

The V1 Population Gains Normalization

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In this issue of *Neuron*, Busse et al. describe the population response to superimposed visual stimuli while Sit et al. examine the spatiotemporal evolution of cortical activation in response to small visual stimuli. Surprisingly, these two studies of V1 report that a single gain control model accounts for their results.

Orientation selectivity is the hallmark of the primary visual cortex (V1). When this property was discovered more than 40 years ago by Hubel and Wiesel, it was thought that the selectivity of cortical cells results only from the organization of feedforward inputs from the visual thalamus. Today we know that the response of cortical cells might be strongly affected by inputs from the entire visual field.

Hubel and Wiesel showed that in V1 cells, the response evoked by lines or bars at specific angles (orientation) is much greater than the response to circular spots of light (Hubel and Wiesel, 1962). However, the first-order cortical neurons that display this property (simple cells) receive their afferent inputs from neurons of the lateral geniculate nucleus (LGN) of the thalamus, which are not orientation selective. How then can this behavior be explained? Hubel and Wiesel suggested a simple model in which simple cells receive feedforward inputs from several LGN neurons with aligned receptive fields. When stimulated by an elongated stimulus, aligned with the collective receptive field structure of these thalamic cells, they are activated simultaneously, causing a large response in simple cells.

Although many predictions of this feedforward model were confirmed experimentally, other predictions failed. One major discrepancy is the observation that the width of orientation tuning curves in V1 is independent of the stimulus contrast (Sclar and Freeman, 1982), a phenomenon called contrast invariance. Since the firing of geniculate cells increases monotonically with contrast, the feedforward model predicts that as contrast is increased, stimuli further away from the preferred orientation will evoke sufficient depolarization to cause firing. Thus, the tuning

curve of V1 neurons is expected to widen when contrast increases (Ferster and Miller, 2000).

Another experimental observation not explained by the simple feedforward model is the strong suppression of responses to a stimulus at the preferred orientation by an orthogonal stimulus, even if the orthogonal stimulus by itself evokes no response (Priebe and Ferster, 2006). The feedforward model predicts that the response to a combination of stimuli is merely the sum of the responses to each individual stimulus.

Subsequently, new models were proposed to account for the experimental findings described above. Roughly, they can be described as belonging to two categories: feedforward models extending the original model of Hubel and Wiesel, and models incorporating feedback inputs. Normalization models, also known as contrast gain control models (Albrecht and Geisler, 1991; Heeger, 1992), belong to the first category. In these models, two pathways determine the response of a cortical neuron. One is a specific filter defined by the neuron's selectivity to the stimulus, as in the feedforward model of Hubel and Wiesel. The second pathway integrates less selective inputs from a wider visual field, and serves as a normalization background. That is, the response of the cell is a result of dividing the input from the first pathway by the input via the second (gain control) pathway (Figure 1). At the level of single cells, contrast gain control models were found to be successful in explaining several key features of visual processing, in particular contrast invariance and cross-orientation suppression.

Visual information, however, is represented by the joint activity of many neurons. Population models of V1 have relied

mostly on data gathered from single neurons, yet neural populations may display qualitatively different behaviors than the units that comprise them. For example, a population of contrast invariant neurons may not be contrast invariant in itself (see below). Therefore, it is not clear whether the aforementioned models, developed to describe the responses of single neurons, can be successfully applied to neuronal populations.

A study by Busse et al. (2009) in this issue of *Neuron* efficiently addresses this question, using multielectrode arrays to record from many neurons in cat V1. Busse and colleagues characterized the tuning curves of multiple simultaneously recorded neurons, and examined how their responses to a superposition of two oriented stimuli sum together. The population response was defined as the average firing rate of neurons grouped according to their preferred orientation. Interestingly, the authors found that a simple normalization model can account for their results.

Initially Busse and her colleagues verified that the population response is contrast invariant and therefore a simple normalization model, composed of a product of a tuning curve and a contrast gain function, may be applied to the population response. How can a population response not exhibit contrast invariance when single neurons are known to be contrast invariant? Consider, for example, a population in which sharply tuned neurons have high contrast thresholds whereas widely tuned cells have low thresholds. In such a population, as contrast is increased, more sharply tuned neurons are recruited, resulting in a sharpening of the population tuning curve. However, the authors find that contrast sensitivity and tuning width are

independent of each other in the population, giving rise to contrast invariant orientation tuning at the population level.

To investigate V1 population responses to more complex stimuli, cats were presented with a sum of two oriented gratings (a plaid), where the contrast of each grating was varied separately. The authors found that the population responses to a combination of stimuli can range from equal weight summation of the responses to the individual stimuli, to a winner-take-all regime in which only one stimulus is represented while the other is virtually ignored. The factor that determines how the responses are summed is the contrast of the respective stimuli. For similar contrast values, an equal weight summation takes place, whereas for large differences in contrast only the response to the high contrast grating is retained. What model can account for this wide range of weight combinations?

Busse, Wade, and Carandini demonstrate that a normalization model for single neurons can be adapted to describe the population response. In this model responses are nonlinearly scaled by their contrast, summed, and then normalized (divided) by the overall contrast of both stimuli. Dividing by the overall constant results in suppression among concurrent stimuli. The nonlinear scaling with contrast results in equal weight summation in the case of similar contrast but amplifies the difference when dissimilar contrasts are used, leading to winner-take-all competition. Thus, the model captures cross-stimulation suppression, and the smooth transition between equal weight summation and winner-take-all, without requiring a change in assigned weights for different stimuli.

Is the normalization performed by V1 cells, or is it already present in the subthreshold input to these neurons? Busse and colleagues found that the normalization model provides a good fit to the average local field potential (LFP) responses of the entire population to plaid stimuli, suggesting that population subthreshold activity in V1 neurons can be described by the same normalization model.

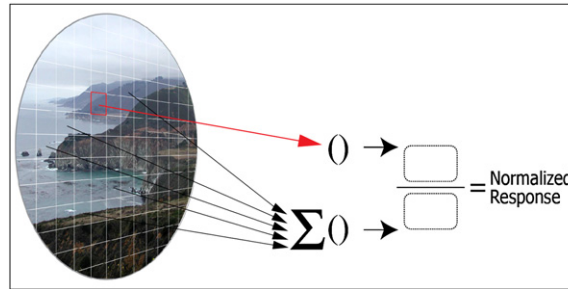


Figure 1. The Normalization Model for Visual Processing

The response of a cortical neuron to visual stimulation is determined by two pathways: (1) excitatory input from its classic receptive field (red), and (2) a gain control component, modulated by a wider range of visual inputs (black). The overall response is determined by the quotient of the two components (each component is also subject to some nonlinearities, not shown here for simplicity).

A second study in this issue of *Neuron*, by Sit et al. (2009), supports Busse and colleagues' finding that population normalization operates already at the subthreshold potential range of upper cortical layers. The authors of this study investigated the responses of V1 neurons to small oriented stimuli in awake monkeys using voltage sensitive dye imaging (VSDI), which reflects changes in membrane potential (Grinvald and Hildesheim, 2004), and examined their spatiotemporal evolution. In spite of the vast difference in methods used in the two studies, Sit and colleagues report that a closely related model accounts for their experimental results.

Previous studies in primate V1 showed cortical activation far beyond the retinotopic mapping of the stimulus (Grinvald et al., 1994). This wide spatial activation is commonly attributed to a spread of activity via lateral connections among cortical neurons. The present study suggests that this may not be the case. Sit and colleagues show that the latency of subthreshold responses of V1 cells, as measured by the VSDI signal, is constant regardless of the distance from the retinotopic center of activation. This result does not agree with the model of lateral propagation, because this model predicts that the latency should increase with distance due to synaptic delays.

A natural candidate to account for the constant latency is the classic feedforward model. If the activation observed using VSDI is due to feedforward connections, then clearly we would expect no

difference in latency. However, further results dismiss the feedforward model. Specifically, the authors find that the area and spatial profile of cortical activation are invariant to contrast. The classic feedforward model predicts that an activation spatial profile will grow wider as contrast is increased, and thus cannot explain the data.

Finally, Sit et al. explore a population gain control model. In their two-stage model, each neuron receives feedforward excitation from neurons in its receptive field pool. In addition, its conductance is modulated by neurons in a normalization pool that

in particular contains the receptive field of the neuron. Increased activity in the normalization pool results in higher conductance in its target neurons and therefore has two major effects on their response: the amplitude is decreased and the time constant is reduced, leading to faster dynamics. The feedforward connectivity explains the constant latency of responses across the entire active region, while the normalization, or gain control, accounts for the invariant profile of spatial spread when contrast varies. The increase in conductance accounts for another experimental observation—the slope of activation increases with proximity to the activation center. In the model, higher conductance for units positioned near the response center, due to higher activity in their normalization pool, reduces their time constant and increases the slope.

Importantly, because the spiking latency depends on the slope of activation, the finding that subthreshold response latency, captured by the VSDI, is independent of the distance from the center of activation region might not be observed via spike measurements. Hence, the use of VSDI reveals an important property of cortical response that proved essential for the conclusions of Sit et al.

Although both studies provide compelling support for contrast gain control in visual processing, it is not immediately clear how the models presented in the two studies are related. Hence, it is worth noting that the conductance model on which the two-layer circuit of Sit et al. is

based was proposed as a possible biophysically plausible implementation of a normalization operation (Carandini and Heeger, 1994), such as the one in Busse et al.

What biophysical mechanisms may be responsible for divisive gain control? Different studies have addressed this question. One candidate mechanism is short-term synaptic depression (Freeman et al., 2002). Widely tuned, visually evoked cortical shunting inhibition may also contribute to contrast normalization. However, intracellular recording studies in vivo of inhibitory tuning curve profiles and changes in evoked conductance in response to plaid stimuli (Priebe and Ferster, 2008) found no support for this view.

Divisive gain control might support higher-level aspects of visual processing beyond the responses of V1 neurons to relatively simple stimuli. Some studies debate the role of normalization in redundancy reduction and efficient coding (Schwartz and Simoncelli, 2001; Shi et al., 2006), while others suggest that

changes in visual processing (sensitivity, gain, etc.) induced by shifts in attention may be explained by a modulation of the input signal by an attentional filter followed by normalization (Reynolds and Heeger, 2009).

Clearly, the functional implications of contrast gain control for downstream visual areas and the contribution of different biophysical mechanisms to its implementation are still open questions. Hopefully, further research and analysis of how large populations process complex stimuli may shed light on these issues.

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Discreet Charm of the GABAergic Bourgeoisie: Superconnected Cells Conduct Developmental Symphonies

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In an exciting study in the December 4th issue of *Science*, Bonifazi and colleagues demonstrated the existence and importance of exceedingly rare but unusually richly connected cells in the developing hippocampus. Manipulating the activity of single GABAergic hub cells modulated network activity patterns, demonstrating their importance for coordinating synchronous activity.

Much to the chagrin of our latte-drinking, sushi-eating, Volvo-driving liberal friends all over, networks in the real world are decidedly not egalitarian but rather aristocratic in nature. Indeed, the disproportionate influence of rare superconnected hubs is well-known in technological, biological, and social networks, including

aviation grids (such as LAX and JFK), biochemical reaction pathways (such as pyruvate and ATP), and the proverbial old boys' networks. For neuroscience in particular, hub-like connectors are considered to be of great potential significance because networks with such aristocratic flavor have been predicted

by theoretical studies to represent a clever compromise between fast computation, economy of wiring, and robustness against random deletions (Buzsáki et al., 2004; Bullmore and Sporns, 2009). However, while we have thoroughly defined neuronal networks lacking superconnected neurons (such as that of