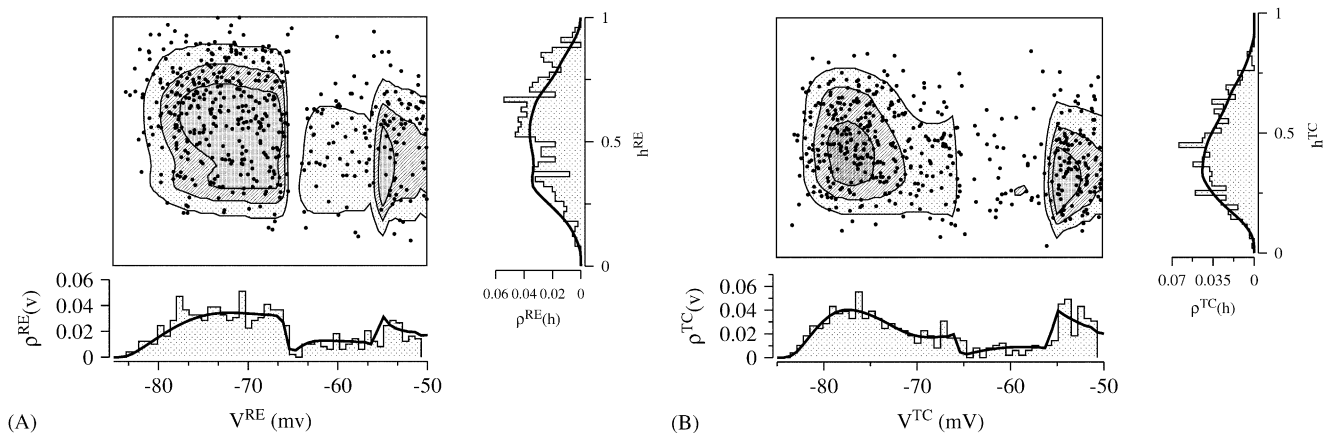


Fig. 3. Comparison between the population density approach and the 500 cell IFB network model. Panels A and B correspond to the RE and TC populations, respectively. *Contour lines* indicate the densities  $\rho^{\text{TC}}(v, h, t)$  and  $\rho^{\text{RE}}(v, h, t)$  of the population density approach and the *scattered points* are a snapshot of the state of each cell in a Monte Carlo simulation of the corresponding IFB network.

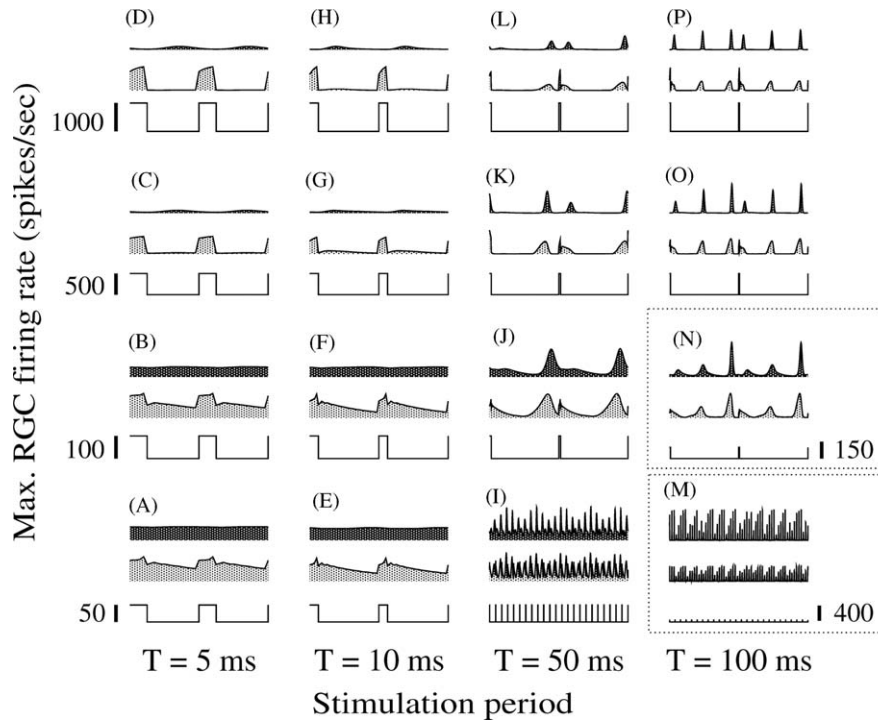


Fig. 4. Parameter study of the responses of the dLGN/PGN network model to simulated optic tract stimulation obtained using the population density approach. Each panel shows the stimulus (*bottom*) and the steady-state TC (*middle*) and RE (*top*) population firing rates for the stimulus parameters indicated by the outer axes. Bars indicate the scale (in spikes/sec) used in a given row with the exception of the panels boxed with dotted lines.

the previous cycle. As the stimulus period is further increased ( $T = 100$  ms) additional bursting is observed: period doubling in panels K and L and complex superharmonic responses in panels I and M.

#### 4. Conclusion

We have successfully used a population density approach [1,4] in a minimal model of the dLGN/PGN network during simulated optic tract stimulation protocols. Importantly the probability density approach was shown to agree well with an equivalent (i.e., same cellular and network parameters) network of coupled IFB point neuron populations as the number of cells in both TC and RE populations increases (Fig. 2). The agreement between the distribution of cells over the state variables  $v$  and  $h$  (Fig. 3) also confirms the quality of our extension of the population density approach to represent the dynamics of two populations of IFB neurons.

We found that the probability density dLGN/PGN network model responses to optic tract stimulation are generally periodic and phase locked to the temporal frequency of the stimulus. Depending on stimulus amplitude and period, one-to-one, one-to-two superharmonic and many-to-many subharmonic responses were observed.

While here we focus on stimulus driven responses, the dLGN/PGN probability density network is capable of rhythmic bursting in the absence of retinal drive (as in the sleeping thalamic slice preparation) and with 30 Hz

spontaneous retinal input (as during sleep; not shown). We have found that convergence between the probability density calculations and Monte Carlo simulations of the corresponding IFB network often converge more rapidly (for smaller  $N$ ) when the size of synaptic jumps is large ( $I_{e,i}^*$  in Eq. (2)). The computation efficiency of the probability density dLGN/PGN calculations presented here is striking. For example, the  $2 \times 1000$  cell simulation of Fig. 2D required two days on a dual 3 GHz processor workstation while the corresponding probability density network calculation required 1 h on the same platform.

#### References

- [1] A.R. Casti, A. Omurtag, A. Sornborger, E. Kaplan, B. Knight, J. Victor, L. Sirovich, A population study of integrate-and-fire-or-burst neurons, *Neural Comput.* 14 (5) (2002) 957–986.
- [2] E. Haskell, D.Q. Nykamp, D. Tranchina, Population density methods for large-scale modelling of neuronal networks with realistic synaptic kinetics: cutting the dimension down to size, *Network Comput. Neural Syst.* 12 (2001) 141–174.
- [3] M.A. Huertas, J.R. Groff, G.D. Smith, Feedback inhibition and throughput properties of an integrate-and-fire-or-burst network model of retinogeniculate transmission, *J. Comput. Neurosci.* 19 (2) (2005) 147–180.
- [4] D.Q. Nykamp, D. Tranchina, A population density approach that facilitates large-scale modeling of neural networks: analysis and an application to orientation tuning, *J. Comput. Neurosci.* 8 (1) (2000) 19–50.
- [5] 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 (1) (2000) 588.



(1998) and holds a Ph.D. in Nuclear Physics from the College of William and Mary (2003).

**Marco A. Huertas** is a research associate at the Department of Applied Science of the College of William and Mary in professor Smith's computational biology laboratory. Huertas' is involved in developing computer simulations and mathematical analysis of models of feedback inhibition in visual thalamus and more recently on excitation-contraction coupling in cardiac myocytes. Originally from Guatemala, Huertas was awarded a scholarship by the Fulbright/LASPAU program



Biophysics Graduate Group at UC Davis (1996) for work performed at the Institute for Theoretical Dynamics with Joel Keizer.

**Gregory D. Smith** is an associate professor in the Department of Applied Science at the College of William and Mary with research interests in computational cell biology and computational neuroscience. Smith's post-doctoral training includes an NRSA Fellowship at Center for Neural Science with John Rinzel at New York University (1998–1999) as well as an IRTA Fellow at the Mathematical Research Branch, NIDDK, NIH (1996–1998). Smith's Ph.D. was awarded by the