However, it is puzzling that the activation of the underlying GABAergic granule cells leads to such changes. Future studies using genetic methods that label a specific subset of neurons or stimulate them by light-gated ion channels will help describe the local neural circuitry in detail.

Interbulbar circuit formation is an intriguing issue in developmental neurobiology. Recent studies have shed light on the molecular basis of olfactory map formation in the OB: OR-derived cAMP signals direct the axonal projection of OSNs by regulating the gene expression of axon guidance/sorting molecules (reviewed by Imai and Sakano, 2007). Spontaneous signaling from ORs, rather than odor-evoked activity, appears to be important in mammalian OSN projection, whereas the intrabulbar projection of external tufted cells is highly dependent on neuronal activity (Marks et al., 2006). Although the intrabulbar connection is monosynaptic, the interbulbar circuit described in the present study is disynaptic, which may require more complicated processing during development. The commissural fibers play an important role in exchanging higher-order information between hemispheres, and studies on the interbulbar circuitry will provide new insights into the molecular mechanisms of the precise wiring between hemispheres.

Another issue raised in the present study is the interhemispheric exchange of olfactory information. The reported failure of interhemispheric communication in the behavioral experiments on the AONpE-lesioned mice may be due to the inability to either "form" the memory or to "transfer" it to the contralateral hemisphere. Alternatively, it may be due to the deficit of the "recall" of memory stored in the contralateral hemisphere. These possibilities are not mutually exclusive and can be dissected and tested with genetic tools to silence the AON in a reversible manner. It is still not well understood where and how olfactory memory is stored and what kinds of neuronal activities lead to learning and recall of olfactory information. The interbulbar circuitry described in the present study will continue to serve as an excellent tool for the study of olfactory memory.

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Au Naturel

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Although adaptation is a ubiquitous property of neurons in the early visual pathway, the functional consequences in the natural visual environment are unknown. In this issue of *Neuron*, Mante et al. show, through a comprehensive set of in vivo experiments in the visual thalamus, that the basic functional mechanisms of adaptation that have been well studied with artificial probes capture the neuronal response in the natural environment and are predictable from properties of the visual scene that may be represented by local neural ensembles.

Nature does nothing uselessly.
—Aristotle, 384–322 BC

It is this compelling idea that has driven neuroscientists for decades to ponder the evolution, development, and function of the brain in the context of the natural environment within which we exist. Simply put, to understand the brain, we cannot ignore our surroundings. Although the key to the mysteries of the endless complexity of the anatomy and function may indeed lie at the interface between the individual and the world, scientific exploration of the brain from this perspective is a vexing task. The idea does not lend itself well to carefully controlled experiments that normally constitute scientific investigation. Nevertheless, confronting this issue may help us move from *what can the brain do?* to *what does the brain*

do? and *why?* In this issue of *Neuron*, Mante et al. bring this perspective to the role of adaptation of the early mammalian visual system in the natural visual environment (Mante et al., 2008).

Although the idea of exploring the visual pathway of the brain with naturalistic visual scenes is not a new one (Creutzfeldt and Nothdurft, 1978), there has been a resurgence of debate within the vision community regarding the use of more naturalistic visual stimuli, as compared to more traditional classes of visual probes (Rust and Movshon, 2005). Although it may superficially seem that researchers pursuing these questions stand on either side of this divide, upon closer inspection it is clear that there is much more consensus than dissent. We all want to understand the sensory pathways in the most ethologically relevant context. The question is how to go about doing so. Beyond the as yet unanswered question as to what constitutes a natural visual scene (or perhaps what does not), two primary problems plague the use of naturalistic scenes in studying the visual pathway. The first one is scientific: natural visual scenes are complex. Although the ubiquitous spatial and temporal correlation structure of natural scenes hinders this line of investigation, it is the sudden, abrupt changes in luminance and contrast that make this problem truly difficult. As objects of varying spatial scales move in and out of the visual field, there are dramatic changes in the distribution of light falling upon the retina (Figure 1), continuously invoking several well-documented, strongly nonlinear, mechanisms of adaptation that have been studied under more well-controlled, isolated conditions (Shapley and Victor, 1978; Shapley and Enroth-Cugell, 1984). The second problem is pragmatic: although challenging, it is important that we connect the foundations of our functional understanding of the visual pathway, which have been built through decades of research utilizing more artificial probes, to the natural visual environment. Doing so would not be the challenging feat that it is, if the natural visual environment were constituted from simple linear combinations of sinusoidal gratings and if the early visual system were linear, neither of which are the case.

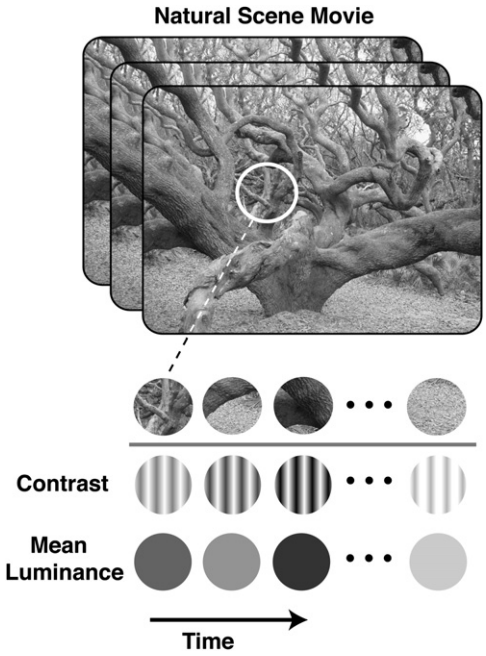

Figure 1. The Nonstationary Statistics of the Natural Visual World

Objects of different spatial scales move in and out of our visual field, due to both self-generated body/eye movement and movement of objects in the physical world. As a result, within a local visual field, outlined in white, the luminance properties vary continuously over time (top row). Changes in contrast (middle row) and mean luminance (bottom row) have been shown to invoke various forms of adaptation at multiple levels of the early visual pathway. How might we relate neural activity in the natural visual environment to what we have learned from conventional probes of the early visual pathway?

Mante and colleagues have directly attacked the above issues, providing a long-needed bridge between the two stimulus worlds (Mante et al., 2008). Through a combination of in vivo electrophysiological recordings in the visual thalamus and functional modeling based on artificial visual stimuli, they generate a model of neural encoding that generalizes to track the response to nonstationary natural visual scenes. Specifically, they constructed a set of functional models using sinusoidal spatial gratings at a range of different mean luminances and contrasts (see Mante et al., 2005). The linear spatiotemporal encoding properties of the model were shown to depend strongly on the stimulus statistics. The "set" of models was then connected by incorporating conductance-based mechanisms that directly shape the linear encoding properties. Through the modification of two conductance parameters linked to luminance and contrast adaptation, the entire range of functional behaviors was captured by a single model. Importantly, the conductance elements were then shown to be derivable from the local properties of the scene (see Bonin et al., 2005). Finally, the model proved to be highly predictive of the recorded responses to natural scene movies, even though it had been constructed from responses to sinusoidal gratings. The key element in predicting the natural scene response was the running computation of quantities capturing important aspects of the mean luminance and local contrast, which enabled the model to "track" the continuous changes in the statistical properties of the highly nonstationary natural scene through the presumed local ensemble neural activity.

What is a model? A model is a hypothetical description of a complex entity or process. Whether aware of it or not, we all use models in our daily lives to help us make decisions and guide our behavior. Otherwise, life is simply a set of observations, without the ability to generalize. The power in a model lies in the degree to which it generalizes. Because of the continuous variations in the statistical properties of the natural visual scene and the sensitivity of the various adaptation mechanisms of the visual pathway to these properties (Lesica et al., 2007), a fixed encoding model developed for a single level of mean luminance and contrast is quite limited relative to the natural environment. By creating an encoding model from a set of experiments involving sinusoidal gratings at different mean luminances and contrasts, and subsequently demonstrating that this model predicts the neuronal response to an entirely different class of visual stimuli based on the visual scene alone, Mante et al. have made this problem general and provided a powerful description of the encoding properties of the pathway. How good is the model? From a qualitative perspective, the model does an excellent job in capturing the episodic nature of the recorded

activity, missing only the details on relatively fine timescales. How do we assess this in a quantitative way? To be fair, the cells do not respond in the same way to repeated presentations of the same visual stimulus, and therefore only some aspects of how the cells respond are explainable from the stimulus. From this perspective, Mante et al. report being able to explain ~60% of the thalamic response that is explainable from the visual scene, as compared to a report of 40% from similar experiments in V1 (David and Gallant, 2005).

For anyone studying the brain, one thing is abundantly clear: neurons do what appears to be an endless list of interesting things. Indeed, scientific study of the brain often seems to be similar to digging a bottomless pit. Upon stepping back, however, an important question emerges: although sensory neurons exhibit a certain behavior that is experimentally repeatable, is it important for the transduction, transformation, and ultimate representation of the external world? How do we know whether capturing 60% of the explainable neural activity is good or bad? Although it may indeed be the case that nature does nothing needlessly, even for sensory neurons, the *needs* may include things other than sensory representation. For example, specific aspects of the neuronal response may be present due to the need to satisfy biophysical or anatomical constraints or due to pressures on metabolic efficiency. Therefore, to frame this issue in the context of communicating sensory information, we might, as an observer of neural activity, ask whether observation of specific aspects of the neural response somehow reduces our uncertainty of what is happening in the outside world. This perspective of decoding has been utilized for several decades (Bialek et al., 1991), and most recently even in human cortical response to natural scenes (Kay et al., 2008). In the study by Kay et al., a large set of natural images was presented to human subjects while monitoring fMRI signals in visual cortex. From a large-scale encoding model that predicts the voxel activity patterns in the fMRI data from the natural images, the identity of a novel image was inferred from the perspective of an observer of the pooled cortical activity. Ultimately, from this perspective, the success of the observer in inferring what is happening in the outside world depends strongly on how well the encoding model captures the relevant features of the visual scene. Of course, we can argue that without a clear map for understanding how the activity of populations of neurons in the sensory pathway is combined to create perception, our game as observer is futile. Nevertheless, this perspective forces us to examine our surroundings and ask questions *relative to the environment we live in*. Recent work in the visual thalamus has shown, through the perspective of an ideal observer, that the relevant timescale for the encoding (and decoding) of natural scenes is on the order of ~10 ms (Butts et al., 2007). The temporal scale over which Mante et al. actually capture the thalamic response, therefore, may be all that is necessary for representation of the natural scene.

So what's left? First, as Mante et al. readily admit, although the proposed model captures a considerable amount of detail in the neuronal response while maintaining relative simplicity, the underlying biophysical mechanisms that give rise to these phenomena are still elusive and are not explicitly part of the model. Recent in vitro work in the isolated retina, however, has been promising in identifying the underlying cellular mechanisms behind different forms of observed adaptation (Baccus and Meister, 2002; Beaudoin et al., 2007), although parallel in vivo work in the intact brain may prove to be a significant technical challenge. In addition, it is likely that what makes this problem particularly difficult as we work our way through the visual pathway is that a variety of different mechanisms give rise to qualitatively, if not quantitatively, similar function, making the source of any observed adaptation difficult to disentangle. Second, the thalamus likely plays a critical role in the transmission of visual information from the periphery to cortex and has been implicated in a number of different dynamic gating processes. Under strong influence originating from a variety of sources, including gross state-dependent neuromodulation and direct cortical feedback, the processing by the thalamic neurons is likely not influenced by properties of the visual scene alone. Finally, and perhaps most importantly, a more complete understanding of the neural code requires consideration of the representation of information not by a single neuron but, instead, across neuronal ensembles, which is undoubtedly important in the adaptation processes. The collective neural activity, and the relative timing of their signals to downstream cortical targets, establishes the foundation for the cortical neural code (Alonso et al., 1996) and thus must be part of any complete description of the neural representation of the natural visual world.

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