demonstration that a glial-expressed factor can directly modulate behavioral output in animals. Future incisive studies like this one will undoubtedly teach us that glia are tightly integrated into many such complex brain functions.

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The Inner Life of Bursts

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In the thalamus, bursts and single spikes are elicited by distinct visual stimuli, suggesting distinct visual functions. In this issue of *Neuron*, Wang et al. make use of intracellular recordings of thalamic neurons in vivo to provide a clear, detailed explanation of how natural stimuli are converted into a neural code that uses both bursts and single spikes.

> What we observe is not nature itself, but nature exposed to our method of questioning.
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> —Werner Heisenberg, 1958

In the course of scientific inquiry, we are often forced to rely on impoverished, indirect observations to laboriously piece together a picture of underlying mechanisms consistent with these observations. Occasionally, we have the great pleasure of peering behind the veil and glimpsing the inner workings at the level below. This is particularly satisfying when a simple, coherent picture emerges, as is the case in the data of Wang et al., in this issue of *Neuron*. This is a beautiful study in which a question of wide interest has been definitively answered: what are the subthreshold currents underlying visually evoked thalamic bursts? This could only be answered by technically challenging experiments of which few laboratories are capable.

Visual signals from the retina pass through the thalamus on the way to cortex. In the last few years, substantial support has accumulated for the hypothesis that thalamic bursts play a key role in sensory information processing, especially for natural scenes. In the earliest recordings from the visual thalamus, a distinctive recurring burst pattern of action potentials was noted. On the basis of in vitro experiments, these bursts were later attributed to a specific ionic conductance, the T current or low-threshold calcium current, I_t. What makes this interesting is that this current is voltage gated: it is inactivated when cells are depolarized, and deinactivated only after sufficiently deep and prolonged hyperpolarization. Thus, if a thalamic cell is relatively close to threshold, the channel remains inactive, and the cell will relay one sensory input spike by one output spike. If the same thalamic cell is resting further from threshold, a sensory input spike may fail to be relayed at all. But if that cell has been quite hyperpolarized, such that the calcium channel has become active, then a sensory input spike can trigger a large calcium influx resulting in a stereotyped burst of spikes. In this way, sensory information from the retina could be faithfully rendered, blocked, or enhanced, depending on the previous membrane voltage of the relay cell. The thalamus could in theory use this mechanism to integrate sensory and

other cues to selectively gate sensory transmission. Interest in this hypothesis has driven research to determine the role of bursts in visual information transmission.

There are two distinct questions to ask about the origin of bursts in a neural response: first, what mechanisms produce the prolonged hyperpolarization that deinactivates or *primes* the calcium channels? And second, once the cell is in the primed state, what depolarizing mechanisms *trigger* the subsequent burst of spikes? During sleep, intrinsic and circuit properties in the thalamus prime and trigger bursts in a rhythmic and synchronous pattern uncoupled from visual input. But during visual stimulation, extracellular data have revealed that the bursts are not rhythmic or synchronous and instead occur at stimulus-locked times (Guido et al., 1995; Reinagel et al., 1999). From this we know that bursts can be visually triggered and thereby constitute part of the visual signal to the brain.

Even though bursts are visually triggered, the priming of the calcium channels could be controlled by nonvisual inputs to the cell, and in that sense, bursting could lack any visual significance. There are several lines of evidence, however, that ongoing visual inputs determine which visually triggered responses will be bursts. Bursts occur at reproducible times in responses to flickering or naturalistic stimuli (Denning and Reinagel, 2005; Lesica and Stanley, 2004). From this we can infer that visual inputs, either feedforward from the retina or feedback from the perigeniculate and visual cortex, must largely control the priming of the channels. Specifically, bursts are triggered by excitatory stimuli that are immediately preceded by inhibitory stimuli (Alitto et al., 2005; Lesica and Stanley, 2004). This pattern is consistent with the idea that bursts occur only after inhibitory visual stimuli hyperpolarize the cell and prime the channel. The functional implication is that bursts indicate surprise: a burst means an excitatory stimulus appeared where there had not been any recently.

Thus, based on rather complicated analysis of extracellular data and reasoning from biophysics, it had been inferred that natural stimuli evoke prolonged epochs of strong hyperpolarization which deinactivate the calcium channels prior to reliably evoked bursts (Lesica et al., 2006). It was not possible to predict whether this hyperpolarization is caused by a lack of recent excitation or an excess of recent inhibition, whether it depends on center-surround antagonism in the receptive field, or whether feedforward or feedback circuits were involved. These questions can be answered only by intracellular recordings, from which it is possible to isolate and separately analyze the subthreshold excitatory and inhibitory postsynaptic potentials (EPSPs and IPSPs) underlying neural responses. In this issue of *Neuron*, Wang and colleagues report the results of these heroic experiments (Wang et al., 2007).

First, Wang and colleagues use intracellular data to show that the center-surround antagonism of thalamic receptive fields is driven by a ''push-pull'' arrangement of synaptic inputs. For example, an ON cell receives synaptic excitation from light in its receptive field center, and synaptic inhibition from light in the surround; but it also receives inhibition from dark stimuli in its center, and excitation from dark stimuli in its surround. A simple feedforward circuit nicely accounts for these data.

Then, using a sophisticated analysis to isolate inhibitory and excitatory components and to compensate for the spatiotemporal correlations in natural scenes, the authors go on to derive a spatial map of the synaptic inputs that precede spikes and bursts during natural movies. The data reveal that certain sequences in natural movies reliably evoke strong feedforward inhibition to the receptive field center, priming the burst mechanism. Subsequent retinal excitatory input to the receptive field center then triggers a calcium spike, resulting in a burst of action potentials. A predictive model demonstrated that these effects are sufficient to predict the reliable production of bursts at specific times in natural movie sequences, even without invoking surround antagonism or inhibition through feedback pathways.

To appreciate the elegance of these experiments, it must be remembered that almost every other study in this field has inferred putative low-threshold calcium spikes on the basis of interspike interval criteria from extracellular recordings. Although this was once validated for one stimulus set, this is a highly indirect method with many caveats. For many stimuli it may be difficult or impossible to distinguish true low-threshold calcium bursts from similar patterns resulting from faithful one-to-one relay of retinal spikes. In this paper (Wang et al., 2007), the authors replicate the same preparation (anesthetized cat), same types of visual stimuli (such as natural movies), and same analysis methods (such as spatio-temporal receptive field mapping) that have been used in the literature to demonstrate visual roles of bursts. Under these conditions, the authors used intracellular recording to observe subthreshold activity in thalamic neurons. By this means they are able to observe T currents and confirm the conclusions in the literature that were previously resting on indirect inferences. With these hard-won data, a major caveat of the existing literature has been put to rest.

Of course many questions remain. The synaptic mechanisms by which downstream neurons decode the information represented by bursts are of obvious interest. The most important limitation of these experiments (like most experiments in the field) is that recordings were obtained from anesthetized animals. It is generally agreed that anesthesia increases the overall frequency of bursts, leading some to worry that bursts may not occur often enough when animals are awake to contribute significantly to visual coding. Several recent studies have reported recordings from the thalamus in alert animals (Bezdudnaya et al., 2006; Guido and Weyand, 1995; Ramcharan et al., 2000; Ruiz et al., 2006; Swadlow and Gusev, 2001; Weyand et al., 2001), but there is still no consensus as to the frequency or properties of bursts in alert animals. Although some studies have failed to observe bursts in alert animals, none of these have replicated the sensory conditions or

computational analysis under which bursts have been found and studied in anesthetized animals. Such an experiment could definitively validate—or invalidate—the accumulated evidence that bursts are important in the visual code. Moreover, recordings in alert animals might uncover additional mechanisms influencing bursting, such as cortical feedback, which may not be strongly engaged under anesthesia.

It is increasingly clear that sensory information is not just relayed, but also processed and transformed at the level of the thalamus. Natural sensory stimuli have been an important experimental tool for uncovering these functions, as exemplified by a study of adaptation in the thalamus also presented in this issue (Lesica et al., 2007). Most sensory modalities have analogous relay stations in the thalamus with similar biophysical and circuit properties, and higher-order thalamic nuclei are hubs for trafficking information between cortical processing areas (Sherman, 2005). The consequence of bursting for the flow of information is thus a fundamental question with broad implications for understanding how the mammalian brain works.

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Appearance Isn't Everything: News on Object Representation in Cortex

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How objects are represented in the visual system is one of the big questions in cognitive neuroscience. In this issue of *Neuron*, Mahon and colleagues present an intriguing study that suggests that properties of objects other than shape can influence the arrangement of object selectivities in visual areas. In the process, the study also points to important caveats regarding the ability of standard fMRI studies to make inferences about neuronal selectivity.

Object recognition is mediated by the so-called ventral visual stream in cortex, in which neuronal tuning specificity and invariance (e.g., to stimulus translation) is gradually built up in a hierarchy of brain areas from primary visual cortex (V1) to inferotemporal/ventral temporal cortex. Monkey electrophysiology studies have shown that a common organizing principle in this and other pathways in cortex appears to be that nearby neurons respond to similar stimuli (such as similarly oriented stimuli in V1), providing experimental support for theoretical models that have argued that arranging neuronal tuning preferences based on physical similarity facilitates local computations in an underlying stimulus parameter space. Another advantage of this mapping principle for hierarchical processing is that it leads to localized, "sparse" codes in which individual objects are represented by activation patterns over confined subpopulations of neurons, producing an efficient representation for downstream processing.

Much recent research and debate has focused on the mapping of