Oscillatory Corticothalamic Response to Somatosensory Input[1]

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Abstract

We construct a model of the thalamocortical feedback loop using the Random Neural Network model to provide a theoretical explanation for cortical and thalamic damped rapid (circa 60-100Hz) oscillations which have been observed in lightly anesthesized rats with somatosensory input Nicolelis (1997). Experimental data corroborates the choice of model parameter settings. Model predictions indicate that positive feedback loops and large signaling delays within cortex significantly determine the oscillatory phenomenon and its duration (i.e. its decay), while positive feedback from cortex to thalamus is needed to exhibit oscillations in thalamus.

Keywords: Somatosensory cortex, thalamocortical projections, cortical oscillations, modelling, random neural network, whisker barrel system.

1 Introduction

Oscillations in thalamus have long been known and studied Steriade (1990,1997), in particular the spindling oscillations observed in anesthesized mammals characterized by sequences of 8-12Hz oscillations of 1-3 second duration. These are *not* the subject of the present study. Rather we direct our attention to the cortico-thalamic feedback system's response to *thalamic stimulation from somatosensory input.*

Significant experimental studies of thalamic and cortical response to whisker stimulation in rats have been reported, including Simons (1989, 1992), Nicolelis (1993,1997) provides the experimental basis for our modeling study. In Nicolelis (1997), where the results reproduced in Figure 1 can be found, short term damped oscillatory behavior in cortex and thalamus is measured in response to a brief (5-7ms) somatosensory input. Our purpose is to provide a model based theoretical investigation of the primary causes of these oscillations. These measurements demonstrate damped oscillatory behavior in somatosensory cortex (SI) and in the ventral posterior medial nucleus of the thalamus (VPM), with periods of 10 to 15 ms, after a short (5-7 ms) stimulation entering through the principal nucleus of the brain stem (PrV) via the spinal nucleus of the trigeminal brain stem complex (SpV). The stimulation results from displacement of a single whisker of the rat during 100 ms. The x-axis shows poststimulus time in units of milliseconds, while the horizontal lines refer to distinct neighboring neurons being measured. The height of the signals refer to firing rates in spikes/sec, with the largest values being 140-150 spikes/sec and the smallest being 0-10 spikes/sec. Two distinct runs of this experiment reported in Nicolelis (1997) yield the plots in Figure 2 for the same six cortical neurons; for a poststimulus time of up to 49 ms the firing rates in spikes/sec of each neuron are reported at two different measurement times.

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Oscillations are less apparent in this data because of the statistical data collection method which is used, by averaging rates over several measurements. The stimulus which enters thalamus at time 5 to 7 ms after t=0 (see Figure 1), elicits a significant response in cortex at time 10-15 ms (see Figure 2), reaching a peak spiking rate at t=20 ms or so, or 10-15 ms after the signal from the brain stem enters thalamus. The cortex's response appears to die out at t=30-35 ms, or 28 to 31 ms after the end of the stimulus from the brain stem. The theoretical model we will present can provide insight into the nature of this response in SpV, VPM and SI which as indicated in Nicolelis (1997) "cannot be defined as discrete representations of the cutaneous periphery".

The RNN or *Random Neural Network* Gelenbe (1989, 1993) which we use is a non-standard recurrent spiked model which differs substantially from existing connexionist models, and is able to carry out similar desirable functions such as learning. Its main advantage is that it describes the spiked random behavior of neurons, and that it can be solved numerically without the use of Monte Carlo simulations even when the network is recurrent. Computations in this model are based on the probability distribution of network state $p(k,t) = \Pr[k(t) = k]$, or with the marginal probability that neuron i is excited $q_i(t) = \Pr[k_i(t) > 0]$. The time-dependent behavior of the model is described by an infinite system of *Chapman-Kolmogorov* equations for discrete state-space continuous Markovian systems. Neuron i, if it is excited, will send spikes to neuron j at a frequency $w_{ij} = w_{ij}^+ + w_{ij}^-$. These spikes will be emitted at exponentially distributed random intervals. In turn, each neuron behaves as a non-linear *frequency demodulator* since it transforms its incoming excitatory and inhibitory spike trains' rates into an "amplitude", which is $q_i(t)$ the probability that neuron i is excited at time t. The stationary probability distribution associated with each cell is used throughout the computations:

$$p(k) = \lim_{t\to\infty} p(k,t), \qquad q_i = \lim_{t\to\infty} q_i(t), \quad i = 1, ..., n. \tag{1}$$

and is given by:

$$q_i = \frac{\sum_{j=1}^n q_j w_{ji}^+ + \Lambda_i}{\sum_{j=1}^n (w_{ij}^+ + w_{ij}^-) + \sum_{j=1}^n q_j w_{ji}^- + \lambda_i} \qquad \text{if } q_i < 1. \tag{2}$$

1.1 The Model

The model we investigate is shown schematically in Figure 3. It is composed of three layers schematically designated as T (thalamus), R (reticular layer) and C (cortex) with the excitatory (+) and inhibitory (-) connections and feedback loops shown in Figure 3. eedback loops – both excitatory and inhibitory – are present both inside cortex and between the various ensembles of cells. Typically, for the somatosensory stimulus that is being discussed here (involving a single whisker of the rat) the number of thalamic cells T involved is of the order of 10^3, while 10^2 cortical cells C would be involved. The model we construct assumes all cortical cells involved are statistically identical, and similarly that all thalamic cells are statistically identical, as are all reticular layer cells. In relation to the work reported in Simons (1989), the thalamic cells T in our model correspond to the thalamo-cortical units (TCU), while the cortical cells C of our model correspond to the "regular spike" barrel units (RSU) of the somatosensory cortex.

We will use the following notation in our presentation. Let x designate some neuronal area being considered: $x = t,\ c,\ r$ for thalamus, cortex and reticular layer, respectively. R_x will denote the observed single cell firing rate in area x as a function of stimulus firing rate e entering the Thalamus. Here area x refers to Thalamus if $x = t$, to Cortex if $x = c$, and to the Reticular area if $x = r$. r_x denotes the intrinsic (maximum) cell firing rate in area x. q_x is the excitation level, or probability of cell firing, for a cell in area x in response to e. Note that $0 \leq q_x \leq 1$. D_{xy}

indicates the time delay for carrying information between region x and region y. In the Random Neural Network Model the relationship:

$$R_x = q_x r_x, \tag{3}$$

holds, so that $R_x \leq r_x$ for each cell in any area x. We will denote by $q_x F_{xy}$ the excitatory rate of firing of a nominal cell of area x to a nominal cell of area y, while $q_x f_{xy}$ will be the corresponding inhibitory firing rate. Note that the $F_{xy},\ f_{xy}$ play the role of nominal connection weights.

Consider a given input signal $e(\tau)$ entering the thalamic region from the brain stem at time τ. While the delay between ensembles is a random variable, we simplify it by taking it to be deterministic. We consider collections of identical cells for each region T, R, C with each cell in a region being connected in the same manner to cells in other regions or (for the case of cortex) to cells in the same layer.

The original RNN model Gelenbe (1989) does not include explicit time delays as signals propagate from one neuron to another. However it is a straightforward manner to introduce such delays in the model, as long as they are assumed to be deterministic. When the delays are stochastic (which will presumably be the realistic situation) we can consider that the model is a "multiply stochastic" one, with a different set of solutions for each set of values of the random variables representing delays. Such delays can represent the propagation time of signals along axons and dendrites as well as synaptic delays, and postsynaptic signal delays within the soma. We will not attempt to enter here into the biophysical nature of delays considered for our model, but just assume that they are present.

This leads to the following system of time delay equations in response to the stimulus signal $e(\tau)$, which captures the most essential features of the corticothalamic feedback system for time $\tau' \geq \tau$:

$$q_c(\tau') = \frac{F_{tc} q_t(\tau' - D_{tc}) + F_{cc} q_c(\tau' - D_{cc})}{r_c + f_{cc} q_c(\tau' - D_{cc})}, \tag{4}$$

$$q_t(\tau') = \frac{F_{ct} q_c(\tau' - D_{ct}) + e(\tau' - D_{et})}{f_{rt} q_r(\tau' - D_{rt}) + r_t}, \tag{5}$$

$$q_r(\tau') = \frac{F_{cr} q_c(\tau' - D_{cr})}{r_r}. \tag{6}$$

This system of equations captures the cortical to cortical excitatory and inhibitory connections, the excitatory projection from thalamus to cortex, the excitatory direct projection from cortex to thalamus and the excitatory connections from cortex to the reticular layer, followed by inhibitory reticular layer to thalamus connections.

These equations assume that all (order of magnitude 10^2) cortical cells are homogenous in their connections and parameters. Similarly all cells in the reticular layer and those in the thalamic layer (order of magnitude 10^2) involved in this specific single somatosensory input also have homogenous connections and parameters. Thus, since the RNN model solution (2) assumes ergodicity, we are exploiting it to predict the expected statistical behavior of three large homogenous interconnected ensembles of cells responding to a time sequence of identical stochastic inputs represent by the input signal rate $e(\tau)$. The cortical cells C of our model correspond to the somatosensory cortex barrel cells. In Simons (1989) the quiescent (i.e. prestimulus) firing behavior of thalamo-cortical units (TCU) is reported. Note that our model assumes that there is *no firing* when there is no input, while in Simons (1989) it is shown that there is significant cell firing (in particular in the thalamic cells (TCU) with on the average nearly 7.89 spikes per 100 ms of prestimulus time, or

0.0789 pulses/ms, 78.9 spikes/sec in our notation). Quiescent firing rates of cortical unit (i.e. RSU in Simons (1989)) are measured to be some 7.24 times smaller or circa 10.9 spikes/sec on the average Simons (1989). It appears that the cells measured in Simons (1989) (layer IV) are not in the same layer as those measured in Nicolelis (1997) (layer V), though their firing characteristics appear to be very similar. An additive correction factor can therefore be proposed as a simple compensation for this quiescent firing effect. We will discuss this point again below when we compare modeling and measurement results.

2 Model Predictions and Discussion

The results throughout this section are obtained by numerically solving the non-linear delay equations (4), (5), (6). Figure 4 shows a first set of model predictions. The column to the right summarizes the parameter settings. At the top right hand side we show the input stimulus and cortical response in terms of a normalized excitation probability of cells. The top right hand side shows the model input stimulus to thalamus $e(\tau)$ in spikes per second (see Figure 1 at the SpV level of the brain stem). The bottom squares show model output in spikes/second: on the left is a cortex cell firing rate (corresponding to measurements of SI in Figure 1) while the right hand square refers to model predictions of thalamic cell firing rates (see VPM of Figure 1).

The input to thalamus in Figure 4 is consistent with the brain stem SpV and PrV data from Figure 1 where the stimulus lasts a total of 4-7 ms, with a maximum spike rate of 120 spikes/second or 0.12 spikes/ms. Maximum cortex cell firing rate observed in the measurements in Figure 2 ranges from 40 to 300 pulses per second or 0.04 to 0.3 pulses/ms. We take an intermediate value in this range for our numerical examples, setting $r_c = 0.1$. The choice of $D_{cc} = D_{ct} = D_{cr} = 10$ is compatible with the value selected for r_c, since for the RNN model the choice of r_c implies that (a) when a cortex neuron is excited it fires on the average each r_c^{-1} milliseconds, and (b) a cortex neuron has an average latency of r_c^{-1} milliseconds between the arrival at its input of signals of sufficient strength to excite it, and the moment it starts emitting its first output spike. Assuming that maximum firing rates in thalamus (VPM) are some ten times higher than in cortex, as are firing rates in the reticular area, we take $r_t,\ r_r = 1$. We have assumed that 20% of cortex to cortex connections are inhibitory, while 80% are taken to be excitatory; Steriade (reports at most 25% cortex to cortex inhibitory connections in certain species of monkeys).

Finally we take 20% of connections from cortex to thalamus to be direct excitatory projections, while 80% are taken to be inhibitory in transit via the reticular layer as shown in Figure 3. These parameter settings lead to the numerical results of Figure 4 with the model parameters which we summarize below:

- $D_{cc} = D_{ct} = D_{cr} = 10ms$
- $r_r = r_t = 1pulse/ms$
- $r_c = 0.1pulses/ms$
- $D_{tc} = D_{et} = D_{rt} = 1ms$
- $F_{cc} = F_{cr} = 0.04$
- $f_{cc} = F_{ct} = 0.01$
- $F_{tc} = f_{rt} = 1$

From Figure 4 we see that response parameters and oscillatory behavior are consistent in the model for cortex with observations in Figures 1 and 2, and the duration of oscillations (circa 50 ms) are comparable to but perhaps slightly greater than those observed in Figure 1. Another corroboration of model predictions concerns the observed latencies to peak response in cortical cells which are reported in Simons (1992) to be of just under $12ms$. This is very consistent with the model predictions in Figure 4 where peak response is observed some 10 *to* $15ms$ after onset of the stimulus.

In Simons (1989) post-stimulus firing rates in thalamic (TCU) cells are reported to be on the average some 1.18 times higher than post-stimulus firing rates over a 20 ms period of cortical (RSU) cells, while our model predictions in Figure 4 seem to yield quasi-identical peak rates. The explanation comes from the fact that our model assumes *no firing* in quiescent state. If we carry out the additive correction we have alluded to at the end of the previous section we would obtain consistent numbers.

The impact of a 7 to 1 ratio in firing rates between thalamus and cortex, and an inverse ratio in signal delays, is shown in Figure 5. Oscillations are still perceptible but have been significantly reduced. Continuing now with the evaluation of the sources of oscillatory behavior in cortex and thalamus, when we keep the set of parameter values of Figure 1 but simply reduce the values of cortical delays to 7 ms (i.e. $D_{cc} = D_{ct} = D_{cr} = 7ms$), the duration of the response in cortex and thalamus is reduced to circa 40 ms, but also the oscillatory behavior is significantly reduced as seen in Figure 6.

To test whether significant delays within cortex are needed, we maintain even lower delays in cortex (as in Figure 6) reduced to 5 ms, and restore a large delay in the corticothalamic projection through the reticular layer and directly ($D_{cr} = D_{ct} = 10ms$). We see in Figure 7 that oscillations in thalamus and cortex have nearly disappeared, demonstrating the dominant effect on oscillatory behavior due to large delays in cortex to cortex connections.

Now returning to the previous 10 ms values of cortical delay, but simply removing all direct positive feedback from cortex to thalamus ($F_{ct} = 0,\ F_{cr} = 0.5$) we obtain the oscillatory behavior in cortex which is observed experimentally, and a duration of response less than 40 ms seen in Figure 2.

This indicates that the oscillatory behavior *in cortex* is dependent on the relative value of delay through cortex compared to thalamus, but that it does not require positive feedback from cortex to thalamus. Positive fedback in cortex and from cortex to thalamus (Figure 4) is needed to produce oscillations *both in cortex and thalamus* as observed in the experimental data Notice that Figures 4, 6, 8 all reproduce oscillations at roughly 100 Hz.

The next question is to see if positive feedback within cortex is needed in order to reproduce oscillatory behavior in the model. In order to verify this point we reduce the proportion of positive feedback in cortex to cortex connections to 20%, and increase negative feedback to 80% (Figure 9). Now total response in cortex and thalamus lasts less than 30 ms, while oscillations have largely disappeared. Removal of all positive feedback connections in cortex and replacing them with negative feedback removes all oscillatory behavior and produces a cortical and thalamic response which is simply proportional to the brain stem input signal (Figure 10).

Our model predictions indicate that cortical and thalamic damped rapid (circa 60 to 100Hz) oscillations are essentially determined by the large ratio of signaling delay from cortical cells to signaling delay from cells of the thalamus and reticular layer, and the positive feedback loops within cortex (for oscillations within cortex), and direct corticothalamic excitatory connections (for oscillations to propagate from cortex to thalamus). Positive feedback within cortex impact

the oscillations, and their duration. Positive feedback from cortex to thalamus is not needed for oscillatory behavior in cortex, but is for oscillatory thalamic behavior. Negative feedback from cortex to thalamus via the reticular layer, and cortex to cortex inhibitory connections, contribute to damping. Future work will investigate the detailed effect of the reticular layer.

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References

[1] Contreras, D. Steriade, M., 1997, State dependent fluctuations of low frequency rhythms in cortico-thalamic networks, Neuroscience 76, 2538.

[2] Gelenbe, E., 1989, Random neural networks with negative and positive signals and product form solution, Neural Computation, 1, 502-511.

[3] Gelenbe, E., 1990, Stability of the random neural network model, Neural Computation, 2, 239-247.

[4] Gelenbe, E., Stafylopatis, A., 1991, Global behavior of homogeneous random neural systems, Applied Math. Modelling, 15, 534-541.

[5] Gelenbe, E., 1993, Learning in the recurrent random neural network," Neural Computation 5, 154-164.

[6] McKenna, T.M., McMullen, M., Schleslinger, M.J., 1994, The brain as a dynamic physical system, Neuroscience 60, 3, pp. 587-605.

[7] Nicolelis, M.A.L., Lin, R.C.S., Woodward, D.J. and Chapin, J.K., 1993, Dynamic and distributed properties of many-neuron ensembles in the ventral posterior medial (VPM) thalamus of awake rats, Proceedings of the National Academy of Sciences 90, 2212-2216.

[8] Nicolelis, M.A.L., Ghazanfar, A.A., Faggin, B., Votaw, S., and Oliveira, L.M.O., 1997, Reconstructing the engram: simultaneous, multiple site, many single neuron recordings", Neuron 18, 529-537.

[9] Simons, D.J., Carvell, G.C., 1989, Thalamocortical response transformation in the rat Vibrissa/Barrel system, Journal of Neurophysiology, 61, 311-330.

[10] Simons, D.J., Carvell, G.C., Hershey, A.E., Bryant, D.P., 1992. Responses of barrel cortex neurons in awake rats and effects of urethane anesthesis, Brain Research, 91, pp. 259–272.

[11] Steriade, M., Jones, E.G., Linas, R.R., 1990, Thalamic Oscillations and Signaling. (John Wiley & Sons, New York).

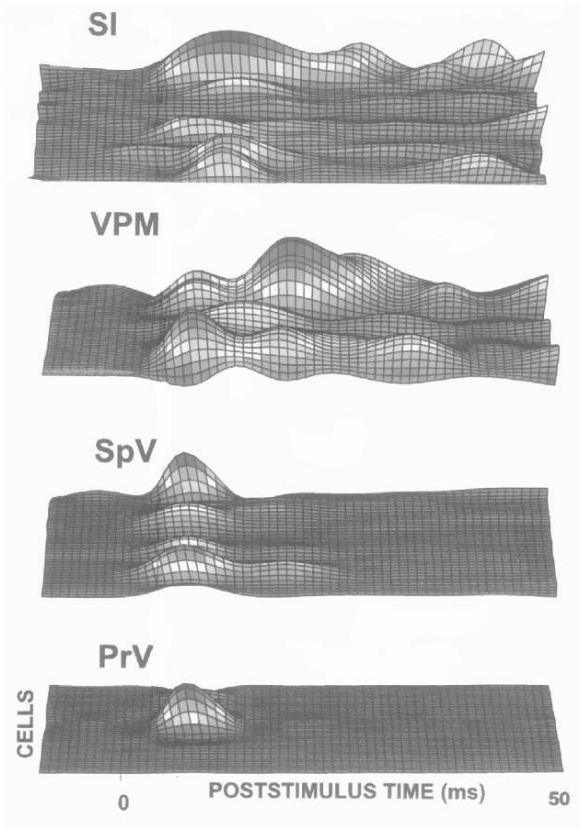

Figure 1: Input from the brain stem (PrV) and response at thalamus (VPM) and cortex (SI), reprinted Nicolelis (1997).

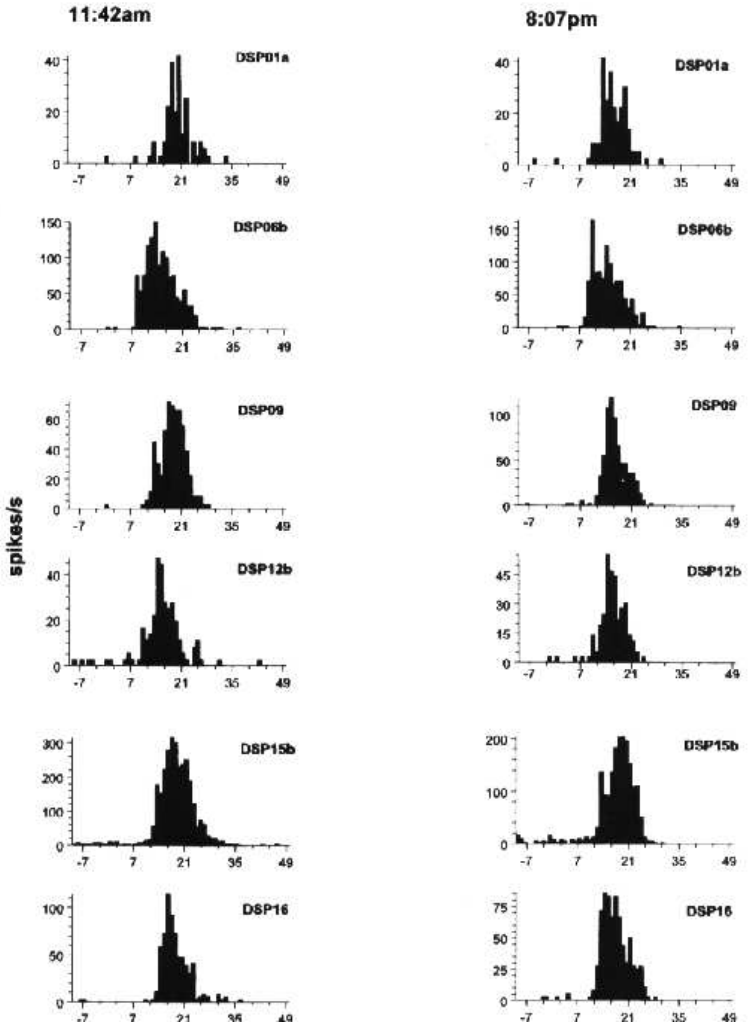

Figure 2: Distinct cell poststimulus firing, reprinted from Nicolelis (1997) .

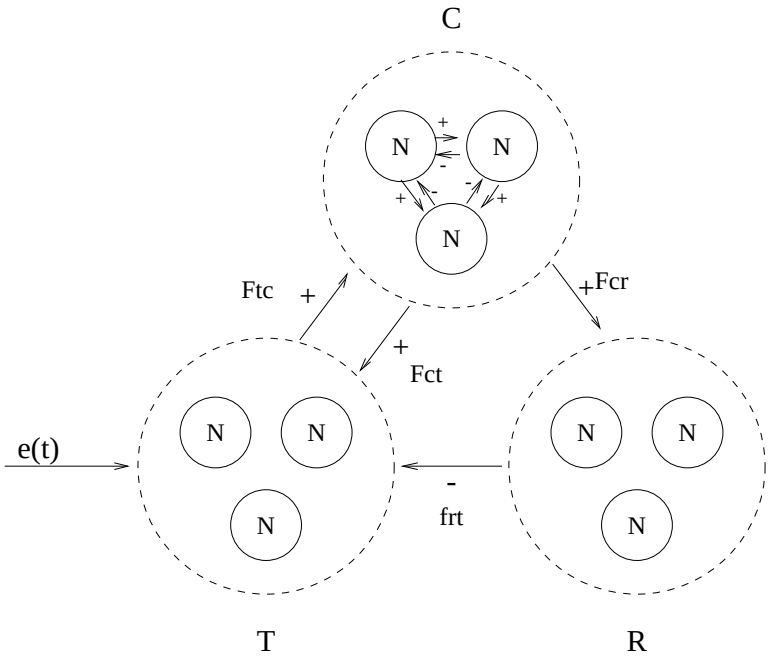

Figure 3: Schematic description of network model

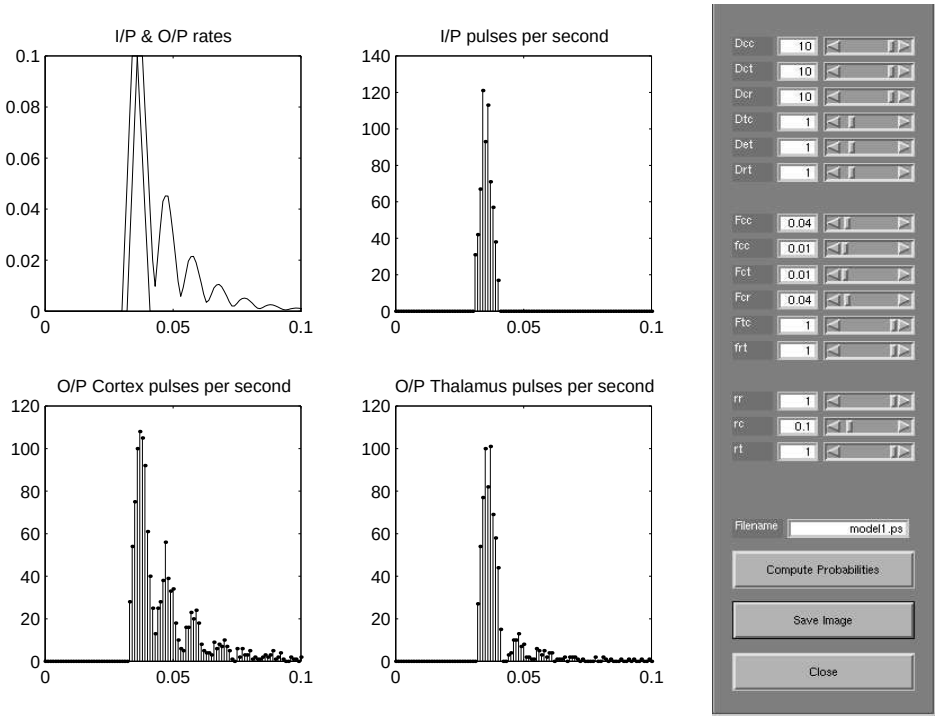

Figure 4: Results from the computational model

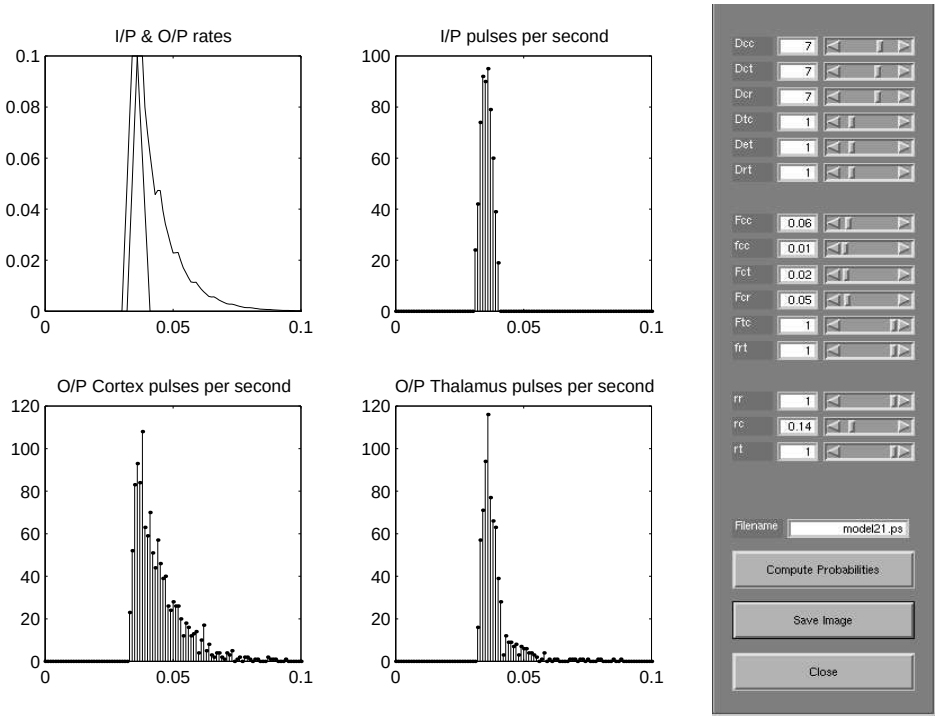

Figure 5: Results from the computational model

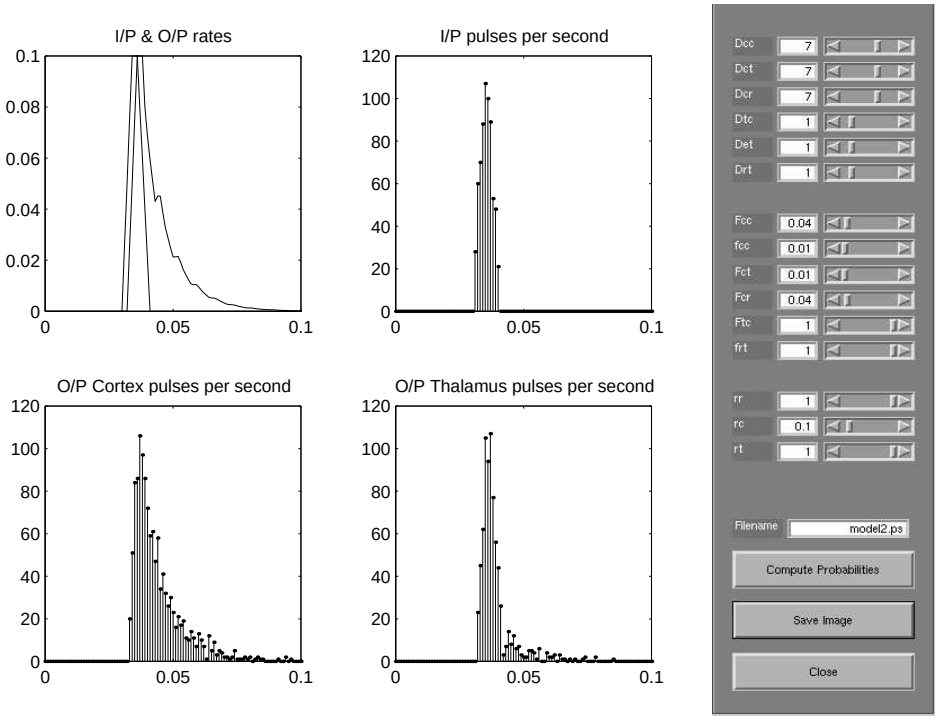

Figure 6: Model with smaller delay through cortex: oscillations have disappeared

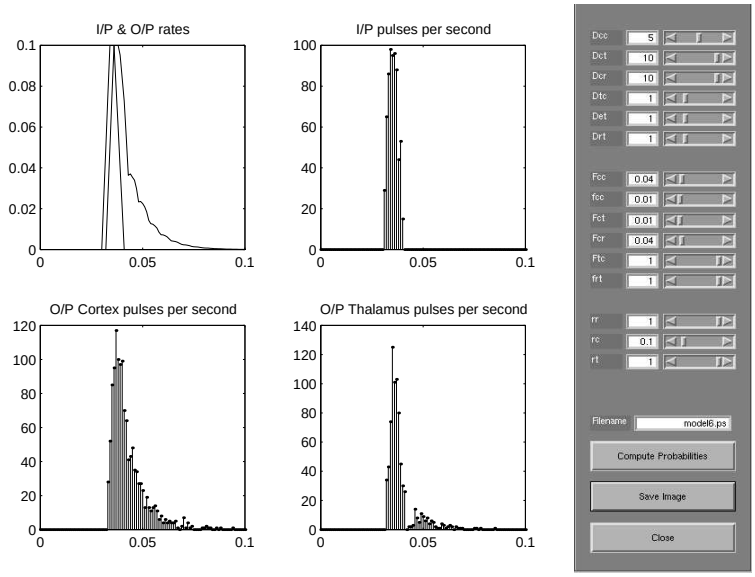

Figure 7: Small delay in cortex, large delay in corticothalamic projections: oscillations are weak

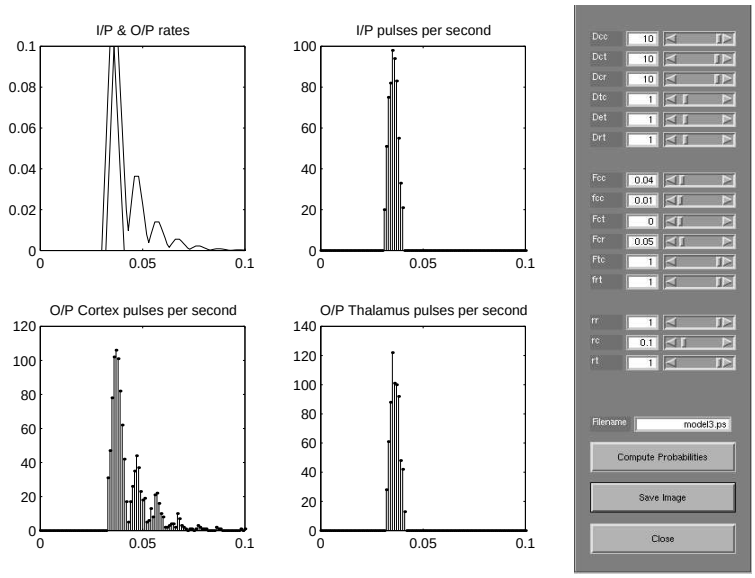

Figure 8: Without positive feedback from cortex to thalamus: cortex oscillates but thalamus does not

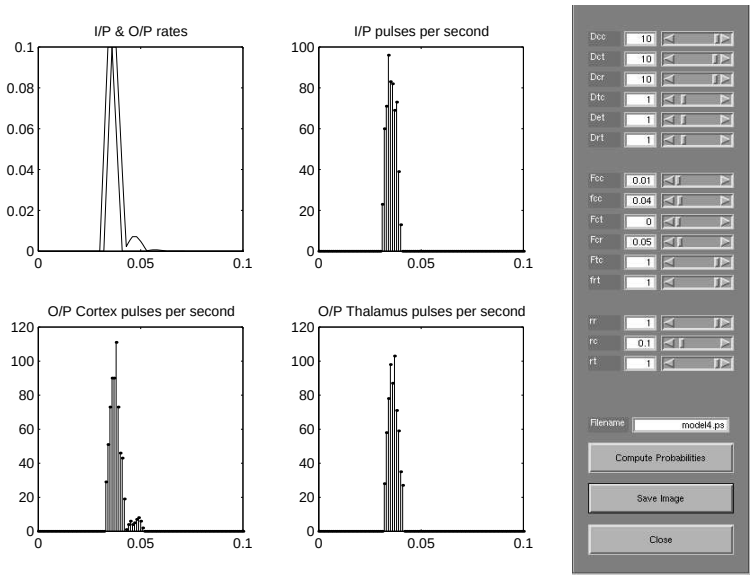

Figure 9: Computational model with dominant negative feedback in cortex

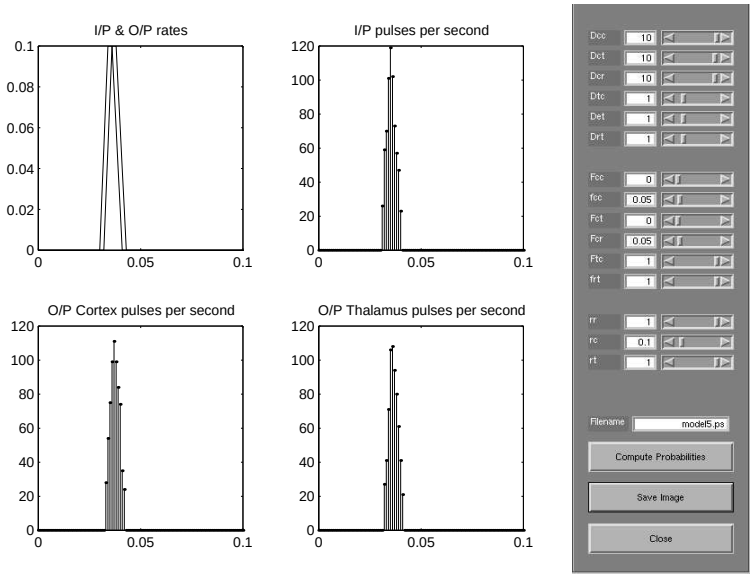

Figure 10: Computational model with only negative feedback in cortex