A population density model of the driven LGN/PGN

Marco A. Huertas
College of William and Mary

Gregory D. Smith
College of William and Mary, gdsmit@wm.edu

Follow this and additional works at: https://scholarworks.wm.edu/appliedsciencepub

Part of the Computational Neuroscience Commons, and the Mathematics Commons

Recommended Citation
10.1093/acprof:oso/9780199235070.003.0008]
8

A POPULATION DENSITY MODEL OF
THE DRIVEN LGN/PGN

Marco A. Huertas and Gregory D. Smith

8.1 Thalamocortical relay nuclei

The thalamus has been called the gateway to the cortex because it transmits sensory information from the periphery to the neocortex through so-called first-order relay nuclei (Sherman and Guillery, 1996). Examples of first-order relays are the dorsal lateral geniculate nucleus (LGN) and the ventral posterior medial (VPM) nucleus of the thalamus. The LGN is a major recipient of retinal ganglion cell (RGC) afferents and represents the first non-retinal stage of visual processing in the mammalian central visual pathway (Sherman and Koch, 1990). The VPM is the main recipient of axonal projections from trigeminal cells that respond to mechanical stimulation of the whiskers in the rat’s mystacial pad (Woolsey and der Loos, 1970, Castro-Alamancos, 2004). For recent comprehensive reviews of the neurobiology of the thalamus and the role of the thalamus in cortical function see (Sherman and Guillery, 2005, Jones, 2007).

Sensory thalamic nuclei such as the LGN and VPM act as state-dependent gateways between the sensory periphery and higher cortical centres (McCormick and Bal, 1997). During sleep, for example, the principal cells of the LGN exhibit rhythmic bursts of action potentials which do not reflect the excitatory glutamatergic drive they receive from spontaneously active retinal ganglion cells (RGCs). This rhythmic bursting may thus be interpreted as a ‘closure’ of the LGN gate. During arousal, this gateway ‘opens’ as thalamocortical (TC) relay neurons of the LGN cease rhythmic bursting, enter tonic mode, and fire conventional action potentials, the timing of which reflects excitatory post-synaptic potentials (EPSPs) received from visually stimulated RGCs.

Several different lines of investigation indicate that it is an oversimplification to view first-order thalamic relay nuclei as passive units that simply relay information to the cortex (Sherman and Koch, 1986, 1990, Sherman and Guillery, 1996, Sherman, 1996). For example, anatomical evidence indicates that only approximately 15% of synapses on LGN relay cells are from RGCs. The remainder originate from subcortical areas, GABAergic local interneurons (IN) of the LGN, GABAergic thalamic reticular (RE) neurons, and striate cortex. Indeed, the neuroanatomical observation that the majority of LGN synapses derive from cortex suggests that thalamic visual processing may not even be predominantly feed-forward. Instead, visual cortex projecting to the LGN and PGN may actively gate retinogeniculate transmission.
There is also a growing body of evidence that LGN relay neurons in awake-behaving and anesthetized cats exhibit transient (as opposed to rhythmic) bursts of action potentials in response to visual stimulation (Guido, Lu, and Sherman, 1992, Weyand, Boudreaux, and Guido, 2001, Guido and Weyand, 1995). When objective criteria are used to divide extracellular records into ‘burst’ and ‘tonic’ responses, it has been observed that LGN relay neurons in both modes can be visually driven (Guido et al., 1995). While tonic responses show little nonlinear distortion and faithfully relay retinal input, relay cells in burst mode have lower spontaneous activity, resulting in an improved signal-to-noise ratio. One bold hypothesis is that these transient, visually driven bursts may signal the presence of stimuli in receptive fields to which attention is not currently directed (Sherman, 1996).

While this specific hypothesis may not be validated, the above observations certainly suggest that the LGN is a dynamic filter under cortical and subcortical control rather than a gateway that can be only completely open (during arousal) or completely closed (during sleep). Indeed, although the classical receptive field properties of LGN relay neurons do not differ markedly from those of the RGCs that innervate them, investigators utilizing spatial and temporal frequency analysis of LGN and PGN cell response properties have long suggested that thalamus has an important dynamic role to play in visual processing, e.g. in contrast gain control (Kaplan, Purpura, and Shapley, 1987, Kaplan, Mukherjee, and Shapley, 1993). However, precisely how stimulus-dependent recruitment of inhibitory mechanisms of the LGN determine what retinal information is filtered out, and what retinal information is faithfully relayed to cortex, is an open question of current research (Casti et al., 2008).

8.2 Sleep oscillations, rhythmic bursts, and arousal

Experimental and theoretical investigations of thalamic activity during sleep have provided an understanding of the biophysical basis of rhythmic oscillations in thalamus that are associated with sleep and certain forms of epilepsy (Destexhe and Sejnowski, 2001, Rush and Rinzel, 1994, Golomb, Wang, and Rinzel, 1996a, Wang, Golomb and Rinzel, 1995, Rinzel et al., 1998). In particular, the 7- to 14-Hz spindle oscillation, which is observed during the onset of sleep, is a well-known phenomenon of coherent brain waves (Steriade and McCarley, 1990, Buzsaki, 2006). Spindle oscillations are an emergent network property of thalamic origin that involves synaptic interactions between excitatory (glutamatergic) thalamocortical (TC) relay neurons and inhibitory (GABAergic) neurons of the thalamic reticular (RE) nucleus, and the intrinsic low-threshold Ca\(^{2+}\) current (\(I_T\)) that both TC and RE cells express (see Fig. 8.1). The details of the mechanisms subserving rhythmic bursting are relevant to thalamic visual processing, because they are also responsible for transient bursts of LGN and PGN cells, and may be involved in other aspects of the gating of retinogeniculate transmission.

In TC cells at rest, the low-threshold Ca\(^{2+}\) current \(I_T\) is largely inactivated; however, \(I_T\) becomes de-inactivated upon hyperpolarization. This allows TC cells
A population density model of the driven LGN/PGN

Inhibitory

FIG. 8.1: Schematic diagram of the interaction between the RE and TC populations (large ellipses) in the Monte Carlo and population density simulations of driven LGN/PGN. The small arrows indicate the population firing rates $r_{TC}$ and $r_{RE}$ in the population density approach (Eqn (8.20)). The large arrows represent the interaction between populations (Eqn (8.24)) that is proportional to the average number of connections between pre- and post-synaptic cells (small circles). Excitatory drive from retinal ganglion cells (RGC) to TC cells is denoted by $i_{RGC}$. Reproduced with permission from Huertas and Smith (2006b).

to respond to release from hyperpolarization with a $Ca^{2+}$ spike that triggers conventional action potentials on its crest. In the simulation shown in Fig. 8.2(c), a minimal TC-like integrate-and-fire-or-burst (IFB) model (Smith et al., 2000) exhibits a post-inhibitory rebound burst in response to hyperpolarizing current injection (details of the IFB model are presented below). While TC cells hyperpolarized from rest may respond with a burst, TC cells depolarized from rest fire tonic spikes. Conversely, RE cells depolarized from rest respond with a burst, and if depolarized further can fire tonic spikes. RE cells burst in response to depolarization rather than hyperpolarization because they differentially express $I_T$ and several other currents. This is illustrated in Fig. 8.2(d), which shows a voltage trace of a RE-like IFB model exhibiting a burst of action potentials in response to depolarizing current injection. In network oscillations of the sleeping thalamus, each cell type provides a synaptic conductance that may cause the other to burst. RE cells periodically provide (through GABAergic synapses) the hyperpolarization necessary for TC cells to respond with post-inhibitory rebound bursts. These TC cell rebound responses then excite RE cells through AMPA synapses and the cycle repeats.

Computational modelling has played an important role in the characterization and analysis of the dynamics of TC and RE neuron membrane currents,
Fig. 8.2: (a), (b): \((V,h)\) phase planes for the TC-like and RE-like IFB models (solid lines, \(dV/dt = 0\); dashed lines, \(dh/dt = 0\); see Eqns (8.1) and (8.2)). Filled circles indicate resting membrane potentials located at the intersection of the \(V\) and \(h\) nullclines \((E^{RE}_L = -71.8\) and \(E^{TC}_L = -62.1\) mV). (c): Applied current pulse of \(\pm 0.6\) µA/cm\(^2\) (upper solid line) and corresponding voltage trace (lower solid line) of TC-like IFB model exhibiting a post-inhibitory rebound (PIR) burst in response to the hyperpolarizing current pulse. (d): Voltage trace (lower solid line) of RE-like IFB model exhibiting a burst of action potentials in response to depolarizing current injection (upper solid line). Parameters as in Table 8.1 save \(C = 1\) µF/cm\(^2\), \(g^{TC}_T = 0.08\) mS/cm\(^2\), \(g^{TC}_{KL} = 0.016\) mS/cm\(^2\), \(g^{RE}_{KL} = 0.031\) mS/cm\(^2\). Adapted with permission from Huertas, Groff, and Smith (2005b).

In particular, the low-threshold Ca\(^{2+}\) current, \(I_T\), and the hyperpolarization-activated nonspecific cation current, \(I_h\) (Destexhe et al., 1996, Destexhe et al., 1998, Zhan et al., 1999, Gutierrez et al., 2001). While the biophysical basis of rhythmic bursting in the thalamus has been extensively modelled (Destexhe, McCormick, and Sejnowski, 1993, Destexhe, Babloyantz, and Sejnowski, 1993, Destexhe et al., 1994a, Destexhe et al., 1994b, Rush and Rinzel, 1994, Wang, Golomb, and Rinzel, 1995, Golomb, Wang, and Rinzel, 1996a, Lytton, Destexhe,
A population density model of the driven LGN/PGN

and Sejnowski, 1996, Destexhe et al., 1996, Rinzel et al., 1998), there are comparatively few computational studies of the dynamic filter properties of thalamic relay nuclei during states of arousal. Kaplan and co-workers published two early studies of the burst and tonic response properties of driven LGN relay cells that included Hodgkin–Huxley (HH)-style simulations emphasizing the role of T-channel kinetics (Mukherjee and Kaplan, 1995, 1998). Firing rate models of retinogeniculate transmission have included feedback from primary visual cortex to the dLGN, but this modelling approach does not account for low-threshold currents or distinguish between burst and tonic spikes (Hayot and Tranchina, 2001). Our own prior work has focused on input/output properties of individual TC neurons (Smith et al., 2000, 2006, Smith and Sherman, 2002) and network studies of the role of feedback inhibition from RE cells in shaping visually-driven TC responses (Huertas, Groff, and Smith, 2005a, 2005b, Huertas and Smith, 2006a, 2006b). Other investigators have used the TC- and RE-like IFB models (Fig. 8.2) as a starting point for computational analysis of the input/output properties of minimal thalamic circuits (Babadi, 2005). In this chapter, we will describe how a large-scale model of sensory relay by the LGN/PGN can be implemented using TC- and RE-like IFB models and the population density methods presented in Chapter 7.

8.3 The integrate-and-fire-or-burst model

Because the integrate-and-fire-or-burst (IFB) model originally presented by Smith et al. (2000) reproduces the salient response properties of TC cells driven by sinusoidal current injection, it is a reasonable starting point for network simulations of LGN/PGN responses driven by RGC input. Briefly, a TC-like IFB model is constructed by adding a slow variable to a classical integrate-and-fire (IF) neuron,

\[
C \frac{dV_{TC}}{dt} = -I_L - g_T m_\infty h_{TC} (V_{TC} - E_T) \tag{8.1}
\]

\[
dh_{TC} \frac{dt}{} = \begin{cases} 
(1 - h_{TC}) / \tau_h^+ & \text{for } V_{TC} < V_h \\
-h_{TC} / \tau_h^- & \text{for } V_{TC} \geq V_h 
\end{cases} \tag{8.2}
\]

where we have expressed the leakage current, \(I_L\), as the sum of potassium and non-specific currents

\[I_L = I_{KL} + I_{NL} = -g_{KL} (V_{TC} - E_{KL}) - g_{NL} (V_{TC} - E_{NL})\,.
\]

A spike occurs when \(V_{TC}\) reaches the threshold \(V_\theta = -50\) mV, and subsequently an absolute refractory period of length \(t_R = 4\) ms is imposed during which \(V_{TC} = V_{\text{reset}} = -55\) mV. The activation of \(I_T\) is idealized here as an instantaneous step function of voltage given by

\[m_\infty (V_{TC}) = \begin{cases} 
0 & \text{for } V_{TC} < V_h \\
1 & \text{for } V_{TC} \geq V_h
\end{cases}\]
with the activation parameter $V_h = -65$ mV corresponding to an all-or-none low-threshold voltage. The slow variable $h_{TC}$ represents de-inactivation of $I_T$ and satisfies Eqn (8.2). When $V_{TC}$ is hyperpolarized below $V_h$, $h_{TC}$ relaxes to 1 with time constant $\tau^+_h = 100$ ms. When $V_{TC}$ is depolarized above $V_h$, $h_{TC}$ exponentially decays with time constant $\tau^-_h = 20$ ms.

Modification of several important parameters converts the TC-like IFB model into an RE-like version. While most of the parameters remain unchanged (e.g., $V_\theta$ and $V_h$), the RE cell leakage reversal potential ($E_{L_{RE}}^{\text{RE}}$) is approximately 9 mV more hyperpolarized than the TC cell leakage reversal potential ($E_{L_{TC}}^{\text{TC}}$). This difference makes the TC-like model resting membrane potential $E_{L_{TC}}^{\text{TC}}$ more depolarized than $V_h$, while the RE-like model $E_{L_{RE}}^{\text{RE}}$ is more hyperpolarized than $V_h$. The parameters chosen lead to the $(V_{TC}, h_{TC})$ and $(V_{RE}, h_{RE})$ phase planes shown in Fig. 8.2(a) and (b). The solid and dashed lines indicate the nullclines for voltage ($dV_{TC}/dt = 0$ and $dV_{RE}/dt = 0$) and $I_T$ de-inactivation ($dh_{TC}/dt = 0$ and $dh_{RE}/dt = 0$), respectively. The vertical branch of the $h_{TC}$ and $h_{RE}$ nullcline (i.e., the vertical dashed line) corresponds to the burst threshold $V_h$ and the vertical dotted lines show the location of the spike threshold ($V_\theta$) and reset ($V_{\text{reset}}$) voltage. The filled circle located at the intersection of the $V_{TC}$ and $h_{TC}$ and $V_{RE}$ and $h_{RE}$ nullclines shows the resting state of the TC- and RE-like IFB neurons in the absence of synaptic input.

The simulated voltage traces of Fig. 8.2(c) showing the TC-like IFB model exhibiting a PIR burst in response to hyperpolarizing current injection can be understood using the phase plane of Fig. 8.2(a) as a consequence of the resting membrane potential ($E_{L_{TC}}^{\text{TC}}$, filled circle) being more depolarized than the burst threshold ($V_h$, vertical dashed line). On the other hand, Fig. 8.2(d) shows simulated voltage traces of an RE-like IFB model exhibiting a burst of action potentials in response to depolarizing current injection. Here also the relative location of the resting membrane potential ($E_{L_{RE}}^{\text{RE}}$) with respect to $V_h$ explains this behaviour (see Fig. 8.2b). Because the maximum conductance for the low-threshold $\text{Ca}^{2+}$ current is greater in the RE-like IFB model ($g_{\text{RE}}^{\text{RE}} = 0.2\text{mS/cm}^2$) than in the TC-like version ($g_{\text{TC}}^{\text{TC}} = 0.08\text{mS/cm}^2$), the RE cell burst response exhibits more action potentials (compare Figs. 8.2c and d).

### 8.4 Synaptic interactions and network connectivity

The LGN/PGN network model presented here is made up of two populations of neurons – one composed of TC-like and the other of RE-like IFB neurons – that interact through excitatory and inhibitory synapses (Fig. 8.1). The TC cells receive excitatory drive from retinal ganglion cells (RGCs) and provide an excitatory input to the RE population, while active RE cells provide feedback inhibition to the TC cells as well as recurrent inhibition to other RE cells (Golomb, Wang, and Rinzel, 1996b; Sanchez-Vives, Bal, and McCormick, 1997, Sanchez-Vives and McCormick, 1997). The response of the TC population that results from these interactions, either in the presence or absence of retinal drive, constitutes the network output. For simplicity, we include neither feed-forward

Following Omurtag et al. (2000a and 2000b) and Nykamp and Tranchina (2000), the excitatory and inhibitory effects of presynaptic action potentials are modelled as instantaneous changes in the membrane potential of postsynaptic neurons. As discussed in Section 7.6.1 of this book, the effect on the postsynaptic cell of an action potential arriving at time $\tilde{t}$ is an instantaneous change in membrane potential with magnitude,

$$\Delta \tilde{V} = \tilde{V}(\tilde{t}^+) - \tilde{V}(\tilde{t}^-) = \left[ 1 - \exp(-\gamma_{e/i}) \right] \left[ E_{e/i} - \tilde{V}(\tilde{t}^-) \right], \quad (8.3)$$

where $\gamma_{e/i}$ is a dimensionless random variable given by

$$\gamma_{e/i} = \frac{1}{C} \int \tilde{g}_{e/i}(t) dt.$$  

In these expressions, tildes indicate random variables, $\tilde{g}_{e/i}(t)$ is the change in conductance due to the synaptic input at time $\tilde{t}$, and $E_{e/i}$ is the reversal potential of the corresponding excitatory (e) or inhibitory (i) synaptic current. Note that the random variable $\gamma_{e/i} = 1 - \exp(-\gamma_{e/i})$ takes values in the range of 0 to 1 and gives the change in the membrane potential at the time of the arriving spike and the excitatory or inhibitory reversal potential, that is,

$$\gamma_{e/i}^* = \left( \frac{\hat{V}(\tilde{t}^+) - \tilde{V}(\tilde{t}^-)}{E_{e/i} - \tilde{V}(\tilde{t}^-)} \right). \quad (8.4)$$

This formulation assumes that changes in membrane potential due to the arrival of an action potential occur on a time-scale much shorter than the membrane’s time-constant. Consequently, the model includes RE-to-TC inhibition mediated by fast (ionotropic) GABA$_A$ receptors, but does not include slower (metabotropic) inhibition mediated by metabotropic GABA$_B$ receptors.

In simulations presented below, the random variable $\gamma_{e/i}$ that corresponds to the magnitude of synaptic events is assumed to be gamma distributed with order $n = 4$ and mean $na_{e/i}$ (see Table 8.1). That is, the continuous probability distribution function $f_{\gamma_{e/i}}(\gamma)$ is given by

$$f_{\gamma_{e/i}}(\gamma) = \frac{\exp(-\gamma/a_{e/i})}{a_{e/i}(n-1)!} \left( \frac{\gamma}{a_{e/i}} \right)^{n-1}, \quad (8.5)$$

from which it follows that the random variable $\gamma_{e/i}^*$ is distributed according to

$$f_{\gamma_{e/i}^*}(\gamma) = \frac{1}{1-\gamma} f_{\gamma_{e/i}}(\gamma') \quad \text{where} \quad \gamma' = -\ln(1-\gamma). \quad (8.6)$$
Interactions between presynaptic and postsynaptic cells also include random synaptic latencies ($\tilde{\tau}$) representing the finite speed of action potential propagation. These latencies are drawn from a truncated gamma distribution that would otherwise be order $n = 9$ with mean $\alpha = 3$ ms (Nykamp and Tranchina, 2000), that is,

$$f_{\tilde{\tau}}(\tau) = \begin{cases} 
\alpha_{\text{norm}} \left(\frac{-\tau}{\alpha}\right)^{\frac{n-1}{\alpha}} & 0 \leq \tau \leq \alpha_{\text{max}} \\
0 & \text{otherwise}
\end{cases}$$

(8.7)

where $\alpha_{\text{max}} = 7.5$ ms and $\alpha_{\text{norm}}$ is a normalization constant. For physiological realism, the relationship between the excitatory and inhibitory synaptic reversal potentials and the spike threshold of the IFB model is assumed to be $E_i < V_0 < E_e$. Thus, when Eqns (8.1) and (8.2) are driven by random synaptic input as described by Eqns (8.3)–(8.6), the state of a neuron initially satisfying $E_i \leq \tilde{V} \leq V_0$ and $0 \leq \tilde{h} \leq 1$ will remain in this range for all time.

To complete the model formulation, we assume that the TC and RE populations each contain $N$ identical IFB neurons (Eqns (8.1) and (8.2)) with the TC- and RE-like parameters of Table 8.1. The random connectivity of the RE and TC cell populations in the LGN/PGN model is specified by a $2 \times 2$ matrix

$$W = (w_{ij}) = \begin{pmatrix} w_{\text{RE,RE}} & w_{\text{RE,TC}} \\
w_{\text{TC,RE}} & 0 \end{pmatrix}$$

(8.8)

with elements indicating the mean number of postsynaptic neurons in population $j$ influenced by the spiking of a presynaptic neuron in population $i$. Typical values of $w_{ij}$ are in the range of 5–50 with the exception of $w_{\text{TC,TC}}$ which is always zero. In the simulations presented below, we do not instantiate a $2N \times 2N$ connectivity matrix consistent with Eqn (8.8) and perform simulations using a fixed network topology. Instead, as suggested by Knight (1972) and Nykamp and Tranchina (2000), presynaptic spikes lead to a postsynaptic event in each and every postsynaptic neuron with probability $p = w_{ij}/N$. The number of postsynaptic potentials evoked by each presynaptic spike is thus a binomially distributed random variable with parameters $N$ and $p$ (and mean $w_{ij}$).

Figures 8.3(a) and (b) show the simulated membrane potential and deactivation gating variable as a function of time for two representative RE cells during a $2 \times 100$ neuron Monte Carlo simulation of the LGN/PGN network described above. Panel (e) shows the same traces in the $(v, h)$-plane along with vertical dashed lines indicating the burst threshold ($V_b$), the resting potential ($V_{\text{reset}}$) of the RE cells. Panels (c), (d), and (f) show the corresponding results for two representative TC cells. As depicted in Fig. 8.1, the LGN/PGN network model is stimulated by excitatory synaptic drive from a population of RGC neurons to the TC population. The RGC-to-TC interaction is one-to-one and the event times for RGC action potentials are simulated as a Poisson point process with an average rate of 60 Hz (not shown). The
A population density model of the driven LGN/PGN

Table 8.1. Parameters for the LGN/PGN population density model following previous experimental and theoretical work (Smith et al., 2000, Huertas, Groff, and Smith, 2005b)(Smith et al., 2000, Huertas et al., 2005b). The parameters representing the magnitude of synaptic events (\(a_{ij}\) in Eqn (8.5)) were chosen to be consistent with experimental estimates. For example, the value of \(a^{RGC}_{RE}\) was chosen so that in the absence of feedback inhibition the TC output correspond to a 50% transfer ratio (Kaplan, Purpura, and Shapley, 1987, Kaplan, Mukherjee, and Shapley, 1993). The values of \(a^{RE}_{TC}\) (TC-to-RE excitation) and \(a^{TC}_{RE}\) (RE-to-TC feedback inhibition) lead to average postsynaptic potentials shown in parentheses when the postsynaptic neuron is at rest. Experimental estimates of the mean number of synaptic connections between populations were used as upper limits on the \(w_{ij}\) (Kim and McCormick, 1998).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Unit</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellular parameters common to the TC- and RE-like IFB models:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(C)</td>
<td>2</td>
<td>(\mu F/cm^2)</td>
<td>membrane capacitance</td>
</tr>
<tr>
<td>(V_0)</td>
<td>-50</td>
<td>mV</td>
<td>integrate-and-fire spike threshold</td>
</tr>
<tr>
<td>(V_{reset})</td>
<td>-55</td>
<td>mV</td>
<td>integrate-and-fire reset voltage</td>
</tr>
<tr>
<td>(t_R)</td>
<td>4</td>
<td>ms</td>
<td>absolute refractory period</td>
</tr>
<tr>
<td>(V_h)</td>
<td>-65</td>
<td>mV</td>
<td>(I_T) activation and inactivation threshold</td>
</tr>
<tr>
<td>(\tau^+_h)</td>
<td>100</td>
<td>ms</td>
<td>(I_T) de-inactivation time constant</td>
</tr>
<tr>
<td>(\tau^-_h)</td>
<td>20</td>
<td>ms</td>
<td>(I_T) inactivation time constant</td>
</tr>
<tr>
<td>(E_T)</td>
<td>120</td>
<td>mV</td>
<td>(I_T) reversal potential</td>
</tr>
<tr>
<td>(E_{NL})</td>
<td>-50</td>
<td>mV</td>
<td>(I_{NL}) reversal potential</td>
</tr>
<tr>
<td>(E_{KL})</td>
<td>-100</td>
<td>mV</td>
<td>(I_{KL}) reversal potential</td>
</tr>
<tr>
<td>Cellular parameters specific to RE:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(g^{RE}_{NL})</td>
<td>0.04</td>
<td>mS/cm(^2)</td>
<td>non-specific leak conductance</td>
</tr>
<tr>
<td>(g^{RE}_{KL})</td>
<td>0.027</td>
<td>mS/cm(^2)</td>
<td>potassium leak conductance</td>
</tr>
<tr>
<td>(g^{RE})</td>
<td>0.2</td>
<td>mS/cm(^2)</td>
<td>low-threshold Ca(^{2+}) conductance</td>
</tr>
<tr>
<td>Cellular parameters specific to TC:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(g^{TC}_{NL})</td>
<td>0.05</td>
<td>mS/cm(^2)</td>
<td>non-specific leak conductance</td>
</tr>
<tr>
<td>(g^{TC}_{KL})</td>
<td>0.02</td>
<td>mS/cm(^2)</td>
<td>potassium leak conductance</td>
</tr>
<tr>
<td>(g^{TC})</td>
<td>0.08</td>
<td>mS/cm(^2)</td>
<td>low-threshold Ca(^{2+}) conductance</td>
</tr>
<tr>
<td>Synaptic parameters:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(E_{AMPA})</td>
<td>0</td>
<td>mV</td>
<td>reversal potential of excitatory synaptic current</td>
</tr>
<tr>
<td>(E_{GABA_A})</td>
<td>-85</td>
<td>mV</td>
<td>reversal potential of inhibitory synaptic current</td>
</tr>
<tr>
<td>(a^{RE}_{TC})</td>
<td>0.0047</td>
<td>–</td>
<td>magnitude of TC to RE excitation (+1.3 mV)</td>
</tr>
<tr>
<td>(a^{TC}_{RE})</td>
<td>0.0119</td>
<td>–</td>
<td>magnitude of RE to TC excitation (-1.0 mV)</td>
</tr>
<tr>
<td>(a^{RGC}_{RE})</td>
<td>0.045</td>
<td>–</td>
<td>magnitude of RGC to RE inhibition (-0.7 mV)</td>
</tr>
<tr>
<td>(w^{TC,TC})</td>
<td>0</td>
<td>–</td>
<td>mean number of TC-to-TC synaptic connections</td>
</tr>
<tr>
<td>(w^{TC,RE})</td>
<td>5–50</td>
<td>–</td>
<td>mean number of TC-to-RE synaptic connections</td>
</tr>
<tr>
<td>(w^{RE,TC})</td>
<td>5–50</td>
<td>–</td>
<td>mean number of RE-to-TC synaptic connections</td>
</tr>
<tr>
<td>(w^{RE,RE})</td>
<td>5–50</td>
<td>–</td>
<td>mean number of RE-to-RE synaptic connections</td>
</tr>
</tbody>
</table>
Fig. 8.3: Panels (a) and (b) show the membrane potential and de-inactivation gating variable as a function of time for two representative RE cells during a $2 \times 100$ neuron Monte Carlo simulation of the LGN/PGN network. Panel (c) shows the same traces in the $(\nu, h)$-plane. Panels (c), (d), and (f) show the corresponding results for two representative TC cells. Reproduced with permission from Huertas and Smith (2006b).

The magnitude of the change in membrane potential due to each synaptic event is distributed according to Eqn (8.5). Note that during burst responses in Fig. 8.3, the gating variable for the low-threshold $\text{Ca}^{2+}$ current of the representative RE and TC neurons decreases (inactivation of $I_T$) with an exponential time constant of $\tau_h^- = 20$ ms and increases (de-inactivation) with time constant $\tau_h^+ = 100$ ms. The instantaneous changes in membrane potential observed in panels (a) and (b) due to the arrival of a presynaptic spike can be observed in panels (e) and (f) as horizontal lines of variable length. Between spikes the trajectories followed by each cell type correspond to solutions to Eqns (8.1) and (8.2). The network connectivity used in this representative simulation is $w_{\text{RE,RE}} = w_{\text{RE,TC}} = w_{\text{TC,RE}} = 5$ and the 60 spikes/s spontaneous retinal input results in population firing rates of 170 and 110 spikes/s for the RE and TC cell populations, respectively.
8.5 Population density formulation

Because the Monte Carlo network simulation of the LGN/PGN presented in the previous section describes the time-evolution of each neuron in the population (either TC or RE), the method faces a computational disadvantage when the number of cells in the population is very large. However, because the neurons in each population are homogeneous in their cell properties – e.g. all RE-like IFB neurons possess the same membrane capacitance, resting membrane potential, and so on – an alternative population density approach can be employed that uses probability density functions to track the distribution of state variables \( V \) and \( h \) within each population (Knight, 1972, Omurtag et al., 2000a, Omurtag et al., 2000b, Nykamp and Tranchina, 2000).

Beginning with Eqns (8.1) and (8.2) we identify the drift rates \( F_v(V, h) \) and \( F_h(V, h) \) such that

\[
\frac{dV}{dt} = F_v(V, h) \tag{8.9}
\]

\[
\frac{dh}{dt} = F_h(V, h) \tag{8.10}
\]

where \( F_v = -(I_L + I_T)/C \), and for clarity we have dropped the superscript TC.

As discussed by (Casti et al., 2002), an infinite homogeneous population of IFB neurons whose state variables satisfy Eqns (8.9) and (8.10) can be described by a two-dimensional probability density function

\[
\rho(V, h, t) dV dh = P\{V < \tilde{V}(t) < V + dV \text{ and } h < \tilde{h}(t) < h + dh\}. \tag{8.11}
\]

Assuming the probability density function is initially restricted to the domain \( E_i \leq V \leq V_\theta \) and \( 0 \leq h \leq 1 \), these densities satisfy a conservation equation of the form

\[
\frac{\partial}{\partial t} \rho(V, h, t) = -\nabla \cdot \vec{J}(V, h, t) + \delta(V - V_{\text{reset}}) \vec{J}_{\text{reset}} \cdot \hat{e}_v \tag{8.12}
\]

where the \( \nabla \) operator is given by

\[
\nabla = \hat{e}_v \frac{\partial}{\partial V} + \hat{e}_h \frac{\partial}{\partial h}.
\]

\( \hat{e}_{v/h} \) are unit vectors in the \((V, h)\)-plane, and the \( \vec{J}_{\text{reset}} \) term is defined below. In Eqn (8.12), the total probability flux \( \vec{J}(V, h, t) \) is composed of two terms:

\[
\vec{J}(V, h, t) = \vec{J}_{\text{int}} + \vec{J}_{\text{ext}}. \tag{8.13}
\]

The first term \( \vec{J}_{\text{int}} \) represents the changes in the probability density due to the intrinsic membrane dynamics of the IFB model,

\[
\vec{J}_{\text{int}}(V, h, t) = [F_v(V, h)\hat{e}_v + F_h(V, h)\hat{e}_h] \rho(V, h, t), \tag{8.14}
\]

\[
\vec{J}_{\text{ext}}(V, h, t) = \vec{J}_{\text{ext}}(V, h). \tag{8.15}
\]
where \(F_v\) and \(F_h\) are the advection rates in the \(v\)- and \(h\)-directions (Eqns (8.9) and (8.10)). The second term in Eqn (8.13) \((\mathbf{J}_{\text{ext}})\) is the extrinsic probability flux that accounts for changes in membrane potential due to synaptic input (Nykamp and Tranchina, 2000),

\[
\mathbf{J}_{\text{ext}} = \hat{e}_v \left[ \eta_e(t) \int_{E_i}^V \tilde{F}_{\gamma^*_e} \left( \frac{V' - V}{E_e - V} \right) \rho(V', h, t) \, dV' \\
- \eta_i(t) \int_V^{V_0} \tilde{F}_{\gamma^*_i} \left( \frac{V' - V}{E_i - V} \right) \rho(V', h, t) \, dV' \right].
\] (8.15)

In this expression, \(E_{e/i}\) is the reversal potential of excitatory/inhibitory synaptic currents and \(\eta_{e/i}\) is the rate of excitatory/inhibitory synaptic events arriving to the population of IFB neurons. To understand the integrals, consider the case of excitatory connections, in which the quantity \(\tilde{F}_{\gamma^*_e} = \frac{1}{\gamma^*_e} \mathbb{P} \{ \gamma^*_e > \gamma \} = \int_{\gamma}^{1} f_{\gamma^*_e} \frac{-\ln(1 - \gamma')}{1 - \gamma'} \, d\gamma'\) (8.16),

where the last equality is given by Eqn (8.6), that is, evaluating \(\tilde{F}_{\gamma^*_e}\) as in Eqn (8.15) gives the probability that \(\tilde{\gamma}_e > (V - V')/(E_e - V')\). Integrating the product of this quantity and the density \(\rho(V', h, t)\) from \(E_i\) to \(V\) and scaling by \(\eta_e(t)\) gives the probability flux of neurons jumping to a membrane potential beyond \(V\) upon receiving excitatory input.

Note that the probability density function evolves in time according to Eqn (8.12) and must remain confined to the physiological region \(E_i \leq V \leq V_0\) and \(0 \leq h \leq 1\). This requirement imposes boundary conditions on \(\rho(V, h, t)\) that correspond to vanishing probability density flux (see Eqn (8.13)). These are

\[
\rho(V = E_i, 0 \leq h \leq 1, t) = 0 \\
\rho(E_i \leq V < V_h, h = 0, t) = 0 \\
\rho(V_h \leq V \leq V_0, h = 1, t) = 0,
\] (8.17, 18, 19)

while \(\rho(E_i \leq V < V_h, h = 1, t)\) and \(\rho(V_h \leq V \leq V_0, h = 0, t)\) are not required to be zero since on those boundaries the drift rates vanish exactly, and \(\rho(V = V_0, 0 \leq h \leq 1, t)\) is also not necessarily zero since even in the absence of external input there can be a net flux through \(V = V_0\) from neurons firing in burst mode.

The component of the total probability flux \(\mathbf{J}\) in the voltage direction \(\hat{e}_v\) at \(V = V_0\) corresponds to the fraction of neurons per unit time crossing the
spike threshold and becoming refractory. Thus, the population firing rate \( r(t) \) is given by
\[
 r(t) = \int_0^1 \mathbf{J}_{\text{spike}}(h, t) \cdot \hat{e}_V \, dh \quad \text{where} \quad \mathbf{J}_{\text{spike}}(h, t) = \mathbf{J}(V = V_0, h, t). \tag{8.20}
\]

It is sometimes convenient to choose a particular value of the de-inactivation gating variable of the low-threshold current (e.g. \( \bar{h} = 0.05 \)) and thereby distinguish burst and tonic portions of the firing rate,
\[
r_{\text{tonic}}(t) = \int_{\bar{h}}^1 \mathbf{J}_{\text{spike}}(h, t) \cdot \hat{e}_V \, dh \quad r_{\text{burst}}(t) = \int_0^{\bar{h}} \mathbf{J}_{\text{spike}}(h, t) \cdot \hat{e}_V \, dh \quad \tag{8.21}
\]

where \( r(t) = r_{\text{tonic}}(t) + r_{\text{burst}}(t) \).

Finally, the probability flux \( \mathbf{J}_{\text{reset}}(h, t) \) in Eqn (8.12) represents neurons leaving the refractory state and becoming responsive with membrane potential \( V = V_{\text{reset}} \). Because the gating variable for the low-threshold Ca\(^{2+}\) current continues to inactivate during the refractory time \( \tau_r \), the flux \( \mathbf{J}_{\text{reset}}(h, t) \) is given by
\[
 \mathbf{J}_{\text{reset}}(h, t) = \begin{cases} e^{\tau_r/\tau_n} \mathbf{J}_{\text{spike}}(he^{\tau_r/\tau_n}, t - \tau_r) & \text{for} \quad he^{\tau_r/\tau_n} \leq 1 \\ 0 & \text{otherwise.} \end{cases} \tag{8.22}
\]

When this expression is used in Eqn (8.12), the boundary conditions given by Eqns (8.17)–(8.19) imply that the probability densities are conserved, that is,
\[
 \int_{E_i} \int_0^{V_0} \rho(V, h, t) \, dh \, dV + \int_{t-\tau_r}^t r(t') \, dt' = 1, \tag{8.23}
\]

where the second integral gives the fraction of neurons in the population that are refractory at time \( t \).

To complete the population density formulation of the LGN/PGN network depicted in Fig. 8.1, we distinguish between the density functions describing the RE and TC populations by writing \( \rho^p(V, h, t) \) where \( p = \text{TC, RE} \). Each density solves equations of the form (8.12)–(8.22) with TC- or RE-like cellular parameters, respectively (Table 8.1). As diagrammed in Fig. 8.1, the network is constructed by associating the rate of excitatory and inhibitory synaptic events with the population firing rate of the presynaptic neuronal populations. The rates \( \eta_{ij}^p(t) \) in Eqn (8.15) are given by
\[
 \eta_{ij}^p(t) = \eta_{ij}^{p,0}(t) + \sum_{q=\text{TC,RE}} w_{ij} \int_0^\infty f_{\bar{z}}(t') r^q(t - t') \, dt' \tag{8.24}
\]

where \( \eta_{ij}^{p,0}(t) \) represents external drive to the population \( p \), and the quantities \( w_{ij} \) are the mean synaptic connectivities (Eqn (8.8)), \( f_{\bar{z}}(t) \) is the probability
distribution function for the synaptic delays (Eqn (8.7)), and \( r^q(t) \) is the firing rate of presynaptic population \( q \) (Eqn (8.20)). In the LGN/PGN model \( \eta_{TC}^{RGC,0} = \eta_{RE,0} = 0 \) and \( \eta_{TC}^{RGC}(t) = r^{RGC}(t) \) because the only external drive is the excitatory retinal input to the TC cell population.

8.6 Numerical method and model parameters

Numerical solution of the population density model described in the previous section can be performed using the total variation diminishing (TVD) scheme of Casti et al. (2002) that is here presented with some important modifications. First, note that Eqn (8.12) can be rewritten in conservative form,

\[
\frac{\partial}{\partial t} \rho(V, h, t) = -\nabla \cdot \left[ J(V, h, t) + \Theta(V - V_{\text{reset}}) J_{\text{reset}}(h, t) \right] \tag{8.25}
\]

where the \( \delta \)-function reaction term is responsible for the Heaviside function \( (\Theta) \) inside the divergence operator and we have dropped the superscripted \( p \)'s for clarity. Next, we discretize the membrane voltage as \( V_j = j \Delta V + E_i \) where \( j = 0, 1, \ldots, N_v \), the number of mesh-points in the \( v \)-direction, and \( \Delta V = (V_p - E_i)/N_v \). Similarly, the low-threshold Ca\(^{2+} \) current gating variable is discretized as \( h_j = j \Delta h \) where \( j = 0, 1, \ldots, N_h \) and \( \Delta h = 1/N_h \). The total probability flux evaluated at \( V_i \) and \( h_j \) is denoted here as \( \tilde{f}_{ij} \) and identified as

\[
\tilde{f}_{ij}(t) = f_{ij}^n \dot{e}_v + f_{ij}^h \dot{e}_h = \tilde{J}(V_i, h_j, t) + \Theta(V_i - V_{\text{reset}}) \tilde{J}_{\text{reset}}(h_j, t).
\tag{8.26}
\]

where the second equality defines \( f^n_{ij} \) and \( f^h_{ij} \). With these preliminaries, the numerical scheme can be written as

\[
\frac{d\rho_{ij}}{dt} = -\frac{1}{\Delta V} [g^n_{ij} - g^n_{i-1,j}] - \frac{1}{\Delta h} [g^h_{ij} - g^h_{ij-1}].
\tag{8.27}
\]

where \( g^n_{ij}, g^n_{i-1,j}, g^h_{ij} \), and \( g^h_{ij-1} \) are given by

\[
g^n_{ij} = f^*_{i+\frac{1}{2},j} + \frac{1}{2} \psi_{i+\frac{1}{2},j} (f_{i,j} - f_{i-\frac{1}{2},j}) + \psi_{i+\frac{1}{2},j} (f_{i+1,j} - f_{i+\frac{1}{2},j}) \tag{8.28}
\]

\[
g^h_{ij} = f^*_{i,j+\frac{1}{2}} + \frac{1}{2} \psi_{i,j+\frac{1}{2}} (f_{i,j} - f_{i,j-\frac{1}{2}}) + \psi_{i,j+\frac{1}{2}} (f_{i,j+1} - f_{i,j+\frac{1}{2}}) \tag{8.29}
\]

and the terms \( f^*_{i+\frac{1}{2},j} \) and \( f^*_{i,j+\frac{1}{2}} \) are first-order Roe fluxes defined by (Casti et al., 2002, Hundsdorfer and Verwer, 2003),

\[
f^*_{i+\frac{1}{2},j} = \frac{1}{2} (f_{i,j} + f_{i+1,j}) - \frac{1}{4} |F_{i,j}^v + F_{i+1,j}^v| (\rho_{i+1,j} - \rho_{i,j})
\tag{8.30}
\]

\[
f^*_{i,j+\frac{1}{2}} = \frac{1}{2} (f_{i,j} + f_{i,j+1}) - \frac{1}{4} |F_{i,j}^h + F_{i,j+1}^h| (\rho_{i,j+1} - \rho_{i,j}).
\tag{8.31}
\]
where \( F^v_{ij} \) and \( F^h_{ij} \) are the discretized \( v \)- and \( h \)-components of the advection rate due to the intrinsic membrane properties of the IFB model (cf. Eqns (8.9) and (8.10)). The quantities \( \psi^+ \) and \( \psi^- \) occurring in Eqns (8.28) and (8.29) are flux limiters given by

\[
\psi^+_{i-1/2,j} = \frac{f_{i+1,j} - f_{i,j-1/2}}{f_{i,j-1/2} - f_{i,j-1}},
\psi^-_{i+1/2,j} = \frac{f_{i,j} - f_{i+1,j}}{f_{i+1,j} - f_{i,j+1/2}}
\]

\[
\psi^+_{i,j-1/2} = \frac{f_{i,j+1} - f_{i,j-1/2}}{f_{i,j-1/2} - f_{i,j-1}},
\psi^-_{i,j+1/2} = \frac{f_{i,j} - f_{i,j+1/2}}{f_{i,j+1/2} - f_{i,j+1}}
\]

where

\[
\psi[r] = \max[0, \min(2r, 1), \min(r, 2)].
\]

Note that the discretized probability flux in the \( v \)-direction given by \( f^v_{ij} \) in Eqn (8.26) includes contributions due to synaptic input and the reset flux \( (f^v_{ij} = F^v_{ij} \rho_{ij} + J^v_{ij}) \) and these fluxes contribute \( \frac{1}{2}(J^v_{ij} + J^v_{i+1,j}) \) to the Rho flux \( f^*_{i+1/2,j} \).

Figure 8.4 shows details of the numerical implementation of the boundary conditions given by Eqns (8.17)–(8.19). As required by the five-point stencil used in Eqns (8.25)–(8.32), two rows and two columns of ‘ghost’ points are shown in addition to the interior and boundary mesh points of the \((V, h)\)-plane. The open circles and squares of Figure 8.4 indicate the unknown probability densities updated using Eqns (8.25)–(8.32), while the filled circles and squares indicate mesh points where the probability density is known to be zero. The open squares located at the \( h = 1 \) boundary for \( V < V_h \) and the \( h = 0 \) boundary for \( V \geq V_h \) are unique in that they are located at the reversal of the \( h \)-component of the advection rate \( F^h(V, h) \) due to the intrinsic dynamics of the IFB model (Eqn (8.10)) and, consequently, probability density can accumulate at these points. For conservation of probability, it is important to set the advection rate to zero at the filled squares located external to the boundaries. Conservation of probability also requires that the ghost points external to boundaries where the advection rate is not reversing (filled circles) use \( F^v_{ij} \) and \( F^h_{ij} \) given by Eqns (8.9) and (8.10).

Note that \( g^v_{ij} \) in Eqn (8.28) corresponds to the magnitude of the total probability flux in the \( V \)-direction at the \((V_i, h_j)\) mesh point. Evaluating this at the \( V = V_0 \) boundary \((i = N_v)\), it provides an approximation to the spiking flux of Eqn (8.20) (as a function of \( h_j \)). Numerical integration along the \( h \)-direction gives the population firing rate (Eqn (8.20)) which is used to calculate the reset flux (Eqn (8.12)) and the rate of synaptic input (Eqn (8.24)). In the simulations presented below, integration in time is performed using Euler’s method with a
fixed time step $\Delta t$ so that the probability density function at the $ij$-mesh point advances according to

$$
\rho_{ij}(t + \Delta t) = \rho_{ij}(t) + \Delta t \left( \frac{dp_{ij}}{dt} \right)
$$

(8.33)

where $dp_{ij}/dt$ is the right-hand side of Eqn (8.27) at time $t$. We use a $100 \times 100$ mesh, $\Delta V = 0.35$ mV, $\Delta h = 0.01$, and $\Delta t = 0.01$ ms.

8.7 Representative Monte Carlo and population density simulations

A representative simulation of the probability density model of the driven LGN/PGN is shown in Fig. 8.5(a) (solid lines). The external drive to the network was chosen to be a complicated function of time varying in the range $0 \leq r_{RGC}^T(t) \leq 200$ spikes per second per cell (lower trace). This time-dependent excitatory input drives the TC cell population – it corresponds to the term $\eta_{TC}^e(t)$ in Eqn (8.24) – and the resulting TC cell activity in turn evokes the

Fig. 8.4: Schematic representation of the mesh used to solve the discretized population density model (Eqns (8.25)–(8.32)). Internal and boundary points in the $(v, h)$-plane are shown as well as two rows and columns of ghost points. Open symbols indicate unknowns while filled symbols indicate points where the probability density is known to be zero. Open squares indicate boundary points where the advection rate of the probability flux evaluates to zero and filled squares indicate ghost points where this advection rate is set to zero to conserve probability. Reproduced with permission from Huertas and Smith (2006b).
Fig. 8.5: Convergence of Monte Carlo simulations (histograms) of the driven LGN/PGN network to the population density model (solid lines) as the number of cells in the TC and RE populations increases from $N = 100$ (a) to 1000 (d). The firing rates $r_{RGC}(t)$ of retinal ganglion cells presynaptic to the TC cell population (lower trace) are shown along with the resulting TC and RE population response (middle and upper traces). Network connectivity is as shown in Fig. 8.1 with $w_{TC,RE} = w_{RE,TC} = w_{RE,RE} = 5$, $a_{RE} = 0.01$, $a_{TC} = a_{RE} = 0.12$, and $a_{RGC} = 0.1$. Reproduced with permission from Huertas and Smith (2006b).

RE cell population response (middle and upper traces, respectively). As shown in Fig. 8.1, feedback inhibition from RE to TC cells and reciprocal RE-to-RE inhibition is also included in these simulations.

In Fig. 8.5(a) the probability density calculation (solid lines) is compared to Monte Carlo simulations of the driven LGN/PGN using the same parameters and 100 cells per population (grey histograms). As expected, the RGC input and the TC and RE responses of the Monte Carlo simulations fluctuate around the population density result (the largest deviation is approximately 28 spikes/s in the TC population). Importantly, Fig. 8.5 (b)–(D) shows that these fluctuations become smaller in Monte Carlo calculations involving 300, 500, and 1000 cells per population. That is, as the number of neurons in each population increases, the Monte Carlo result converges to the population density calculation (shown on each panel).
Fig. 8.6: Snapshot of the Monte Carlo and probability density calculations of Fig. 8.5 at $t = 300$ ms for the RE (a) and TC (b) cell populations. Contour plots in (a) and (b) show the probability density functions $\rho_{RE}$ and $\rho_{TC}$, respectively, while the filled circles show the state of 500 RE and 500 TC neurons in the corresponding Monte Carlo simulation. The marginal distribution functions $\rho_p^V(V, t)$ and $\rho_p^h(h, t)$ (Eqns (8.34) and (8.35)) for the membrane potential and low-threshold Ca$^{2+}$ current gating variable confirm that the probability density (solid lines) and Monte Carlo (grey histograms) models are in agreement. Parameters as in Fig. 8.5(c). Reproduced with permission from Huertas and Smith (2006).
and

\[ \rho_p^p(h, t) \, dh = P\{h < \tilde{h}(t) < h + dh\} = \int_{\varepsilon_i}^{\varepsilon_f} \rho^p(V, h, t) \, dV. \]  

(8.35)

where the superscript \( p \) can be either TC or RE.

The marginal distribution function for RE and TC cell voltage presented in Fig. 8.6 shows a significant fraction of both populations hyperpolarized below the burst threshold \( V_h \), with the low-threshold \( \text{Ca}^{2+} \) current more de-inactivated in the TC population. Notice also that the marginal densities show both cell types have a non-zero probability density at \( V = V_\theta \) indicating advection across the firing threshold mediated by the T-current (Eqn (8.14)). While this drift of probability density across the spike threshold corresponds to intrinsic membrane properties generating burst spikes, the significant population firing rate of both the TC (67 spikes/s) and RE (39 spikes/s) populations also includes the RGC-to-TC and TC-to-RE excitation fluxes (Eqn (8.15)).

8.8 Oscillatory responses of the LGN/PGN model

As discussed in Section 8.1, potassium leakage conductances \( g_{ KL}^{TC/RE} \) representing increased or decreased cholinergic neuromodulatory action of the brain stem lead to changes in the resting membrane potential of both TC and RE cells. These changes are such that during sleep states the mutual action of both cell populations favour the appearance of self-sustaining oscillatory responses composed of bursts of action potentials. On the other hand, during states of vigilance, the changes in \( g_{ KL} \) decrease the sustainability of such oscillatory responses.

Figure 8.7 shows that in the absence of retinal input the LGN/PGN model is capable of rhythmic bursting. These rhythmic oscillations (solid lines in both panels) are composed almost entirely of burst spikes (Eqn (8.21)) and their occurrence is not particularly sensitive to the average number of connections between TC and RE populations, but the frequency of oscillation is influenced by changes in \( w_{TC,RE} \) and \( w_{RE,TC} \) (Eqn (8.24)). When the potassium leakage conductance in both TC and RE cells \( (g_{ KL}^{TC/RE}) \) is changed to represent arousal of the LGN/PGN network, the rhythmic oscillations may be eliminated or persist depending on the strength of the network connectivity. In Fig. 8.7(b) we observe an example where the network connectivity of the model allows rhythmic oscillations to be sustained even in the aroused state. These oscillatory responses are indicated by the dotted lines. On the other hand, in Fig. 8.7(a) the network connectivity allowed rhythmic oscillations only when the values of \( (g_{ KL}^{TC/RE}) \) corresponded to the sleep state, while in the aroused state no oscillations are observed.

When the LGN/PGN network model is driven by constant retinal input, and the values of the potassium leakage conductances are chosen to correspond to the awake state, the response of the system depends strongly on the strength of the driving input and the magnitude of the synaptic connections between the TC and RE populations. Parameter studies varying the average
Stochastic methods in neuroscience

Fig. 8.7: Rhythmic bursting of the LGN/PGN population density model in the absence of retinal drive. Each panel shows the population firing rate (thick black line) for RE cells (upper panels) and TC cells (lower panels). Network connectivity is $[w_{RE,RE}, w_{RE,TC}, w_{TC,RE}] = [10, 5, 5]$ in (a) and $[10, 50, 5]$ in (b). When $\gamma_{KL}$ is changed to represent arousal of the LGN/PGN network (Table 8.1), the rhythmic oscillations still persist in (b) (black dotted lines) but are eliminated in (a), which is clear from the absence of dotted lines. Adapted with permission from Huertas and Smith (2006b).

number of synaptic connections – i.e. changing the entries of the $W$ matrix defined in Eqn (8.8) – show that at high retinal input ($r_{RGC} \approx 200$ spikes/s) the network response is often time-independent. In these simulations the RE population firing rate is composed mostly of tonic spikes while the TC population response always contained a mixture of both burst and tonic spikes (not shown). However, at more moderate values of time-homogeneous retinal drive ($r_{RGC} \approx 30$ spikes/s), the response of each population depends dramatically on the mean number of synaptic connections. Interestingly, network connectivities can be found where the TC and RE populations exhibit oscillatory responses in response to constant retinal input. For example, a 17 Hz oscillation emerges in the presence of constant retinal input of 15 spikes/s when the mean number of TC-to-RE synaptic connections is $w_{TC,RE} = 10$ and the mean number of RE-to-TC and RE-to-RE inhibitory connections are $w_{RE,TC} = 50$ and $w_{RE,RE} = 10$, respectively.

Figure 8.8 presents another interesting example: a low-frequency oscillatory response that emerges in the presence of constant retinal input of 15 spikes/s when the mean number of TC-to-RE synaptic connections is $w_{TC,RE} = 20$ and the mean number of inhibitory connections are $w_{TC,RE} = w_{RE,RE} = 10$. In this figure, the thick black lines indicate population firing rates and the dark and light grey areas represent burst and tonic spikes, respectively (Eqn (8.21)). Such low-frequency oscillatory responses are not exhibited in the absence of retinal input and are clearly distinguishable from the sleep spindle-like responses shown in Fig. 8.7. These low-frequency oscillations are also not observed in the absence of the reciprocal RE-to-RE connection, and this feedback inhibition appears to be responsible for the decrease in RE population firing rate that occurs.
8.9 Conclusion

We have shown how the population density modelling approach, discussed in more detail in Chapter 7, can be used to simulate a large-scale network model of the LGN/PGN (Fig. 8.4). This approach accurately computes the distribution of membrane potential $V$ and de-inactivation variable $h$ of a large number of cells in each population (Fig. 8.6). As discussed in Chapter 7, the computational efficiency of this multivariate population density approach is not as dramatic as that observed in univariate simulations (in our hands approximately 30-fold). An important open question is whether dimension reduction techniques can be successfully applied in this context (Ly and Tranchina, 2007).

It is also important to note the exclusive use of fast synapses in the LGN/PGN network model presented here. While interactions mediated through fast (ionotropic) GABA$_A$ and AMPA receptors are sufficient for our present purposes, the dynamics of slow (metabotropic) synaptic interactions such as those associated with GABA$_B$ receptors play important physiological roles in the LGN/PGN network (Cox, Zhou, and Sherman, 1998, Cox and Sherman, 2000, Cox, Reichova, and Sherman, 2003, Govindaiah and Cox, 2004). Such slow kinetics could be implemented using an additional dynamic variable (say $q$) to the IFB model. This would increase the dimensionality of the probability densities, $\rho^p(V, h, q, t)$, and lead to computationally more demanding numerical integration of the resulting advection-reaction equations (Eqn (8.12)). Alternative implementations that do not increase the number of dimensions might also be employed (Haskell, Nykamp, and Tranchina, 2001).
References


References


Woolsey, TA and der Loos, H Van (1970, Jan). The structural organization of layer IV in the somatosensory region (SI) of mouse cerebral cortex. the description of a cortical field composed of discrete cytoarchitectonic units. *Brain research*, 17, 205–42.