Webber, Roxanna M. and Garrett B. Stanley. Transient and steady-state adaptation dynamics of cortical adaptation. J Neurophysiol 95: 2923–2932, 2006. First published February 8, 2006; doi:10.1152/jn.01188.2005. Adaptation is a ubiquitous property of all sensory pathways of the brain and thus likely critical in the encoding of behaviorally relevant sensory information. Despite evidence identifying specific biophysical mechanisms contributing to sensory adaptation, its functional role in sensory encoding is not well understood, particularly in the natural environment where transient rather than steady-state activity could dominate the neuronal representation. Here, we show that the heterogeneous transient and steady-state adaptation dynamics of single cortical neurons in the rat vibrissa system were well characterized by an underlying state variable. The state was directly predictable from temporal response properties that capture the time course of postexcitatory suppression following an isolated vibrissa deflection. Altering the initial state, by preceding the periodic stimulus with an additional vibrissa deflection, strongly influenced single-cell transient cortical adaptation responses. Despite the different transient activity, neurons reached the same steady-state adapted response with a time to steady state that was independent of the initial state. However, the differences in transient activity observed on small time scales were not present when activity was integrated over the longer time scale of a stimulus cycle. Taken together, the results here demonstrate that although adaptation can have significant effects on transient neuronal activity and direction selectivity, a simple measure of the time course of suppression following an isolated stimulus predicted a large portion of the observed adaptation dynamics.

Introduction

Adaptation is a phenomenon widely observed at multiple levels of processing across all sensory pathways of the brain (Hellweg et al. 1977; Ohzawa et al. 1982; Wilson 1998). Acting over a range of time scales, adaptation has been implicated in both shifting the sensitivity of the system to maximize the dynamic range of encoding and priming the system for responses to novel stimuli (Abbott et al. 1997; Fairhall et al. 2001; Muller et al. 1999). Rapid adaptation, a type of sensory adaptation for which response attenuation has been shown to develop and recover on time scales of milliseconds to seconds, has been reported in response to sensory stimuli in the visual and somatosensory cortices (Chung et al. 2002; Muller et al. 1999; Nelson 1991). Although steady-state adaptation properties have been characterized in many sensory pathways (Ahissar et al. 2001; Eggermont 1991; Shapley and Victor 1979), little is known regarding the transient component of adaptation. The transient dynamics could be particularly important in understanding neural coding in the natural environment, where the statistics of the sensory inputs are continuously changing, and transient rather than steady-state dynamics may dominate the representation.

Rats use their vibrissae to actively explore the environment and to perform tasks of detection and discrimination by sweeping (whisking) the vibrissa array across objects at frequencies between 6 and 12 Hz (Brecht et al. 1997; Carvell and Simons 1990; Guic-Robles et al. 1989; Welker 1964). Although whisking is not restricted to a single plane of motion (Bermejo et al. 2002), it can be idealized in a two-dimensional anterior-posterior plane. Recent studies have explored the steady-state neuronal responses to stimuli in the whisking frequency range. It has been shown that repetitive periodic stimuli in the rat vibrissa system induce adaptation first at the level of the thalamus (Chung et al. 2002; Hartings et al. 2003; Sosnik et al. 2001) and at lower frequencies (4–6 Hz) in cortical neurons (Ahissar et al. 2001; Chung et al. 2002; Khatiri et al. 2004). Higher frequencies of periodic stimulation generally result in low- or band-pass properties of the steady-state response (Ahissar et al. 2001; Garabedian et al. 2003; Khatiri et al. 2004; Webber and Stanley 2004). It has been postulated that the initial transient adaptation dynamics in the rat vibrissa system could be related to the time course of suppression after a single vibrissa deflection (Hartings et al. 2003; Webber and Stanley 2004), although a direct relationship has not yet been established experimentally.

In this study, we investigated the neural response when vibrissae were deflected in two directions within a single plane. We inferred the time course of postexcitatory suppression after an isolated vibrissa deflection by measuring the relative response to a second deflection at varying time intervals after the first deflection. We show that this temporal response property of a cell predicted the corresponding transient and steady-state adaptation dynamics observed in response to periodic stimuli presented around natural whisking frequencies. The relatively complex neural activity observed during adaptation was well characterized by a simple underlying “state,” which varied over time as a function of the suppression induced throughout the stimulus history. For individual neurons, we altered the initial state by inserting an additional deflection prior to the onset of the periodic stimulus. This gave rise to fundamentally different transient adaptation responses yet led to an invariant steady-state response. Furthermore, despite the variable responses observed at fine temporal scales, when integrated over a stimulus cycle, the transient firing rate was also independent of the initial state. Although adaptation alters transient neuronal activity and direction selectivity, the observed adaptation
dynamics were largely predicted by a simple measure of the time course of suppression after an isolated stimulus.

METHODS

Surgical preparation

Thirteen female adult Sprague-Dawley rats weighing 250–300 g (Charles River Facility, Wilmington, MA) were used in the experiments. Surgical procedures were the same as previously described (Webber and Stanley 2004). Briefly, animals were initially sedated with 2% vaporized isoflurane, anesthetized with an intraperitoneal injection of pentobarbital sodium (50 mg/kg), and transferred to a stereotaxic frame (Kopf Instruments, Tujunga, CA) for surgery and recording. A craniotomy (2 × 2 mm) was performed on the left parietal bone above the vibrissa (barrel) region of the primary somatosensory cortex (Paxinos and Watson 1998). The edges of the craniotomy were sealed with bone wax, and mineral oil was applied to cover and protect the exposed dura. After surgery, supplemental doses of pentobarbital (12.5 mg/kg) were administered as necessary to maintain a light level of anesthesia. The physiological condition of the animals was assessed through the respiratory rate, pinch reflexes, and corneal reflexes. Body temperature was maintained at 38°C with a heating pad. At the termination of the experiment, animals were killed with an overdose of pentobarbital sodium. All procedures were approved by the Animal Care and Use Committee at Harvard University and in accordance with guidelines established by the National Institutes of Health.

Electrophysiological recordings and vibrissa stimulation

A sharp tungsten microelectrode (5–7 MΩ, FHC, Bowdoinham, ME) was slowly advanced through the cortex until a cell was encountered between 600 and 800 µm below the surface. Neuronal signals were amplified (A-M Systems, Sequim, WA), band-pass filtered (300 Hz to 5 kHz), and acquired at 20 kHz. Single-unit activity was discriminated off-line using standard template matching techniques and physiologically plausible refractory periods. All recorded cells were excitatory regular spiking units (RSUs) within the barrel field (Simons 1978; Zhu and Connors 1999), and the principal vibrissa (PV) was determined through manual deflection as the vibrissa that elicited the largest neuronal response.

Vibrissa deflection was controlled by inserting the PV into a glass pipette fixed to the end of a piezoelectric bending actuator (Polytech PI, Auburn, MA) positioned 10 mm from the vibrissa pad. Vibrissae were deflected with a filtered square-wave pattern to minimize mechanical ringing of the actuator (Simons 1983; Webber and Stanley 2004). The square wave was smoothed with a one-sided Gaussian filter of 1-ms SD, which did not interfere with the smallest inter-deflection intervals (IDIs) used in this study. The actuator was calibrated to produce 700-µm deflections with maximum velocities between 100 and 155 mm/s. Deflections from rest to the plateau were defined as “away” from rest, and deflections from the plateau to resting position were defined as “back” to rest. The data collection and actuator were controlled using LabWindows acquisition/control software (National Instruments, Austin, TX) and the C++ programming language.

Stimulus protocols

The study includes recordings from 41 single units. All PVs were deflected with a paired-deflection protocol, consisting of a filtered square wave with time intervals between away and back deflections ranging from 20 to 250 ms IDIs (see Fig. 2a). The PV was first deflected with the paired-deflection stimulus beginning at rest with the first deflection away from rest and the second deflection back to rest. In a separate set of trials, the PV was deflected with the paired-deflection stimulus in the opposite direction, beginning at the plateau position with the first deflection back to rest and the second deflection away from rest, using the same IDIs. Each IDI was presented 90 times with 1 s of rest between trials.

The standard adaptation protocol consisted of deflecting the PV from rest with a filtered square wave of 50% duty cycle (see Fig. 1a). The inverted adaptation protocol was the same as the standard, but preceded by an additional deflection in the back direction (beginning away from rest with 1st deflection back to rest; see Fig. 5, B and D). For 19 cells, the PV was deflected in the rostral-caudal plane with the standard adaptation protocol at 2, 4, 6, 8, and 16 Hz. Thirteen cells were stimulated at 4, 6, 8, and 16 Hz with the standard and inverted adaptation protocols. Each stimulus train was 5 s long and presented 20 times with 10 s of rest between each presentation. Although whisking is not restricted to a single plane of motion (Bermejo et al. 2002), it can be idealized in a two-dimensional anterior-posterior plane. Therefore in this study, vibrissae were deflected primarily in the two directions of the rostral-caudal plane. For nine cells in this study, the PV was deflected with standard and inverted adaptation protocols in five directions (rostral, rostro-dorsal, dorsal, caudo-dorsal, and caudal) at 4 and 6 Hz or 6 and 8 Hz. For this set of cells, each stimulus train was 3 s long and presented 20 times with 10 s of rest between trains. Data analyses indicated that the phenomena observed for rostral-caudal stimulation were present in multiple directions; therefore all responses were combined for average response measures.

Characterization of postexcitatory suppression

The paired-deflection protocol was used to determine the amount of suppression after a single deflection in a given direction. Neuronal suppression after a deflection was inferred from the activity of a cell in response to a subsequent deflection at varying IDIs (Fanselow and Nicolelis 1999; Kyriazi et al. 1994; Webber and Stanley 2004). The area under the curve (AUC) for the first 30 ms of the peristimulus time histogram (PSTH, 3-ms bins) after the second deflection of the square wave was calculated at all IDIs for each neuron and normalized by the AUC obtained for a single deflection in that direction to form response-suppression curves. The response-suppression curve is analogous to the normalized “off response” measures previously reported (Kyriazi et al. 1994), except that here the on deflection was not always in the maximal response direction. Two response-suppression curves were formed for each neuron, one representing suppression after an away from rest deflection (α) and one representing suppression after a back to rest deflection (β). All error bars represent 1 SE above and below the mean and were determined through bootstrapping methods applied to the dataset (i.e., dividing the full number of trials into multiple smaller subsets of trials to calculate the mean and SE). The t₀ value, or the IDI for which the response reached 50% of the maximum value, was determined for all of the response-suppression curves by interpolating between known points using a shape-preserving piece-wise cubic interpolation in Matlab (The Mathworks, Natick, MA).

Characterization of adaptation

The adaptation to periodic stimuli was defined as a deviation from the observed response to an isolated deflection. PSTHs were calculated as the average number of spikes occurring in 3-ms bins across trials unless otherwise stated. The average neuronal response after each deflection was determined by computing the AUC of the PSTH for a 30-ms bin after the relevant deflection. Responses in each direction were normalized to an isolated deflection response in the associated direction to account for the directional selectivity of neurons. The adaptation response trajectories for each neuron were fit with second-order polynomial functions using a nonlinear least-squares method.
The adaptation response was divided into transient and steady-state portions. Neurons reached a stable response level in <1 s of stimulation for all tested frequencies. Therefore the steady-state response was conservatively defined as the average response per deflection from 1 to 3 s after initiation of the stimulus for each direction. The transient portion was defined as the time period from stimulus initiation until the polynomial fit in each direction reached a level within 1 SE of the corresponding steady-state response.

Simulations

All simulations in this study were performed using a predictive method described previously based on nonlinear interactions of the response-suppression curves within a deflection sequence (Webber and Stanley 2004). Briefly, to predict the neural response, this method used parametric forms of the $\alpha$ and $\beta$ response-suppression curves described in the preceding text, and the response magnitudes for isolated deflections in the given directions. Parametric response-suppression curves were formed from a sigmoidal hyperbolic tangent function

$$x(t_{\text{Ref}}) = \frac{1}{2} \left[ \tanh(t_{\text{Ref}} - t_{\text{IDT}}/\tau) + 1 \right]$$

where $t_{\text{Ref}}$ was the time associated with the IDI. The curve was characterized by two parameters, $\tau$ and $t_{\text{IDT}}$, describing the rise time of the sigmoid and the time at which the function reaches 50% of the maximum value, respectively. This function was previously found to be representative, on average, of observed response-suppression curves (Webber and Stanley 2004). For simulations, $\tau$ was held constant at 50 ms (consistent with experimental data) and $t_{\text{IDT}}$ was varied, unless otherwise stated. An identical formulation was used for $\beta$.

For a sequence of deflections, the response to each deflection was influenced by the amount of suppression induced by prior deflections. The response to a given deflection was expressed as the response to a single deflection in isolation, denoted by $\hat{r}$, scaled by the “state” of the system at that time, denoted by $x$. Values of the state $<1$ represent a suppression of the excitatory response compared with its isolated response, and values $>1$ represent an amplification. The underlying state was directly related to the amount of suppression induced by prior deflections, and therefore a function of the response-suppression curves. Consider, as a simple example, the first three deflections of the sequence in Fig. 3A. After a long period of rest, the response to the first deflection is identical to that observed in isolation. The response to the second deflection is scaled by the suppression induced from the first deflection or the value of the response-suppression curve at the relevant IDI. In addition to suppression of the excitatory portion of the second response, the suppression the second deflection normally induces will also be altered (denoted as the effective suppression, solid lines in Fig. 3A). The response to the third deflection then depends on the effective suppression from the second deflection, resulting in a slightly larger response than would be expected based on the observed suppression curves. Dashed lines in Fig. 3A represent the measured $\alpha$ and $\beta$ curves for comparison with the effective curves. Additionally, if time intervals are short enough, the first deflection can directly suppress the response to the third deflection (Webber and Stanley 2004). The combination of these effects resulted in the underlying state, which evolved over time based on the history of the stimulus. Note that for simplicity of illustration, the example in Fig. 3A is for a case where the IDI is long enough to preclude a direct interaction between the suppression induced by the first deflection and the response to the third deflection.

The preceding argument was formalized and extended for periodic stimulus patterns. Each deflection of the vibrissa, at time $t_{\text{IDT}}$, was indexed and referred to as the $i$th deflection. For a periodic stimulus, the deflections occurred at multiples of the inter-deflection interval, $t_{\text{IDT}}$. The state at the $i$th deflection in a sequence, $x_{i\text{Ref}}$, was predicted from a combination of the effective suppression induced by the two previous deflections (the $(i - 1)$th deflection and the $(i - 2)$th deflection). For any deflection of the vibrissa, the state was determined by

$$x_{i\text{Ref}} = \begin{cases} \alpha_{i\text{Ref}}(2t_{\text{Ref}})\beta_{i\text{Ref}}(t_{\text{Ref}}) & i = 1, 3, 5, \ldots \\
\beta_{i\text{Ref}}(2t_{\text{Ref}})\alpha_{i\text{Ref}}(t_{\text{Ref}}) & i = 2, 4, 6, \ldots \end{cases}$$

The effective scaling of the response to the $i$th deflection was determined recursively

$$\beta_{i\text{Ref}}(t_{\text{Ref}}) = \frac{\beta(t_{\text{Ref}})}{\alpha(t_{\text{Ref}})}$$

$$\alpha_{i\text{Ref}}(t_{\text{Ref}}) = \frac{\alpha(t_{\text{Ref}})}{\beta_{i-1\text{Ref}}(t_{\text{Ref}}) + \beta(t_{\text{Ref}})(1 - \alpha_{i-1\text{Ref}}(t_{\text{Ref}}))}$$

with initial conditions $\alpha_{i\text{Ref}}(0) = 1$, $\beta_{i\text{Ref}}(0) = 1$ for $i < 1$, and $\alpha_{i\text{Ref}}(\cdot) = \alpha(\cdot)$. These functional forms were previously shown to predict steady-state responses to periodic stimuli (Webber and Stanley 2004). Note that these expressions are purely functions of the measured response-suppression curves. The response at each deflection was predicted as

$$r_i = \begin{cases} x_{i\text{Ref}} & i = 1, 3, 5, \ldots \\
x_{i\text{Ref}} & i = 2, 4, 6, \ldots \end{cases}$$

where the superscripts $a$ and $b$ denote away and back deflections, respectively. For the standard stimulus protocol, an odd index denotes an away deflection, and an even index denotes a back deflection, with the opposite indexing for the inverted stimulus protocol. This recursive function scales the nominal response, $\tilde{r}_i$, by the underlying state determined from the stimulus history.

R E S U L T S

We investigated the transient and steady-state adaptation responses of SI cortical neurons to repetitive vibrissa stimulation at frequencies between 2 and 16 Hz (see METHODS for stimulus details). The average response of all 41 recorded cells to a 6-Hz stimulus is represented by the PSTH shown in Fig. 1A. The response was large for the first deflection but quickly adapted to the periodic stimulus. The bottom panel depicts the average normalized firing rate in a 30-ms window after each deflection in the two stimulus directions (away; back) and a second-order polynomial fit to the data. Although the height of the PSTH was greatly reduced after the first deflection, the width of the PSTH increased, which resulted in the firing rate within the chosen window adapting to ~50% of the isolated response. The responses were normalized to an isolated response in the associated direction to account for neuronal direction selectivity. The response to the away deflections exhibited a gradual decrease over time. In contrast, the response to deflections in the back direction began in a suppressed state relative to an isolated response, due to the preceding away deflection, and exhibited a slight increase before reaching steady state.

The adaptation response was divided into two portions, transient and steady state (Fig. 1A, Bottom). The steady-state response for each direction was calculated as the average response over the time period from 1 to 3 s after the onset of the stimulus. At all recorded frequencies (2–16 Hz), the average responses to the away and back directions adapted to the same fraction of the full response at steady state (Fig. 1B). The steady-state response exhibited low-pass characteristics with neurons adapting more at higher frequencies of stimulation. The transient portion was defined as the time period from stimulus initiation until the polynomial fit in each direction...
reached a level within 1 SE of the corresponding steady-state response. The average time required to reach steady state (the length of the transient portion) gradually decreased as a function of stimulus frequency (Fig. 1C). Note, however, that this decrease was less than would be predicted if it were linearly dependent on the total number of deflections within a fixed time interval.

**Adaptation dynamics differ across single neurons**

Previous studies have shown that the time course of suppression after a single vibrissa deflection is a temporal response property that varies across cells (Simons 1985) and largely predicts the response of cells to temporal stimulus patterns (Webber and Stanley 2004). Here, we hypothesized that the transient and steady-state adaptation responses were predictable on a cycle-by-cycle basis from the time course of the postexcitatory suppression induced by a single deflection. To explore this, we inferred the time course of the postexcitatory suppression by deflecting the PV at IDIs between 20 and 250 ms (Fig. 2A, top) and calculating the AUC of the PSTH for 30 ms after the second deflection. The responses were normalized to the AUC of an isolated deflection in the same direction to form a response-suppression curve. Two response-suppression curves were formed for each cell to account for the directional selectivity of barrel neurons. The α curve represents the suppression after a deflection away from rest, and the β curve represents the suppression after a deflection back to rest to account for the two directions in the periodic stimulus patterns. The average normalized α and β curves for all recorded cells are shown in Fig. 2A. To compare the time course of suppression for the two directions, the times at which the response-suppression curves reached 50% of the maximum response ($t_{50}$) were calculated by interpolating between known points to find the time at which the curve equaled 0.5 of the normalized maximum. The average α and β response-suppression curves were similar in time course, as quantified by their $t_{50}$ values ($t_{50}^\alpha = 92$ ms, $t_{50}^\beta = 100$ ms), shown with the dashed lines in Fig. 2A. However, the time course of suppression in the two stimulus directions can differ greatly for individual cells. Figure 2B shows $t_{50}^\alpha$ versus $t_{50}^\beta$ for all recorded cells with each circle representing a single cell. Note that many of the circles lie away from the unity slope line (gray line), indicating that the time course of suppression is directionally dependent.

Similarly, although the average response of all neurons adapted to the same percentage of the isolated response for both directions at steady state (Fig. 1B), single neurons exhibited a diverse range of steady-state responses in the two stimulus directions. Figure 2C shows the 6-Hz steady-state response in the away direction versus the back direction for all recorded cells. The adapted responses ranged from cells that adapted to the same amount in both directions (close to the unity slope line) to cells that only responded to one of the two directions at steady-state (away from the unity slope line).

**FIG. 1.** Transient and steady-state adaptation dynamics. **A.** Top: periodic square wave stimulus at 6 Hz, beginning at rest with alternating away-from-rest and back-to-rest vibrissa deflections. Middle: corresponding average peristimulus time histogram (PSTH; 1-ms bins) for all 41 recorded cells. Bottom: average firing rate in a 30-ms window after each deflection of the stimulus (○, away from rest; □, back to rest). solid line, 2nd-order polynomial fit to the data. The portion of the response prior to reaching steady state is termed the transient portion. All panels are plotted on the same time scale. **B:** average steady-state response in a 30-ms window after deflections at frequencies between 2 and 16 Hz in both the away and back directions (○, away; □, back). C: average time to reach steady state at frequencies between 2 and 16 Hz. Error bars represent ± 1 SE.

**FIG. 2.** Adaptation responses vary across single neurons. **A.** Top: representative square waves used in paired-deflection study beginning at rest and beginning away from rest. Inter-deflection intervals (IDIs) ranged from 20 to 250 ms. **Bottom:** average response-suppression curve for all 41 recorded cells after a deflection in the away from rest direction (left) and after a deflection in the back direction (right). Vertical dashed lines, $t_{50}$ values for the response-suppression curves. **B:** calculated $t_{50}$ values in the away and back directions for all recorded cells. Filled circles, single-cell examples shown in Fig. 4. **C:** normalized 6-Hz steady-state responses in the away and back directions for all recorded cells. Gray lines, the unity slope line. Error bars represent ± 1 SE.
**Simulation of adaptation dynamics**

We hypothesized that the asymmetries in the time course of suppression for the two stimulus directions were predictive of the wide variety of observed adaptation responses. Previously, we developed a prediction method that used the time course of the response-suppression curves to predict the steady-state frequency response to periodic stimuli (Webber and Stanley 2004). Here, we extended the prediction method to simulate the neuronal response to each deflection of a periodic stimulus to characterize both transient and steady-state response components. Briefly, the response to each deflection was determined by scaling the expected response to a stimulus in isolation by the underlying state, which was a function of the suppression induced by the preceding stimulus deflections. Figure 3 demonstrates the calculation of the underlying state for the case where the IDI was sufficiently long enough to preclude direct suppression of the response to the third deflection (therefore \( \alpha(2t_{\text{IDI}}) = 1 \); see METHODS for a full description of the simulations). The state is a function of the measured response-suppression curves (\( \alpha \); black, \( \beta \); gray), and depends on the stimulus history. The response to the second deflection is scaled by the \( \alpha \) curve at the relevant IDI, which also alters the amount of suppression normally induced by the second deflection (denoted as the *effective* suppression). Therefore the state at the time of the third deflection, and all subsequent deflections, was calculated from the *effective* \( \alpha \) and \( \beta \) curves (solid lines, black and gray, respectively). The measured \( \alpha \) and \( \beta \) curves are shown in dashed lines for comparison. The symbols (●, away; □, back) represent the scaling of the response to each deflection of the stimulus, predicted by the underlying state.

We performed simulations to investigate whether asymmetries in \( t_{50} \) values of the response-suppression curves could produce the observed range of behaviors illustrated in Fig. 2C. Figure 3B, top, shows idealized \( \alpha \) and \( \beta \) curves with similar parameters (\( \alpha \): \( \tau_{\alpha} = 45, t_{50}^\alpha = 115; \beta \): \( \tau_{\beta} = 50, t_{50}^\beta = 120 \), all reported in ms), the simulated response to a 6-Hz periodic stimulus, and the simulated steady-state response at frequencies from 2 to 16 Hz. The simulated response in the away direction decreased and the response in the back direction increased slightly before converging at steady state for all frequencies. This type of behavior was denoted as convergent, referring to the convergence of the away and back response trajectories at steady state.

Figure 3B, middle, demonstrates a situation with a longer time course of suppression (\( t_{50} \) value) after a deflection in the away direction than in the back direction (\( \alpha \): \( \tau_{\alpha} = 50, t_{50}^\alpha = 120; \beta \): \( \tau_{\beta} = 50, t_{50}^\beta = 90 \)), similar to cell 2 (below the gray line) in Fig. 2B. The simulation showed a consistently large response in the away direction and little or no response in the back direction. This behavior was denoted as divergent-\( \parallel \), indicating that the away and back response trajectories remained separated (\( \parallel \)) and the direction of the first deflection was the dominant response direction throughout the adaptation response. Figure 3B, bottom, demonstrates the opposite situation where the time course of suppression was longer after a deflection in the back direction (\( \alpha \): \( \tau_{\alpha} = 50, t_{50}^\alpha = 90; \beta \): \( \tau_{\alpha} = 50, t_{50}^\beta = 120 \)), similar to cell 3 (above the gray line) in Fig. 2B. In this case, the simulated away direction response was quickly attenuated and the back direction response increased until it was consistently large at steady state. This type of behavior was denoted as divergent-X, indicating that the away and back response trajectories cross (\( X \)) before reaching different values at steady state. For this case, the dominant response direction at steady state was the direction that was initially suppressed during the transient portion of the response. For both examples of divergent responses, simulations predicted that a larger response in one direction compared with the other direction at steady state would be observed at frequencies between 4 and 8 Hz (Fig. 3, B, right).

**Adaptation dynamics are predicted by postexcitatory suppression**

The simulations suggest that the relative time course of suppression in the two directions affects the transient and steady-state adaptation responses of neurons. To test this hypothesis, we predicted the adaptation response of all recorded neurons from their respective response-suppression curves. Figure 4A, left, shows the response of cell 1 (on the gray line) in Fig. 2B to a 6-Hz periodic stimulus. There was a large probability of a spike in response to the first deflection of the stimulus and decreased probability of firing in response to later deflections with the response adapting to similar values in both directions at steady state. The dashed lines represent the
response of the cell predicted from its response-suppression curves. This cell converged to the same percentage of adaptation in both directions for all recorded frequencies (Fig. 4A, right), similar to the average steady-state response in Fig. 1.

Cell 2 (below the gray line) in Fig. 2B consistently responded to the away deflections and rarely responded to the back deflections at 6 Hz as illustrated by Fig. 4B. The dashed lines show the response predicted from the cell’s measured response-suppression curves. It is important to note that this cell responded to both directions in isolation, and therefore this phenomenon was not simply the result of strong directional tuning. The response to the away deflection did not decrease throughout the stimulus period, whereas the response to the back direction was suppressed by the initial away deflection and remained suppressed throughout the trial. The response to the away deflection did not decrease throughout the periodic stimulus, whereas the response to the away direction decreased until it was consistently large at steady state (Fig. 4C). There was also period doubling at steady state for this case, but 180° out of phase with the response shown in Fig. 4B. The dominant response direction at steady state for frequencies between 4 and 8 Hz was the direction that was initially suppressed during the transient portion of the response (Fig. 4C, right).

To determine how well the response was predicted for all recorded cells, we calculated a measure of the change in direction dominance between the 1st stimulus cycle and the steady state of the cell. This was compared with the same measure for the prediction. Specifically, we first calculated the difference between the away and back responses to the first stimulus cycle as a measure of the initial dominant direction. We then calculated the difference between the away and back responses at steady state as a measure of the dominant direction at steady state. To determine the change in direction dominance, we calculated the difference between the away and back responses at steady state as a measure of the dominant direction at steady state. To determine the change in direction dominance, we calculated the difference between the away and back responses at steady state as a measure of the dominant direction at steady state. To determine the change in direction dominance, we calculated the difference between the away and back responses at steady state as a measure of the dominant direction at steady state.

Figure 4C shows the response of cell 3 (above the gray line) in Fig. 2B to a 6-Hz stimulus along with the prediction from the response-suppression curves. This cell exhibited a large response to the first few away deflections but was quickly attenuated for subsequent away deflections. The response to the back deflections was initially suppressed, but grew as the response to the away direction decreased until it was consistently large at steady state (Fig. 4C). There was also period doubling at steady state for this case, but 180° out of phase with the response shown in Fig. 4B. The dominant response direction at steady state for frequencies between 4 and 8 Hz was the direction that was initially suppressed during the transient portion of the response (Fig. 4C, right).

To determine how well the response was predicted for all recorded cells, we calculated a measure of the change in direction dominance between the response to the first stimulus cycle and the steady-state response of the cell. This was compared with the same measure for the prediction. Specifically, we first calculated the difference between the away and back responses to the first stimulus cycle as a measure of the initial dominant direction. We then calculated the difference between the away and back responses at steady state as a measure of the dominant direction at steady state. To determine the change in direction dominance, we calculated the difference between the away and back responses at steady state as a measure of the dominant direction at steady state. To determine the change in direction dominance, we calculated the difference between the away and back responses at steady state as a measure of the dominant direction at steady state. To determine the change in direction dominance, we calculated the difference between the away and back responses at steady state as a measure of the dominant direction at steady state.
reflecting the fact that the dominant response direction changed between the first stimulus cycle and steady state. Figure 4D shows the actual measure versus the predicted measure for all recorded cells at frequencies between 4 and 8 Hz, along with the regression line (gray line). The prediction and the actual response were well correlated ($r = 0.7$).

**Initial state affects only the transient dynamics**

The preceding recordings were all performed with the initial deflection in the away direction; however, the suppression after an excitatory response has been shown to be directionally dependent (Simons 1985). Therefore we hypothesized that preceding the periodic stimulus with a deflection in the opposite direction would induce a different amount of suppression at the onset of the stimulus, placing the neuron in a different initial state and significantly alter the subsequent adaptation response. To test this hypothesis, a subset of the recorded neurons (22/41) were presented with the standard adaptation stimulus, with the PV beginning away from rest and initially deflected in the back to rest direction (Fig. 5, stimulus pattern). Aside from the initial location of the PV and the initial state and significantly alter the subsequent adaptation response. To test this hypothesis, a subset of the recorded neurons (22/41) were presented with the standard adaptation stimulus, with the PV beginning away from rest and initially deflected in the away direction; however, the suppression after an excitatory response has been shown to be directionally dependent (Simons 1985). Therefore we hypothesized that preceding the periodic stimulus with a deflection in the opposite direction would induce a different amount of suppression at the onset of the stimulus, placing the neuron in a different initial state and significantly alter the subsequent adaptation response. To test this hypothesis, a subset of the recorded neurons (22/41) were presented with the standard adaptation stimulus, with the PV beginning away from rest and initially deflected in the back to rest direction (Fig. 5, stimulus pattern). Aside from the initial location of the PV and the initial direction of deflection, these stimuli were otherwise identical.

Preceding the standard stimulus with an additional back deflection had the effect of changing divergent-|| behavior into divergent-X behavior and vice versa. Figure 5 shows the response of two representative single neurons to the standard (top) and inverted (bottom) periodic stimulus patterns. The neuron in Fig. 5, A and B, responded to an 8-Hz standard adaptation stimulus in the away direction but was suppressed in the back direction, consistent with divergent-|| behavior. In contrast to the observed response to the standard stimulus, the response to the inverted stimulus was consistent with divergent-X behavior. The cell responded strongly to the first few cycles in the back direction and then adapted to little or no response at steady state. The response to the away direction was suppressed for the first few deflections, but as the back response decreased, the away response increased until the neuron consistently responded to the away direction at steady state. The results for a second representative single unit to a 6-Hz stimulus are shown in Fig. 5, C and D. For the standard stimulus, this cell showed an initial preference to respond in the away direction, but transitioned to respond to back deflections at steady state, consistent with divergent-X behavior. For the inverted stimulus, it consistently responded to the back deflections but not to the away deflections, both in the initial transient and the steady-state response, consistent with divergent-|| behavior.

For both illustrated cells, the steady-state responses in the standard and inverted cases were similar (PSTH and average response of the last 5 cycles shown), despite dramatic differences in the transient portion of the response. This phenomenon was noted for all recorded cells. To quantify this, the average response of all cells to the standard (■) and inverted (□) stimulus patterns at specific times during the trial was calculated for the away (top) and back (bottom) trajectories (Fig. 6A). For the first two cycles (First), the average responses to the two stimuli were very different, became more similar by the third and fourth cycles (Mid), and were not statistically different at steady state (S-S, Mann-Whitney U test: $P > 0.2$). Figure 6B shows the average time to steady state across frequencies for the standard and inverted stimuli. The time to steady state was not significantly different between the standard and inverted stimuli (Mann-Whitney U test, 4 Hz: $P = 0.65$, 6 Hz: $P = 0.51$, 8 Hz: $P = 0.23$). Despite differences in the transient activity for the standard and inverted stimulus patterns, neurons reached the same steady-state response in the same average amount of time independent of the initial state.

Given that neurons reached the same steady-state response regardless of the initial state, one possibility is that the response at steady state simply reflects the directional selectivity of the cell for the two stimulus directions. To investigate this, we calculated a measure of the change in directional selectivity between isolated responses and steady-state responses. Specifically, we first calculated the difference between the away and back responses in isolation, a conventional measure of the cell’s directional selectivity (Simons 1978). We then calculated the difference between the away and back responses at steady state, the cell’s adapted direction selectivity. The difference between these two values provides a measure of the shift in direction selectivity during adaptation. A negative number represents a shift of the selectivity toward the away direction, a positive number indicates a shift toward the back direction, and a number close to zero indicates that the steady-state response is representative of the conventional measure of directional selectivity. Figure 6C shows this change in direc-
Adaptation is a ubiquitous property of sensory encoding, observed across multiple sensory modalities and over a range of time scales. The results presented here show that in the vibrissa pathway a significant portion of the observed rapid cortical adaptation to tactile stimulus patterns was predictable from simple temporal response properties of single neurons. The relative time course of postexcitatory suppression after a single vibrissa deflection predicted the observed heterogeneity in both transient and steady-state adaptation dynamics. For many cells, the dominant response direction at steady state was different from that which would be predicted in response to isolated stimuli, suggesting that adaptation alters neuronal direction selectivity. Altering the initial state, by preceding the stimulus with an additional vibrissa deflection, strongly influenced single cell transient adaptation responses, yet resulted in an invariant steady-state response. Furthermore, despite observed differences in transient activity at fine temporal scales, when neural activity was integrated over the time window of a stimulus cycle, neuronal firing rate during the transient portion of the response was also independent of the initial state. Taken together, the results here demonstrate that although adaptation can have significant effects on transient neuronal activity and direction selectivity, a simple measure of the time course of suppression after an isolated stimulus predicts a large portion of the observed adaptation dynamics.

**Adaptation dynamics**

In this study, cortical neurons exhibited a gradual decrease in responsiveness to repetitive stimuli over the 2- to 16-Hz frequency range until reaching a frequency-dependent steady-state response as previously observed (Ahissar et al. 2001; Chung et al. 2002; Khatri et al. 2004). The time to steady state gradually decreased from 700 ms to ~500 ms as the frequency of stimulation increased. These results agree with previous findings, where cortical cells were found to reach steady state more rapidly at stimulation frequencies of 20–40 Hz, although the time course was not fully investigated (Khatri et al. 2004). It should be noted that by defining one period of the stimulus as containing both an away and back deflection, an 8-Hz stimulus described here is comparable to a 16-Hz stimulus used for studies with a single stimulus direction. Our findings demonstrate that the time to reach steady state is slower than would be predicted if the development of adaptation were simply linearly dependent on the number of stimuli presented in a given amount of time. However, the process does not appear to have a single time constant associated with it, in which the time to steady state would be invariant of the stimulus frequency.

Here we observed that cells with a similar time course of suppression in both directions of deflection exhibited responses of alternating magnitude to the first few deflections of a periodic stimulus before converging to the same steady-state adapted response. These transient adaptation dynamics have been observed in thalamic cells in response to periodic pulsatile vibrissa deflections (Hartings et al. 2003) and in local field potential recordings at the cortical level (Castro-Alamancos 2004). Repetitive pulsatile deflections in a single direction would induce the same time course of suppression after each stimulus and are thus analogous to the convergent cells shown.
here. Cells with differing amounts of suppression in the two directions tended to respond more strongly to one direction than the other at steady state, resulting in an alternating response pattern (divergent). Typically, the direction that induced a longer time course of suppression was the direction to which the neuron responded more vigorously at steady state, whereas the response to deflections in the other direction was suppressed. For example, consider a case in which the time course of suppression is longer for a deflection in the away direction as compared with the back direction. The longer time course of suppression associated with the away direction increases the probability that the response to the subsequent back deflection will be suppressed. If so, there will be less suppression associated with the back direction, allowing for a larger response to the next away deflection. This pattern propagates, causing the away response to dominate throughout the stimulus and at steady state. Neurons with divergent behavior exhibited strong steady-state direction selectivity. Interestingly, we found that the directional selectivity of a neuron in response to isolated stimuli did not predict the directional selectivity at steady state (see Fig. 6C), suggesting that the directional selectivity of a cell is a parameter that dynamically changes throughout adaptation. This is similar to findings in the visual system that tuning properties such as orientation preference and receptive field extent can dynamically change during the presentation of a stimulus (Kohn and Whitsel 2002; Ringach et al. 1997).

Similar asymmetries exist across vibrissae, where the time course of suppression after a primary vibrissa deflection is greater than that for the deflection of an adjacent vibrissa (Simons 1985). This asymmetry would predict divergent adaptation dynamics in response to spatiotemporally distributed patterns consisting of alternating deflections of the primary and adjacent vibrissa, consistent with experimental observations (A. Boloori and G. B. Stanley, unpublished observations). Taken together, these results suggest that the dynamics described here may be a general phenomenon of neuronal response to spatiotemporal stimulus patterns.

Relating adaptation to postexcitatory suppression

It has been hypothesized that there is a direct functional relationship between the time course of postexcitatory suppression and the adaptation response to periodic stimuli (Hartings et al. 2003; Webber and Stanley 2004). Here we have shown that the neuronal response to a periodic stimulus was predictable from nonlinear combinations of the postexcitatory suppression induced by previous deflections, which we refer to as the underlying state. This suggests that the observed state could be reflective of the underlying state of the mechanisms responsible for adaptation.

Mechanisms identified as contributors to cortical adaptation, such as activity-dependent depression of thalamocortical synapses (Chung et al. 2002), depression of recurrent excitatory cortical synaptic connections (Petersen 2002), and intracortical inhibition, have also been shown to be engaged by single stimulus events. Paired-pulse suppression has been observed at thalamocortical synapses with interstimulus intervals ranging between 10 and 2,000 ms in vitro (Gil et al. 1997). Intracellular studies have shown that thalamocortical excitatory postsynaptic potentials (EPSPs) depress in response to a periodic stimulus in vivo and in vitro with a 40–50% decrease in EPSP amplitude occurring by the second pulse in the stimulus (Chung et al. 2002; Gil et al. 1997). Similarly, synaptic connections between cortical excitatory neurons exhibit paired-pulse depression and depression to periodic stimulus patterns (Petersen 2002). Intracortical inhibition has a similar time scale in response to an isolated stimulus as the observed time course of response suppression with inhibitory postsynaptic potentials that can extend >100 ms after presentation of the stimulus (Carvell and Simons 1988; Higley and Contreras 2003; Moore and Nelson 1998; Zhu and Connors 1999). Therefore the time course of suppression measured in this study is probably due to a combination of the preceding mechanisms that ultimately contribute to adaptation.

It should be noted, however, that the predictions from the postexcitatory suppression tend to slightly overestimate the steady-state response (Webber and Stanley 2004), underestimate the time to steady state (see Fig. 6D), and do not account for the recovery time of the neuron after periodic stimulation. Underlying processes, such as synaptic depression, could require repeated stimulation to be fully activated would not be completely reflected in the observed postexcitatory suppression and could account for the discrepancies between observed and predicted steady-state activity and time course of adaptation. Furthermore, the prolonged recovery process could be due to the recovery time of thalamocortical synapses (Chung et al. 2002) and the relatively long time constants associated with intracortical inhibitory (GABA\(_\text{B}\)) dynamics (Garabedian et al. 2003).

Possible implications of the observed dynamics

To explore the possible implications of adaptation for neural encoding, consider an observer that only receives sensory information via the firing rate of SI neurons, from which discriminations between different stimuli must ultimately be made. Here we focused our analysis on neuronal firing rate, although other response features, such as timing of spikes, can play a role in the encoding process during adaptation (Ahissar et al. 2000; Higley and Contreras 2006; A. Boloori and G. B. Stanley, unpublished observations). We found that altering the initial state of adaptation by preceding a periodic stimulus with an extra vibrissa deflection strongly influenced the transient adaptation response but did not affect the steady-state response. Heuristically, the standard and inverted stimuli in Fig. 5 differ only in the initial direction of deflection and thus could logically result in a neuronal representation that is invariant to this difference. Our results suggest several possibilities regarding the relative roles of transient and steady-state activity in establishing a stable neural representation of sensory features. One possibility is that the initial transient activity confounds the representation and that reaching steady state would be required to form a stable neural representation. Here we showed that cortical neurons do indeed reach the same steady-state representation, in the same amount of time, despite variable transient activity for the different stimuli. In this case, time to steady state would be the limiting factor for a stable representation.

A second possibility is that despite differences in observed responses for different initial states, the transient activity still serves to establish a consistent representation of the sensory
stimuli. For a two-alternative forced-choice task in which rats were trained to discriminate between two similar textures, well-trained rats occasionally chose a “whisk-and-go” strategy in which only one discriminandum was whisked before the decision was made, resulting in a correct choice 73% of the time. On average, the voluntary contact time between the vibrissa and the texture, prior to decision, was ~700 ms (Carvell and Simons 1990). These results suggest that the animal could use the transient neural representation from a single whisking bout to discriminate the textures. Here we showed that the transient activity integrated over a stimulus cycle could potentially produce a stable neuronal representation as it was independent of the initial manner by which the vibrissa was engaged (Fig. 6D). A representation of this type would require that an observer have knowledge of the time interval of the cycle. This could be accessible from efferent copies of motor control of whisking in cases where the stimulus periodicity is due to active whisking (Ahrens and Kleinfeld 2004; Kleinfeld et al. 2002). However, given that the time course of adaptation could be altered in the awake animal (Castro-Alamancos 2004), further studies of adaptation in behavioral settings would be needed to completely disentangle these issues.

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