

Model description

Here, the model published in Suffczynski et al, 2004 is described. The diagram of the Simulink model is shown in Fig. 1. It consists of four (PY, IN, TC and RE) interconnected neuronal populations. In each population, incoming impulses generate postsynaptic currents which are integrated giving rise to mean membrane potential of the population. The latter is transformed to population output (i.e. firing rate) through nonlinear transfer function. Each element of the model is described successively. Parameter values are summarized in Table 1.

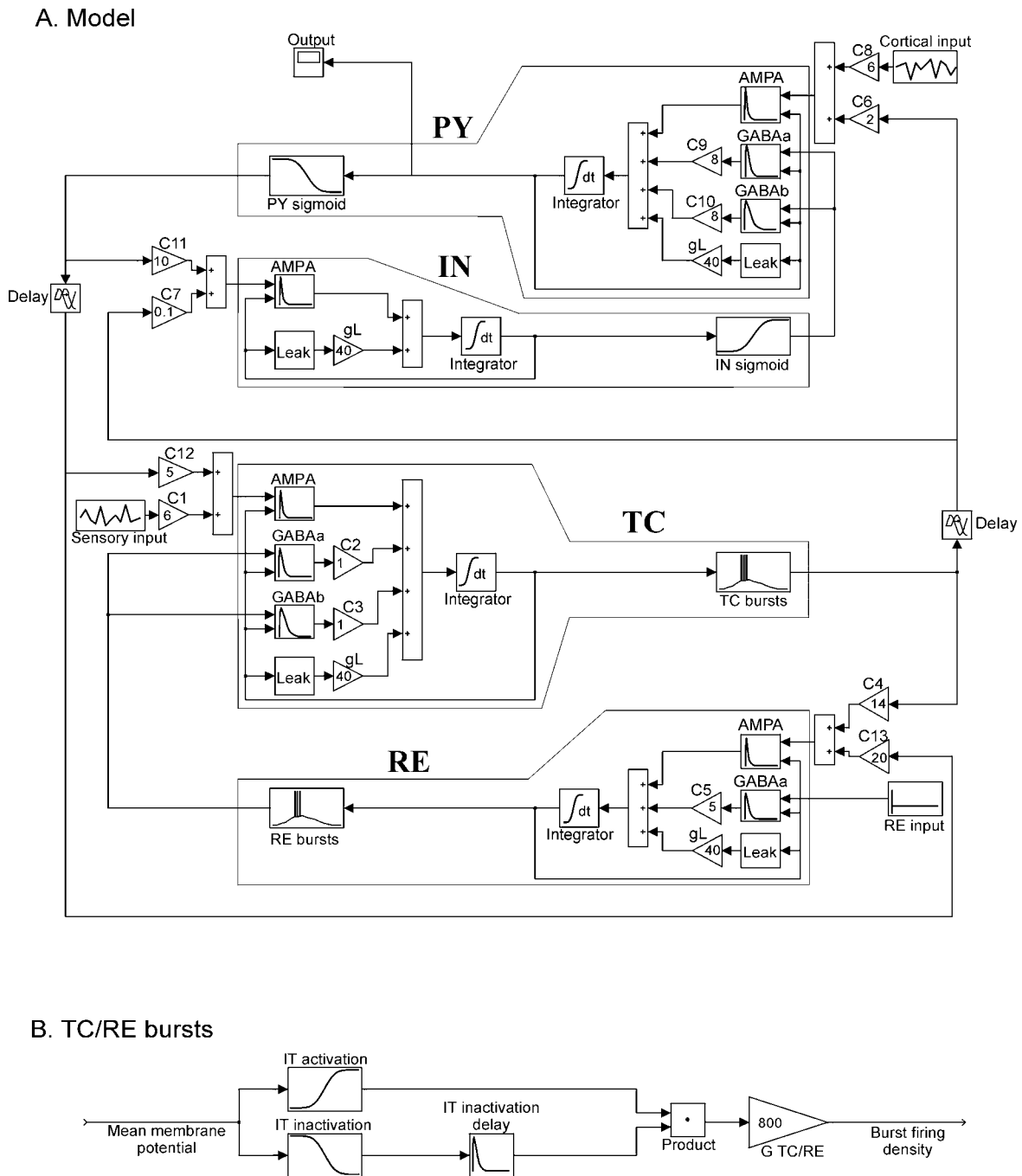


Fig. 1 Model diagram. A. Thalamocortical network model consisting of interconnected cortical and thalamic modules. B. Details of the blocks that represent the generation of TC/RE bursts.

Synaptic transmission

To simulate synaptic transmission we used the general membrane equation:

$$C_m dV^{(i)}/dt = -\Sigma I_{syn}^{(i)} - g_{leak}(V^{(i)} - V_{leak}^{(i)}), \quad i = \{TC, RE, PY, IN\} \quad (1)$$

$$I_{syn}^{(i)} = g_{syn}^{(i)}(t)(V^{(i)} - V_{syn}^{(i)}) \quad (2)$$

where V is the membrane potential, C_m is the membrane capacitance, g_{leak} is the leak current conductance, $g_{syn}(t)$ is the synaptic current conductance, V_{leak} and V_{syn} are the reversal potentials of leak current and synaptic current, respectively.

Synaptic conductances were modeled by convolving incoming action potential sequence ($pulse_{syn}$) with a synaptic impulse response function (h_{syn}):

$$g_{syn}^{(i)}(t) = \int h_{syn}(t - \tau) pulse_{syn}^{(i)}(\tau) d\tau \quad (3)$$

$$h_{syn}(t) = A_{syn}[\exp(-a_{1syn} t) - \exp(-a_{2syn} t)],$$

$$a_{2syn} > a_{1syn}, \quad syn = \{AMPA, GABA_A, GABA_B\} \quad (4)$$

Additionally, following the observation (Kim et al., 1997) that high stimulus intensity is needed to activate GABA_B receptor, we assumed that the amplitude of the GABA_B postsynaptic current increases nonlinearly with the spiking rate of the RE and IN populations. The nonlinear activation function of GABA_B receptors in RE and IN cells has the form:

$$B(F) = \{1 + \exp[(F - \theta_G)/\sigma_G]\}^{-1}, \quad F = \{F^{\{RE\}}, F^{\{IN\}}\} \quad (5)$$

Table 2 gives synaptic currents in four neuronal populations (to use with equations (1,2) and pulse densities contributing to each synaptic current (to use with equation (3,16,17)):

Table 2 over here

Mean membrane potential to firing rate conversion

Conversions from mean membrane potential to pulse densities in cortical populations are of the sigmoidal form:

$$F^{(j)}(V^{(j)}) = G_S / (1 + \exp[(V^{(j)} - \theta_S)/\sigma_S]), \quad j = \{PY, IN\} \quad (6)$$

Conversions from mean membrane potential to pulse densities in thalamic populations took into account the burst firing of thalamic cells that occurs at the hyperpolarized membrane potential levels of these cells. A burst generated by thalamic neuron consists of a low threshold spike (LTS) mediated by I_T calcium current and fast sodium spikes on the top of the LTS. In a population, the relative number of cells that fire LTS at the time t is equal to the proportion of cells in which I_T current is de-inactivated and which, at the same time, are depolarized above the threshold for LTS generation. To account for this behavior we introduced new variables $n_{inf}(V)$ and $m_{inf}(V)$. These functions are the steady-state functions of the mean membrane voltage of the population V and express the fractions of cells in which I_T current is de-inactivated and activated, respectively, as a function of clamped value of V . If we assume that activation of the I_T current is immediate at the appropriate value of membrane potential V , the fraction of cells in which the I_T current is activated at time t is given by $m_{inf}(V(t))$. We also assume that reaching a steady state of I_T current de-inactivation is delayed with respect to membrane potential change and this delay is accounted for by convolving the

steady state de-inactivation function $n_{inf}(V)$ with a delay function (h_n). Finally, we assume that each LTS triggers a burst of fast action potentials at the frequency G .

The pulse density associated with burst firing of the thalamic population is:

$$F^{(k)}(V^{(k)}) = G^{(k)} m_{inf}^{(k)}(V^{(k)}) n^{(k)}(V^{(k)}), \quad k = \{TC, RE\} \quad (7)$$

$$n^{(k)}(V^{(k)}) = \int h_n(t - \tau) n_{inf}^{(k)}(V^{(k)}) d\tau \quad (8)$$

$$h_n(t) = N[\exp(-n_1 t) - \exp(-n_2 t)], \quad n_2 > n_1, N = n_1 n_2 / (n_2 - n_1) \quad (9)$$

The activation (m_{inf}) and inactivation (n_{inf}) functions of the I_T current are of the sigmoidal form:

$$f_{inf}(V) = \{1 + \exp[(V - \theta_f^k) / \sigma_f^k]\}^{-1} \quad f = \{m, n\} \quad (10)$$

The scheme of the transformation between the mean membrane potential and the average firing rate in a burst mode is depicted in Fig. 1B.

Connectivity

The coupling constants $c_1 - c_{13}$ represented the average number of synaptic contacts between different cell types. For the purpose of investigating temporal dependencies between cortical and thalamic activities we introduced time delays in both thalamocortical and corticothalamic projections. They correspond to finite propagation velocity of action potentials.

Model's inputs and output

The TC population received an external excitatory input P that represents glutamatergic sensory inputs from the ascending afferents. This was modelled as a random signal (Gaussian white noise) with a DC component. The PY population received cortical excitatory input P_{Cx} that stands for the glutamatergic input from other pyramidal cells, not included in the lump. This was also modelled as a random signal with a DC offset. Noise generators used for cortical and thalamic input signals were independent. The rationale behind using Gaussian noise as input signals derives from the assumption that these signals reflect averages of many independent processes with stochastic components. Finally, the RE population received an inhibitory DC offset signal Q representing the inhibitory bias from the neighboring RE cells. DC values of noise inputs were set such that the system was in the bistable regime. The standard deviations of noise inputs were about three times smaller than the range of the bistability domain. The output of the model, V_{Cx} , was the mean membrane potential of the pyramidal cell population.

Generic set of equations

Integral equation of the form:

$$\eta(t) = \int h(t - \tau) p(\tau) d\tau \quad (11)$$

where $h(t)$ is double exponential function

$$h(t) = A[\exp(-a_1 t) - \exp(-a_2 t)] \quad (12)$$

gives second order differential equation:

$$p(t) = 1/A(a_2 - a_1) [a_1 a_2 \eta(t) + (a_1 + a_2) d\eta(t)/dt + d^2\eta(t)/dt^2] \quad (13)$$

which reduces to two first order differential equations:

$$d\zeta(t)/dt = A(a_2 - a_1)p(t) - a_1a_2\eta(t) - (a_1 + a_2)\zeta(t) \quad (14)$$

$$d\eta(t)/dt = \zeta(t) \quad (15)$$

The full set of equations (without time delays in thalamocortical and corticothalamic projections) consists of the following equations:

(1), (2), (5), (6), (7), (10) and

$$d\zeta^{(i)}_{\text{syn}}(t)/dt = A_{\text{syn}}(a_{2\text{syn}} - a_{1\text{syn}}) \text{pulse}^{(i)}_{\text{syn}}(t) - a_{1\text{syn}}a_{2\text{syn}} g^{(i)}_{\text{syn}}(t) - (a_{1\text{syn}} + a_{2\text{syn}})\zeta^{(i)}_{\text{syn}}(t),$$

$$i = \{\text{TC, RE, PY, IN}\}, \text{syn} = \{\text{AMPA, GABA}_A, \text{GABA}_B\} \quad (16)$$

$$dg^{(i)}_{\text{syn}}(t)/dt = \zeta^{(i)}_{\text{syn}}(t) \quad (17)$$

$$d\zeta^{(k)}(t)/dt = N(n_2 - n_1) n^{(k)}_{\text{inf}}(V^{(k)}) - n_1n_2 n^{(k)}(V^{(k)}) - (n_1 + n_2)\zeta^{(k)}(t),$$

$$k = \{\text{TC, RE}\} \quad (18)$$

$$dn^{(k)}(t)/dt = \zeta^{(k)}(t) \quad (19)$$

Parameter	Interpretation	Reference value	Source
C_m	Membrane capacitance	$1 \mu\text{F}/\text{cm}^2$	[4]
g_{leak}	Leak current conductance	$0.04 \text{ mS}/\text{cm}^2$	Value between $0.01 \text{ mS}/\text{cm}^2$ [4] and $0.1 \text{ mS}/\text{cm}^2$ [8]
V_{leak}	Reversal potential of leak current	$V_{leak}^{PY} = -70 \text{ mV}$, $V_{leak}^{IN} = -70 \text{ mV}$, $V_{leak}^{TC} = -65 \text{ mV}$, $V_{leak}^{RE} = -72 \text{ mV}$	Resting potential of PY and IN: [3], of TC: reported range -61 mV , -70 mV ([1],[4]), of RE: reported range -67 mV , -84 mV ([2], [4])
A_{AMPA} , a_{1AMPA} , a_{2AMPA} , V_{AMPA}	Amplitude, decay and rise times of synaptic conductance, reversal potential for AMPA postsynaptic current	$A_{AMPA} = 10^{-2} \text{ mS}/\text{cm}^2$, $a_{1AMPA} = 105 \text{ s}^{-1}$, $a_{2AMPA} = 2500 \text{ s}^{-1}$, $V_{AMPA} = 0 \text{ mV}$	[4]
A_{GABAA} , a_{1GABAA} , a_{2GABAA} , V_{GABAA}	Amplitude, decay and rise times of synaptic conductance, reversal potential for GABA _A postsynaptic current	$A_{GABAA} = 0.1 \text{ mS}/\text{cm}^2$, $a_{1GABAA} = 85 \text{ s}^{-1}$, $a_{2GABAA} = 2500 \text{ s}^{-1}$, $V_{GABAA} = -75 \text{ mV}$	[4]
A_{GABAB} , a_{1GABAB} , a_{2GABAB} , V_{GABAB}	Amplitude, decay and rise times of synaptic conductance, reversal potential for GABA _B postsynaptic current	$A_{GABAB} = 1.25 * 10^{-3} \text{ mS}/\text{cm}^2$, $a_{1GABAB} = 20 \text{ s}^{-1}$, $a_{2GABAB} = 40 \text{ s}^{-1}$, $V_{GABAB} = -100 \text{ mV}$	[4]
θ_G, σ_G	Threshold and slope for GABA _B receptor activation function	$\theta_G = 8 \text{ pps}$, $\sigma_G = -0.01 \text{ pps}$	Free parameters
θ_S, σ_S , G_S	Threshold, slope and amplitude of sigmoid function in PY and IN	$\theta_S = 7 \text{ mV}$, $\sigma_S = -2 \text{ mV}$, $G_S = 50 \text{ pps}$	[5]
$\theta_m^{TC}, \sigma_m^{TC}$, $\theta_n^{TC}, \sigma_n^{TC}$	Threshold and slope of activation and inactivation functions of I _T current in TC	$\theta_m^{TC} = 6 \text{ mV}$, $\sigma_m^{TC} = 2 \text{ mV}$, $\theta_n^{TC} = -16 \text{ mV}$, $\sigma_n^{TC} = 6 \text{ mV}$	Thresholds [4], slopes – free parameters
$\theta_m^{RE}, \sigma_m^{RE}$, $\theta_n^{RE}, \sigma_n^{RE}$	Threshold and slope of activation and inactivation functions of I _T current in RE	$\theta_m^{RE} = 16 \text{ mV}$, $\sigma_m^{RE} = -2 \text{ mV}$, $\theta_n^{RE} = -6 \text{ mV}$, $\sigma_n^{RE} = 6 \text{ mV}$	Thresholds [4], slopes – free parameters
n_1, n_2	Decay and rise times of I _T inactivation delay function in TC and RE	$n_1 = 40 \text{ s}^{-1}$, $n_2 = 130 \text{ s}^{-1}$	Inactivation time constant of I _T current in TC is $\sim 20 \text{ s}^{-1}$ [4]
$G^{(TC)}$, $G^{(RE)}$	Firing frequency of single burst	$G^{(TC)} = G^{(RE)} = 800 \text{ pps}$	$\sim 450 \text{ pps}$ [6]
c_1, c_2, c_3 , c_4, c_5	Average number of synaptic connections in thalamic lump	$c_1 = 6$ (afferent cell → TC, AMPA), $c_2 = 1$ (RE → TC, GABA _A),	10 for RE → TC, TC → RE, RE → RE connections [9]

		$c_3 = 1$ (RE \rightarrow TC, GABA _B), $c_4 = 14$ (TC \rightarrow RE, AMPA), $c_5 = 5$ (RE \rightarrow RE, GABA _A)	
c_6, c_7	Average number of synaptic thalamocortical connections	$c_6 = 2$ (TC \rightarrow PY, AMPA), $c_7 = 0.1$ (TC \rightarrow IN, AMPA)	[7]
c_8, c_9, c_{10}	Average number of synaptic connections in cortical lump	$c_8 = 6$ (PY \rightarrow PY, AMPA), $c_9 = 8$ (IN \rightarrow PY, GABA _A), $c_{10} = 8$ (IN \rightarrow PY, GABA _B), $c_{11} = 10$ (PY \rightarrow IN, AMPA)	11 for PY \rightarrow PY, PY \rightarrow IN, IN \rightarrow PY connections [3]
c_{12}, c_{13}	Average number of synaptic corticothalamic connections	$c_{12} = 5$ (PY \rightarrow TC, AMPA), $c_{13} = 20$ (PY \rightarrow RE, AMPA)	21 for PY \rightarrow TC, PY \rightarrow RE connections [3]
τ	Time delay in thalamocortical and corticothalamic fibers	8 ms	It corresponds to distance 1.2 cm, propagation velocity 1.5 m/s.
P, σ_P	Mean and standard deviation of the sensory input noise	$P = 11$ pps, $\sigma_P = 1$ pps	Free parameters
P_{Cx}, σ_{PCx}	Mean and standard deviation of the cortical input noise	$P_{Cx} = 13.5$ pps, $\sigma_{PCx} = 1$ pps	Free parameters
Q	Mean of the inhibitory input to RE	$Q = 12$ pps	Free parameter

Table 1. Model parameters, interpretation, reference values and sources of reference. Abbreviations: pps – pulses per second, PY, IN, TC, RE – populations of cells: pyramidal, interneurons, thalamocortical, and reticular nucleus, respectively. References: [1] Bal et al. (1995a), [2] Bal et al. (1995b), [3] Destexhe and Sejnowski (2001), [4] Golomb et al. (1996), [5] Jansen and Rit (1995), [6] McCormick and Bal (1997), [7] Sherman and Koch (1986), [8] Wang et al. (1991), [9] Wang et al. (1995). ‘Free parameters’ in column four of the table are those parameters for which no physiological data were available and were freely chosen by us in order to obtain acceptable results.

$V^{(i)}$	$g_{\text{syn}}^{(i)}$	$\text{pulse}_{\text{syn}}^{(i)}$
$V^{(\text{TC})}$	$g_{\text{AMPA}}^{(\text{TC})}$	$c_1P + c_{12}F^{(\text{PY})}$
	$g_{\text{GABAA}}^{(\text{TC})}$	$c_2F^{(\text{RE})}$
	$g_{\text{GABAB}}^{(\text{TC})}$	$c_3F^{(\text{RE})} B(F^{(\text{RE})})$
$V^{(\text{RE})}$	$g_{\text{AMPA}}^{(\text{RE})}$	$c_4F^{(\text{TC})} + c_{13}F^{(\text{PY})}$
	$g_{\text{GABAA}}^{(\text{RE})}$	c_5Q
$V^{(\text{PY})}$	$g_{\text{AMPA}}^{(\text{PY})}$	$c_8P_{\text{Cx}} + c_6F^{(\text{TC})}$
	$g_{\text{GABAA}}^{(\text{PY})}$	$c_9F^{(\text{IN})}$
	$g_{\text{GABAB}}^{(\text{PY})}$	$c_{10}F^{(\text{IN})} B(F^{(\text{IN})})$
$V^{(\text{IN})}$	$g_{\text{AMPA}}^{(\text{IN})}$	$c_7F^{(\text{TC})} + c_{11}F^{(\text{PY})}$

Table 2. Synaptic currents and pulse densities. The table summarizes firing densities (3rd column) which contribute to AMPA, GABA_A and GABA_B synaptic conductances (2nd column) in four neuronal populations (1st column).

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