Multiplicative Gain Changes Are Induced By Excitation or Inhibition Alone

Brendan K. Murphy[1] and Kenneth D. Miller[1,2]
[2]Depts. of Physiology and Otolaryngology
[1]Biophysics Graduate Program
[1]W.M. Keck Center for Integrative Neuroscience
[2]Sloan-Swartz Center for Theoretical Neurobiology at UCSF
University of California
San Francisco, CA 94143-0444
Email: murphy@phy.ucsf.edu, ken@phy.ucsf.edu

Address Correspondence To:
Brendan Murphy
Dept. of Physiology, UCSF
513 Parnassus
SF, CA 94143-0444
Phone: 415-476-1007
Fax: 415-476-4929
Email: murphy@phy.ucsf.edu

Abstract

We model the effects of excitation and inhibition on the gain of cortical neurons. Previous theoretical work has concluded that excitation or inhibition alone will not cause a multiplicative gain change in the curve of firing rate vs. input current. However, such gain changes *in vivo* are measured in the curve of firing rate vs. stimulus parameter. We find that when this curve is considered, and when the non-linear relationships between stimulus parameter and input current and between input current and firing rate *in vivo* are taken into account, then simple excitation or inhibition alone can induce a multiplicative gain change.

Introduction

Gain modulation is a roughly multiplicative or divisive change in a neuron's tuning curve to one stimulus parameter as some other parameter or state is modified. Such gain changes are frequently observed in the responses of cortical neurons, and are thought to play an important role in neural computations (reviewed in Salinas and Thier 2000). A number of factors have been shown to influence the gain of cortical neurons, including eye position(Andersen and Mountcastle 1983, Boussaoud et al. 1993) and attention(McAdams and Maunsell 1999, Treue and Martinez Trujillo 1999). Gain modulation can also be induced pharmacologically: Fox et al. (1990) found that by iontophoretically applying NMDA to neurons in cat V1, they could increase the gain of the neuron's contrast response curve.

Despite the apparent importance of multiplicative gain modulation in the cortex, the mechanisms responsible for producing such gain changes are not well understood (but, see Chance et al. 2002, Fox and Daw 1992, Salinas and Abbott 1996). In particular, it has been concluded that simple excitation or inhibition alone cannot achieve a gain change (*e.g.* Chance et al. 2002, Holt and Koch 1997). Instead, it has recently been shown that concurrent, balanced increases in background excitation and inhibition together, which cause an increase in current noise and in conductance with no net depolarization or hyperpolarization, can serve to divisively decrease gain (Chance et al. 2002). These conclusions were based on examining the gain of the relationship between injected current and firing rate. However, multiplicative gain changes in cortex *in vivo* are observed in the relationship between a *stimulus parameter* and firing rate. Here we consider the non-linear relationship between stimulus parameter and injected current, as well as the non-linear relationship between injected current and firing rate. We show that multiplicative gain changes arise robustly from the simple addition of excitation or inhibition alone, provided the modulating excitation or inhibition is small relative to the peak of the tuning curve of the driving excitation. That is, the observed cortical gain changes can be induced if the modulating influence simply adds or subtracts excitation or inhibition.

An important part of our model is the large background synaptic conductances to which neurons are subject *in vivo*, which give rise to a noisy sub-threshold membrane potential (Anderson et al. 2000). A noisy sub-threshold membrane potential in turn gives rise to an expansive power law relationship between the average membrane potential and the firing rate of a neuron (Hansel and van Vreeswijk 2002, Miller and Troyer 2002). This non-linear relationship between voltage, or input current, and firing rate, along with the non-linear relationship between stimulus parameter and input current, together cause excitation or inhibition alone to yield roughly multiplicative gain changes in neuronal responses. We demonstrate this using both simulations of an integrate-and-fire model neuron and a simple analytical model.

Model

We use two models to study the effects of inhibition and excitation on the gain of visual cortical neurons. The first is a conductance-based integrate-and-fire model neuron. Its input includes noise conductances designed to match voltage noise observed *in vivo* (Anderson et al. 2000), which make the RMS voltage noise about 5 mV. The second is a simplified analytical model of the neuron that qualitatively reproduces the results of the numerical simulations very well.

We assume that our integrate-and-fire model neuron receives a stimulus-driven excitatory Poisson input. The rate of this input is a function of a stimulus parameter, and it is designed to model synaptic input from an earlier stage of visual processing. By varying the stimulus parameter, and therefore the rate of the stimulus-driven input, we construct a plot of stimulus parameter versus the response of the model neuron. We then study how the gain of the model neuron's response to the stimulus is altered by additional excitation or inhibition in the form of glutamate or GABA receptor binding drugs, direct injected current, or an additional Poisson input. The application of drugs binding to glutamate or GABA receptors is modeled by opening a constant conductance of the appropriate type.

An intuitive understanding of the numerical results can be gained by considering a simple analytical model of the neuron. We express the neuron's state in terms of the *shadow voltage*, defined to be the voltage the neuron would have if it did not spike or undergo post-spike voltage resets. The effect of the voltage noise in the model neuron is to make the neuron's firing rate depend on its mean shadow voltage as a power law (Hansel and van Vreeswijk 2002, Miller and Troyer 2002). Using this power law relationship, and the fact that the shadow voltage is linear in the mean input, we derive an expression for the gain of the neuron in terms of both its stimulus-driven input and any modulatory excitation or inhibition.

Results

We show that a cortical neuron that adds its inputs at the level of voltages, but raises this net input to a power significantly greater than one to produce an output, can effectively compute a multiplication of the inputs (or more strictly, of functions of the inputs: the output R is given by $R \approx f(i_1)g(i_2)$ where i_1 and i_2 are the inputs and f and g are some functions). Furthermore if the input voltages are nonlinear functions of a stimulus parameter, then this multiplication will not produce a mere left- or right-shift of the curve of output vs. parameter. Multiplication computed in this manner is only approximate. The approximation is accurate, though small systematic differences remain (which agree with small differences seen physiologically), when one of the inputs is substantially smaller than the other over the range in which the larger input produces a substantial response.

Conclusion

Given some assumptions about the common properties of cortical neurons, specifically the non-linear ways that their input firing rates depend on the properties of a stimulus and their output firing rates depend on their input, we have shown that it should be expected that a smaller input will multiplicatively modulate the gain of the response to a larger input. While other mechanisms may of course also play a role in experimentally observed gain changes, we are proposing that multiplicative gain changes are a normal property of the cortex, the natural outcome of these simple attributes of cortical neurons.

References

Andersen R and Mountcastle V (1983) The influence of the angle of gaze upon the excitability of the light-sensitive neurons of the posterior parietal cortex. *J Neurosci* , 3:532–48.

Anderson JS, Lampl I, Gillespie D, and Ferster D (2000) The contribution of noise to contrast invariance of orientation tuning in cat visual cortex. *Science*, 290:1968–1972.

Boussaoud D, Barth T, and Wise S (1993) Effects of gaze on apparent visual responses of frontal cortex neurons. *Exp Brain Res* , 93:423–34.

Chance F, Abbott L, and A.D. R (2002) Gain modulation from background synaptic input. *Neuron*, 35:773–782.

Fox K and Daw N (1992) A model for the action of NMDA conductances in the visual cortex. *Neural Comput* , 4:59–83.

Fox K, Sato H, and Daw N (1990) The effect of varying stimulus intensity on NMDA-receptor activity in cat visual cortex. *J Neurophysiol* , 64:1413–1428.

Hansel D and van Vreeswijk C (2002) How noise contributes to contrast invariance of orientation tuning in cat visual cortex. *J Neurosci* , 22:5118–5128.

Holt GR and Koch C (1997) Shunting inhibition does not have a divisive effect on firing rates. *Neural Comput* , 9:1001–1013.

McAdams C and Maunsell J (1999) Effects of attention on orientation-tuning functions of single neurons in macaque cortical area v4. *J Neurosci* , 19:431–41.

Miller KD and Troyer TW (2002) Neural noise can explain expansive, power-law nonlinearities in neural response functions. *J Neurophysiol* , 87:653–659.

Salinas E and Abbott L (1996) A model of multiplicative neural responses in parietal cortex. *Proc Nat Acad Sci USA*, 93:11956–61.

Salinas E and Thier P (2000) Gain modulation: a major computational principle of the central nervous system. *Neuron*, 27:15–21.

Treue S and Martinez Trujillo J (1999) Feature-based attention influences motion processing gain in macaque visual cortex. *Nature*, 399:575–9.