Oscillations and Long-Lasting Correlations in a Model of the Lateral Geniculate Nucleus and Visual Cortex

KYLE L. KIRKLAND, ADAM M. SILLITO, HELEN E. JONES, DAVID C. WEST, AND GEORGE L. GERSTEIN

Department of Neuroscience, University of Pennsylvania, Philadelphia, Pennsylvania 19104; and Department of Visual Science, Institute of Ophthalmology, London EC1V 9EL, United Kingdom

Received 12 November 1999; accepted in final form 14 June 2000

INTRODUCTION

The lateral geniculate nucleus (LGN) is the thalamic relay for the mammalian visual system, receiving input from the retina and projecting to the visual cortex. But the intricate circuitry and numerous other inputs and projections of the LGN (Sherman and Koch 1998), including massive feedback from the visual cortex, suggest that it is more than just a relay; what other functions the LGN may have, however, have not been clearly demonstrated.

Sillito et al. (1994) reported significant correlations in the spike trains of cat LGN cells when co-stimulated by a drifting grating (even after the stimulus-induced covariation was removed) but only with an intact visual cortex. This experiment, along with other recent work (Kaplan et al. 1993; Marrocco et al. 1996), indicates that the LGN may play an important role in processing visual information. However, the LGN correlations in the Sillito et al. (1994) data, which are presumably due to neural interactions such as shared input or synaptic connections, last much longer than might be anticipated from the stimulus-driven responses. Because neural interactions are generally of short duration, the time frame of the Sillito et al. (1994) analysis, and the further analysis and modeling of Kirkland and Gerstein (1998), was limited to a few hundred milliseconds. Surprisingly, when the time frame of analysis was extended (Brody 1998), the experimental data showed correlations that have durations of seconds.

What caused these long-lasting correlations? One possible explanation involves long-lasting variables, which has been explored by Brody (1998). Further investigation of the model of Kirkland and Gerstein (1998) offers some intriguing alternative ideas based on the complex anatomy and physiology of the LGN. One important feature of our model is LGN bimodality (Sherman 1996). The two states, or modes, are usually referred to as "burst" and "tonic." The burst mode is associated with hyperpolarized membrane potentials, which de-inactivates low-threshold (LT) channels and makes LGN relay cells tend to respond to stimuli with a short, high-frequency burst; in tonic mode, LGN stimulus responses tend to be a more linearly graded series of spikes related to stimulus strength. Another important feature in our model—though it was not deliberately incorporated—is that it reproduces the well-known spindle oscillations of the thalamocortical system (McCormick and Bal 1997; Steriade et al. 1993). These 7–15 Hz oscillations are usually identified with states of low arousal or sleep and are generated, in part, by LT channels. These two features of the LGN may be involved in producing the long-lasting correlations seen in Sillito et al. (1994).

METHODS

Model

All simulations were done with a slightly modified copy of GENESIS, including the addition of a new object which presented drifting gratings and bar stimuli to a simplified layer of cells (the input layer). The only other modifications were enhancements of the spiking mechanism for cells (used for spike generation when voltage-gated channels were not present), and formatting the output of the simulator for use with our analysis programs.

A schematic diagram of the model (Kirkland and Gerstein 1998) is shown in Fig. 1, along with a list of important parameter values. The model consists of an input layer ("retina"), an LGN layer, and a cortex layer. Each layer consists of a 24 × 24 array of cells. The cells of the input layer have the center-surround receptive field typical of the well-known spindle oscillations of the thalamocortical system (McCormick and Bal 1997; Steriade et al. 1993). These 7–15 Hz oscillations are usually identified with states of low arousal or sleep and are generated, in part, by LT channels. These two features of the LGN may be involved in producing the long-lasting correlations seen in Sillito et al. (1994).

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked "advertisement" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.
cells generally have very low spontaneous firing rates—and therefore cortical cells having other orientations would be slight—since cortical the stimuli were also horizontal, we believe that the contribution of horizontal bars (all stimuli are horizontally oriented). Because all of actions, 2 rows of 4 LGN cells); all cortical cells are thus “tuned” to tory input from a horizontal row of four LGN cells (in some simula-

The synaptic connections between the LGN and cortex are very excitatory for LGN cells topographically close to the cortical cell and inhibitory to an annulus of LGN cells further away. The region of excitation was a subset of LGN cells in a 3 × 3 region centered on the retinotopic location of the cortical cell; the subset was chosen ran-
domly with a probability of connection of about 0.6. The annulus of inhibition was composed of the two surrounding rings and the prob-
ability of connection was about 0.5. There is some experimental evidence for such a structure in cortical feedback (He 1997; Tsumoto et al. 1978; Yan and Suga 1996), and simulation studies have shown it to be important both for stability and for modeling some physio-
logical mechanisms (Kirkland and Gerstein 1998, 1999; Xing and Gerstein 1996).

Cortical cells, but not LGN or retinal cells, were locally connected: except for the edges, each cortical cell made excitatory synapses with a subset of neighboring cells in the surrounding two rings and inhibi-

FIG. 1. Schematic diagram of the model and list of parameter values. Top left: a stimulus grating and a typical retinal cell receptive field; below are the 3 networks and representative connections (only 1 cell’s connections are shown). Excitatory synaptic connections are black, inhibitory are gray. Right: a list of important parameters and their value ranges. rg, retinogeniculate; gc, geniculocortical; cg, corticogeniculate; ml, corticocortical; exc, excitatory; inh, inhibitory. This figure was adapted from Fig. 2 and Table 1 of Kirkland and Gerstein (1998).

retinal ganglion cells; the size of the RFs was assumed to be about one to two visual degrees in diameter. The relative strengths of the excitatory center and inhibitory surround were adjusted so that full field illumination gave only a small response (over baseline). The input layer cells fired independently, but there was always partial overlap between neighboring cell RFs. The length of the grating or bar stimuli typically spanned 8–10 cells, which in the model was about 3–5°. In an earlier version, neighboring input cells were slightly correlated, but the results were similar to that of the independent firing models. The input layer cells are simply Poisson-like spike train generators; the output is modulated by an activation variable that is the convolution of the RF structure with the portion of the stimulus falling in the RF (Wehmeier et al. 1989).

Each input layer cell makes a strong excitatory connection to a single LGN cell, so the LGN RF is structurally the same as the input layers. The LGN cells have two compartments: a soma, with voltage-gated LT calcium channels, and a passive dendrite. The cortical cells have a single compartment. In a few earlier simulations, LGN and cortical cell somas had sodium and potassium voltage-gated channels; but in most cases, a spike was pasted on the output of the cells when the membrane potential reached threshold, followed by a short refrac-
tory period and after-hyperpolarization.

The synaptic connections between the LGN and cortex are very important for the model’s performance. Cortical cells receive excita-
tory input from a horizontal row of four LGN cells (in some simula-
tions, 2 rows of 4 LGN cells); all cortical cells are thus “tuned” to horizontal bars (all stimuli are horizontally oriented). Because all of the stimuli were also horizontal, we believe that the contribution of cortical cells having other orientations would be slight—since cortical cells generally have very low spontaneous firing rates—and therefore ignorable.

Feedback from the cortex to the LGN has a specific structure:
resulting matrix contains only correlations due to the firing rates (sometimes this doesn’t work—see DISCUSSION for details). We generally average over all possible shifts, which provides a smooth function called the “shift predictor.” The matrix bins are also typically transformed into correlation coefficients (Aertsen et al. 1989).

To the right of the matrix is the coincidence histogram, which is a one-dimensional display of the paradiagonal area indicated by the bracket at the top right corner of the matrix. The histogram at far right is a cross-correlogram, computed by summing along the matrix paradiagonals.

For a tutorial on the JPST, see http://mulab.physiol.upenn.edu/jpst.html.

RESULTS

Figure 2A shows a JPST from the data of Sillito et al. (1994). (The anatomy of a JPST is described briefly in the methods section.) The time window is 900 ms and encompasses three separate bar passes of the grating for each of the two LGN neurons as can be seen in the PSTHs on the bottom and left side of the matrix. The correlation along the diagonal of the matrix, and summarized in the central peak of the cross-correlogram, shows the near coincident firing of the two neurons, above that expected from the (covarying) firing rates. Such correlations were only found with an intact visual cortex.
An interesting and unexpected result is the correlations at delays of 300 ms, as seen in the off-diagonal peaks of the cross-correlogram and the circled region of the matrix. The response of one neuron was therefore correlated with the response of the other neuron to a different bar pass of the grating, even after correcting for firing rates. This result is typical for the Sillito et al. (1994) data.

Figure 2B shows a JPSST from the model, using data reported in Kirkland and Gerstein (1998). As in the experiment, the stimulus was a drifting grating (with slightly higher drift velocity); the result is strikingly similar to the experimental data and is also commonly found, with varying degrees of prominence, in virtually all of the model data. Since there were no variables with long time constants, the off-diagonal correlations found in the model were very surprising.

We investigated the model’s off-diagonal correlations by a brief exploration of parameter space. We measured the amount of off-diagonal correlation by computing the average height of the two side peaks in the cross-correlogram, as a percentage of the central peak height; only cross-correlograms with a significant central peak were used. Since the peak is made up of coincidental firing activity, which is more than that expected by chance, the height of a peak is a rough measure of correlation strength; peak area is more difficult to compute and, since the extent of the negative side lobes did not affect the results, peak height was an accurate measure. Figure 3 shows the results.

One parameter that significantly affects the amount of off-diagonal correlation is inhibition (Fig. 3A): a reduction in cortical feedback inhibition produces a corresponding reduction in off-diagonal correlations. Another way to significantly reduce off-diagonal correlation is to reset the parameters of the LT channel after each stimulus, i.e., after each sweep of a bar of the grating (Fig. 3B). The percentage of off-diagonal correlation depends on the number and location of affected LGN cells; in Fig. 3B, ■ represents horizontal rows of LGN cells with reset LT channels (or in 1 case, a vertical column that was perpendicular to the stimulus). The results implicate the LT channel in the off-diagonal peaks. Note, however, that when the affected LGN cells were perpendicular to the stimulus (last entry in Fig. 3B), no significant reduction in off-diagonal correlation occurred.

Display of the correlations at higher resolution reveals another interesting phenomenon. The cross-correlogram in Fig. 4A is from the Sillito et al. (1994) data shown in Fig. 2A. There is a curious “ripple” or oscillation in the cross-correlogram, with a frequency of about 10 Hz. Figure 4B shows a spectral analysis of the cross-correlogram. Cross-correlograms from the model have similar features (see the diagonal cross-correlogram in Fig. 2B), although the frequency of the oscillation is slightly higher. Visibly obvious oscillations in cross-correlograms are often encountered in model data with more than half of our simulations having them. Such oscillations were seen much less often in the experimental data; among the data that have been checked, only about 10–20% show prominent oscillations as in Fig. 4A. But as reported in Sillito et al. (1994), only 19 of 37 cell pairs (51%) had significant correlations; thus about 20–40% of these showed oscillations; this is a considerable portion.

The frequency of this oscillation is similar to the spindle oscillation (7–15 Hz). In model simulations having prominent oscillating cross-correlograms, we searched the rasterplots of the individual cells for signs of oscillations at this frequency. Surprisingly, the neurons’ spike trains showed no obvious oscillatory pattern, unlike the pairwise cross-correlograms.

However, the model is capable of producing prominent spindle-like oscillations. Such oscillations, which are obvious both in single neuron spike trains and in group activity, can be induced by lowering the membrane potential of some LGN cells. The frequency of these oscillations was slightly higher than the spindle oscillations observed in experimental preparations. In some simulations, we induced spindle-like oscillations in LGN cells whose RFs are outside of the area stimulated by the grating (but not outside of the area that gets feedback from stimulus-induced cortical activity due to divergent connections). In these simulations, a clear increase is easily seen in the prominence and number of oscillating cross-correlograms (Fig. 4C). The membrane potentials of the LGN cells also show signs of oscillating. The model cross-correlations increase in
duration, often lasting seconds, similar to those commonly seen in the experimental data. In the model, the long-lasting correlations seem to be a consequence of shared oscillatory input to LGN cells.

**DISCUSSION**

Off-diagonal peaks in the JPST (Fig. 2, A and B) of the model and experimental data suggest a longer interaction between neurons than is physiologically expected. In our model, the strength of cortical inhibition to the LGN is critical. Earlier results indicated that the cortical inhibitory input could switch LGN modes (although we were not aware of the oscillation at the time of our prior publication) (Kirkland and Gerstein 1998); but if that is the reason cortical inhibition produces off-diagonal correlations, it is not obvious how it works. One possible scenario: the periodic nature of the stimulus, in conjunction with the cortical inhibitory input to the LGN, creates...
a sort of resonance phenomenon in which the geniculocortical network weakly oscillates. Resonance is well known in engineering and physics, particularly when objects are stimulated at their so-called natural frequency. Oscillation can produce off-diagonal peaks if its period is fairly constant, but if the oscillation is weak it may not be easily detected in other measurements (electroencephalography or rasterplots, for example). We will call this a subliminal oscillation.

What about the long-lasting correlations (of seconds duration) in the data of Sillito et al. (1994)? Correlations of this duration occur in the model when part of the geniculocortical system is oscillating. Alternatively, Brody (1998) proposes that the long-lasting correlations are due to a slow, cortically driven covariation in membrane potential. In both of these two hypotheses, the shift predictor (used to correct for stimulus-induced firing rate changes in the neurons under study) fails to be an appropriate corrector. The shift predictor in our “subliminal oscillation” hypothesis fails to account for nonstimulus locked oscillation; in the “slow covariation” hypothesis, the shift predictor is fooled by nonstimulus locked covariation in the membrane potentials of the cells. The generic term for these situations is “nonstationarity”; unfortunately, neural spike trains are susceptible to nonstationarities (Perkel et al. 1967) (see also http://mulab.physiol.upenn.edu/cross-correlation.html). There is currently no well-established procedure for dealing with this problem, although some solutions have been proposed (Brody 1999; A.M.H.J. Aertsen, personal communication).

The two hypotheses are not mutually exclusive. A slow covariation in cellular membrane potentials can produce long-lasting correlations (Brody 1998) but does not explain all the data. It certainly cannot explain the oscillations in the cross-correlograms. Of course, our hypothesis also fails to explain all the data; however, given the multimodal nature of the LGN, heterogeneity is not very surprising. What we have shown here is that long-lasting correlations can be generated by not only slow covariations but also by relatively fast oscillations. From the data of Sillito et al. (1994), we cannot conclusively determine if either (or perhaps both) of these hypotheses are correct. However, intracellular LGN recordings would certainly be able to do so since in Brody’s hypothesis the membrane potentials would slowly covary, whereas in our hypothesis they would oscillate.

A point of contention for our model is that the model’s long-lasting correlations require a continuous oscillation. There is evidence for cortical involvement in spatially synchronizing LGN oscillations (Contreras et al. 1996). But electroencephalography traces typically show only episodic, not continuous, spindle oscillations. However, suppose that subliminal oscillations exist; then oscillations seen in the thalamocortical system may not be as episodic as originally believed. Perhaps a subliminal oscillation constantly exists in the system, or part of the system, which is only episodically increased to easily detectable levels. The oscillation could arise from network activity, as in our simulations and those of Traub et al. (1996), or a small number of cells (Gray and McCormick 1996). One could check this idea by looking for a phase relationship between “episodes” of the oscillation.

We should also mention that the feature-linked aspects of the synchronization reported in Sillito et al. (1994) are not strongly affected by the results reported here. Our model shows similar behavior, i.e., LGN cells are not significantly synchronized when simultaneously stimulated by spots of flashing light (when the correlation function is corrected for firing rates), but the cells are synchronized by moving bars and gratings. This synchronization could be used in feature-linked processing (Sillito et al. 1994) or perhaps as part of an attention system, as we have speculated elsewhere (Kirkland and Gerstein 1998). However, the physiological significance (if any) of the long-term correlations is not obvious.

This research was supported by National Institute of Mental Health Grant MH-46428 and National Research Council Program grants.

REFERENCES


