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Rapid Sensory Adaptation Redux: A Circuit Perspective

Clarissa J. Whitmire[1] and Garrett B. Stanley[1,*]
[1]Wallace H. Coulter Department of Biomedical Engineering, Georgia Institute of Technology and Emory University, Atlanta, GA 30332, USA
*Correspondence: garrett.stanley@bme.gatech.edu
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Adaptation is fundamental to life. All organisms adapt over timescales that span from evolution to generations and lifetimes to moment-by-moment interactions. The nervous system is particularly adept at rapidly adapting to change, and this in fact may be one of its fundamental principles of organization and function. Rapid forms of sensory adaptation have been well documented across all sensory modalities in a wide range of organisms, yet we do not have a comprehensive understanding of the adaptive cellular mechanisms that ultimately give rise to the corresponding percepts, due in part to the complexity of the circuitry. In this Perspective, we aim to build links between adaptation at multiple scales of neural circuitry by investigating the differential adaptation across brain regions and sub-regions and across specific cell types, for which the explosion of modern tools has just begun to enable. This investigation points to a set of challenges for the field to link functional observations to adaptive properties of the neural circuit that ultimately underlie percepts.

Introduction

To live is to adapt to the world around us. This is a notion so embedded in our way of thinking and our language that even though we all know it when we see it, it remains difficult to define precisely what adaptation means. On long timescales, species evolve to adapt characteristics that are favorable for survival. Adapt or die! On shorter timescales, individual organisms adapt behaviorally in response to changes in their environment, as, for example, an animal adapts their scavenging behavior to take advantage of a new food source when the previous one is suddenly no longer available. On even faster timescales, we are all familiar with our eyes adapting as we move from the bright sunlight to a dark room, or as we become accustomed to the sensation of clothing on our bodies, or as we quickly adapt our gait in response to a new pair of shoes. The binding agent among all of these different phenomena seems to be time—adaptation is a change in function that takes time to develop (be it fast or slow) and time to dissipate. Although it is certainly the case that these different notions of adaptation at disparate timescales arise from different mechanisms and engage different systems within our bodies, they collectively embody something profound that connects them: the ability of organisms to respond to changes in the environment.

On the timescale relevant for an individual organism, there are still many forms of adaptation, but none perhaps as well studied as rapid sensory adaptation of the nervous system, a ubiquitous property of all sensory pathways that has profound effects both perceptually and neurophysiologically (Figure 1). From a historical perspective, there is documented evidence of the perceptual effects of rapid sensory adaptation going back several centuries. For example, Aristotle observed in 350 BC a phenomenon that later came to be referred to as the visual "waterfall" illusion, with perceived visual motion of stationary objects following a fixed gaze on moving objects for just a few seconds. Over the last few decades, adaptation paradigms have been implemented in psychophysical studies to more precisely determine the extent to which persistent exposure to a sensory input affects our perception. For example, fundamental properties of the visual pathway include adaptation to visual contrast (Georgeson and Harris, 1984; Greenlee and Heitger, 1988), visual orientation (Blakemore and Campbell, 1969a, 1969b), visual motion (Anstis et al., 1998; Sekuler and Ganz, 1963; Wohlgemuth, 1911), and even complex visual features such as faces (Webster and MacLeod, 2011). For reviews of visual adaptation, see Clifford et al. (2007) and Kohn (2007). Although a very wide range of adaptive phenomena has been observed both psychophysically and neurophysiologically at the single-neuron level across different sensory pathways, until now we have not been in a position to pose questions in the context of circuits and networks to ultimately enable us to link these to behavior for a more holistic view of rapid sensory adaptation.

In this Perspective, we revisit this classical issue in sensory neuroscience and consider multiple levels of investigation into rapid sensory adaptation to build from intrinsic adaptive properties of a single neuron to adaptive properties within common circuit motifs (Figure 1). Specifically, we will ask (1) how we disambiguate adaptation effects occurring within a single neuron from those inherited presynaptically or generated locally in the context of the highly interconnected and detailed anatomy of our sensory pathways and (2) how differential adaptation of neurons by synapse type, cell type, or stimulus tuning develops the adaptive circuit properties observed, and if this is generalized across circuit motifs. Here, we seek to open these questions up in the context of the modern tools that are making it possible to dissect the function of complex circuits relevant for behavior, and to pose some questions related to how we as organisms navigate the dynamics of the world in which we live.

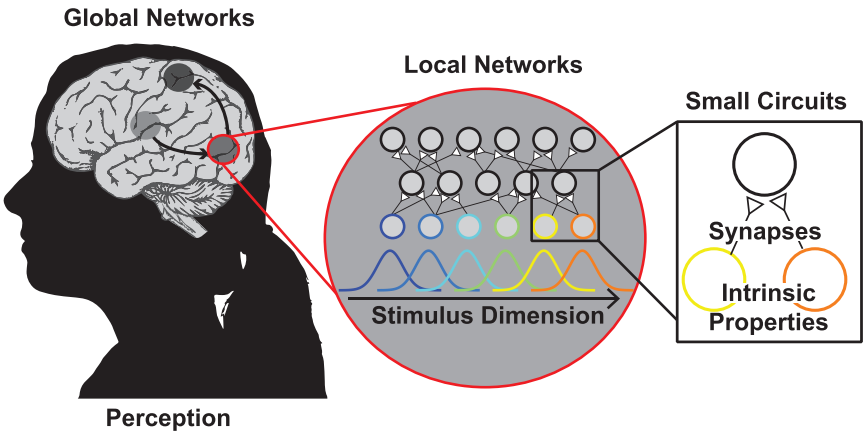

Figure 1. Concepts of Adaptation Span from Intrinsic Currents in a Single Neuron to the Perception of a Sensory Stimulus
Brain image edited from Livingstone, BIODIDAC.

Encoding Framework

While there is significant evidence that changes in neural function occur on longer timescales in response to changes in sensory environment and peripheral modification of the sensory organ (Buonomano and Merzenich, 1998; Gilbert, 1998; Karmarkar and Dan, 2006; Suga and Ma, 2003), our focus in this Perspective is the rapid sensory adaptation that occurs on the timescale of milliseconds to seconds that represents the ability of the pathway to dynamically adjust to the recent sensory environment. Despite extensive psychophysical investigation of many different rapid sensory adaptation phenomena, the underlying neural basis for most of these observations remains elusive even though neural signatures of the corresponding perceptual phenomena have been observed at multiple stages of processing across different sensory pathways.

Here we consider how the neural circuitry gives rise to these rapid adaptation effects in the context of a sensory encoding framework that relates the firing activity of individual neurons to the sensory stimulus driving them. Perhaps the simplest form of this encoding framework is a class of models that maps sensory inputs to observed neuronal activity, whose basic form has been widely applied in capturing coding properties of sensory pathways since the 1960s (de Boer and Kuyper, 1968; Eggermont et al., 1983), known as linear-nonlinear models (Schwartz et al., 2006; Simoncelli et al., 2004). In this two-stage model framework, the first stage can be envisioned to represent the aggregate synaptic input to the neuron in question, while the second stage represents the overall gain of the input-output relationship combined with some elements of spike generation. We might thus think of the first stage as representative of the synaptically driven feature selectivity or filtering of the neuron, and the second stage as an intrinsic property of the neuron (Figure 2A). Throughout this Perspective, we will use this model as a framework for describing how adaptation reshapes the encoding properties of the pathway. It is important to note that within the context of this framework, we define adaptation as a change in functional properties, be it through changes in synaptic feature selectivity and/or intrinsic neuronal properties. But this naturally begs the question as to what properties that we observe, if any, are static, instantaneous properties (e.g., tuning properties such as contrast sensitivity in the visual pathway), and which are dynamic due to adaptation (e.g., contrast adaptation in the visual pathway), as the tools we use to measure functional properties often require time averaging, which would obscure any adaptive process and likely change the very properties that we are attempting to measure.

Intrinsic Adaptation in a Single Neuron

What is the role of the individual neuron in adaptation? On timescales of tens of milliseconds, individual neurons exhibit intrinsic properties of rapid adaptation, such as spike frequency adaptation, that are independent of any network-level phenomenon. Spike frequency adaptation is a well-described component of neural activity that is present in nearly every neuron type, whereby the rate of spiking will decrease in response to constant synaptic input. There are multiple somatic currents that have been implicated in mediating spike frequency adaptation (Benda and Herz, 2003), including M-currents (Constanti and Brown, 1981), calcium-activated and sodium-activated potassium currents (Bhattacharjee and Kaczmarek, 2005; Lancaster and Nicoll, 1987; Sanchez-Vives et al., 2000), and slow recovery from the inactivation of sodium channels (Fleidervish et al., 1996), as well as dendritic activity-dependent effects such as reduced efficacy of distal inputs due to slow sodium channel de-inactivation (Häusser et al., 2000; Jung et al., 1997). An increase in the spiking threshold, possibly due to the slow recovery of sodium channels (Azouz and Gray, 2000; Toib et al., 1998), has also been identified as an intrinsic activity-dependent mechanism to induce spike frequency adaptation (Henze and Buzsáki, 2001; Pozzorini et al., 2013; Wilent and Contreras, 2005a). Each of these mechanisms allows a single neuron to modulate its firing rate in an activity- and cell-type-dependent manner (Mensi et al., 2012), and the effect is not subtle (for review of biophysical mechanisms that enable single-neuron computation, see Silver, 2010). These intrinsic adaptation properties have been observed across many different pathways and cell types.

A tantalizing hypothesis was asserted by Barlow in the 1960s that proposed that sensory pathways evolve and adapt to efficiently process information (Barlow, 1961). Without the ability to adapt to constant input, neurons would be fundamentally limited in the dynamic range of encoding that could be achieved.

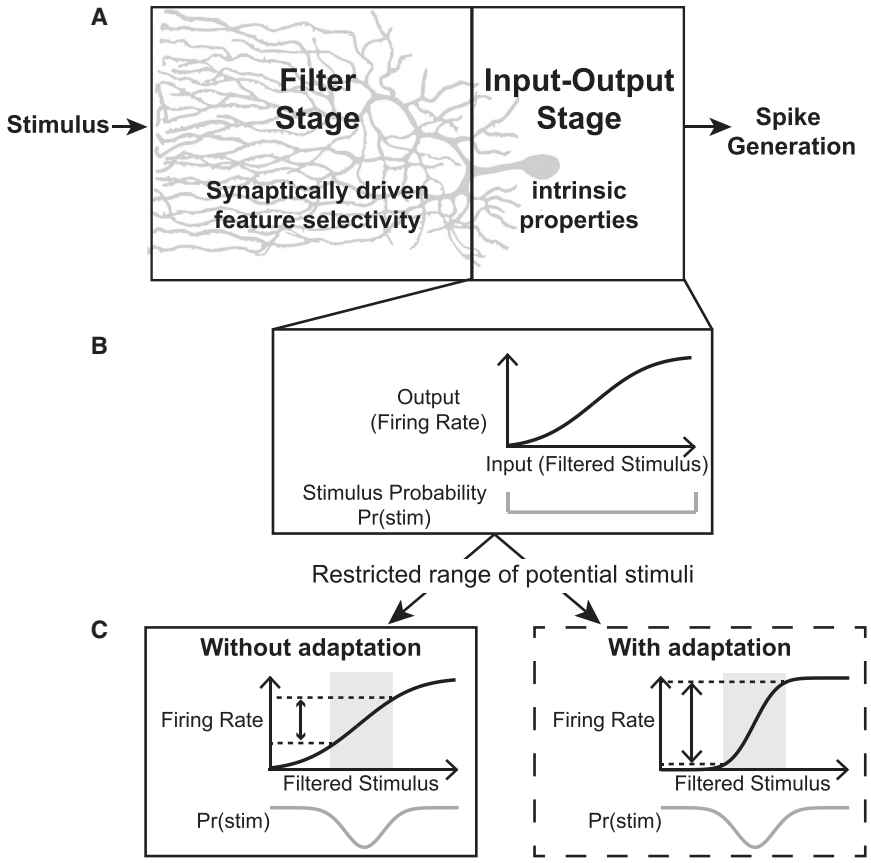

Figure 2. Intrinsic Adaptation Allows Rescaling of the Input-Output Function

(A) Sensory encoding models have classically described two stages of transformation from the sensory stimulus to the spike output. The first stage can be envisioned as a filter stage where the sensory stimulus is filtered by the feature selectivity of a given neuron. The second stage can be described as an input-output stage that transforms the filtered stimulus input into a firing rate output.

(B) A neuron has a finite amount of spikes that can be elicited in a given time window. If a neuron is tuned to encode a finite number of potential stimuli, the neuron could encode each input linearly such that there is a one-to-one mapping between the input and the output.

(C) Realistically, a neuron will not encounter every possible stimulus in a short time window, so the range of potential stimuli is likely restricted. Without adaptation, the input-output function for the neuron would not rescale, which would limit the dynamic range of the outputs (left, gray shading). With adaptation, the input-output function can be rescaled to shift the dynamic firing range of the neuron to the stimulus range that is likely (right, gray shading). Neuron image adapted from Ramon y Cajal, 1889 (RIKEN, 2014).

If the neuron did not display intrinsic adaptation, it would faithfully encode information in a fairly straightforward way, for the neural response would be unchanged regardless of stimulus input. However, because of the fixed gain, the stimulus intensity would be encoded only at a very coarse resolution, as quantified by the range of inputs captured by the input-output relationship. If we consider the information to be captured in the spike count or firing rate of the individual neurons over a short time window, each neuron is limited in the total number of inputs that it can differentially encode across the full input range (Figure 2B). If, however, the recent input range is restricted such that only a subset of potential stimuli is likely to be encountered, these non-adapting neurons cannot adjust and will continue to act as rigid look-up tables that are only able to encode a finite number of stimuli across a limited fixed range of firing rates (Figure 2C, left). In contrast, the ability of an individual neuron to adapt to constant input represents a fundamental capability of the neuron to dynamically shift its operating point and expand the dynamic range to accommodate a finer resolution of encoding over the relevant range (Figure 2C, right). This method of remapping the nonlinearity to match the input distribution, known as histogram equalization, maximizes the response entropy to optimize the encoding (Dayan and Abbott, 2001; Laughlin and Hardie, 1978).

Adaptive gain rescaling, or the dynamic rescaling of the input-output function to match the statistics of the input, has been demonstrated at multiple stages of processing across several sensory modalities (Fairhall et al., 2001; Maravall et al., 2007, 2013). Using in vitro recordings, adaptive gain rescaling can also be generated in response to current injection using only intrinsic properties of the neurons (Díaz-Quesada and Maravall, 2008; Mease et al., 2013). Furthermore, this rescaling is not instantaneous; the time course of gain rescaling is dependent on the duration of the stimulus (Fairhall et al., 2001). Intrinsic adaptation currents occur on multiple timescales (La Camera et al., 2006) that may serve to tune the timescale of adaptation to the input statistics (Lundstrom et al., 2008). In fact, it has been proposed that spike frequency adaptation employs temporal whitening whereby the output spikes of an individual neuron are decorrelated to improve information transmission within a single neuron (Huang et al., 2016; Pozzorini et al., 2013). While intrinsic adaptation can account for many of the adaptive properties described here, neurons obviously do not act in isolation but instead are embedded in a network. In highly interconnected neural circuitry, intrinsic adaptation properties of a single neuron will elicit widespread changes in information processing when interpreted in the context of network activity (Gjorgjieva et al., 2014). Observations of the coding properties associated with any individual recorded neuron indicate a potential compounding of the intrinsic cell properties of all cells feeding into the neuron in question combined with the adaptation effects occurring at the synapse between them.

Adaptation at the Chemical Synapse

Beyond the intrinsic properties of a single neuron, rapid adaptation has also been described in the context of a modulation of the

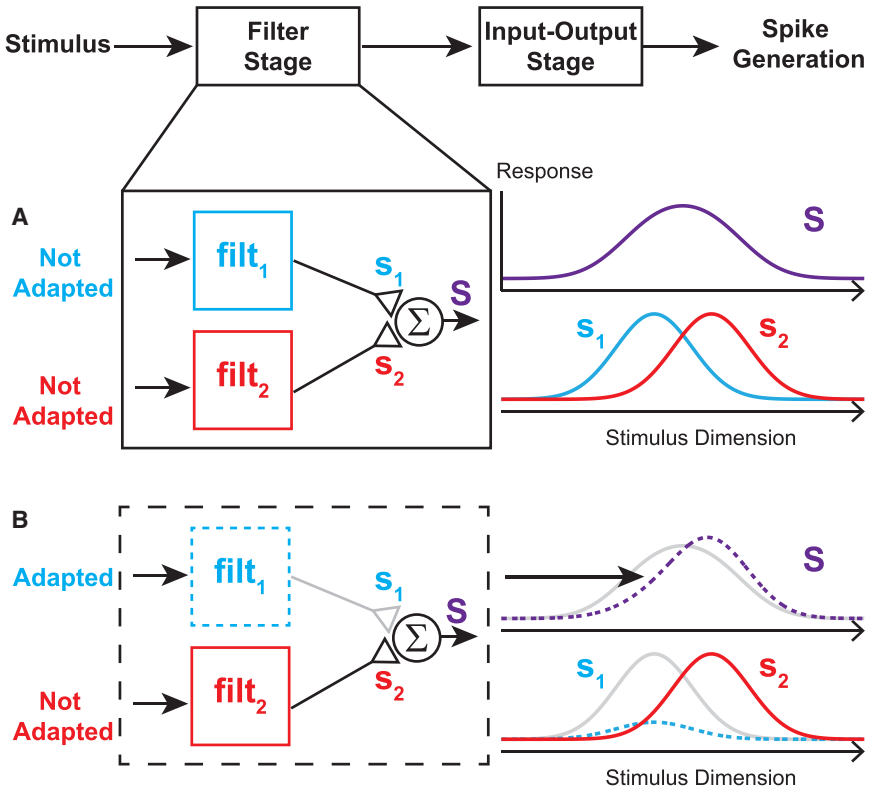

Figure 3. Synaptic Plasticity Dynamically Alters Feature Selectivity in an Input-Specific Manner

(A) The feature selectivity of a neuron is determined by its presynaptic inputs. In a simplistic scenario, the feature selectivity of a neuron (S, purple) could be the sum of the feature selectivity of its presynaptic inputs (s_1, s_2; blue, red, respectively).

(B) When the synaptic drive from one presynaptic population (s_1, dashed) is adapted, the synapse projecting downstream may become depressed (gray). The reduced drive from one synaptic input will cause the feature selectivity of the downstream cortical neuron to momentarily shift away from the adapted population (purple, dashed).

synaptic inputs to a measured neuron, captured as synaptic efficacy (Sen et al., 1996). Similar to intrinsic adaptation properties, rapid synaptic plasticity has been proposed as a potential neural mechanism to implement gain control (Abbott et al., 1997), as well as to decorrelate spike sequences (Goldman et al., 1999). However, in contrast to intrinsic adaptation effects of a single neuron that are indifferent to the input, rapid synaptic plasticity represents an input-specific change in the synaptic drive to a postsynaptic neuron (Chance and Abbott, 2001). Repeated spiking activity from a presynaptic neuron can lead to reduced or enhanced postsynaptic potentials depending on whether the synapse is depressing or facilitating. Paired-pulse studies have revealed that rapid synaptic depression, where increased presynaptic activity reduces the synaptic efficacy, persists for hundreds of milliseconds to seconds, while sustained stimulation can produce even longer lasting effects (Regehr, 2012). Short-term facilitation, where increased presynaptic activity enhances the synaptic efficacy, occurs on the timescale of tens to hundreds of milliseconds (Zucker and Regehr, 2002). In addition to chemical synaptic transmission, electrical synapses also show activity-dependent plasticity (Haas et al., 2016). In terms of nomenclature, note that changes in synaptic transmission have been described as a form of short-term plasticity, but it occurs on the same timescale as the activity-dependent adaptation effects we consider here, and thus is functionally tangled. Activity-dependent synaptic adaptation compounds the adaptive effects described for single-neuron input-output models by providing a mechanism to fundamentally alter the feature selectivity of neurons.

As information is transmitted from one neuron to the next, adaptive changes in synaptic transmission will directly impact the encoding in downstream neurons through modulation to the overall amplitude of the synaptic drive. Depression at the thalamocortical synapse has been implicated as a major contributing factor underlying the reduction in firing activity seen for cortical adaptation in the somatosensory pathway (Chung et al., 2002; Lundstrom et al., 2010), although it is certainly not the only contributing factor (Ganmor et al., 2010). In a simple hypothetical scenario, we can consider the effects of adaptive changes in the amplitude of sensory drive on the feature selectivity of a neuron that receives input from two distinct populations of presynaptic neurons (Figure 3A). If the sensory drive adapts only one population of these neurons such that the neurons are fatigued and the synapses are sufficiently depressed, the feature selectivity of the postsynaptic neuron will dynamically shift away from the tuning of the adapted presynaptic population (Figure 3B). With constantly ongoing and fluctuating sensory environments, the feature selectivity of neurons will rapidly shift in an activity-dependent manner. In the context of our simplified model framework introduced previously, even moderate selectivity in plasticity could fundamentally change the feature selectivity embodied in the first filtering stage. Indeed, rapid stimulus-dependent changes in the filter properties have been demonstrated in the visual (Lesica et al., 2007; Sharpee et al., 2006), auditory (Theunissen et al., 2000), and somatosensory (Ramirez et al., 2014) pathways.

In addition to modulating the amplitude of the synaptic response, adaptation also shifts the temporal dynamics of the synaptic drive (Chance et al., 1998). Repetitive stimulation has been shown to increase the latency of the evoked response in sensory neurons (Ahissar et al., 2000) as well as decrease the trial-to-trial timing precision in the onset of the neural response (Desbordes et al., 2008; Higley and Contreras, 2006). However, at intermediate adaptation levels, repetitive stimulation can improve temporal precision (Eggermont, 1991; Garabedian et al., 2003), suggesting that adaptation effects are non-monotonic and likely reflect more subtle schemes. In addition to

altering the temporal precision of the evoked response of a single neuron, adaptation has also been shown to alter the synchrony of spiking across neurons (Wang et al., 2010b). In many neural pathways, coordinated presynaptic spike timing is important, as synchronous population activity is hypothesized to play a major role in the successful transmission of information (Abeles, 1982), perhaps best exemplified in the thalamocortical circuit in the gating of information flow to cortex (Bruno, 2011; Jones, 2002; Tiesinga et al., 2008; Wang et al., 2010a). Due to synaptic integration in cortical neurons, for example, the change in temporal dynamics with sensory adaptation has been identified as a key player underlying the synchrony-mediated trade-off between signals that are well suited for detection and those that allow fine discrimination between different inputs (Ollerenshaw et al., 2014; Wang et al., 2010b).

While these studies provide general principles about the adaptive effects of ongoing sensory stimulation on synaptic transmission, there are also substantial differences in the adaptation of the synaptic efficacy as a function of cell type. In the thalamocortical pathway, synaptic efficacy varies as a function of both the pre- and postsynaptic neuron properties. Recordings from cortical neurons have demonstrated thalamocortical synapses are more effective than corticocortical synapses (Gil et al., 1999), but they also depress to a greater extent (Gil et al., 1997). Furthermore, by separating cortical responses into regular-spiking and fast-spiking populations, it has been shown that thalamocortical axons make stronger connections onto fast-spiking inhibitory interneurons (Cruikshank et al., 2007) that also depress more (Beierlein et al., 2003) than thalamocortical connections onto regular-spiking excitatory neurons. The variability of synaptic properties based on both pre- and postsynaptic neuron properties presents a fairly complicated interaction that is difficult to interpret (Reyes et al., 1998). However, recent work taking advantage of advances in genetic cell-type labeling and stimulation techniques has begun to articulate these cell-type-specific synaptic properties in controlled experimental conditions that do not rely on imperfect classification of cell type based on waveform characteristics (Crandall et al., 2015; Jouhanneau et al., 2015; Pala and Petersen, 2015). As we begin to pull together the synaptic properties between different cell types and anatomical regions, these experimental advances will uncover the role of individual cell types in the development of adaptive synaptic properties within functional circuits to develop generalized principles of neural coding.

Importantly, much of our knowledge of the neurophysiological underpinnings of rapid sensory adaptation was developed in the anesthetized animal, while all of our knowledge of the perceptual effects of sensory adaptation was reported from the awake subject. Brain state plays an important role in shaping spontaneous neural activity, as well as sensory-evoked responses (Anderson et al., 2000; Buonomano and Maass, 2009; McCormick et al., 2015; Petersen et al., 2003; Poulet and Petersen, 2008; Zagha and McCormick, 2014), and therefore will impact encoding properties in the sensory pathways. Given that the state of the synapse is a function of activity levels, it follows that reduced synaptic efficacy will be present in thalamocortical neurons during states of arousal or with ongoing neural activity (Boudreau and Ferster, 2005; Castro-Alamancos and Oldford, 2002). In awake sensing conditions, organisms are constantly bombarded with a continuous stream of sensory information. The continuity of sensation has led some to hypothesize that depressing synapses, such as those found in feedforward sensory information transmission, are always in some state of depression during natural sensing (Borst, 2010; Reinhold et al., 2015). The difference between the state of the brain during most neurophysiological recordings and the state of the brain during conscious perception of adaptation may suggest potential differences in encoding (Castro-Alamancos, 2004). While the absolute neural responses likely vary with state, there is significant evidence to suggest that many of the neural adaptation effects, such as reductions in neural activity levels (Ollerenshaw et al., 2014; Stoelzel et al., 2015), shifts in encoding states (Whitmire et al., 2016), and changes in population coding (Gutnisky and Dragoi, 2008), seen in the anesthetized animal are also present in the awake animal. The qualitative ability to rapidly adapt neural properties appears to be a conserved mechanism across brain states. While extrapolating additional results from the anesthetized animal to the awake preparation will require significant validation, we can begin to make clear and testable predictions about how the neural activity may change in the awake state and the implications for adaptive sensory encoding.

Differential Adaptation of Specific Populations of Tuned Neurons

Moving from adaptation between pairs of neurons to adaptation across circuits, there is evidence that the properties of the ongoing sensory stimulation will differentially activate distinct populations of tuned neurons. In the auditory pathway, ‘‘oddball’’ paradigms that reduce the dimensionality of the stimulus space to a single dimension, such as frequency, have been used extensively to study this phenomenon known in the auditory field as stimulus-specific adaptation (SSA) (Ulanovsky et al., 2003). SSA is defined by a reduced response to a frequent stimulus (standard) that does not affect, or minimally affects, the response to a rare stimulus (deviant) on a trial-by-trial basis (Pérez-González and Malmierca, 2014). SSA has been identified in the non-lemniscal stations of the inferior colliculus (Ayala and Malmierca, 2015; Malmierca et al., 2009) and the thalamus (Anderson et al., 2009; Antunes et al., 2010), while primary auditory cortex (A1) is the first lemniscal station that shows strong SSA (Taaseh et al., 2011). SSA has also been identified in these brain regions in the awake animal (von der Behrens et al., 2009; Duque and Malmierca, 2015; Richardson et al., 2013), further underscoring the ubiquity of neural adaptation across brain states.

While the origin of SSA in the auditory pathway is debated, it is generally accepted to be generated from a network phenomenon because it cannot be explained from the intrinsic properties of the neurons alone (Malmierca et al., 2015). Instead, a model of adaptation in narrow frequency channels has been proposed that suggests SSA is due to the differential adaptation of tuned populations of presynaptic neurons (Figure 4A). As discussed previously in the context of synaptic plasticity, presynaptic neurons tuned to the standard stimulus (Figure 4, blue) will experience synaptic depression in response to the standard stimulus presentation and therefore will elicit reduced sensory drive in the postsynaptic neurons (Figure 4C, dashed lines). In a separate

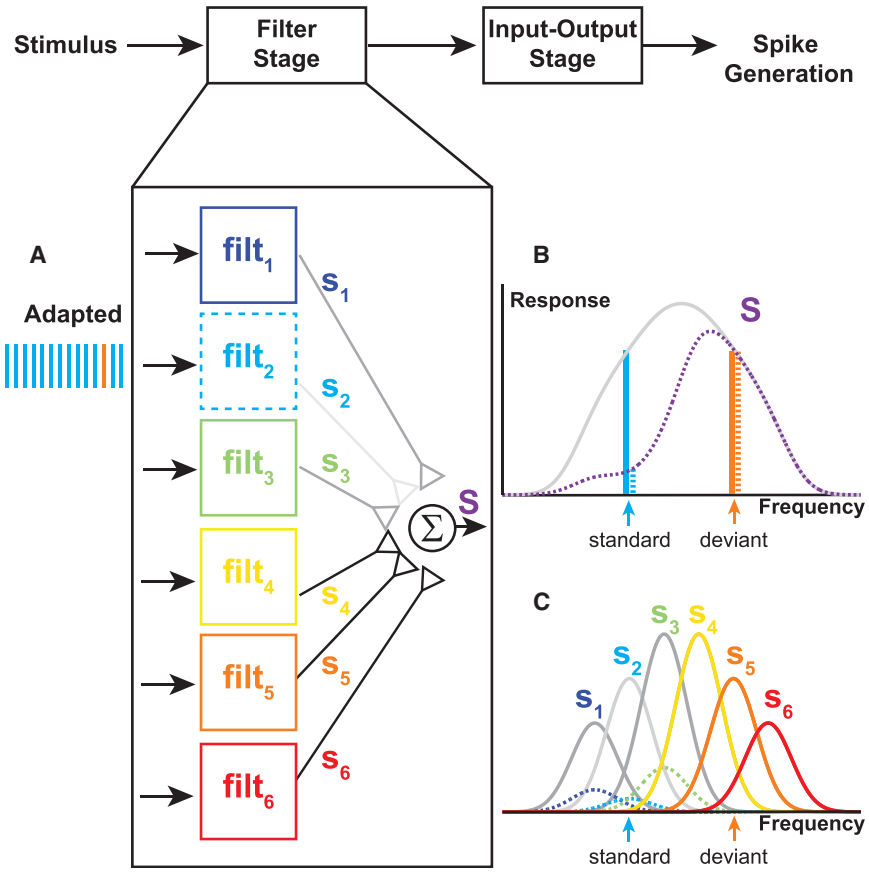

Figure 4. SSA Can Be Partially Explained by the Adaptation in a Narrow Frequency Model

(A) The frequency tuning of a neuron in primary auditory cortex (A1) could be inherited from the frequency tuning of its presynaptic inputs. In an SSA paradigm, one off-peak frequency for the A1 is used as the "standard" stimulus that is presented frequently (blue), while a second off-peak frequency is used as the infrequently presented "deviant" stimulus (orange). Repetitive "standard" stimulation will depress the feedforward synapses (gray).

(B) The evoked responses to the deviant and standard stimuli are approximately equal without adaptation (solid vertical lines). The evoked response to the standard stimulus is greatly reduced when adapted, while the deviant stimulus is largely unaffected (dashed vertical lines).

(C) It has been proposed that differential adaptation of the presynaptic populations that are tuned to the standard stimulus will reduce the inputs from those neurons (dashed frequency tuning curves) and shift the frequency tuning of the A1 neuron (B, purple dashed line).

population of presynaptic neurons that are tuned to the deviant stimulus (Figure 4, orange), the standard stimulus will not evoke a response and therefore the synapses in this population will not be depressed (Mill et al., 2011; Taaseh et al., 2011) (Figure 4C, solid lines, warm colors). When these differentially tuned populations of neurons drive a common downstream brain region, the postsynaptic population integrating their inputs will demonstrate SSA simply due to differential adaptation of the stimulus-selective neurons (Figure 4B, dashed line). Recent evidence further supports this model by demonstrating that SSA is not present for intensity oddball paradigms where presumably the same population of neurons would be activated by the standard and the deviant (Duque et al., 2016). This simple theoretical model provides a framework for a network-level adaptation whereby information is differentially processed by complementary populations of neurons to generate an adaptation effect not necessarily present in the presynaptic populations.

Although the adaptation in narrow frequency channel model presents a simple feedforward mechanism for the generation of SSA from the upstream driving inputs, it has been shown that the model is insufficient to fully account for the properties of SSA seen in A1 (Hershenhoren et al., 2014; Yaron et al., 2012), suggesting that there are also locally generated mechanisms of SSA. In A1, there are a variety of cell types classified broadly into excitatory and inhibitory neurons that form complex cortical circuits that are proposed to enhance SSA (Taaseh et al., 2011).

These functionally distinct classes of neurons likely contribute differentially to the function of the cortical circuit and, in this case, to the generation or enhancement of SSA locally within A1. Using traditional electrophysiological techniques, it is incredibly difficult to deconstruct the role of each cell type in cortical function. However, the advent of genetic tools has made it possible to perform cell-type-specific circuit dissection (Luo et al., 2008). In the auditory pathway, the implementation of these genetic tools has demonstrated that SSA is evident in both excitatory neurons and inhibitory neurons in A1 (specifically, somatostatin-positive (SOM) and parvalbumin-positive (PV) GABAergic interneurons) (Chen et al., 2015; Natan et al., 2015). Systematic investigation of the role of SOM and PV interneurons suggests that the two inhibitory cell types are actually playing complementary roles in the enhancement of SSA in excitatory cortical neurons (Natan et al., 2015). In this work, Natan et al. found that PV interneurons amplify SSA through non-specific inhibition while SOM interneurons amplify SSA by selectively suppressing excitatory responses to the standard tone. These cell-type-specific adaptation effects demonstrate that all interneurons are not equal in the context of adaptation and information coding (Moore et al., 2010), but questions still remain about how these cell types work together within and across brain regions to generate functional percepts. It is possible that the adaptation in narrow frequency channel model represents an inherited mechanism of adaptation in A1 while the differential adaptation of cell types within A1 represents a locally generated mechanism to enhance SSA. However, understanding the mechanisms underlying SSA is significantly more complex than this. These sensory pathways are highly interconnected and receive a significant number of top-down influences in addition to the bottom-up and local influences described here (Malmierca et al., 2015). However,

only recently have the tools been available to perform circuit-level assessments of functional properties using fast and reversible control of discrete cell types to enable answers to these fundamental questions of adaptation. Using these techniques, we will be able to quantify the adaptive properties across neuron populations that may differ genetically but function together as one efficient unit. Only by understanding the role each population plays in information processing will we be able to understand the true function of the circuitry.

The SSA paradigm has become an excellent tool to probe the neural response along a single dimension of the sensory stimulus space. There have also been demonstrations of a similar phenomenon to auditory SSA, although likely a different neural correlate, in human event-related potentials known as mismatch negativity in response to auditory stimuli (Escera and Malmierca, 2014; Farley et al., 2010; Grimm and Escera, 2012; Khouri and Nelken, 2015). Although neural signatures of SSA have been most widely studied in the context of frequency in the auditory pathway, it has also been demonstrated in the context of a range of tuning property dimensions in the visual pathway (Baylis and Rolls, 1987; Miller et al., 1991; Ringo, 1996; Sawamura et al., 2006) and in slice recordings in response to spatially separated electrical stimuli (Eytan et al., 2003). Many forms of adaptation have been identified in the visual pathway, but adaptation of orientation tuning is one dimension of the visual space that has been investigated most extensively. As shown for frequency-specific adaptation in the auditory pathway, orientation-specific adaptation can shift the orientation tuning of primary visual cortex (V1) neurons away from the adapting orientation (Benucci et al., 2013; Dragoi et al., 2000; Felsen et al., 2002; Jin et al., 2005). The adaptation of orientation tuning is stronger with longer adaptation stimulation (Patterson et al., 2013) and more prominent for neurons at the center of orientation pinwheels where there is the most access to multiple orientation directions (Dragoi et al., 2001) (but see Sengpiel and Bonhoeffer, 2002). Interestingly, orientation responses are also quickly adapted by simultaneous presentation of a stimulus at a different orientation (Mrsic-Flogel and Hübener, 2002).

What might be the perceptual consequences of such phenomena? While not completely understood in terms of the electrophysiology, perhaps because of the distributed nature of the activity, the perceptual ''waterfall'' illusion described previously is also thought to arise from a differential adaptation of visual neurons tuned for specific directions of motion (Anstis et al., 1998). Prolonged exposure to motion in one direction preferentially adapts neurons tuned to that direction, resulting in biased population codes (Zavitz et al., 2016) and ultimately a biased percept of subsequent stimuli (Levinson and Sekuler, 1976). Until we are truly able to identify the neural basis of perception, it will be extremely difficult to directly link the perceptual effects to the underlying neural correlates. However, the commonality of this phenomenon across sensory modalities, brain regions, and species suggests that differential adaptation of distinct neuronal populations is a conserved adaptive response where the response properties of neurons, and ultimately perception, are adaptive on a moment-by-moment basis.

Differential Adaptation of Excitatory and Inhibitory Neurons

Given that the differential adaptation of sub-populations of neurons could profoundly shape neural activity, to what extent does the anatomical wiring influence these effects? Throughout all neural pathways, there are a number of common circuit motifs that are believed to perform canonical functions for neural processing (Miller, 2016). In sensory pathways, disynaptic feedforward inhibition is a common motif, exemplified in the thalamocortical projection where sensory information transmitted from the thalamus will elicit a stereotyped pattern of excitation followed by inhibition at the level of the primary sensory cortex (Isaacson and Scanziani, 2011) (Figure 5, solid lines). The rapid onset of the inhibition that follows excitation is likely due to feedforward inhibition from thalamocortical inputs that synapse onto both excitatory and inhibitory cortical neurons (Cruikshank et al., 2007; Miller et al., 2001; Wilent and Contreras, 2005b; Wu et al., 2006). Disynaptic feedforward inhibition has been proposed as a mechanism to enable cortical neurons to be particularly sensitive to the timing of their inputs within a window of integration (Wehr and Zador, 2003). Furthermore, the sequence of excitation followed by inhibition that generates precise timing sensitivity appears to represent a common circuit motif for neural processing within brain regions that receive excitatory projections and contain interneurons, including primary sensory cortex (Gabernet et al., 2005; Higley and Contreras, 2006; Wehr and Zador, 2003), hippocampus (Buzsáki, 1984; Finch et al., 1988; Pouille and Scanziani, 2001), amygdala (Bissière et al., 2003), and visual thalamus (Blitz and Regehr, 2005). While this conserved circuit motif leads to a repeatable excitation-inhibition activation pattern, the temporal aspects of the dynamic interaction between the excitatory and inhibitory conductances are also variable as a function of the input. In the presence of adaptation, the onset of inhibition relative to excitation shifts such that the cortical window of integration can lengthen to allow integration over longer time windows (Gabernet et al., 2005; Higley and Contreras, 2006). While the absolute duration of the cortical integration window is debated, it is believed to be on the order of milliseconds when the pathway is not adapted and on the order of tens of milliseconds in the presence of adaptation (Gabernet et al., 2005). Elongation of the excitability period of cortical neurons is paired with shifts in thalamic synchrony, which ultimately controls the gating of signals to cortex (Wang et al., 2010b).

In our simplified modeling framework, the summed output across filters can now be separated by the sign of interaction to generate both excitatory and inhibitory filters (Figure 6). In the visual pathway, the filter component of a thalamic encoding model can be described as a combination of an excitatory filter with a temporally lagging inhibitory filter (Butts et al., 2011), which is consistent with disynaptic feedforward inhibition (Figure 6A). Because the excitatory and inhibitory inputs interact in a complex manner, adaptation of these two components will have profound effects on the temporal feature selectivity and timing of responses. Contrast adaptation, for example, has been linked to changes in temporal dynamics and gain in the visual system (Shapley and Victor, 1979; Solomon et al., 2004). Contrast is obviously an important parameter for visual

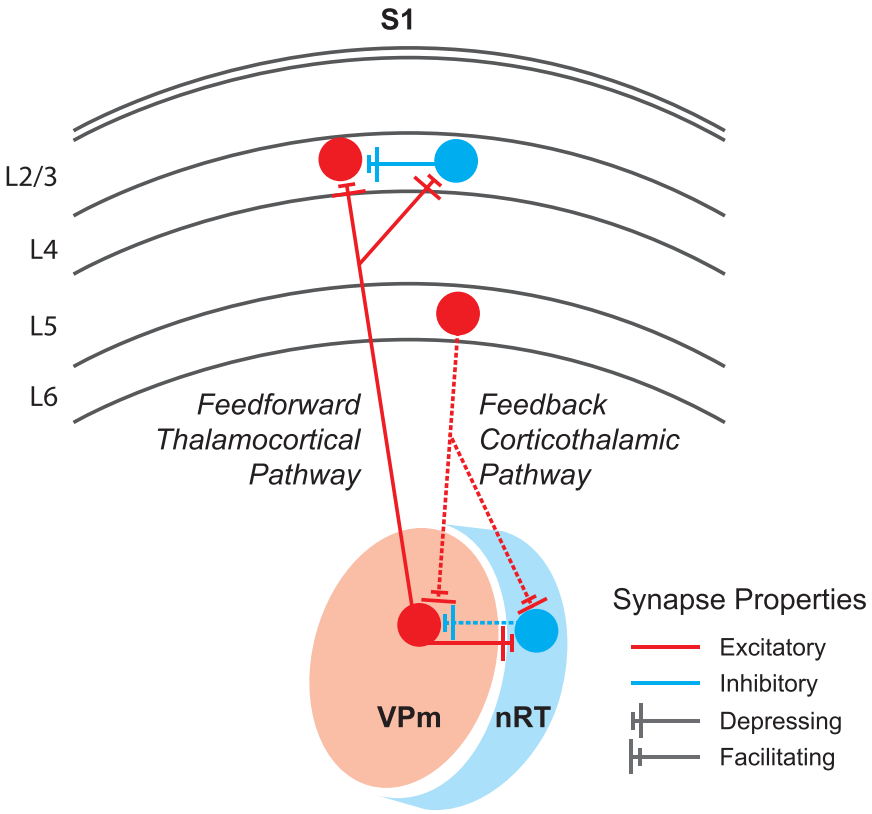

Figure 5. Feedforward Inhibition in the Thalamocortical and Corticothalamic Pathways of the Rodent Vibrissa System

The feedforward thalamocortical inputs from the ventral posteromedial (VPm) thalamus project to both excitatory and inhibitory neurons in layer 4 of primary sensory cortex (S1L4; solid lines). The corticothalamic feedback inputs from S1 L6 provide direct excitation to VPm and feedforward inhibition to VPm mediated through the reticular nucleus of the thalamus (nRT; dashed lines). While the exact properties of these feedforward and feedback pathways differ in detail, the similar feedforward inhibition motif leads to common adaptive properties.

processing, and contrast sensitivity is considered one of the fundamental instantaneous/static properties of visual neurons. Interestingly, however, contrast sensitivity is typically measured with the presumption that it is a static property of the pathway, obscuring any adaptive process that may be going on. In the context of adaptation, with an increase in contrast in a switching paradigm, the adapted linear filters for lateral geniculate nucleus (LGN) neurons show faster temporal dynamics and a decrease in the gain of the input-output function relative to a low contrast condition (Figure 6B) (Lesica et al., 2007; Mante et al., 2005). However, it is difficult to estimate dynamic feature selectivity to robustly capture adaptive behaviors across stimulus conditions (Lesica and Stanley, 2005, 2006; Stanley, 2002) because the feature selectivity of a neuron (Fritz et al., 2003; Lesica et al., 2007; Sharpee et al., 2006; Ulanovsky et al., 2003) can change rapidly with only a short adapting stimulus. This suggests that the fundamental features of a stimulus that drive a neuron to fire are flexible on rapid timescales such that adaptation can reshape what information is transmitted through the sensory pathway, which has even more profound effects if there is differential adaptation across excitatory and inhibitory inputs.

In addition to differentially modulating the timing of the excitatory and inhibitory inputs in response to punctate stimuli, adaptation has also been shown to differentially modulate the overall amount of the excitatory and inhibitory synaptic drive onto an L4 excitatory cortical neuron (Heiss et al., 2008). The thalamocortical synapses onto both excitatory and inhibitory neurons will depress with ongoing sensory drive, leading to an overall reduction in the absolute amount of excitation and inhibition (Chung et al., 2002; Reinhold et al., 2015). However, the effect of adaptation is greater for inhibition than for excitation (Gabernet et al., 2005) such that the excitatory-inhibitory balance is transiently shifted toward excitation (Cohen-Kashi Malina et al., 2013; Heiss et al., 2008). While extracellular recordings have shown that spiking activity in fast-spiking inhibitory neurons can sustain higher firing frequencies than excitatory neurons during sustained stimulation (Khatri et al., 2004), both the input synapse from the thalamus and the output synapse to the regular-spiking neuron show substantial depression (Beierlein et al., 2003; Gabernet et al., 2005). Furthermore, the recovery of inhibition from adaptation is slower than the recovery of excitation, which can provide a period of facilitation immediately following adaptation (Cohen-Kashi Malina et al., 2013). At first glance, it may seem contradictory that adaptation of cortical L4 neurons results in both a transient shift toward excitation and a reduced suprathreshold spiking response to ongoing stimulation. However, the marked reduction in excitation due to depression of the thalamocortical synapse prevents the cortical neurons from reaching spiking threshold. Consistent with this view, recent work in the rodent whisker pathway found a net depolarization of the membrane potential was elicited in the barrel cortex in response to an adaptation stimulus, but the depolarization was paired with a reduction in the excitatory postsynaptic potential amplitude (Ramirez et al., 2014). Note that there is also recent evidence of thalamic projections to other layers of cortex (Constantinople and Bruno, 2013), but the role of these connections in adaptive gating is currently unknown.

While this has been well studied in the feedforward thalamocortical pathway, disynaptic feedforward inhibition is also a circuit motif in the corticothalamic pathway from primary sensory cortex to the lemniscal nucleus of the thalamus mediated through the reticular nucleus (nRT) (Figure 5, dashed lines, rodent vibrissa pathway). The results described here have been investigated in the context of the rodent vibrissa pathway, but

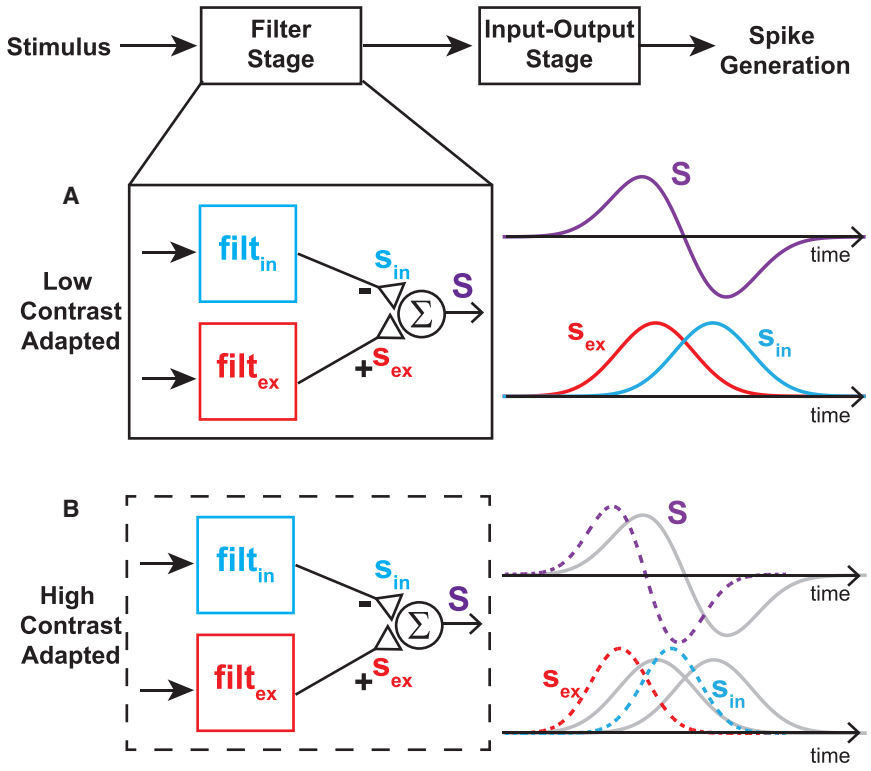

Figure 6. Shifts in Contrast Adaptation Can Sharpen Temporal Dynamics of Receptive Fields

(A) The feature selectivity of a neuron will incorporate both excitatory and inhibitory inputs. In this example, the inhibitory input is simply a temporally shifted version of the excitatory input (right, bottom). The subtraction of these two temporal features results in a biphasic feature selectivity (right, top).

(B) In the high-contrast adapted condition, the excitatory and inhibitory filters are more temporally precise (right, bottom), leading to a temporally sharpened component of the receptive field (right, top).

likely apply more broadly. In contrast to the feedforward processing of the thalamocortical pathway where thalamocortical synapses depress, corticothalamic synapses show short-term facilitation (Cruikshank et al., 2010; Deschênes and Hu, 1990; Landisman and Connors, 2007). Yet similar to the thalamocortical circuit of the rodent vibrissa pathway, repeated activation of the corticothalamic feedback (S1L6) to whisker thalamus (VPm) also results in decreased inhibition in the VPm (Crandall et al., 2015). Given that the reticular thalamus (nRT) is the only known source of inhibitory input to VPm (Pinault, 2004), this suggests that nRT must be exhibiting greater adaptation than the excitatory feedback input from S1L6. As demonstrated for inhibitory neurons in cortex, inhibitory neurons in thalamus (nRT) can also maintain high tonic firing rates during repetitive whisker (Hartings et al., 2003) or S1L6 stimulation, but with reduced levels of inhibition in the postsynaptic excitatory neurons (VPm) due to robust short-term synaptic depression at the nRT-VPm synapse (Crandall et al., 2015). Furthermore, sustained activation of S1L6 will lead to a net depolarization of the membrane potentials in VPm (Mease et al., 2014), as was seen in both thalamus (Jubran et al., 2016) and cortex (Ramirez et al., 2014) in response to repetitive stimulation of the whiskers. Finally, nRT responses also recover much more slowly than VPm responses (Ganmor et al., 2010), as was demonstrated for the level of inhibitory synaptic drive in cortex (Cohen-Kashi Malina et al., 2013).

The parallels between these highly interconnected feedforward and feedback pathways of the thalamocortical system present what may be a fundamental component of dynamic neural encoding. Differential adaptation of excitatory and inhibitory neural populations provides a mechanism to shift the properties of synaptic integration and therefore the function of the circuit, specifically in the context of timing. Timing in sensory circuits plays an important role in stimulus representation (Desbordes et al., 2008; Montemurro et al., 2007), and work in the visual system has shown how the temporal precision of the pathway is matched to the statistics of the input (Butts et al., 2007). Adaptation modulates not only temporal precision within neurons, but also synchronous firing across neurons (Wang et al., 2010b). Furthermore, transitions in the coding properties of the pathway in response to adaptation also extend to state-related firing, such as burst-tonic firing in the thalamus (Lesica and Stanley, 2004; Lesica et al., 2006; Whitmire et al., 2016), that could underlie the shift in information processing modes (Ollerenshaw et al., 2014).

Pooled Population Effects

While adaptation has cell-type-specific effects, there are also large-scale properties of adaptation due to pooled population effects. Normalization has been proposed as a canonical computation of neural circuits whereby a neuron's response is normalized by the pooled neural activity of the local circuitry (Carandini and Heeger, 2011). Normalization was originally proposed to explain responses in V1 (Heeger, 1992), but the principles have since been demonstrated in a wide range of studies, including processing in visual thalamus (Bonin et al., 2005) and inferior temporal cortex (Kaliukhovich and Vogels, 2016), olfactory processing (Olsen et al., 2010), multisensory integration (Ohshiro et al., 2011), visual attention (Reynolds and Heeger, 2009), and context-dependent decision making (Louie et al., 2013). While the exact biophysical mechanism underlying this computation depends upon the neural architecture (Sato et al., 2016), this activity-dependent computation has a common theme: normalization of the neural response.

Although the relationship between normalization and adaptation is not clear, the normalization computation occurs on timescales relevant for the rapid adaptation discussed here. As such, normalization could represent an added layer of

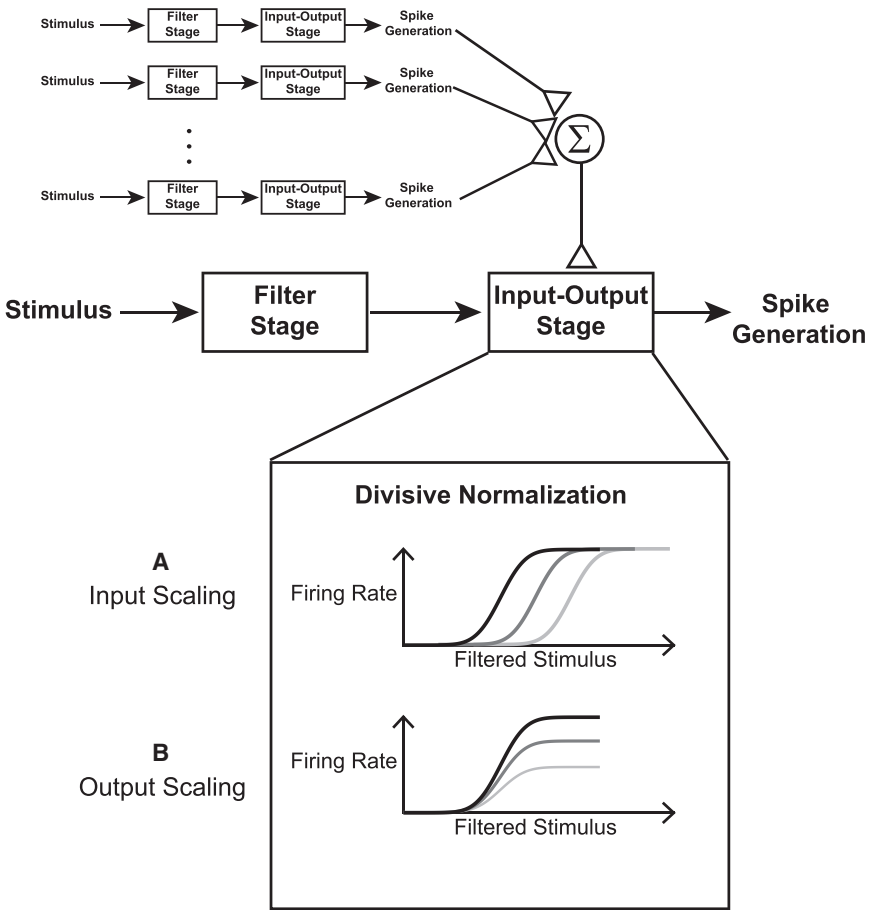

Figure 7. Divisive Normalization Modulates the Input-Output Tuning Function

Although not typically described in conjunction with sensory adaptation, divisive normalization could also be considered a pooled adaptation effect where the firing activity across neurons can reshape the input-output function of an individual cell in an activity-dependent manner. There are two methods of input-output scaling that have been proposed and demonstrated in different sensory pathways. (A) Input scaling refers to shifting the input-output curve laterally while (B) output scaling refers to scaling the input-output curve vertically. Both scaling mechanisms represent an activity-dependent network mechanism to shift the encoding of sensory neurons.

population-level adaptation effects to modulate sensory responses. Normalization can be visualized as a form of gain control whereby the activity of the circuit serves as negative feedback for the input-output function. In the context of the model framework described here, the response of any given neuron is still a cascade of its feature selectivity that is shaped by synaptic inputs and a second nonlinearity stage associated with intrinsic properties and some elements of spike generation, but this second stage input-output function is now modulated by the population activity (Figure 7). Whereas we previously discussed shifts in the nonlinearity due to intrinsic adaptation currents, normalization presents an additional modulation due to pooled neural activity. Depending on the mechanism of action, normalization can scale the input to the nonlinearity (Figure 7A) or the output of the nonlinearity (Figure 7B). In the olfactory processing of *Drosophila*, Olsen et al. implemented a sensory paradigm to investigate the role of lateral inhibition in generating normalization that takes advantage of the highly structured odorant tuning to independently stimulate the neuronal population of interest and the surrounding neuronal populations (Olsen et al., 2010). In this work, inclusion of lateral inhibition (through a non-specific odorant stimulus) led to input scaling as the normalization effect in this pathway (Figure 7A). In visual processing of macaque V1, Cavanaugh et al. implemented a spatial integration paradigm to investigate divisive normalization in the context of response gain (Cavanaugh et al., 2002). In this work, a receptive field model identified output scaling as the best fit to the experimental data (Figure 7B). Importantly, while both input and output rescaling have been demonstrated in olfactory and visual processing, the underlying neural correlates of normalization vary based on the circuitry. Normalization described for the olfactory pathway of *Drosophila* is likely mediated through increased inhibition while divisive normalization in visual cortex may actually result from a decrease in synaptic excitation rather than an increase in inhibition (Sato et al., 2016). Yet despite these varying mechanisms, the normalization computation appears conserved across different pathways and brain structures (Carandini and Heeger, 2011). Note that much of the existing literature providing empirical support for the normalization computation does not explicitly include time as an element (time to develop, time to dissipate). However, given that the normalization is activity dependent, it is very likely that the effects fit within our definition of adaptation as requiring time to manifest.

Given the prevalence of normalization computations in the brain, we might ask how this compares to other rapid adaptation mechanisms described thus far. Previously, we discussed mechanisms to drive changes in the feature selectivity of sensory-driven neurons such as SSA or changes in excitatory-inhibitory conductances. The role of normalization is not necessarily to drive changes in the feature selectivity of the neuron, but instead to modulate the neural response in more subtle ways. In the visual pathway, for example, normalization has been used to describe the role of the non-classical receptive field in modulating cortical responses. The classical receptive field is defined as the region of visual space that elicits firing from the sensory neuron (Hubel and Wiesel, 1959), while the non-classical receptive field is the visual space that extends beyond the classical receptive field (Allman et al., 1985). Simultaneous activation of the classical and non-classical receptive fields will reduce the evoked response relative to stimulation of the classical receptive

field alone (Jones et al., 2001), giving non-classical receptive field the description of a suppressive field (Bonin et al., 2005). The suppressive field normalizes the neural response relative to the stimulus intensity in the non-classical receptive field (Carandini and Heeger, 2011), but not without purpose. Visual stimulation with natural movies has shown that stimulation of the non-classical receptive field increases the efficiency of information transmission (Vinje and Gallant, 2002), as expected for sensory adaptation, through intracortical network interactions (Haider et al., 2010). Building on the complexity of the adaptive modulation of feature selectivity, normalization represents the ability of the neural circuitry to pool information across neurons to fundamentally alter the input-output relationship. There is still much to learn, however, about how these mechanisms might operate dynamically in a transient environment, and about the timescales over which the normalization takes place.

Implications of Highly Interconnected Circuitry in Adaptive Coding

As described throughout this Perspective, adaptation effects will build and compound from a single neuron to a single synapse to a small circuit to a local network before eventually forming adaptive percepts. In order to interpret network activity in the context of highly interconnected circuitry, we must consider the detailed anatomy of our sensory pathways and how these canonical microcircuits might give rise to the adaptive neural responses discussed here.

Disentangling Inherited and Locally Generated Adaptation Effects

Thus far, we have primarily discussed adaptation within the thalamocortical circuit. But things become increasingly complex as we consider how adaptation shapes encoding across entire pathways in which the fundamental properties of a given neuron can be rapidly altered by recent sensory drive. In the rodent vibrissa pathway, somatosensory information is transduced by the primary sensory neurons in the whisker follicle and then transmitted from the vibrissa to the brainstem and then to the thalamus before reaching primary somatosensory cortex (Diamond et al., 2008). If we consider the cortical response to repetitive whisker stimulation, we can ask how much of the rapid adaptation seen in cortex is generated locally compared to how much is inherited from rapid adaptation at earlier stages of the pathway. Rapid adaptation has been quantified in the most basic sense as the change in the spike counts (firing rate) in response to repetitive stimulation. In the vibrissa pathway, the amount of spike count adaptation increases at each stage of the processing pathway from the brainstem to the thalamus to cortex (Ganmor et al., 2010). This would suggest, perhaps unsurprisingly, that at least some basic components of adaptation are inherited from one brain region to the next. However, as we have discussed, there are also mechanisms of adaptation that are generated locally rather than inherited only from presynaptic adaptation effects. Locally generated adaptation effects have been described perceptually by ''higher-order'' adaptation whereby a subject adapts to higher-order stimulus features, such as face adaptation, that cannot be entirely inherited from non-face selective regions (Strobach and Carbon, 2013; Webster et al., 2004) in the absence of complex scenarios that seem exceedingly unlikely. While the effects of face adaptation can be seen perceptually, it is difficult to identify the neural correlates of higher-order adaptation (Fox and Barton, 2007). However, this dichotomy between inherited and locally generated adaptive processes likely exists at each stage of sensory processing for even very simple sensory stimuli. In the visual pathway, the inheritance of adaptation has been studied from LGN to V1 (Dhruv and Carandini, 2014; King et al., 2016) and from V1 to the middle temporal (MT) region of cortex (Patterson et al., 2014). For example, by silencing V1 optogenetically, King et al. were able to dissociate local cortical processing from the feedforward adapted thalamic input to determine the relative weights of inherited versus locally generated contrast adaptation effects. If we begin to consider the commonality of neural processing between excitatory and inhibitory neurons or differential adaptation of tuned populations of neurons, we can begin to extrapolate the effects on information processing as each stage of processing inherits earlier adaptation effects and locally generates additional encoding shifts.

Adaptation Effects in Highly Interconnected Circuitry

It is also important to consider that sensory information is not only being processed in a feedforward manner from the periphery to the cortex, but instead there are an immense number of feedback projections that suggest information is processed in a highly complex way. A particularly salient example is the thalamocortical circuit. While we traditionally study the feedforward projections from thalamus to cortex, it is well documented that the vast majority of synapses onto a thalamic neuron are actually cortical in origin (Varela, 2014). While these synapses are more modulatory in nature than the sensory drive (Sherman and Guillery, 1998), the sheer volume suggests an important role of corticothalamic feedback in information transmission. Furthermore, the feedback circuit motifs share anatomical and functional properties with the feedforward circuit, such as disynaptic feedforward inhibition and common adaptation responses for excitatory and inhibitory neurons at each stage of processing, as described above in the context of the rodent vibrissa pathway. Recent evidence from the SSA literature that has sought to disentangle the role of feedforward SSA generation from feedback SSA modulation suggests that while SSA can be inherited in a feedforward manner, it is refined subcortically through cortical feedback (Malmierca et al., 2015). Similar to the roles of specific cell types in the enhancement of SSA in cortex, the ability of cortical feedback to modulate information transmission presents a complementary role for modulatory feedback in rapid sensory encoding. Disentangling the role of any given neuron in inducing or demonstrating sensory adaptation will likely require a more sophisticated understanding of artificial stimulation techniques (Millard et al., 2015) that can be implemented in conjunction with cell-type specificity and real-time feedback control of neural activity to functionally decouple causally related variables (Grosenick et al., 2015; Newman et al., 2015). By understanding the part each neural component plays in building the network-level response, we can begin to understand the functional role of the circuitry in dynamic encoding.

Implications of Adaptation Paradigms for Natural Sensing and Behavior

While significant progress in the field has demonstrated various adaptive properties across neural circuits, the experimental paradigms employed are still restricted in their scope due to practical limitations of experimental preparations. How do we bridge the electrophysiological findings developed under reduced sensory stimulus adaptation paradigms to natural sensing environments? And further, what are the implications of these dynamic encoding properties demonstrated in neurophysiological studies on information encoding and ultimately sensory perception? While the answers to these questions remain abstract, we can begin to piece together prior experimental results to propose a few open questions for the field.

Extrapolating Adaptation Effects from Simplified Experimental Paradigms to Natural Sensing

In probing the dynamics of neural pathways, a simple paired-pulse paradigm has been widely utilized to capture the dynamics in the simplest possible manner. This paired-pulse paradigm has built the foundation for our understanding of synaptic facilitation and depression dynamics (Stevens and Wang, 1995) and sensory-evoked cortical dynamics (Simons, 1985). Although experimentally and analytically attractive, these kinds of pairs of probes separated in time only capture second-order interactions. The immediate question becomes whether or not second-order dynamics are sufficient to explain the neural dynamics observed in more realistic regimes. More specifically, does this kind of characterization make accurate predictions when extended to even just a triplet of stimuli or, more importantly, to complex temporal patterns? In the rodent vibrissa pathway, pairs of punctate whisker stimuli have been commonly employed to quantify neural dynamics (Simons, 1985). However, models built from the cortical response to a pair of whisker stimuli alone are insufficient to fully predict even the cortical response to just a triplet of whisker stimuli (Webber and Stanley, 2004). As the patterns of whisker stimuli become increasingly complex, the encoding must expand to incorporate the temporal interactions across stimuli that capture the interplay between excitatory and inhibitory circuitry (Boloori et al., 2010). Similar findings from the crustacean neuromuscular junction demonstrate that the dynamic synaptic response to temporally random stimuli has a temporal dependence on recent spiking history that cannot be predicted by the response to a single stimulus alone (Sen et al., 1996).

Even in spike-timing-dependent plasticity experiments where the stimulation occurs over a longer time period, the depression/potentiation dynamics are dependent on these more complex spiking patterns within neurons as opposed to simply the single pair of pre- and postsynaptic spikes (Froemke and Dan, 2002). The addition of more complicated, yet more realistic, spiking patterns did not refute earlier findings developed using paired-pulse paradigms but instead added another layer of interaction in the spike trains. As we consider how to scale our adaptation principles developed from studies of a single dimension of the sensory space to a naturalistic scene, existing models from simpler stimulation paradigms should be used as the foundation of these neural interactions that can be expanded to identify the appropriate stimulus interactions to incorporate under more complex stimulation paradigms.

Returning to the more general modeling framework discussed here, we might ask to what extent an adaptation effect such as SSA identified along a single stimulus dimension maps to the adaptation of the full feature selectivity of a neuron. Within this context lies a catch-22: the time frame over which these adaptive changes in feature selectivity occur is fairly fast, yet the ability to capture the feature selectivity through approaches such as reverse correlation requires sufficient measurement time (and spikes) to robustly capture the dynamics. By restricting the stimulus space when using an SSA paradigm, the overall data requirement is reduced and the adaptive modulation to the tuning function can be measured. Connecting general descriptions of feature selectivity to the tuning properties associated with a reduced dimension stimulus space is therefore difficult, particularly in the context of rapid adaptation, which exists on the timescale of milliseconds to seconds. Multiple layers of interaction between the sensory stimulus and the evoked neural response paired with limited sampling capabilities may seem like an intractable problem. However, there is evidence that rapid modulation of feature selectivity is present in the spectrotemporal receptive fields of A1 neurons (Fritz et al., 2003) as well as the spatiotemporal receptive fields of V1 neurons (Debanne et al., 1998; Lesica et al., 2007). Future work should be aimed at bridging the gap between tuning results from a limited stimulus space and tractable assessments of more general feature selectivity.

Perceptual Implications of Sensory Adaptation

Despite a long history of scientific investigation, the link between neural adaptation and perceptual adaptation remains unknown. However, in a few cases, this link has become more salient due to the pairing of new experimental techniques with creative experimental design. One particularly valuable example aimed at linking cortical adaptation with behavioral perception using optogenetics techniques provided a clear relationship between the adaptation of evoked cortical responses and the perceptually based response of the rodent (Musall et al., 2014). While there are a limited number of studies making this link, significant work has been done to bridge the gap using estimates of information from the neural spiking data to predict task performance using encoder-decoder frameworks. From an information-theoretic perspective, the differential adaptation of different populations of neurons based on tuning, cell type, circuit dynamics, and so on presents a very interesting coding problem. In a complex sequence of encoding through a pathway, it would seem imperative to understand the degree of adaptation that occurs at each point in the chain and whether decoding of the signals ultimately requires knowledge of the adaptation (Seriès et al., 2009).

Recent evidence has linked the effects of sensory adaptation to the specific information processing tasks of detection and discrimination. The efficient coding hypothesis put forth by Barlow proposed optimization of sensory encoding, but without explicit consideration for varying task demands. The flexibility of organisms to perform a variety of behaviors, such as dynamically shifting between detection and discrimination modes, may require a more expansive view of optimization than that reflected in our classical framework. In the somatosensory pathway, spatial discrimination tasks have been well studied due to the

distributed nature of the sensation. More than half a century ago, von Békésy noted that the perceived size of a tactile stimulus decreased with increasing frequency of a repetitive sensory stimulus (von Békésy, 1957). Perceptual studies in human tactile sensing further suggested that somatosensory adaptation enhanced spatial discrimination between stimuli through vibrotactile input to the fingertip (Goble and Hollins, 1993, 1994; Tannan et al., 2006; Vierck and Jones, 1970), and subsequent studies have investigated the spatial sharpening of representations in somatosensory cortex in response to repetitive, ongoing sensory inputs (Lee and Whitsel, 1992; Moore et al., 1999; Sheth et al., 1998; Simons et al., 2005; Tommerdahl et al., 2002), posited as a potential explanation for enhanced spatial acuity (Lee and Whitsel, 1992; Moore et al., 1999; Vierck and Jones, 1970). These results have been expanded to investigate the underlying neural correlates of spatial discrimination in multiple animals models of somatosensation, including the monkey fingertip (Simons et al., 2005) and the rodent vibrissa pathway (Ollerenshaw et al., 2014).

More importantly, however, is the assertion that the adaptation mediates a trade-off between detectability and discriminability (Moore, 2004) that has been linked behaviorally and electrophysiologically (Ollerenshaw et al., 2014; Wang et al., 2010b; Zheng et al., 2015), controlling the nature of the utility of the sensory representation in a dynamically changing environment. Importantly, the adaptive switch from a detection to a discrimination mode is highly stimulus dependent. Adaptation of a particular stimulus dimension will only enhance discrimination performance when the test stimulus is similar to the adapting stimulus (Blakemore and Campbell, 1969b; Sekuler and Ganz, 1963; Tommerdahl et al., 2005). In a sensory environment that is filled with rich stimuli that are continuously changing, dynamic changes to sensory encoding on fast timescales presents a mechanism to rapidly shift information processing states with respect to the current state of the world and therefore the perceptual capabilities of an organism.

Conclusions

As we stated at the onset, we all know what adaptation is, but in the nervous system, it is hard to define and harder still to identify what it is not. Words like evolution, development, plasticity, and adaptation may be bound together philosophically as a way organisms face a changing environment, but they are implemented through wildly different mechanisms on entirely different spatial and temporal scales. Focusing on rapid sensory adaptation over timescales of milliseconds to seconds, we have laid out a wide range of biophysical mechanisms that can contribute to, and compound, effects within and across networks. While the perceptual effects of adaptation are sometimes dramatic, the neural signatures that we think are related can be subtle, and likely distributed and hard to interpret. The rapid adaptation effects described here vary as a function of cell type, synapse type, feature selectivity, and anatomical connectivity. Due to the complexity of neural recordings, most experimental adaptation evidence is analyzed with respect to only a single region of the brain. However, this becomes increasingly difficult to interpret when we consider the inherited effects of adaptation as information is transmitted from one processing stage to the next as well as the highly interconnected circuitry that is constantly providing feedback between processing centers. The set of tools that are emerging in the field enable, for the first time, the ability to dissect the potential neural underpinnings of complex phenomena like adaptation. Importantly, at key stages of processing, the nervous system is exquisitely organized, and the anatomical connectivity is likely to play a major role in determining the link between the perceptual effect and the underlying neural activity that drives it.

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REFERENCES

Abbott, L.F., Varela, J.A., Sen, K., and Nelson, S.B. (1997). Synaptic depression and cortical gain control. Science *275*, 220–224.

Abeles, M. (1982). Role of the cortical neuron: integrator or coincidence detector? Isr. J. Med. Sci. *18*, 83–92.

Ahissar, E., Sosnik, R., and Haidarliu, S. (2000). Transformation from temporal to rate coding in a somatosensory thalamocortical pathway. Nature *406*, 302–306.

Allman, J., Miezin, F., and McGuinness, E. (1985). Stimulus specific responses from beyond the classical receptive field: neurophysiological mechanisms for local-global comparisons in visual neurons. Annu. Rev. Neurosci. *8*, 407–430.

Anderson, J., Lampl, I., Reichova, I., Carandini, M., and Ferster, D. (2000). Stimulus dependence of two-state fluctuations of membrane potential in cat visual cortex. Nat. Neurosci. *3*, 617–621.

Anderson, L.A., Christianson, G.B., and Linden, J.F. (2009). Stimulus-specific adaptation occurs in the auditory thalamus. J. Neurosci. *29*, 7359–7363.

Anstis, S., Verstraten, F.A.J., and Mather, G. (1998). The motion aftereffect. Trends Cogn. Sci. *2*, 111–117.

Antunes, F.M., Nelken, I., Covey, E., and Malmierca, M.S. (2010). Stimulus-specific adaptation in the auditory thalamus of the anesthetized rat. PLoS ONE *5*, e14071.

Ayala, Y.A., and Malmierca, M.S. (2015). Cholinergic modulation of stimulus-specific adaptation in the inferior colliculus. J. Neurosci. *35*, 12261–12272.

Azouz, R., and Gray, C.M. (2000). Dynamic spike threshold reveals a mechanism for synaptic coincidence detection in cortical neurons in vivo. Proc. Natl. Acad. Sci. USA *97*, 8110–8115.

Barlow, H. (1961). Possible principles underlying the transformation of sensory messages. In Sensory Communication, W. Rosenblith, ed. (MIT Press), pp. 217–234.

Baylis, G.C., and Rolls, E.T. (1987). Responses of neurons in the inferior temporal cortex in short term and serial recognition memory tasks. Exp. Brain Res. *65*, 614–622.

Beierlein, M., Gibson, J.R., and Connors, B.W. (2003). Two dynamically distinct inhibitory networks in layer 4 of the neocortex. J. Neurophysiol. *90*, 2987–3000.

Benda, J., and Herz, A.V.M. (2003). A universal model for spike-frequency adaptation. Neural Comput. *15*, 2523–2564.

Benucci, A., Saleem, A.B., and Carandini, M. (2013). Adaptation maintains population homeostasis in primary visual cortex. Nat. Neurosci. *16*, 724–729.

Bhattacharjee, A., and Kaczmarek, L.K. (2005). For K+ channels, Na+ is the new Ca2+. Trends Neurosci. *28*, 422–428.

Bissière, S., Humeau, Y., and Lüthi, A. (2003). Dopamine gates LTP induction in lateral amygdala by suppressing feedforward inhibition. Nat. Neurosci. *6*, 587–592.

Blakemore, C., and Campbell, F.W. (1969a). On the existence of neurones in the human visual system selectively sensitive to the orientation and size of retinal images. J. Physiol. *203*, 237–260.

Blakemore, C., and Campbell, F.W. (1969b). Adaptation to spatial stimuli. J. Physiol. *200*, 11P–13P.

Blitz, D.M., and Regehr, W.G. (2005). Timing and specificity of feed-forward inhibition within the LGN. Neuron *45*, 917–928.

Boloori, A.-R., Jenks, R.A., Desbordes, G., and Stanley, G.B. (2010). Encoding and decoding cortical representations of tactile features in the vibrissa system. J. Neurosci. *30*, 9990–10005.

Bonin, V., Mante, V., and Carandini, M. (2005). The suppressive field of neurons in lateral geniculate nucleus. J. Neurosci. *25*, 10844–10856.

Borst, J.G.G. (2010). The low synaptic release probability in vivo. Trends Neurosci. *33*, 259–266.

Boudreau, C.E., and Ferster, D. (2005). Short-term depression in thalamocortical synapses of cat primary visual cortex. J. Neurosci. *25*, 7179–7190.

Bruno, R.M. (2011). Synchrony in sensation. Curr. Opin. Neurobiol. *21*, 701–708.

Buonomano, D.V., and Maass, W. (2009). State-dependent computations: spatiotemporal processing in cortical networks. Nat. Rev. Neurosci. *10*, 113–125.

Buonomano, D.V., and Merzenich, M.M. (1998). Cortical plasticity: from synapses to maps. Annu. Rev. Neurosci. *21*, 149–186.

Butts, D.A., Weng, C., Jin, J., Yeh, C.I., Lesica, N.A., Alonso, J.M., and Stanley, G.B. (2007). Temporal precision in the neural code and the timescales of natural vision. Nature *449*, 92–95.

Butts, D.A., Weng, C., Jin, J., Alonso, J.M., and Paninski, L. (2011). Temporal precision in the visual pathway through the interplay of excitation and stimulus-driven suppression. J. Neurosci. *31*, 11313–11327.

Buzsáki, G. (1984). Feed-forward inhibition in the hippocampal formation. Prog. Neurobiol. *22*, 131–153.

Carandini, M., and Heeger, D.J.D. (2011). Normalization as a canonical neural computation. Nat. Rev. Neurosci. *13*, 51–62.

Castro-Alamancos, M.A. (2004). Absence of rapid sensory adaptation in neocortex during information processing states. Neuron *41*, 455–464.

Castro-Alamancos, M.A., and Oldford, E. (2002). Cortical sensory suppression during arousal is due to the activity-dependent depression of thalamocortical synapses. J. Physiol. *541*, 319–331.

Cavanaugh, J.R., Bair, W., and Movshon, J.A. (2002). Nature and interaction of signals from the receptive field center and surround in macaque V1 neurons. J. Neurophysiol. *88*, 2530–2546.

Chance, F.S., and Abbott, L.F. (2001). Input-specific adaptation in complex cells through synaptic depression. Neurocomputing *38–40*, 141–146.

Chance, F.S., Nelson, S.B., and Abbott, L.F. (1998). Synaptic depression and the temporal response characteristics of V1 cells. J. Neurosci. *18*, 4785–4799.

Chen, I.-W., Helmchen, F., and Lütcke, H. (2015). Specific early and late oddball-evoked responses in excitatory and inhibitory neurons of mouse auditory cortex. J. Neurosci. *35*, 12560–12573.

Chung, S., Li, X., and Nelson, S.B. (2002). Short-term depression at thalamocortical synapses contributes to rapid adaptation of cortical sensory responses in vivo. Neuron *34*, 437–446.

Clifford, C.W.G., Webster, M.A., Stanley, G.B., Stocker, A.A., Kohn, A., Sharpee, T.O., and Schwartz, O. (2007). Visual adaptation: neural, psychological and computational aspects. Vision Res. *47*, 3125–3131.

Cohen-Kashi Malina, K., Jubran, M., Katz, Y., and Lampl, I. (2013). Imbalance between excitation and inhibition in the somatosensory cortex produces post-adaptation facilitation. J. Neurosci. *33*, 8463–8471.

Constanti, A., and Brown, D.A. (1981). M-Currents in voltage-clamped mammalian sympathetic neurones. Neurosci. Lett. *24*, 289–294.

Constantinople, C.M., and Bruno, R.M. (2013). Deep cortical layers are activated directly by thalamus. Science *340*, 1591–1594.

Crandall, S.R., Cruikshank, S.J., and Connors, B.W. (2015). A corticothalamic switch: controlling the thalamus with dynamic synapses. Neuron *86*, 768–782.

Cruikshank, S.J., Lewis, T.J., and Connors, B.W. (2007). Synaptic basis for intense thalamocortical activation of feedforward inhibitory cells in neocortex. Nat. Neurosci. *10*, 462–468.

Cruikshank, S.J., Urabe, H., Nurmikko, A.V., and Connors, B.W. (2010). Pathway-specific feedforward circuits between thalamus and neocortex revealed by selective optical stimulation of axons. Neuron *65*, 230–245.

Dayan, P., and Abbott, L.F. (2001). Information theory. In Computational and Mathematical Modeling of Neural Systems (MIT Press), pp. 123–150.

de Boer, R., and Kuyper, P. (1968). Triggered correlation. IEEE Trans. Biomed. Eng. *15*, 169–179.

Debanne, D., Shulz, D.E., and Fregnac, Y. (1998). Activity-dependent regulation of 'on' and 'off' responses in cat visual cortical receptive fields. J. Physiol. *508*, 523–548.

Desbordes, G., Jin, J., Weng, C., Lesica, N.A., Stanley, G.B., and Alonso, J.-M. (2008). Timing precision in population coding of natural scenes in the early visual system. PLoS Biol. *6*, e324.

Deschênes, M., and Hu, B. (1990). Electrophysiology and pharmacology of the corticothalamic input to lateral thalamic nuclei: an intracellular study in the cat. Eur. J. Neurosci. *2*, 140–152.

Dhruv, N.T., and Carandini, M. (2014). Cascaded effects of spatial adaptation in the early visual system. Neuron *81*, 529–535.

Diamond, M.E., von Heimendahl, M., Knutsen, P.M., Kleinfeld, D., and Ahissar, E. (2008). 'Where' and 'what' in the whisker sensorimotor system. Nat. Rev. Neurosci. *9*, 601–612.

Díaz-Quesada, M., and Maravall, M. (2008). Intrinsic mechanisms for adaptive gain rescaling in barrel cortex. J. Neurosci. *28*, 696–710.

Dragoi, V., Sharma, J., and Sur, M. (2000). Adaptation-induced plasticity of orientation tuning in adult visual cortex. Neuron *28*, 287–298.

Dragoi, V., Rivadulla, C., and Sur, M. (2001). Foci of orientation plasticity in visual cortex. Nature *411*, 80–86.

Duque, D., and Malmierca, M.S. (2015). Stimulus-specific adaptation in the inferior colliculus of the mouse: anesthesia and spontaneous activity effects. Brain Struct. Funct. *220*, 3385–3398.

Duque, D., Wang, X., Nieto-Diego, J., Krumbholz, K., and Malmierca, M.S. (2016). Neurons in the inferior colliculus of the rat show stimulus-specific adaptation for frequency, but not for intensity. Sci. Rep. *6*, 24114.

Eggermont, J.J. (1991). Rate and synchronization measures of periodicity coding in cat primary auditory cortex. Hear. Res. *56*, 153–167.

Eggermont, J.J., Johannesma, P.M., and Aertsen, A.M.H. (1983). Reverse-correlation methods in auditory research. Q. Rev. Biophys. *16*, 341–414.

Escera, C., and Malmierca, M.S. (2014). The auditory novelty system: an attempt to integrate human and animal research. Psychophysiology *51*, 111–123.

Eytan, D., Brenner, N., and Marom, S. (2003). Selective adaptation in networks of cortical neurons. J. Neurosci. *23*, 9349–9356.

Fairhall, A.L., Lewen, G.D., Bialek, W., and de Ruyter Van Steveninck, R.R. (2001). Efficiency and ambiguity in an adaptive neural code. Nature *412*, 787–792.

Farley, B.J., Quirk, M.C., Doherty, J.J., and Christian, E.P. (2010). Stimulus-specific adaptation in auditory cortex is an NMDA-independent process distinct from the sensory novelty encoded by the mismatch negativity. J. Neurosci. *30*, 16475–16484.

Felsen, G., Shen, Y.S., Yao, H., Spor, G., Li, C., and Dan, Y. (2002). Dynamic modification of cortical orientation tuning mediated by recurrent connections. Neuron *36*, 945–954.

Finch, D.M., Tan, A.M., and Isokawa-Akesson, M. (1988). Feedforward inhibition of the rat entorhinal cortex and subicular complex. J. Neurosci. *8*, 2213–2226.

Fleidervish, I.A., Friedman, A., and Gutnick, M.J. (1996). Slow inactivation of Na+ current and slow cumulative spike adaptation in mouse and guinea-pig neocortical neurones in slices. J. Physiol. *493*, 83–97.

Fox, C.J., and Barton, J.J.S. (2007). What is adapted in face adaptation? The neural representations of expression in the human visual system. Brain Res. *1127*, 80–89.

Fritz, J., Shamma, S., Elhilali, M., and Klein, D. (2003). Rapid task-related plasticity of spectrotemporal receptive fields in primary auditory cortex. Nat. Neurosci. *6*, 1216–1223.

Froemke, R.C., and Dan, Y. (2002). Spike-timing-dependent synaptic modification induced by natural spike trains. Nature *416*, 433–438.

Gabernet, L., Jadhav, S.P., Feldman, D.E., Carandini, M., and Scanziani, M. (2005). Somatosensory integration controlled by dynamic thalamocortical feed-forward inhibition. Neuron *48*, 315–327.

Ganmor, E., Katz, Y., and Lampl, I. (2010). Intensity-dependent adaptation of cortical and thalamic neurons is controlled by brainstem circuits of the sensory pathway. Neuron *66*, 273–286.

Garabedian, C.E., Jones, S.R., Merzenich, M.M., Dale, A., and Moore, C.I. (2003). Band-pass response properties of rat SI neurons. J. Neurophysiol. *90*, 1379–1391.

Georgeson, M.A., and Harris, M.G. (1984). Spatial selectivity of contrast adaptation: models and data. Vision Res. *24*, 729–741.

Gil, Z., Connors, B.W., and Amitai, Y. (1997). Differential regulation of neocortical synapses by neuromodulators and activity. Neuron *19*, 679–686.

Gil, Z., Connors, B.W., and Amitai, Y. (1999). Efficacy of thalamocortical and intracortical synaptic connections: quanta, innervation, and reliability. Neuron *23*, 385–397.

Gilbert, C.D. (1998). Adult cortical dynamics. Physiol. Rev. *78*, 467–485.

Gjorgjieva, J., Mease, R.A., Moody, W.J., and Fairhall, A.L. (2014). Intrinsic neuronal properties switch the mode of information transmission in networks. PLoS Comput. Biol. *10*, e1003962.

Goble, A.K., and Hollins, M. (1993). Vibrotactile adaptation enhances amplitude discrimination. J. Acoust. Soc. Am. *93*, 418–424.

Goble, A.K., and Hollins, M. (1994). Vibrotactile adaptation enhances frequency discrimination. J. Acoust. Soc. Am. *96*, 771–780.

Goldman, M.S., Nelson, S.B., and Abbott, L.F. (1999). Decorrelation of spike trains by synaptic depression. Neurocomputing *26–27*, 147–153.

Greenlee, M.W., and Heitger, F. (1988). The functional role of contrast adaptation. Vision Res. *28*, 791–797.

Grimm, S., and Escera, C. (2012). Auditory deviance detection revisited: evidence for a hierarchical novelty system. Int. J. Psychophysiol. *85*, 88–92.

Grosenick, L., Marshel, J.H., and Deisseroth, K. (2015). Closed-loop and activity-guided optogenetic control. Neuron *86*, 106–139.

Gutnisky, D.A., and Dragoi, V. (2008). Adaptive coding of visual information in neural populations. Nature *452*, 220–224.

Haas, J.S., Greenwald, C.M., and Pereda, A.E. (2016). Activity-dependent plasticity of electrical synapses: increasing evidence for its presence and functional roles in the mammalian brain. BMC Cell Biol. *17* (*Suppl 1*), 14.

Haider, B., Krause, M.R., Duque, A., Yu, Y., Touryan, J., Mazer, J.A., and McCormick, D.A. (2010). Synaptic and network mechanisms of sparse and reliable visual cortical activity during nonclassical receptive field stimulation. Neuron *65*, 107–121.

Hartings, J.A., Temereanca, S., and Simons, D.J. (2003). Processing of periodic whisker deflections by neurons in the ventroposterior medial and thalamic reticular nuclei. J. Neurophysiol. *90*, 3087–3094.

Häusser, M., Spruston, N., and Stuart, G.J. (2000). Diversity and dynamics of dendritic signaling. Science *290*, 739–744.

Heeger, D.J. (1992). Normalization of cell responses in cat striate cortex. Vis. Neurosci. *9*, 181–197.

Heiss, J.E., Katz, Y., Ganmor, E., and Lampl, I. (2008). Shift in the balance between excitation and inhibition during sensory adaptation of S1 neurons. J. Neurosci. *28*, 13320–13330.

Henze, D.A., and Buzsáki, G. (2001). Action potential threshold of hippocampal pyramidal cells in vivo is increased by recent spiking activity. Neuroscience *105*, 121–130.

Hershenhoren, I., Taaseh, N., Antunes, F.M., and Nelken, I. (2014). Intracellular correlates of stimulus-specific adaptation. J. Neurosci. *34*, 3303–3319.

Higley, M.J., and Contreras, D. (2006). Balanced excitation and inhibition determine spike timing during frequency adaptation. J. Neurosci. *26*, 448–457.

Huang, C.G., Zhang, Z.D., and Chacron, M.J. (2016). Temporal decorrelation by SK channels enables efficient neural coding and perception of natural stimuli. Nat. Commun. *7*, 11353.

Hubel, D.H., and Wiesel, T.N. (1959). Receptive fields of single neurones in the cat's striate cortex. J. Physiol. *148*, 574–591.

Isaacson, J.S., and Scanziani, M. (2011). How inhibition shapes cortical activity. Neuron *72*, 231–243.

Jin, D.Z., Dragoi, V., Sur, M., and Seung, H.S. (2005). Tilt aftereffect and adaptation-induced changes in orientation tuning in visual cortex. J. Neurophysiol. *94*, 4038–4050.

Jones, E.G. (2002). Thalamic circuitry and thalamocortical synchrony. Philos. Trans. R. Soc. Lond. B Biol. Sci. *357*, 1659–1673.

Jones, H.E., Grieve, K.L., Wang, W., and Sillito, A.M. (2001). Surround suppression in primate V1. J. Neurophysiol. *86*, 2011–2028.

Jouhanneau, J.-S., Kremkow, J., Dorrn, A.L., and Poulet, J.F.A. (2015). In vivo monosynaptic excitatory transmission between layer 2 cortical pyramidal neurons. Cell Rep. *13*, 2098–2106.

Jubran, M., Mohar, B., and Lampl, I. (2016). The transformation of adaptation specificity to whisker identity from brainstem to thalamus. Front. Syst. Neurosci. *10*, 56.

Jung, H.Y., Mickus, T., and Spruston, N. (1997). Prolonged sodium channel inactivation contributes to dendritic action potential attenuation in hippocampal pyramidal neurons. J. Neurosci. *17*, 6639–6646.

Kaliukhovich, D.A., and Vogels, R. (2016). Divisive normalization predicts adaptation-induced response changes in macaque inferior temporal cortex. J. Neurosci. *36*, 6116–6128.

Karmarkar, U.R., and Dan, Y. (2006). Experience-dependent plasticity in adult visual cortex. Neuron *52*, 577–585.

Khatri, V., Hartings, J.A., and Simons, D.J. (2004). Adaptation in thalamic barreloid and cortical barrel neurons to periodic whisker deflections varying in frequency and velocity. J. Neurophysiol. *92*, 3244–3254.

Khouri, L., and Nelken, I. (2015). Detecting the unexpected. Curr. Opin. Neurobiol. *35*, 142–147.

King, J.L., Lowe, M.P., Stover, K.R., Wong, A.A., and Crowder, N.A. (2016). Adaptive processes in thalamus and cortex revealed by silencing of primary visual cortex during contrast adaptation. Curr. Biol. *26*, 1295–1300.

Kohn, A. (2007). Visual adaptation: physiology, mechanisms, and functional benefits. J. Neurophysiol. *97*, 3155–3164.

La Camera, G., Rauch, A., Thurbon, D., Lüscher, H.R., Senn, W., and Fusi, S. (2006). Multiple time scales of temporal response in pyramidal and fast spiking cortical neurons. J. Neurophysiol. *96*, 3448–3464.

Lancaster, B., and Nicoll, R.A. (1987). Properties of two calcium-activated hyperpolarizations in rat hippocampal neurones. J. Physiol. *389*, 187–203.

Landisman, C.E., and Connors, B.W. (2007). VPM and PoM nuclei of the rat somatosensory thalamus: intrinsic neuronal properties and corticothalamic feedback. Cereb. Cortex *17*, 2853–2865.

Laughlin, S.B., and Hardie, R.C. (1978). Common strategies for light adaptation in the peripheral visual systems of fly and dragonfly. J. Comp. Physiol. *128*, 319–340.

Lee, C.J., and Whitsel, B.L. (1992). Mechanisms underlying somatosensory cortical dynamics: I. In vivo studies. Cereb. Cortex *2*, 81–106.

Lesica, N.A., and Stanley, G.B. (2004). Encoding of natural scene movies by tonic and burst spikes in the lateral geniculate nucleus. J. Neurosci. *24*, 10731–10740.

Lesica, N.A., and Stanley, G.B. (2005). An LGN inspired detect/transmit framework for high fidelity relay of visual information with limited bandwidth. In Brain, Vision, and Artificial Intelligence, M. De Gregorio, V. Di Maio, and C. Musio, eds. (Springer), pp. 177–186.

Lesica, N.A., and Stanley, G.B. (2006). Decoupling functional mechanisms of adaptive encoding. Network *17*, 43–60.

Lesica, N.A., Weng, C., Jin, J., Yeh, C.-I., Alonso, J.-M., and Stanley, G.B. (2006). Dynamic encoding of natural luminance sequences by LGN bursts. PLoS Biol. *4*, e209.

Lesica, N.A., Jin, J., Weng, C., Yeh, C.-I., Butts, D.A., Stanley, G.B., and Alonso, J.M. (2007). Adaptation to stimulus contrast and correlations during natural visual stimulation. Neuron *55*, 479–491.

Levinson, E., and Sekuler, R. (1976). Adaptation alters perceived direction of motion. Vision Res. *16*, 779–781.

Louie, K., Khaw, M.W., and Glimcher, P.W. (2013). Normalization is a general neural mechanism for context-dependent decision making. Proc. Natl. Acad. Sci. USA *110*, 6139–6144.

Lundstrom, B.N., Higgs, M.H., Spain, W.J., and Fairhall, A.L. (2008). Fractional differentiation by neocortical pyramidal neurons. Nat. Neurosci. *11*, 1335–1342.

Lundstrom, B.N., Fairhall, A.L., and Maravall, M. (2010). Multiple timescale encoding of slowly varying whisker stimulus envelope in cortical and thalamic neurons in vivo. J. Neurosci. *30*, 5071–5077.

Luo, L., Callaway, E.M., and Svoboda, K. (2008). Genetic dissection of neural circuits. Neuron *57*, 634–660.

Malmierca, M.S., Cristaudo, S., Pérez-González, D., and Covey, E. (2009). Stimulus-specific adaptation in the inferior colliculus of the anesthetized rat. J. Neurosci. *29*, 5483–5493.

Malmierca, M.S., Anderson, L.A., and Antunes, F.M. (2015). The cortical modulation of stimulus-specific adaptation in the auditory midbrain and thalamus: a potential neuronal correlate for predictive coding. Front. Syst. Neurosci. *9*, 19.

Mante, V., Frazor, R.A., Bonin, V., Geisler, W.S., and Carandini, M. (2005). Independence of luminance and contrast in natural scenes and in the early visual system. Nat. Neurosci. *8*, 1690–1697.

Maravall, M., Petersen, R.S., Fairhall, A.L., Arabzadeh, E., and Diamond, M.E. (2007). Shifts in coding properties and maintenance of information transmission during adaptation in barrel cortex. PLoS Biol. *5*, e19.

Maravall, M., Alenda, A., Bale, M.R., and Petersen, R.S. (2013). Transformation of adaptation and gain rescaling along the whisker sensory pathway. PLoS ONE *8*, e82418.

McCormick, D.A., McGinley, M.J., and Salkoff, D.B. (2015). Brain state dependent activity in the cortex and thalamus. Curr. Opin. Neurobiol. *31*, 133–140.

Mease, R.A., Famulare, M., Gjorgjieva, J., Moody, W.J., and Fairhall, A.L. (2013). Emergence of adaptive computation by single neurons in the developing cortex. J. Neurosci. *33*, 12154–12170.

Mease, R.A., Krieger, P., and Groh, A. (2014). Cortical control of adaptation and sensory relay mode in the thalamus. Proc. Natl. Acad. Sci. USA *111*, 6798–6803.

Mensi, S., Naud, R., Pozzorini, C., Avermann, M., Petersen, C.C., and Gerstner, W. (2012). Parameter extraction and classification of three cortical neuron types reveals two distinct adaptation mechanisms. J. Neurophysiol. *107*, 1756–1775.

Mill, R., Coath, M., Wennekers, T., and Denham, S.L. (2011). A neurocomputational model of stimulus-specific adaptation to oddball and Markov sequences. PLoS Comput. Biol. *7*, e1002117.

Millard, D.C., Whitmire, C.J., Gollnick, C.A., Rozell, C.J., and Stanley, G.B. (2015). Electrical and optical activation of mesoscale neural circuits with implications for coding. J. Neurosci. *35*, 15702–15715.

Miller, K.D. (2016). Canonical computations of cerebral cortex. Curr. Opin. Neurobiol. *37*, 75–84.

Miller, E.K., Gochin, P.M., and Gross, C.G. (1991). Habituation-like decrease in the responses of neurons in inferior temporal cortex of the macaque. Vis. Neurosci. *7*, 357–362.

Miller, K.D., Pinto, D.J., and Simons, D.J. (2001). Processing in layer 4 of the neocortical circuit: new insights from visual and somatosensory cortex. Curr. Opin. Neurobiol. *11*, 488–497.

Montemurro, M.A., Panzeri, S., Maravall, M., Alenda, A., Bale, M.R., Brambilla, M., and Petersen, R.S. (2007). Role of precise spike timing in coding of dynamic vibrissa stimuli in somatosensory thalamus. J. Neurophysiol. *98*, 1871–1882.

Moore, C.I. (2004). Frequency-dependent processing in the vibrissa sensory system. J. Neurophysiol. *91*, 2390–2399.

Moore, C.I., Nelson, S.B., and Sur, M. (1999). Dynamics of neuronal processing in rat somatosensory cortex. Trends Neurosci. *22*, 513–520.

Moore, C.I., Carlen, M., Knoblich, U., and Cardin, J.A. (2010). Neocortical interneurons: from diversity, strength. Cell *142*, 189–193.

Mrsic-Flogel, T., and Hübener, M. (2002). Visual cortex: suppression by depression? Curr. Biol. *12*, R547–R549.

Musall, S., von der Behrens, W., Mayrhofer, J.M., Weber, B., Helmchen, F., and Haiss, F. (2014). Tactile frequency discrimination is enhanced by circumventing neocortical adaptation. Nat. Neurosci. *17*, 1567–1573.

Natan, R.G., Briguglio, J.J., Mwilambwe-Tshilobo, L., Jones, S.I., Aizenberg, M., Goldberg, E.M., and Geffen, M.N. (2015). Complementary control of sensory adaptation by two types of cortical interneurons. eLife *4*, 1–27.

Newman, J.P., Fong, M.F., Millard, D.C., Whitmire, C.J., Stanley, G.B., and Potter, S.M. (2015). Optogenetic feedback control of neural activity. eLife *4*, e07192.

Ohshiro, T., Angelaki, D.E., and DeAngelis, G.C. (2011). A normalization model of multisensory integration. Nat. Neurosci. *14*, 775–782.

Ollerenshaw, D.R., Zheng, H.J.V., Millard, D.C., Wang, Q., and Stanley, G.B. (2014). The adaptive trade-off between detection and discrimination in cortical representations and behavior. Neuron *81*, 1152–1164.

Olsen, S.R., Bhandawat, V., and Wilson, R.I. (2010). Divisive normalization in olfactory population codes. Neuron *66*, 287–299.

Pala, A., and Petersen, C.C.H. (2015). In vivo measurement of cell-type-specific synaptic connectivity and synaptic transmission in layer 2/3 mouse barrel cortex. Neuron *85*, 68–75.

Patterson, C.A., Wissig, S.C., and Kohn, A. (2013). Distinct effects of brief and prolonged adaptation on orientation tuning in primary visual cortex. J. Neurosci. *33*, 532–543.

Patterson, C.A., Wissig, S.C., and Kohn, A. (2014). Adaptation disrupts motion integration in the primate dorsal stream. Neuron *81*, 674–686.

Pérez-González, D., and Malmierca, M.S. (2014). Adaptation in the auditory system: an overview. Front. Integr. Nuerosci. *8*, 19.

Petersen, C.C.H., Hahn, T.T.G., Mehta, M., Grinvald, A., and Sakmann, B. (2003). Interaction of sensory responses with spontaneous depolarization in layer 2/3 barrel cortex. Proc. Natl. Acad. Sci. USA *100*, 13638–13643.

Pinault, D. (2004). The thalamic reticular nucleus: structure, function and concept. Brain Res. Brain Res. Rev. *46*, 1–31.

Pouille, F., and Scanziani, M. (2001). Enforcement of temporal fidelity in pyramidal cells by somatic feed-forward inhibition. Science *293*, 1159–1163.

Poulet, J.F.A., and Petersen, C.C.H. (2008). Internal brain state regulates membrane potential synchrony in barrel cortex of behaving mice. Nature *454*, 881–885.

Pozzorini, C., Naud, R., Mensi, S., and Gerstner, W. (2013). Temporal whitening by power-law adaptation in neocortical neurons. Nat. Neurosci. *16*, 942–948.

Ramirez, A., Pnevmatikakis, E.A., Merel, J., Paninski, L., Miller, K.D., and Bruno, R.M. (2014). Spatiotemporal receptive fields of barrel cortex revealed by reverse correlation of synaptic input. Nat. Neurosci. *17*, 866–875.

Regehr, W.G. (2012). Short-term presynaptic plasticity. Cold Spring Harb. Perspect. Biol. *4*, a005702.

Reinhold, K., Lien, A.D., and Scanziani, M. (2015). Distinct recurrent versus afferent dynamics in cortical visual processing. Nat. Neurosci. *18*, 1789–1797.

Reyes, A., Lujan, R., Rozov, A., Burnashev, N., Somogyi, P., and Sakmann, B. (1998). Target-cell-specific facilitation and depression in neocortical circuits. Nat. Neurosci. *1*, 279–285.

Reynolds, J.H., and Heeger, D.J. (2009). The normalization model of attention. Neuron *61*, 168–185.

Richardson, B.D., Hancock, K.E., and Caspary, D.M. (2013). Stimulus-specific adaptation in auditory thalamus of young and aged awake rats. J. Neurophysiol. *110*, 1892–1902.

RIKEN (2014). What makes purkinje neurons unique? Cutting edge methods reveal. ScienceDaily, www.sciencedaily.com/releases/2014/06/140605140232.htm.

Ringo, J.L. (1996). Stimulus specific adaptation in inferior temporal and medial temporal cortex of the monkey. Behav. Brain Res. *76*, 191–197.

Sanchez-Vives, M.V., Nowak, L.G., and McCormick, D.A. (2000). Cellular mechanisms of long-lasting adaptation in visual cortical neurons in vitro. J. Neurosci. *20*, 4286–4299.

Sato, T.K., Haider, B., Häusser, M., and Carandini, M. (2016). An excitatory basis for divisive normalization in visual cortex. Nat. Neurosci. *19*, 568–570.

Sawamura, H., Orban, G.A., and Vogels, R. (2006). Selectivity of neuronal adaptation does not match response selectivity: a single-cell study of the FMRI adaptation paradigm. Neuron *49*, 307–318.

Schwartz, O., Pillow, J.W., Rust, N.C., and Simoncelli, E.P. (2006). Spike-triggered neural characterization. J. Vis. *6*, 484–507.

Sekuler, R.W., and Ganz, L. (1963). Aftereffect of seen motion with a stabilized retinal image. Science *139*, 419–420.

Sen, K., Jorge-Rivera, J.C., Marder, E., and Abbott, L.F. (1996). Decoding synapses. J. Neurosci. *16*, 6307–6318.

Sengpiel, F., and Bonhoeffer, T. (2002). Orientation specificity of contrast adaptation in visual cortical pinwheel centres and iso-orientation domains. Eur. J. Neurosci. *15*, 876–886.

Seriès, P., Stocker, A.A., and Simoncelli, E.P. (2009). Is the homunculus "aware" of sensory adaptation? Neural Comput. *21*, 3271–3304.

Shapley, R., and Victor, J.D. (1979). The contrast gain control of the cat retina. Vision Res. *19*, 431–434.

Sharpee, T.O., Sugihara, H., Kurgansky, A.V., Rebrik, S.P., Stryker, M.P., and Miller, K.D. (2006). Adaptive filtering enhances information transmission in visual cortex. Nature *439*, 936–942.

Sherman, S.M., and Guillery, R.W. (1998). On the actions that one nerve cell can have on another: distinguishing "drivers" from "modulators". Proc. Natl. Acad. Sci. USA *95*, 7121–7126.

Sheth, B.R., Moore, C.I., and Sur, M. (1998). Temporal modulation of spatial borders in rat barrel cortex. J. Neurophysiol. *79*, 464–470.

Silver, R.A. (2010). Neuronal arithmetic. Nat. Rev. Neurosci. *11*, 474–489.

Simoncelli, E.P., Paninski, L., Pillow, J.W., and Schwartz, O. (2004). Characterization of neural responses with stochastic stimuli. In The New Cognitive Neurosciences, Third Edition, M. Gazzaniga, ed. (MIT Press).

Simons, D.J. (1985). Temporal and spatial integration in the rat SI vibrissa cortex. J. Neurophysiol. *54*, 615–635.

Simons, S.B., Tannan, V., Chiu, J., Favorov, O.V., Whitsel, B.L., and Tommerdahl, M. (2005). Amplitude-dependency of response of SI cortex to flutter stimulation. BMC Neurosci. *6*, 43.

Solomon, S.G., Peirce, J.W., Dhruv, N.T., and Lennie, P. (2004). Profound contrast adaptation early in the visual pathway. Neuron *42*, 155–162.

Stanley, G.B. (2002). Adaptive spatiotemporal receptive field estimation in the visual pathway. Neural Comput. *14*, 2925–2946.

Stevens, C.F., and Wang, Y. (1995). Facilitation and depression at single central synapses. Neuron *14*, 795–802.

Stoelzel, C.R., Huff, J.M., Bereshpolova, Y., Zhuang, J., Hei, X., Alonso, J.-M., and Swadlow, H.A. (2015). Hour-long adaptation in the awake early visual system. J. Neurophysiol. *114*, 1172–1182.

Strobach, T., and Carbon, C.C. (2013). Face adaptation effects: reviewing the impact of adapting information, time, and transfer. Front. Psychol. *4*, 318.

Suga, N., and Ma, X. (2003). Multiparametric corticofugal modulation and plasticity in the auditory system. Nat. Rev. Neurosci. *4*, 783–794.

Taaseh, N., Yaron, A., and Nelken, I. (2011). Stimulus-specific adaptation and deviance detection in the rat auditory cortex. PLoS ONE *6*, e23369.

Tannan, V., Whitsel, B.L., and Tommerdahl, M.A. (2006). Vibrotactile adaptation enhances spatial localization. Brain Res. *1102*, 109–116.

Theunissen, F.E., Sen, K., and Doupe, A.J. (2000). Spectral-temporal receptive fields of nonlinear auditory neurons obtained using natural sounds. J. Neurosci. *20*, 2315–2331.

Tiesinga, P., Fellous, J.-M.M., and Sejnowski, T.J. (2008). Regulation of spike timing in visual cortical circuits. Nat. Rev. Neurosci. *9*, 97–107.

Toib, A., Lyakhov, V., and Marom, S. (1998). Interaction between duration of activity and time course of recovery from slow inactivation in mammalian brain Na+ channels. J. Neurosci. *18*, 1893–1903.

Tommerdahl, M., Favorov, O., and Whitsel, B.L. (2002). Optical imaging of intrinsic signals in somatosensory cortex. Behav. Brain Res. *135*, 83–91.

Tommerdahl, M., Hester, K.D., Felix, E.R., Hollins, M., Favorov, O.V., Quibrera, P.M., and Whitsel, B.L. (2005). Human vibrotactile frequency discriminative capacity after adaptation to 25 Hz or 200 Hz stimulation. Brain Res. *1057*, 1–9.

Ulanovsky, N., Las, L., and Nelken, I. (2003). Processing of low-probability sounds by cortical neurons. Nat. Neurosci. *6*, 391–398.

Varela, C. (2014). Thalamic neuromodulation and its implications for executive networks. Front. Neural Circuits *8*, 69.

Vierck, C.J., Jr., and Jones, M.B. (1970). Influences of low and high frequency oscillation upon spatio-tactile resolution. Physiol. Behav. *5*, 1431–1435.

Vinje, W.E., and Gallant, J.L. (2002). Natural stimulation of the nonclassical receptive field increases information transmission efficiency in V1. J. Neurosci. *22*, 2904–2915.

von Békésy, G. (1957). Neural volleys and the similarity between some sensations produced by tones and by skin vibrations. J. Acoust. Soc. Am. *29*, 1059.

von der Behrens, W., Bäuerle, P., Kössl, M., and Gaese, B.H. (2009). Correlating stimulus-specific adaptation of cortical neurons and local field potentials in the awake rat. J. Neurosci. *29*, 13837–13849.

Wang, H.-P., Spencer, D., Fellous, J.-M., and Sejnowski, T.J. (2010a). Synchrony of thalamocortical inputs maximizes cortical reliability. Science *328*, 106–109.

Wang, Q., Webber, R.M., and Stanley, G.B. (2010b). Thalamic synchrony and the adaptive gating of information flow to cortex. Nat. Neurosci. *13*, 1534–1541.

Webber, R.M., and Stanley, G.B. (2004). Nonlinear encoding of tactile patterns in the barrel cortex. J. Neurophysiol. *91*, 2010–2022.

Webster, M.A., and MacLeod, D.I.A. (2011). Visual adaptation and face perception. Philos. Trans. R. Soc. Lond. B Biol. Sci. *366*, 1702–1725.

Webster, M.A., Kaping, D., Mizokami, Y., and Duhamel, P. (2004). Adaptation to natural facial categories. Nature *428*, 557–561.

Wehr, M., and Zador, A.M. (2003). Balanced inhibition underlies tuning and sharpens spike timing in auditory cortex. Nature *426*, 442–446.

Whitmire, C.J., Waiblinger, C., Schwarz, C., and Stanley, G.B. (2016). Information coding through adaptive gating of synchronized thalamic bursting. Cell Rep. *14*, 795–807.

Wilent, W.B., and Contreras, D. (2005a). Stimulus-dependent changes in spike threshold enhance feature selectivity in rat barrel cortex neurons. J. Neurosci. *25*, 2983–2991.

Wilent, W.B., and Contreras, D. (2005b). Dynamics of excitation and inhibition underlying stimulus selectivity in rat somatosensory cortex. Nat. Neurosci. *8*, 1364–1370.

Wohlgemuth, A. (1911). On the after-effect of seen movement. Br. J. Psychol. Monogr. *1* (*Suppl.*), 1–117.

Wu, G.K., Li, P., Tao, H.W., and Zhang, L.I. (2006). Nonmonotonic synaptic excitation and imbalanced inhibition underlying cortical intensity tuning. Neuron *52*, 705–715.

Yaron, A., Hershenhoren, I., and Nelken, I. (2012). Sensitivity to complex statistical regularities in rat auditory cortex. Neuron *76*, 603–615.

Zagha, E., and McCormick, D.A. (2014). Neural control of brain state. Curr. Opin. Neurobiol. *29*, 178–186.

Zavitz, E., Yu, H.-H., Rowe, E.G., Rosa, M.G., and Price, N.S. (2016). Rapid adaptation induces persistent biases in population codes for visual motion. J. Neurosci. *36*, 4579–4590.

Zheng, H.J.V., Wang, Q., and Stanley, G.B. (2015). Adaptive shaping of cortical response selectivity in the vibrissa pathway. J. Neurophysiol. *113*, 3850–3865.

Zucker, R.S., and Regehr, W.G. (2002). Short-term synaptic plasticity. Annu. Rev. Physiol. *64*, 355–405.