Synchronization as a mechanism for attentional gain modulation[1]

Paul H. E. Tiesinga[a,b,2], Jean-Marc Fellous[b], Emilio Salinas[c], Jorge V. José[d] and Terrence J. Sejnowski[b,e]

[a] *Department of Physics & Astronomy, University of North Carolina at Chapel Hill, 184 Phillips Hall, Chapel Hill NC 27599, USA.*

[b] *Sloan-Swartz Center for Theoretical Neurobiology, Computational Neurobiology Lab, and Howard Hughes Medical Institute, The Salk Institute, 10010 N. Torrey Pines Rd, La Jolla, CA 92037, USA.*

[c] *Department of Neurobiology and Anatomy, Wake Forest University School of Medicine, Winston-Salem, NC 27157, USA.*

[d] *Physics Department and CIRCS, Northeastern University, Boston, MA 02115, USA.*

[e] *Division of Biological Sciences University of California at San Diego, La Jolla, CA 92093, USA.*

Abstract

Responses of neurons in monkey visual cortex are modulated when attention is directed into the receptive field of the neuron: the gain or sensitivity of the response is increased or the synchronization of the spikes to the local field potential (LFP) is increased. We investigated, using model simulations, whether the synchrony of inhibitory networks could link these observations. We found that, indeed, an increase in inhibitory synchrony could enhance the coherence of the model neurons with the simulated LFP, and could have different effects on the firing rate. When the firing rate vs current (f-I) response curves saturated at high I, attention yielded a shift in sensitivity; alternatively, when the f-I curves were non-saturating, the most significant effect was on the gain of the response. This suggests that attention may act through changes in the synchrony of inhibitory networks.

Key words: synchronization, gamma oscillations, selective attention

[1] This work was supported by the Sloan-Swartz Center for Theoretical Neurobiology at the Salk Institute, the Howard Hughes Medical Institute and the University of North Carolina at Chapel Hill.

[2] Corresponding author, `tiesinga@physics.unc.edu`

1 Introduction

Physiological correlates of attention have been studied by recording the response of cortical neurons in Macaque monkey to either oriented gratings (area V4) or random dot patterns moving in different directions (area MT) (6; 12). The firing rate in these cases was tuned for orientation or direction, respectively. When attention was directed into the receptive field of the recorded neuron the following changes were observed (compared with attention directed outside the receptive field). Attention could increase the gain of the firing rate response while the neuron remained tuned for orientation/direction (6; 12), and this effect was approximately multiplicative. Attention could also increase the coherence of the neuron's discharge with the local field potential (3). When the contrast of the stimulus was varied there could be saturation effects: attention did not increase the firing rate anymore at high contrasts (7).

Cortical interneurons are part of dedicated networks connected by gapjunctions and chemical inhibitory synapses (4; 5). Interneuron networks synchronize when activated by excitatory neurotransmitters or neuromodulators. The firing rate of cortical output neurons is modulated by the resulting synchronous inhibition. Here we explore using model simulations and *in vitro* experiment, the hypothesis that selective attention is mediated by changes in synchrony of local interneuron networks.

When the effect of attention is modeled as an increase in synchrony of interneuron networks, we find that: attention increases the coherence of spike trains with the local field potential; the firing rate can increase with attention or remain the same depending on stimulus strength; attention results either in a gain change of firing rate response curves or a shift in the sensitivity, depending on the extent of interneuron network activation. Thus, changes in interneuron synchrony could potentially underlie a variety of seemingly unrelated observations.

2 Methods

Modeling synchronous inhibitory inputs. A model interneuron network produced an oscillatory activity that consisted of a sequence of synchronized spike volleys (2). Each spike volley is characterized by the mean number of spikes in a volley a_{IV}, their spike-time dispersion σ_{IV}, and oscillation frequency f_{osc} (equal to the number of volleys per second).

The method for obtaining synchronous volleys is given in Ref. (11). Each spike in the volley produced an exponentially decaying conductance pulse, $\Delta g_{inh} \exp(-t/\tau_{inh})$ in the postsynaptic cell (inh stands for inhibitory), yielding a current $I_{syn} = \Delta g_{inh} \exp(-t/\tau_{inh})(V - E_{GABA})$. In this expression t is the time since the input spike arrival, $\tau_{inh} = 10$ ms is a decay constant, Δg_{inh} is the unitary synaptic conductance, V is the postsynaptic membrane potential, and $E_{GABA} = -75\ mV$, is the reversal potential. The resulting train of conductance pulses drove a single compartment neuron with Hodgkin-

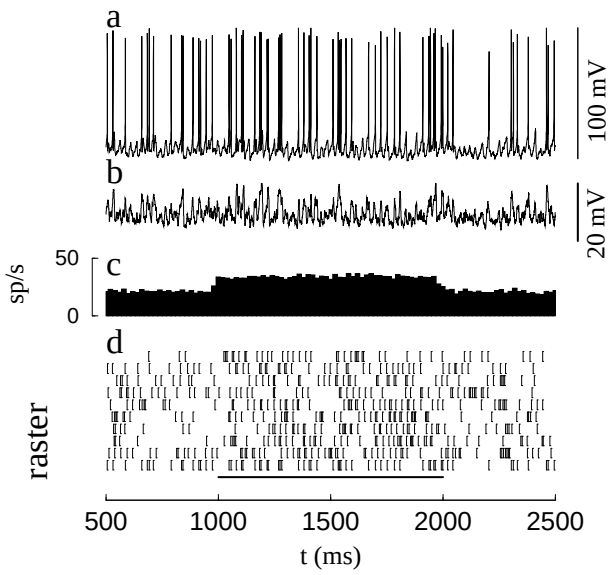

Fig. 1. Increasing inhibitory input synchrony led to an increased firing rate. We show (a) the membrane potential, (b) the local field potential (LFP), (c) the firing rate as a function of time, and (d) the rastergram of the first ten trials. During the time interval between $t = 1000$ and 2000 ms (indicated by the bar in (d)), σ_{IV} was reduced from 4 ms to 2 ms.

Huxley voltage-gated sodium and potassium channels, a passive leak current, the synaptic currents described above, and a white noise current with mean I and variance $2D$ (11).

Stimulus and attention. The model was run under four sets of parameters representing the following experimental conditions: attention was either directed away or toward the receptive field of the neuron, in combination with a stimulus either present or absent in the receptive field. The effects of attention were modeled by changing the parameters of the synchronous inhibitory drive. The value of σ_{IV} was reduced in the attended state, leading to an increase in input synchrony. The stimulus-induced synaptic inputs that drove the neuron were not temporally patterned. The model neuron either received a temporally homogeneous excitatory Poisson process with rate λ_{exc}, or it was driven by a random white noise current with mean I and variance $2D$.

Experiment. To validate the computer model, neurophysiological experiments in slice were performed. These were carried out in accordance with animal protocols approved by the N.I.H.. Coronal slices of rat pre-limbic and infra limbic areas of prefrontal cortex were obtained from 2 to 4 weeks old Sprague-Dawley rats. We recorded from regularly spiking layer 5 pyramidal cells that were identified morphologically. Current was injected into the neuron using dynamic clamp (10) to mimic the effect of a oscillatory inhibitory synaptic drive. Full experimental details are in Ref. (1).

3 Results

The model can account for results obtained in vivo. Results on attentional modulation of the firing rate and coherence of V4 neurons in macaque cortical area V4 were recently reported in three key papers (6; 7; 3). We reproduced the results by McAdams & Maunsell (6) and those of Fries and coworkers (3) under the assumption that attention modulates the synchrony of local interneuron networks (results not shown).

Gain modulation on neurons with highly variable spike trains. Cortical neurons can fire at high rates with a coefficient of variation (CV) between 0.5 and 1.5. A potential consequence of driving neurons with a synchronous oscillatory inhibitory drive is a decrease in variability (11). Therefore, we investigated whether attentional modulation by inhibitory synchrony could operate on neurons with high CV values (Figure 1). The model neuron was driven by a noisy synchronous inhibitory drive, a temporally homogeneous excitatory Poisson process and a white noise current. The effects of attentional modulation were simulated by decreasing σ_{IV} from 4 ms to 2 ms during the time interval between $t = 1000$ and 2000 ms. During the non-attended state ($t < 1000$ ms), the firing rate was 22.3 Hz and CV= 1.0. During the attended state the firing rate increased to 34.6Hz, with $CV = 0.78$. The spike field coherence (see Ref.(3)) in the gamma-frequency band ($34 - 44$ Hz) increased by 59%.

Attentional modulation of $f - I$ curves. Ascending sensory inputs can often be represented as a depolarizing current I. The resulting firing rate that such an input elicits is determined by the $f - I$ curve, the shape of which depends on the modulating inputs to the receiving neuron. These inputs may represent the value of an additional variable, such as attentional state. There are important computational consequences when modulating inputs change the gain of the $f - I$ curve multiplicatively (8). We investigated how inhibitory synchrony altered the $f - I$ curves.

In Figure 2A we compare the $f - I$ curves obtained in a slice experiment for $\sigma_{IV} = 1$ ms to those for $\sigma_{IV} = 4$ ms for two different neurons. The response could saturate as a function of I (Fig. 2Ab), in which case reducing σ_{IV} led to a shift of the $f - I$ curve to the left. In the other case, the response could be nonsaturating (Fig. 2Aa) and multiplicative gain changes are in principle possible. We studied using numerical simulations the changes in $f - I$ over a wide range of parameters (Figure 2B). For $a_{IV} = 10$ (see Methods), the $f - I$ curves were nonsaturating (Figure 2Ba). The degree of multiplicative gain modulation was investigated by rescaling and shifting all curves, $f \to f/\lambda_f$ and $I \to I - \Delta_I$, to fit to the curve for $\sigma_{IV} = 1$ms. We found shifts $|\Delta_I|$ up to $0.6\mu A/cm^2$ and λ_f as low as 0.5. This indicates that the main effect of inhibition for this parameter range is gain modulation. For $a_{IV} = 50$, the $f - I$ curves saturated at a rate equal to the inhibitory oscillation frequency, f_{osc} (Figure 2Bb). The $f - I$ curves were well fitted by a sigmoid function, $f = A/2(1 + \tanh(\lambda_I(I - \Delta_I))$. Increasing σ_{IV} shifted the curve to the right ($\Delta_I > 0$) and stretched it (λ_I decreased). Hence, for this set of parameters

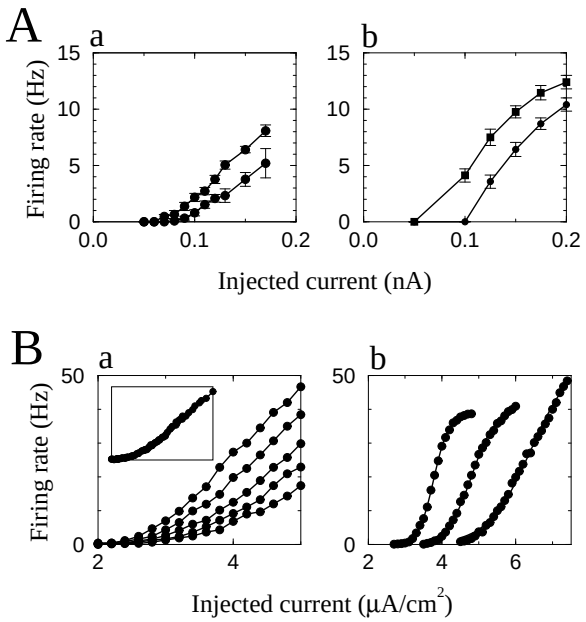

Fig. 2. Subtractive and divisive modulation of $f-I$ curves with inhibitory synchrony. (A) $f-I$ curves for two different neurons in slices of rat prefrontal cortex. The firing rate did not saturate in (a), whereas it did saturate in (b). In (a) and (b), for the top curve $\sigma_{IV} = 1$ ms and for the bottom curve $\sigma_{IV} = 4$ ms. (B) Model results. (a) Multiplicative gain modulation with inhibitory synchrony. $a_{IV} = 10$, from top to bottom $\sigma_{IV} = 1$, 2, 3, 4 and 5 ms. Inset: all curves could be overlaid by a shift in the current and a rescaling of the firing rate axis. (b) Shift in neural sensitivity with inhibitory synchrony, $a_{IV} = 50$, from left to right, $\sigma_{IV} = 1$, 3, and 5 ms. The solid lines are fits to a sigmoid function, filled circles are simulation results.

the change in gain was minimal.

The input activity a_{IV} is proportional to the size of the network times the mean number of neurons that are active on each cycle. The latter is determined by the extent of electric and chemical synaptic coupling, the former is determined by the extent of interneuron network activation by the stimulus. Hence, for small networks together with relatively focal activation of interneuron networks, attention leads to gain changes, whereas for large networks and stimuli that cause strong and widespread activation of the interneuron network, attention leads to a shift in sensitivity.

4 Discussion

Visual scenes with enormous spatial and temporal information richness are transduced into spike trains in the sensory pathway. Human psychophysics indicates that only a small part of this information is consciously accessible. For instance, differences between two images shown in rapid succession are only visible when the subject is told to pay attention to the particular spatial location of the change (9). The mechanism for this process, selective attention, remains unclear. The neural correlate of selective attention has recently been studied in Macaque monkeys (6; 7; 3). A key finding is that attention modulates both the mean firing rate of a neuron in response to a stimulus (6; 7) as

well as the coherence with other neurons responsive to the stimulus (3).
Here we presented a simple model that could reconcile these three observations. Sensory input was represented as a constant depolarizing current that was tuned for orientation and increased with contrast. Attention acted by changing the synchrony of local interneuron networks. First, increases in inhibitory synchrony led to increased coherence of output spike trains with the local field potential (Figure 1). Second, in slice experiments we observed $f-I$ curves that either saturated or did not saturate (Figure 2). For the curves that did not saturate, the firing rate always increased with inhibitory synchrony. In that case, inhibitory synchrony could lead to gain changes. For the curves that did saturate, the firing rate did not increase further with stimulus strength at high contrast. The saturation firing rate was equal to the inhibitory oscillation frequency. However, we found that the neuron could also saturate at rates corresponding to aperiodic excitatory activity, yielding a larger range of saturation rates. We are presently investigating constraints on the possible saturation rates.

To summarize, modulating inhibitory synchrony can account for the experimental observations on attentional modulation of single neuron activity. The question that remains for future study is how attention can selectively modulate inhibitory synchrony in cortical circuits.

References

[1] J-M Fellous, M Rudolph, A Destexhe, and TJ Sejnowski. *Neuroscience, in press*, 2003.

[2] M Diesmann, MO Gewaltig, and A Aertsen. *Nature*, 402:529–533, 1999.

[3] P Fries, JH Reynolds, AE Rorie, and R Desimone. *Science*, 291:1560–1563, 2001.

[4] M Galarreta and S Hestrin. *Nature*, 402:72–75, 1999.

[5] JR Gibson, M Beierlein, and BW Connors. *Nature*, 402:75–79, 1999.

[6] CJ McAdams and JH Maunsell. *J Neurosci*, 19:431–441, 1999.

[7] JH Reynolds, T Pasternak, and R Desimone. *Neuron*, 26:703–714, 2000.

[8] E Salinas and P Thier. *Neuron*, 27:15–21, 2001.

[9] DJ Simons. *Visual Cognition*, 7:1–15, 2000.

[10] AA Sharp, MB O'Neil, LF Abbott, and E Marder. *J Neurophysiol*, 69:992–995, 1993.

[11] PHE Tiesinga, J-M Fellous, JV José, and TJ Sejnowski. *Network*, 13:41–66, 2002.

[12] S Treue and Martinez Trujillo JC. *Nature*, 399:575–579, 1999.