Visual Neuroscience (1995), **12**, 191–205. Printed in the USA.

Adaptation aftereffects in single neurons of cat visual cortex: Response timing is retarded by adapting

ALAN B. SAUL

Department of Neurobiology, University of Pittsburgh School of Medicine, Pittsburgh

(RECEIVED April 18, 1994; ACCEPTED August 1, 1994)

Abstract

Extracellular single-unit recordings were made from simple cells in area 17 of anesthetized cats. Cells were tested with drifting gratings under control and adapted conditions. Response amplitude and phase were measured as a function of either contrast or temporal frequency. Adapting not only reduces amplitude, but also retards phase. Adaptation alters the responses of simple cells in a particular way: the onset of the response to each cycle of a sinusoidally modulated stimulus is delayed. Once cells start to respond during each cycle, however, they generally recover to control levels, and the offset of the response is unaffected by adapting. The timing aftereffects are independent of the amplitude aftereffects. Timing aftereffects are tuned around the adapting temporal frequency, with a bias toward lower temporal frequencies. Adaptation thus modifies cortical responses even more specifically then previously thought. Firing rates are depressed primarily at response onset, even after several stimulus cycles have occurred following the end of adapting. Because all cells appear to adapt in this way, the data offer an opportunity to theorize about cortical connectivity. One implication is that inhibition onto a simple cell arises from other simple cells with similar response properties that fire a half-cycle out of phase with the target cell.

Keywords: Adaptation aftereffects, Visual cortex, Simple cells, Response timing, Intracortical inhibition

Introduction

Cortical cells tend to be activated only by specific situations. To understand the origins of cortical response specificity, typical experiments alter responses in some controlled way. This paper arises out of one such manipulation, where adaptation is used to modify response properties. Adaptation refers here to the process by which short-term experience affects responses, and particularly how an adapting stimulus induces aftereffects, changes in responses that persist after the adapting stimulus is removed. Adapting affects spatial- and temporal-frequency tuning and direction selectivity; the mechanisms underlying these response properties can be studied through the parallel changes in receptive-field structure. For instance, adapting can change spatial-frequency tuning by reducing responses at and below the optimal frequency more than at higher frequencies (Saul & Cynader, 1989*a*). Since the optimal spatial frequency is inversely related to the spatial wavelength of the receptive field (Movshon et al., 1978), the receptive-field map should also be altered by adapting.

The changes in response properties and receptive-field structure revealed by adapting can shed light on the connectivity in cortex and on the arrangement of thalamic afferents to single cortical cells. Many of these relationships can be fruitfully characterized in terms of space and time. Spatial receptive-field structure has been studied far more than temporal structure, but the timing of neuronal responses to sensory stimuli has recently received increasing attention (Hamilton et al., 1989; Saul & Humphrey, 1990, 1992*b*; DeAngelis et al., 1993; McLean et al., 1994). This paper will show how adapting affects response timing, as part of an effort to understand spatiotemporal receptive-field structure.

Adaptation aftereffects have been observed in single cells of cat visual cortex by many investigators over the past 20 years (Maffei et al., 1973, 1986; Vautin & Berkley, 1977; von der Heydt et al., 1978; Movshon & Lennie, 1979; Kulikowski et al., 1981; Dean, 1983; Albrecht et al., 1984; Ohzawa et al., 1985; Hammond et al., 1985, 1986, 1989; Hammond & Mouat, 1988; Maddess et al., 1988; Marlin et al., 1988, 1991, 1993; Saul & Cynader, 1989*a*,*b*; Bonds, 1991; Pettet & Gilbert, 1992; Giaschi et al., 1993). In a typical experiment, a high-contrast stimulus is presented in a cell's receptive field for about a minute. The response to this stimulus declines during this period, and responses to subsequently presented test stimuli are weaker than they were prior to adapting. Consistent findings from these previous studies include (1) practically every cortical cell adapts,

Reprint requests to: Alan B. Saul, Department of Neurobiology, University of Pittsburgh School of Medicine, 3500 Terrace St., Pittsburgh, PA 15261, USA.

whereas subcortical cells do not; (2) aftereffects are observable after a few seconds of adapting, and persist for seconds; (3) despite the presence of a nonspecific fatigue-like component, the tuning of aftereffects is specifically related to the adapting stimulus; (4) adaptation produces a rightward shift of the contrast response function; and (5) both directions of motion are affected by adapting, with differences between the directions varying across investigations.

Despite the numerous investigations of adaptation, we still know little about the underlying mechanisms. In all of the previous physiological studies, aftereffects have been measured in terms of decreased responses in the adapted state relative to a control state, or, equivalently, as shifts of the contrast response function. Timing has been ignored. This paper communicates details of a simple phenomenon: visual cortical cells show reliable, consistent changes in response timing when adapted. Adapted response histograms from simple cells are systematically shifted toward later times. This observation is true of nearly every simple cell. It occurs primarily for test stimuli that are similar to the adapting stimulus. The timing aftereffects are largely independent of the amplitude aftereffects. The changes in response phase induced by adaptation occur primarily at low temporal frequencies, in contrast to amplitude aftereffects that are stronger at high temporal frequencies. The temporal-frequency dependence of the phase aftereffects shows that adaptation does not produce a pure delay of the response. For clarity, results on the contrast dependence of aftereffects are presented before the main results on temporal-frequency tuning. These experiments provide hints as to the mechanisms underlying adaptation by going beyond previous observations that only considered response strength. They also have implications for cortical connectivity. In addition, the importance of response timing in generating cortical specificity is reinforced.

Some of these results have been presented in abstract form (Saul, 1993).

Methods

Animal preparation

The details of the surgical procedures have been described previously (Saul & Humphrey, 1990, 1992*a*,*b*). Female adult cats weighing 2–3 kg were anesthetized with 4% halothane in nitrous oxide and oxygen. Flaxedil (gallamine triethiodide, 15 mg) was administered i.v. for paralysis and the animal was artificially respired. Heart rate, rectal temperature, and expired CO_2 were monitored. The halothane concentration was adjusted to maintain a state of strong synchronization in the electroencephalogram (EEG) during the remainder of the surgery and mild synchronization during recording. A small craniotomy was made over left visual cortex at about P4/L1, and the dura was carefully reflected to expose just enough of the cortex to permit electrode placement. All penetrations in this study were verified histologically to be in area 17. Eccentricities ranged from 0.7 deg to 21 deg, with most cells falling between 5 deg and 10 deg.

All incisions and pressure points were infused with lidocaine HCl to further reduce the possibility of discomfort. The intravenous infusion included 5 mg/kg-h of Flaxedil and 0.7 mg/kg-h of d-tubocurarine in 5% dextrose and lactated Ringer's solution, and was delivered at a rate of about 5 ml/h. Rectal temperature was maintained at about 37.5°C through a feedback-controlled heating pad. End-tidal CO_2 was kept at 4%, and heart rate was in the range of 150–240 beats/min. Periodic spectral analyses of the electroencephalogram showed most of the power was at frequencies below 10 Hz. In later experiments, arterial blood pressure was continuously monitored and maintained at about 100 mm Hg. The skull was attached to cross bars to permit removal of the ear and eye bars while keeping the skull position rigid in stereotaxic coordinates.

Pupils were dilated with atropine and nictitating membranes were retracted with phenylephrine HCl. Zero-power contact lenses were placed on the eyes which were frequently bathed with 1.5% saline. The eyes were refracted by slit retinoscopy and focus at 57 cm was corrected if necessary with lenses placed in front of the eyes. Contact lenses containing 3-mm artificial pupils were placed over the eyes. A small piece of a mirror was attached to the edge of a contact lens and a laser beam was reflected off the mirror onto the tangent screen. This permitted continuous monitoring of changes in eye position. Eye movements were negligible in the recordings presented here.

Recording

Micropipettes filled with 10% HRP in 0.2 M KCl in Tris buffer were used for all recordings in this study. These pipettes were beveled to final impedances of 50–100 MΩ. In the brain, the impedance would often go up to 100–200 MΩ as the electrodes clogged. They could be temporarily cleared while advancing by overcompensating the capacitance to induce ringing. Stable recordings could be obtained over many hours. Single units were well isolated, although on rare occasions a second unit interfered and data collection was terminated. These electrodes have been shown to record from small as well as large cells (Humphrey & Weller, 1988).

Stimulation

Visual stimuli were generated on a Tektronix 608 monitor running at a 200-Hz frame rate placed 57 cm from the tested eye. Drifting grating stimuli were generated by a Picasso (Innisfree, Inc., Cambridge, MA) controlled directly by an LSI-11 computer which was in turn controlled by a Macintosh Quadra 900 running Igor Pro (WaveMetrics, Inc., Lake Oswego, OR). Stimulus parameters were carefully calibrated, but contrast values shown below are not reliable at the highest contrasts plotted (above about 0.8 contrast). In many cases contrasts of 1 are stated for simplicity, but these values were slightly smaller in reality because of ambient light. The mean luminance was 15 cd/m^2 for all experiments.

Initial hand-plotting and preliminary quantitative tests permitted estimation of tuning and in particular optimal values of orientation, spatial and temporal frequencies, and direction. The experiments presented here consisted of repeated presentations of adapting and test stimuli (Saul & Cynader, 1989*a*,*b*), all of which were drifting gratings. The test stimuli varied as a function of either contrast or temporal frequency. Each trial was divided into an adapting and a test portion. Typically, 8 s of adapting stimulation were followed by 4 s of test stimulation. Only responses during the test portion are analyzed. During the adapting portion either a drifting grating was present or the screen was blank, with a luminance of 15 cd/m^2. Trials on which the blank screen was present were used to measure con-

trol responses to each test stimulus. Trials on which a drifting grating was present during the adapting portion generated the adapted responses which were then compared to the control responses. Several different adapting stimuli were often used in a single run.

Special efforts were made to reduce possible transient effects. In all experiments reported here, test stimuli actually commenced 100 ms earlier than nominally indicated, and lasted a total of 4.1 s. Thus, the first 100 ms following onset of the test stimulus were ignored, and responses were derived from histograms that averaged over the last 4 s of each trial.

Most studies of adaptation in single cells have used trials that last on the order of minutes. Saul and Cynader (1989*a*) previously showed that aftereffects can be observed with briefer trials. In that study contrasts were near threshold, where amplitude aftereffects are most clearly revealed. In the present study higher contrasts were necessary in order to study timing. However, aftereffects were still observable even with brief trials, permitting more conditions to be tested and the tuning of the aftereffects to be determined. The tradeoff is that weaker aftereffects were observed. Strong aftereffects are sacrificed to some extent in order to study their tuning. To increase aftereffect strengths, spatial frequencies were generally chosen to be slightly lower than optimal, and temporal frequencies just higher than optimal (Saul & Cynader, 1989*a*,*b*).

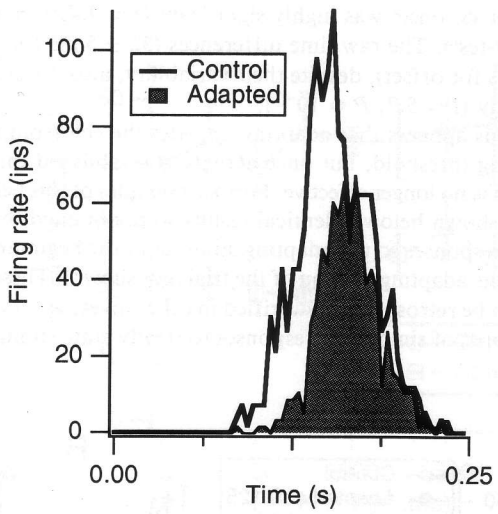

Fig. 1. Averaged histograms from a simple cell tested with a 0.28 cycles/deg grating drifting at 4 Hz in the preferred direction. Contrast was 0.25. A total of 144 cycles (16 cycles per trial × 9 trials) are included in each of the two histograms. The control responses were obtained from 4-s test trials that followed 8 s of zero contrast; the adapted responses were from identical, interleaved test trials that followed 8 s of stimulation with a 0.125 contrast grating that was otherwise like the test grating.

Analysis

Spike arrival times for the test portion of each trial were used to increment bins (bin width varied slightly with stimulus temporal frequency, but was typically 3.90625 ms) in histograms whose length was equal to the test stimulus period. For example, if the test stimulus drifted at 2 Hz, the histogram would have a length of 500 ms, and eight stimulus cycles would be averaged in the histogram because the test portion lasted 4 s. The first harmonic amplitude and phase were then computed for this histogram. These responses were averaged over the 5–10 iterations for each condition to derive means and standard errors of both amplitude and phase.

Adapted and control responses were compared by computing the *t*-score between them. This index divides the difference of the means by the square root of the summed-squared standard errors. It effectively normalizes the response difference so that aftereffects can be seen in weak responses or small absolute differences as well as in strong responses and large differences. It also gives a sense of statistical significance, since for normally distributed data this score serves as the statistic for Student's *t*-test. Here it is used as an index of the strength of aftereffects rather than as a statistic from which to compute probabilities that aftereffects are significant, since population data are obtained by averaging *t*-score values. To perform such averaging the test variable (contrast or temporal frequency) was normalized by computing its distance from the adapting stimulus in octaves (Saul & Cynader, 1989*a*,*b*).

Results

Histograms

The first harmonic response phase will be the primary measure used to describe response timing. However, this index does not provide details about the time course of the response. We need to consider response histograms to see why phase is retarded by adapting. In Fig. 1, the averaged peristimulus-time histograms (PSTHs) are presented for a simple cell's responses to 4-s presentations of a 0.28-cpd grating at a contrast of 0.25 drifting in the preferred direction at 4 Hz. Both histograms show responses to the same test stimulus, but the open PSTH is derived from trials following 8 s of zero contrast and the shaded one from trials following adapting for 8 s at a contrast of 0.125. The onset of the excitatory response in the adapted condition is delayed, the amplitude is reduced, but the offset of the response is unaffected by adapting. Note that only one spike was evoked in the adapted condition during the time when the stimulus began to drive the cell in the control condition, despite the fact that this averaged histogram includes data from stimulus cycles occurring long after the end of the adapting stimulus. Thus, the aftereffect clearly endured for at least 4 s following 8 s of adapting, although the test stimulus itself may have an important role in maintaining the aftereffect. At any rate, the difference between the onset and offset of the response is not due to decay of aftereffect strength, but instead suggests that the mechanisms underlying the aftereffects differentially influence these components of the response.

Onsets and offsets were estimated for all histograms by comparing the times when responses crossed the half-maximal level. These computations required considerable smoothing to disambiguate the level crossings. As will be shown below, the changes in onset times induced by adapting decrease dramatically with temporal frequency. The differences between adapted and control times were therefore multiplied by stimulus temporal frequency, obtaining shifts as portions of a cycle. Onsets were delayed an average of 0.055 ± 0.004 cycles whereas offsets were not consistently changed by adapting (0.006 ± 0.004 cycles, $N = 192$). The difference between the adaptation-induced change

in offset *vs.* onset was highly significant ($t = 9.4$, $P = 10^{-17}$, paired t-test). The raw time differences (32 ± 5 ms for onset, 7 ± 4 ms for offset), despite their variability, also differed significantly ($t = 5.7$, $P = 10^{-7}$).

It thus appears that adapting impedes the cell from reaching firing threshold, but once activity is established this suppression is no longer effective. Further examples of this behavior will be shown below. Identical results were obtained by comparing responses to the adapting stimulus at the beginning and end of the adapting portion of the trial (not shown). These findings can be retrospectively verified in other investigators' data. All records of simple cell responses to steady-state stimuli lasting on the order of 10 s should show these effects. The present study provides details of this phenomenon obtained through systematically controlled experiments in which temporal frequency or contrast were varied.

Aftereffects as a function of contrast

Contrast-response functions were obtained from ten cells under control and adapted conditions. An example is shown in Fig. 2 (the data in Fig. 1 were taken from this experiment). This cell was tested at 20 contrasts and adapted at 2 contrasts. As the *adapting* contrast increases from 0.125 to 0.5, the magnitude

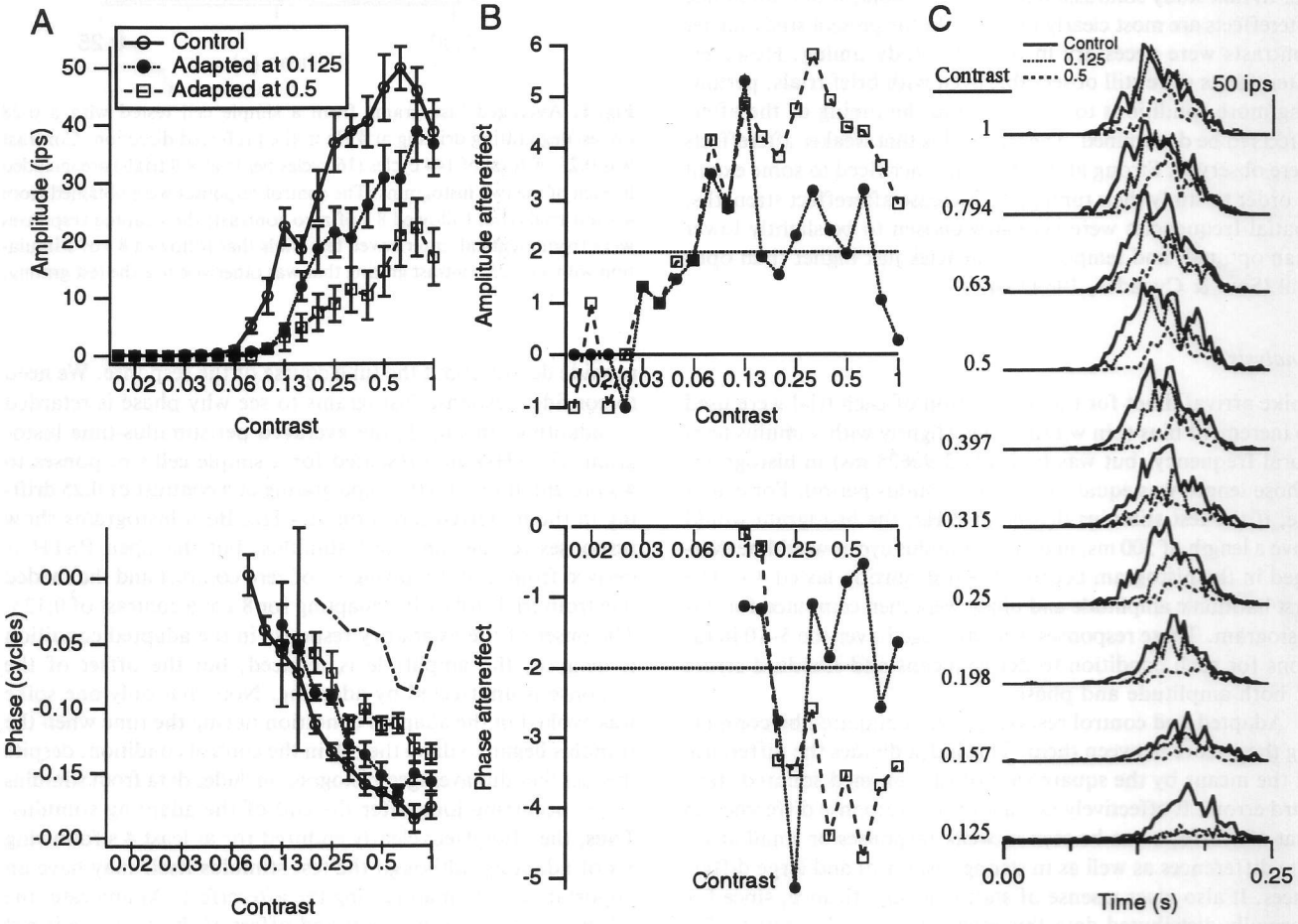

Fig. 2. A: Contrast-response functions in three different states of adaptation are plotted. Increasing phase values correspond to later responses. Markers indicate means over the nine trials, and error bars show standard errors of these means. All gratings had a spatial frequency of 0.28 cycles/deg and a temporal frequency of 4 Hz. Adapting stimuli had contrasts of 0, 0.125, or 0.5. Test contrasts ranged from about 0.01 to 1 in steps of a third of an octave. The broken line in the phase graph shows the phase values that would be predicted if the timing aftereffects depended solely on the rightward shift between the control and adapted-at-0.5 amplitude data and on the control phase advance with contrast. This prediction is contrasted with the measured values shown by the square symbols and dashed line. B: The adapted responses were compared to the control responses by means of the t-score (control mean minus adapted mean divided by the square root of the summed squared standard errors) between them. The amplitude aftereffects are positive (amplitudes are reduced by adapting) once control threshold is reached, and the aftereffects from adapting at 0.5 contrast are stronger than those from adapting at 0.125 at high test contrasts. The phase aftereffects are negative (phase values are increased by adapting) once the adapted threshold is reached (since the variance of the phase means are too high below threshold). The timing aftereffects are also stronger at the higher adapting contrast. C: Averaged histograms are shown for the ten highest test contrasts and for each of the three adapting conditions. The scale bar at the top applies to all histograms. The control responses (solid lines) have earlier onsets than the adapted responses (dotted and dashed lines).

of both amplitude and phase aftereffects increases. The mean responses are shown in Fig. 2A, and a measure of aftereffect strength (the *t*-score between the control and adapted responses) is plotted in Fig. 2B. The dotted lines indicate a convenient but somewhat arbitrary level of 2.0 that serves as a reference for when to consider aftereffects to be strong. Clear aftereffects are seen with both adapting contrasts once the test contrast reaches threshold. The timing aftereffects are not as apparent as the amplitude aftereffects at low contrasts because more spikes need to be obtained in both control and adapted conditions to see the changes in timing than in amplitude. Histograms corresponding to the high contrast (0.125 to 1) test stimuli for this experiment are shown in Fig. 2C. The retarded phase values can again be seen to reflect late onsets. The responses following adapting at 0.5 also have later onsets than those adapted at 0.125.

Note that the phase *vs.* contrast functions in Fig. 2A show a phase advance with increasing contrast. The histograms in Fig. 2C can also be seen to arise and decay earlier with increasing contrast. This phase advance has been previously described (Dean & Tolhurst, 1986; Carandini & Heeger, 1994), and presumably reflects in part the retinal contrast gain control present in the responses of ganglion cells (Shapley & Victor, 1981; Victor, 1987, 1988) and partly intracortical mechanisms. Given the fact that adapting shifts the response amplitude *vs.* contrast function to the right, do the phase aftereffects simply reflect the corresponding rightward shift of the phase *vs.* contrast function? Three lines of evidence will be presented here to show that this is not the case. One way to evaluate this possibility is to compute the expected adapted phase values by shifting the control phase values by the rightward shift seen in the amplitude data. These computations* revealed that the phase aftereffects are not due to such a simple dependence on the amplitude aftereffects and the phase advance with contrast. The broken line in Fig. 2A (and also in Figs. 3–6) shows the predicted phase values for the adapted-at-0.5 case, based on the amplitude data and the control phase values. The predicted phase values are much larger than the actual values, despite the strong timing aftereffects induced by this adapting stimulus. In other words, the amplitude curve shifted farther to the right than the phase curve.

Less-simplistic predictions might be expected to provide a better fit to the data, but there are deeper problems with the hypothesis that the timing aftereffects are directly related to the phase advance with contrast. Although there are not yet any thorough studies of the cortical phase advance, it varies across cells and temporal frequency, as in the retina and lateral geniculate nucleus (Victor, 1987, 1988; Saul & Humphrey, 1990). In two cells in this series, no phase advance was present (at least for low temporal frequencies), yet timing aftereffects were still observed. Fig. 3 shows an example where phase was actually retarded with increasing contrast. If timing aftereffects were related to the contrast shift seen in the amplitude data, then

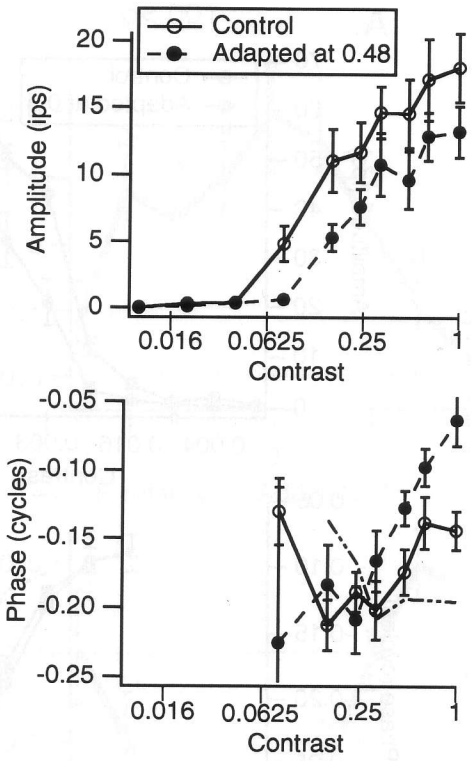

Fig. 3. Contrast-response functions from a cell that did not show a phase advance with contrast when tested at 4 Hz and 0.32 cycles/deg in the preferred direction and adapted at 0.48 contrast. The ten test contrasts were 0.01, 0.02, 0.04, 0.08, 0.16, 0.24, 0.32, 0.48, 0.64, and 1. Each condition was tested ten times, with 8-s adapting portions and 4-s test portions. The broken line again shows the prediction of the adapted phase values based on the amplitude data and the control phase values.

adapting would advance the phase in this case (as indicated by the broken line). Instead, the normal aftereffect of retarded phase was seen.

To complete the evidence against the hypothesis that timing aftereffects represent no more than a shift along the contrast axis, note that histograms shift with contrast in a different way than they do with adaptation. With decreasing contrast, both onsets and offsets occur later in the stimulus cycle. Adaptation instead only delays onsets. In summary, adaptation does not commute with the amplitude/phase relation, timing aftereffects are independent of the phase advance with contrast, and decreasing contrast shifts both onsets and offsets of response histograms. These results show that phase aftereffects do not correspond in a simple way to the phase advance associated with contrast gain control. However, the present results leave unresolved the important question of how adaptation is related to contrast gain control.

The consistency of the aftereffects reported here was striking. To illustrate this point, further examples are illustrated in Figs. 4–6. These three cells span the range of degree of aftereffects, from strong in Figs. 4 and 5 to weak in Fig. 6. The amplitude and phase values are shown, along with histograms. Note how the amplitude and phase aftereffects are poorly correlated, with a tendency for the amplitude aftereffects to be stronger at lower contrasts than the phase aftereffects. The example in

*The predicted adapted phase values were obtained by finding the control phase value at the contrast that gave a control amplitude equal to the adapted amplitude:

$$\phi^{\text{predicted}}_{\text{Adapted}}(c) = \phi_{\text{Control}}[A^{-1}_{\text{Control}}(A_{\text{Adapted}}(c))]$$

In mathematical words, this tests the commutativity of adapting with the relation between amplitude and phase.

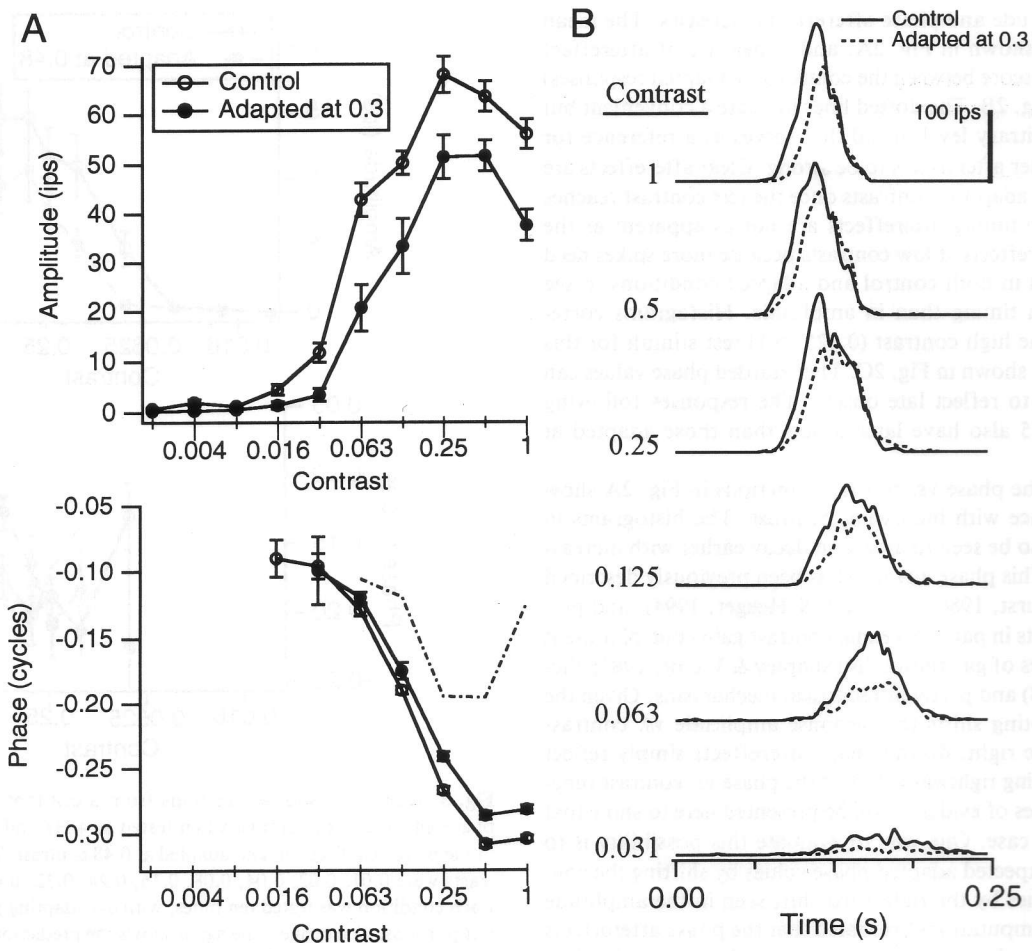

Fig. 4. Data from a cell tested at ten contrasts ranging from about 0.002 to 1 in octave steps at 0.125 cycles/deg and 4 Hz in the preferred direction. Adapting and test portions of the trials lasted 8 s and 4 s, respectively, with ten iterations. The adapting contrast was 0.3.

Fig. 5, in particular, shows how amplitude can be unaffected even though the timing is strongly retarded. The histograms from these cells demonstrate the consistent asymmetry in the effects of adaptation on onset *vs.* offset.

To average data from different cells, aftereffects as measured by the *t*-score index were plotted *vs.* the difference (in octaves) between the test and adapting contrasts. Population results, from ten cells, are shown in Fig. 7. The hypothesis that these means did not differ from zero was tested by a one-tailed *t*-test, and points where this hypothesis was rejected are indicated with star symbols. The averaged amplitude aftereffects show little dependence on contrast over a five-octave range. Highly significant aftereffects were found even two octaves above the adapting contrast. This is consistent with previous reports that adapting induces a rightward shift of the contrast-response function over a broad range of contrasts.

The phase aftereffects are significant over a narrower range, only within one octave of the adapting contrast. Timing aftereffects disappear at low contrasts, but this is due at least in part to the fact that responses are too poor at low contrast to observe reliable aftereffects. Aftereffects appear to remain strong at high contrasts, but adapting contrasts tended to be fairly high in this sample (mostly 0.5), yielding few points at contrasts more than 1.5 octaves above the adapting contrast (that is, in the +2 octave bin).

The absolute change in response amplitude induced by the adapting stimulus is not very meaningful because of the wide range of amplitudes seen in the control condition. This is the reason for presenting a normalized measure such as the *t*-score index used here, or a ratio measure used by many others. In contrast, response phase values lie in a uniform range and the amount of phase delay caused by the adapting stimulus provides a useful measure of the aftereffect. Typically, this delay amounts to about 0.05 cycles, independent of temporal frequency (see below). The average change in phase is plotted in Fig. 7, and, like the *t*-score measure, reaches significance within one octave on either side of the adapting contrast. Over this sample, which included some points that showed no aftereffect, phase values were retarded on average about 0.02 cycles.

Aftereffects as a function of temporal frequency

Temporal-frequency tuning was tested in control and adapted states in 19 cells. Previous work has demonstrated that amplitude aftereffects are tuned in the temporal-frequency domain, in that frequencies near the adapting temporal frequency are

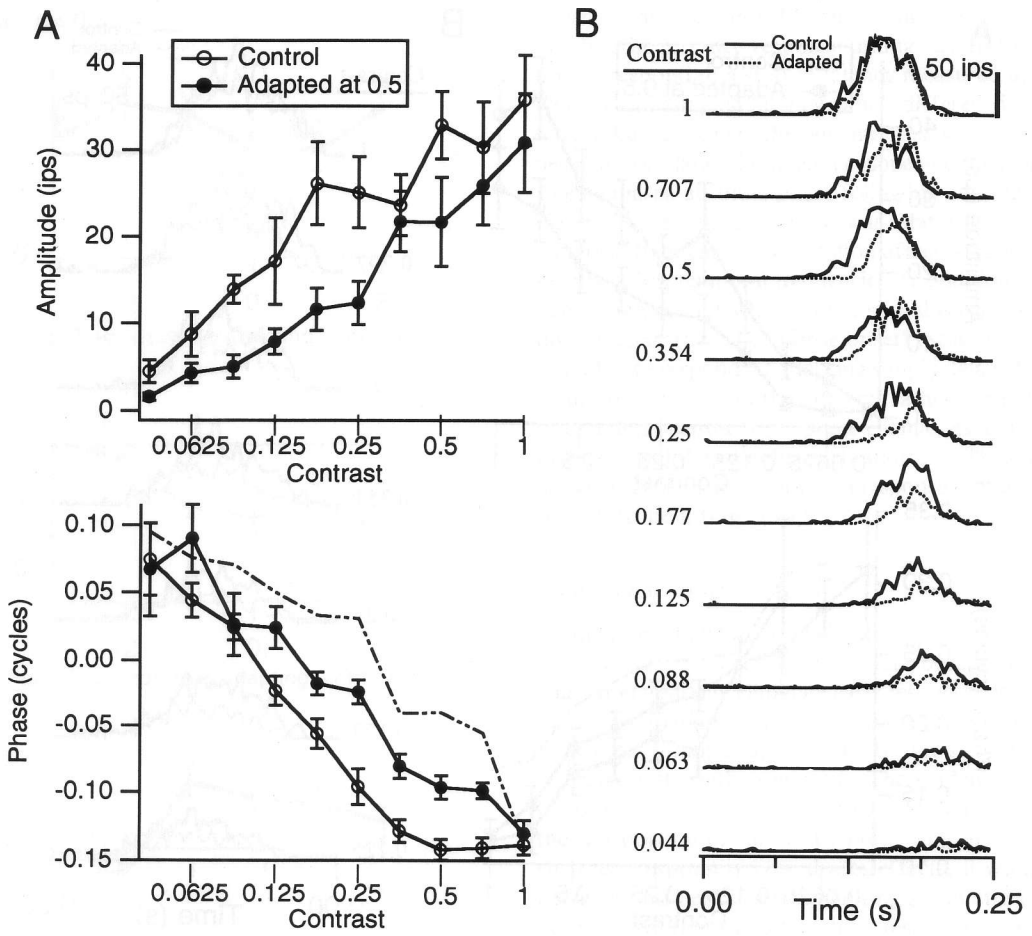

Fig. 5. This cell was tested at 0.15 cycles/deg and 4 Hz in the preferred direction at contrasts ranging from about 0.04 to 1 in half-octave steps, and adapted at 0.5 contrast. Other parameters are like those in Fig. 4.

most strongly affected, with a bias toward higher temporal frequencies (Maddess et al., 1988; Saul & Cynader, 1989*b*). In the present experiments, these results were extended to the tuning of phase aftereffects. Fig. 8 shows an experiment in which a simple cell was tested at ten temporal frequencies and adapted at four temporal frequencies. The 0.25-Hz points have been removed from these graphs for clarity because responses were negligible there (as they were at 16 Hz). The control amplitude tuning shows a preferred temporal frequency of about 2 Hz. The adapted tuning is similar but of lower amplitude, with some shifts of the optimal frequency.

Response phase increases fairly linearly as a function of temporal frequency (Lee et al., 1981; Hamilton et al., 1989; Saul & Humphrey, 1990, 1992*b*; Reid et al., 1992). The slope corresponds to a latency, or integration time, which ranges from 40–200 ms in primary visual cortical cells (Hamilton et al., 1989; Saul & Humphrey, 1992*b*; Reid et al., 1992). The intercept of the phase *vs.* temporal-frequency line depends on the receptive-field structure, but contains an arbitrary shift that is not accounted for in these data alone, since the position of the grating relative to the receptive field is not determined. However, for our purposes it is the comparison between the control and adapted phase that matters, so this arbitrary shift is canceled. The adapted phase values are consistently slightly later than the control values. The difference is typically about 0.03–0.05 cycles. For many of the adapted/control pairs, this small difference is significant at the $P < 0.01$ level using a standard univariate *t*-test (as well as by circular statistics tests), since their standard errors are about 0.01 cycles. Because these changes occur primarily at low temporal frequencies (1–3 Hz), the intercepts of the phase *vs.* temporal-frequency lines change more than the slopes. The intercept was increased from −0.018 cycles in the control condition to 0.037, 0.063, 0.046, or 0.014 cycles in the adapted conditions, whereas the slopes ranged from the control value of 66 ms to 54, 58, 63, and 73 ms.

Fig. 8B shows histograms from this experiment. Responses can be seen to occur later in the stimulus cycle as temporal frequency increases. Again, the main effects of adapting were to decrease response amplitude and to delay response onsets but not offsets. The adapted responses started later than the control response in every case, but recovered later in the cycle.

The change in response timing induced by adapting is treated as a change in phase values rather than as a pure delay because the degree to which phase is altered is relatively constant across temporal frequency. Fig. 9 compares the phase-change and time-delay alternatives, for the 8-Hz adapting data from Fig. 8. When plotted as a change in phase values, the aftereffect is fairly constant at about 0.06 cycles. Replotting the same data as a pure

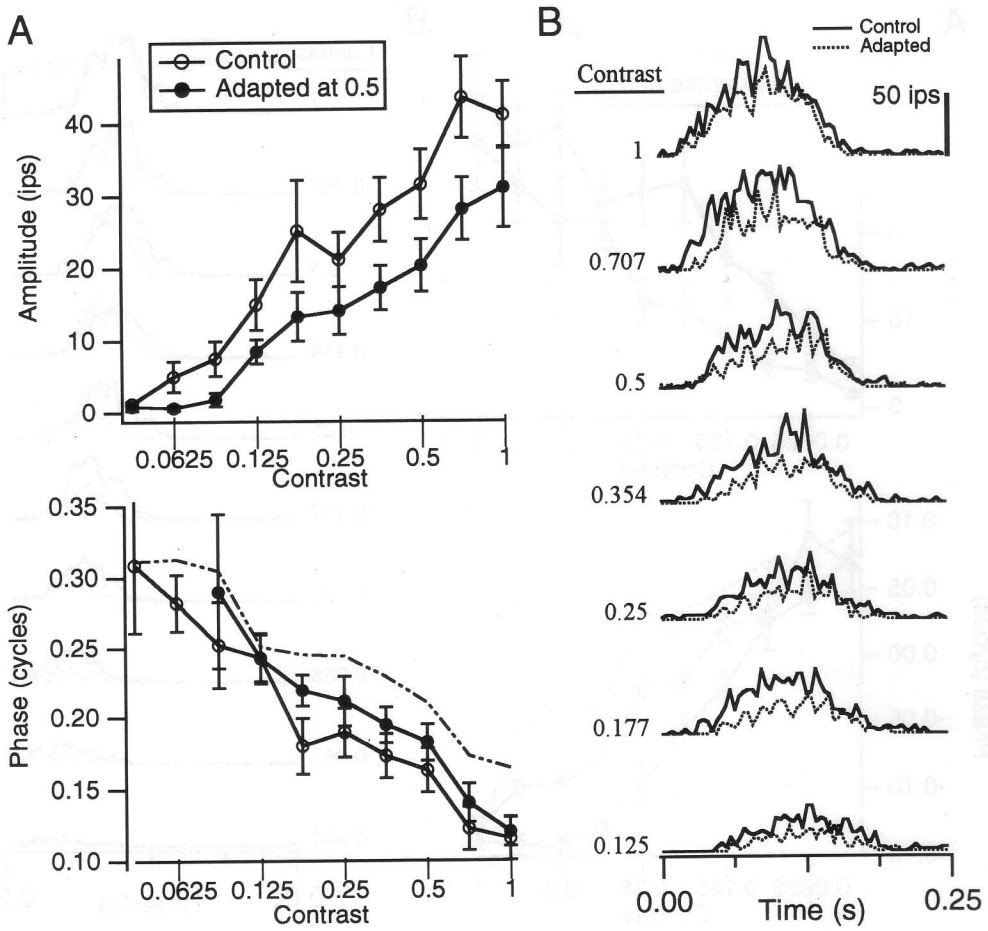

Fig. 6. Weaker aftereffects were obtained from this cell tested at 0.3 cycles/deg and 4 Hz in the preferred direction. Other parameters are as in Fig. 5. The histograms in B have been rotated by a half-cycle for clarity.

delay (by dividing by temporal frequency) therefore shows a decreasing function of temporal frequency, with delays ranging from about 60–10 ms. The time delay induced by adapting always decreases with temporal frequency, as will be emphasized below. It is more appropriate to present the data in the frequency domain rather than the time domain.

For comparison across cells, aftereffect strengths were computed using the *t*-score measure, and plotted as a function of test temporal frequency relative to adapting temporal frequency. These values were then averaged across the 19 cells tested in this way. Fig. 10 shows the average amplitude and timing aftereffect tuning, as well as the average change in the response phase value itself. The distribution of adapting temporal frequencies used resembled the range of optimal frequencies observed in area 17 simple cells (c.f. Fig. 4A in Saul & Humphrey, 1992*a*). The geometric mean of the adapting temporal frequencies was 2.3 Hz. As observed previously (Saul & Cynader, 1989*b*), the amplitude aftereffects are broadly tuned around the adapting frequency. Several studies have observed that aftereffects are stronger at high temporal frequencies (Maddess et al., 1988; Saul & Cynader, 1989*b*; Bonds, 1991). No bias was observed for higher temporal frequencies in this small sample, although when the subset of data for adapting and testing in the same direction was considered (not shown) a slight bias was seen. The timing aftereffects are also tuned around the adapting frequency, with some bias for lower temporal frequencies. Phase is significantly retarded in the population for temporal frequencies within an octave of the adapting frequency, and at two octaves below as well. Note that timing was not delayed at high temporal frequencies (i.e. 2–3 octaves above the adapting frequency), even though amplitude was reduced there. The different tuning of the amplitude and phase data suggests that these two measures of aftereffects are not correlated, and that the phase aftereffects are not dependent on the amplitude aftereffects. The total sample of 538 points where amplitude and phase aftereffects were measured showed only a weak correlation ($r = -0.2$; the negative correlation reflects the tendency to have reduced amplitude and increased phase following adapting).

The slopes (latencies) and intercepts (absolute phase values) were measured from the phase *vs.* temporal-frequency data in the control and adapted conditions. These two measures characterize timing behavior well (Saul & Humphrey, 1990, 1992*b*). Latency comprises delays and integration times due to filtering and other processing. Absolute phase includes timing properties related to the stimulus cycle (whether responses are to bright or dark, and how transient or sustained and lagged or nonlagged the responses are). Fig. 11 shows histograms of the differences between control and adapted values of these param-

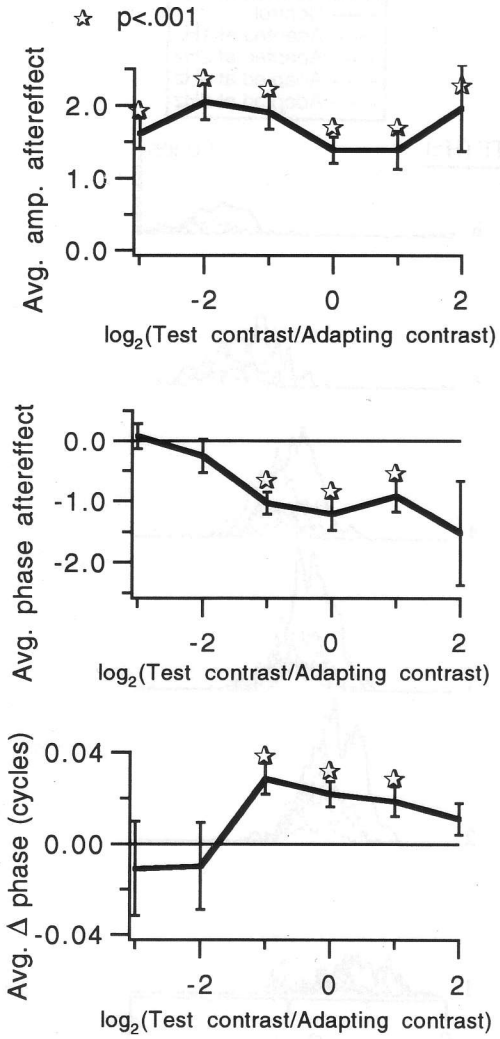

Fig. 7. Population data based on ten cells from which contrast-response functions were obtained in control and adapted states. Test contrasts were normalized to the adapting contrast by computing the difference in octaves between them. The indices of aftereffect strength (the *t*-scores for amplitude and phase and the pure phase shift induced by adapting) were then put into octave-wide bins and averaged. Shown here are the means and standard errors of those indices. The number of points in each bin from −3 to +2 octaves are 44, 36, 55, 46, 32, and 6, respectively. The stars mark those means that differ significantly from 0. Most data were obtained from adapting near 0.5 contrast and 4 Hz. Test temporal frequency always matched the adapting temporal frequency.

eters, along with their correlation. As discussed for the example of Fig. 8, latencies were not consistently increased by adapting, whereas absolute phase values were almost always retarded. The absolute phase data has a clear mode shifted to the right of zero, with only three points out of 35 showing advanced absolute phase. The average absolute phase difference induced by adapting was 0.05 cycles, and the adapted absolute phase values differed highly significantly from the control values.

In contrast, the latency differences were somewhat mixed, with a mean of 10 ms that is equivalent to about two bin widths in the original histograms. The adapted latencies were slightly *shorter* than the control latencies on average, clearly indicating that the retarded response timing caused by adapting does not correspond to a shift in latency measured in this way. The control and adapted latency values differed significantly ($P = 0.005$), but, as seen at the bottom, this is apparently due to the negative correlation between the slope and intercept parameters. The increased absolute phase following adapting forced latencies to decrease because phase was relatively unaffected at high temporal frequencies. Adaptation affects phase values predominantly at low temporal frequencies. In addition or alternatively, adaptation affects where in the stimulus cycle spikes occur or do not occur (i.e. at response onset) rather than how long the cell takes to respond. If adapting simply delayed responses, this would be reflected in the latency, rather than absolute phase, since a delay causes larger phase changes as temporal frequency increases and the stimulus cycle shortens. Thus, as pointed out above, the effect of adapting on response timing can not be considered to be a time delay.

Time course of aftereffects

As mentioned above, aftereffects appeared to persist for several seconds. This is important here because transient effects could preferentially eliminate early responses as opposed to later responses, thereby inducing a shift in response timing. In other words, the timing changes could be due simply to the decay of aftereffect strength over time. The evidence contradicts this hypothesis. The data were reanalyzed, ignoring the first 2 s of the test portion of the trials, preserving only the final 2 s. If such test responses showed aftereffects, it would argue for a persistent influence of the adapting stimulation. A caveat was noted above that the intervening test stimulation could *maintain* the aftereffect, but this would contradict the idea that the timing changes are due to *decaying* aftereffects.

Fig. 12A shows representative data from a cell that was tested at a range of temporal frequencies and adapted at 2 Hz. Responses at 1 and 2 Hz, in control and adapted states, are shown for the entire 4 s of testing as well as for the final 2 s. The latter responses were nearly indistinguishable from the earlier ones. In the adapted histograms, no spikes are present at control response onset even during the last 2 s of testing.

The caveat mentioned above was directly addressed by testing three cells with a range of delays between the end of adapting and the start of testing. How much do aftereffects decay during this delay? To keep the test conditions comparable, only the onset of the test stimulus was delayed, so that all conditions ended 4 s after the adapting stimulus was removed. Thus, in Fig. 12B, nine test conditions were presented, with delays ranging from 0 to 2000 ms. All stimuli were gratings drifting in the preferred direction at 0.15 cycles/deg and 4 Hz, with 8-s adapting portions at either 0 or 0.5 contrast, and test gratings at 0.25 contrast. Each test stimulus had a different duration because of the delay, so that the duration was 4000 ms minus the delay. Because fewer cycles were presented at longer delays, reliability tends to decrease with increasing delay. Delays longer than 2 s were not used because of this problem. The delays were chosen so that an integral number of cycles of the 4-Hz stimulus was completed in every case. Aftereffects persisted for about 2 s, weakening somewhat with increasing delay. The timing aftereffects consisted of a phase change of about 0.04 cycles at short delays, decaying to about 0.02 cycles at longer delays.

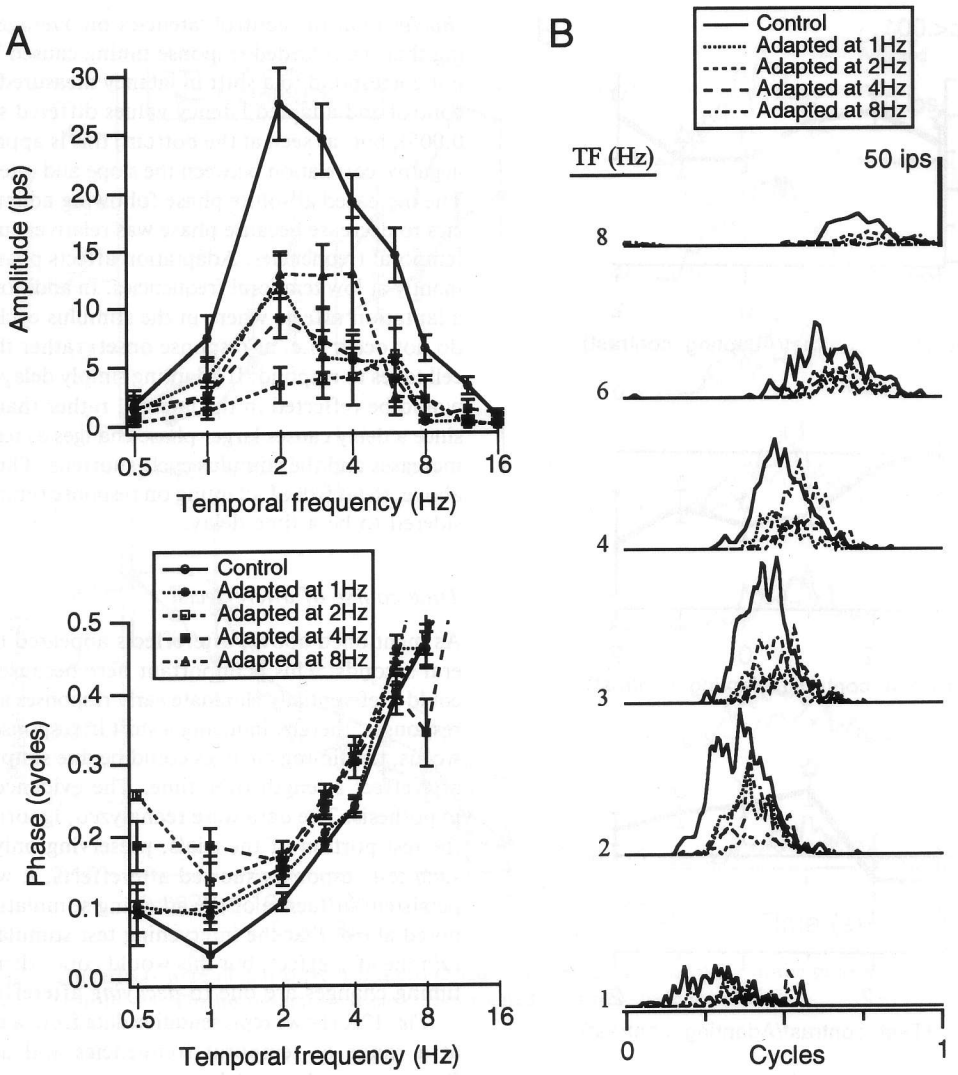

Fig. 8. A: Responses are shown to gratings of 0.3 cycles/deg and 0.2 contrast drifting in the preferred direction at a range of temporal frequencies under several adapting conditions. Adapting stimuli were presented for 10 s, followed by 4-s test portions. Each condition was tested either eight or nine times. Phase increases fairly linearly with temporal frequency, but the temporal-frequency axis is plotted logarithmically. The phase axis and the temporal-frequency axes have been truncated for clarity, omitting some responses that were negligibly weak. B: Histograms for those temporal frequencies where reasonable levels of response were obtained are plotted for each of the adapting states. The time base varies with temporal frequency. The control responses have earlier onsets than the adapted responses in almost every case. These histograms have been rotated by a half-cycle for clarity.

Adaptation therefore produces short-term changes in cortical activity that specifically affect response onsets.

Discussion

Adaptation affects the timing of visual responses as well as their amplitude. Responses occur later following adapting. These retarded phase values are seen near the adapting temporal frequency, typically within an octave of the adapting stimulus. Timing aftereffects show a bias toward low temporal frequencies. This bias is opposite that seen for amplitude aftereffects, which are biased toward high temporal frequencies (Maddess et al., 1988; Saul & Cynader, 1989*b*; Bonds, 1991). The dissociation of timing and amplitude aftereffects implies that *when* a cell responds can be altered without changing how strongly it responds. Some of these findings on the tuning of phase aftereffects are subject to the problem that amplitude aftereffects can preclude the observation of phase changes, because few spikes are evoked in the adapted condition. For instance, reliable phase values are more difficult to obtain at low contrasts and at high temporal frequencies. However, in many cells a bias was present even when responses were adequate to yield small standard errors of the phase means (as in Fig. 8).

Since contrast advances response phase in most cells, the decreased apparent contrast (rightward shift) following adapting would be expected to retard phase. However, the timing

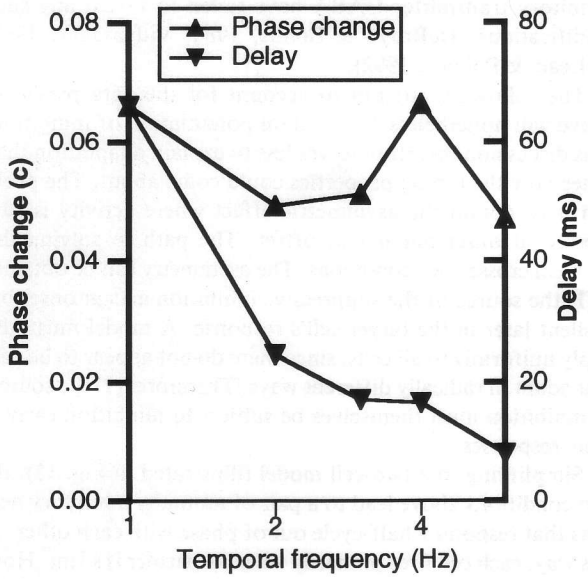

Fig. 9. The difference between the control and adapted at 8-Hz response phase values is plotted in two ways for the data from Fig. 8. The phase difference is shown against the left axis with triangles that point upward, and the time difference is plotted against the right axis with downward triangles. The delay values are obtained by dividing the phase differences by the temporal frequency. Adapting retards phase relatively constantly across temporal frequency compared to the effect on time delays, which are very short at high frequencies.

aftereffects do not correspond to changes in apparent contrast for several reasons. For one, adapting retards phase even when there is no phase advance with contrast. For another, both onset and offset of response shift with contrast, but only the onset is delayed by adapting.

The most remarkable result is the consistent lack of firing at the time of control response onset, and the subsequent recovery of activity. This demonstrates the specificity of adaptation in a new sense. Adaptation does not cause a generalized increase in threshold or other fatigue-like processes, but acts on only a limited subset of a neuron's response repertoire. Dean (1983), by similarly examining histograms, showed that adapting does not simply raise thresholds. He shifted the peaks of the adapted histograms to align them with the control waveforms, and therefore discarded the data behind the key finding of the present work. Just as this finding can falsify hypotheses about adaptation, it can provide inspiration for further modeling.

Mechanisms

The substrate for neuronal adaptation aftereffects is unknown, but several investigators have speculated that a potentiation of mutually inhibitory interactions is involved (Dealy & Tolhurst, 1974; Wilson, 1975; Vautin & Berkley, 1977; Movshon & Lennie, 1979; DeBruyn & Bonds, 1986; Saul & Cynader, 1989*b*; Heeger, 1992; Wilson & Humanski, 1993). This suggestion corresponds to the feeling that adaptation is a gain control process involving dampening of the entire cortical network. However, no direct evidence supports this idea, and attempts to modify aftereffects by iontophoretic application of antagonists to the

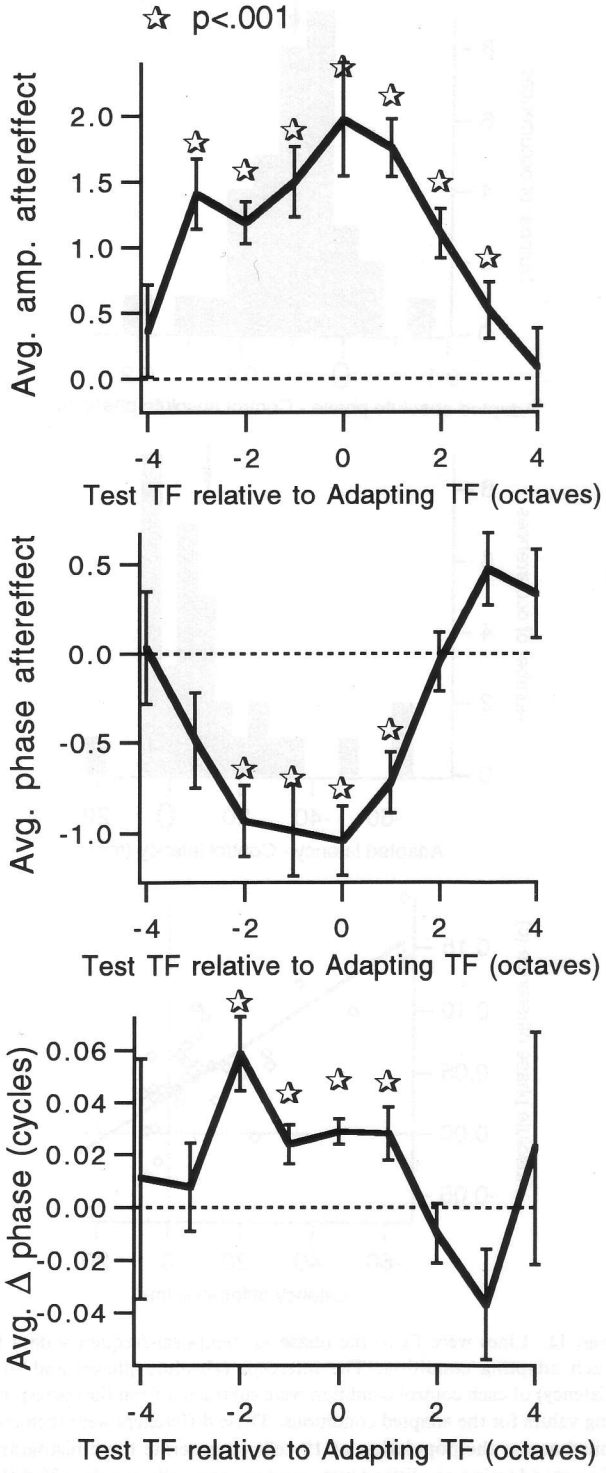

Fig. 10. Population data from 19 cells for the temporal-frequency tuning of aftereffects. As in Fig. 7, three measures of aftereffect strength are shown, plotted against test temporal frequency relative to adapting temporal frequency. Means and standard errors are shown for points ranging from −4 to +4 octaves, where the number of points in each of these nine bins was 20, 38, 59, 70, 80, 94, 83, 62, and 32, respectively. Some of these points were derived from conditions where the adapting and test direction matched and others where adapting and test directions were opposite. Opposite direction points numbered 4, 10, 17, 19, 21, 25, 24, 18, and 10 out of the sample sizes given above. As in Fig. 7, stars indicate means that differ from 0 at the 0.001 level.

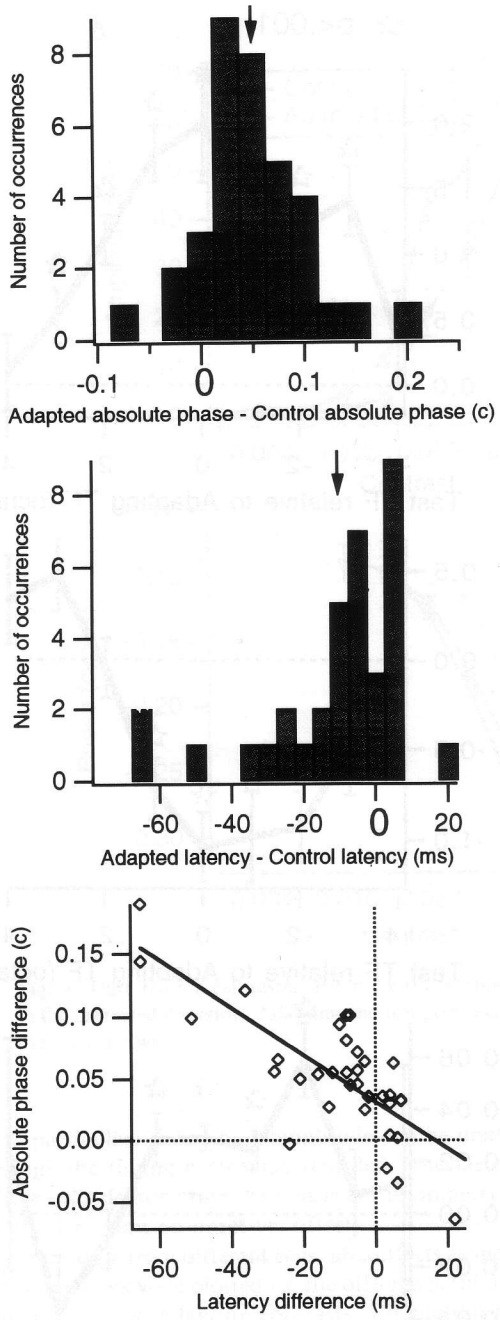

Fig. 11. Lines were fit to the phase *vs.* temporal-frequency data for each adapting condition. The intercept (absolute phase) and slope (latency) of each control condition were subtracted from the corresponding values for the adapted conditions. These differences were then compiled across the population of 19 cells to generate these histograms. Several adapting conditions were used in some cells, yielding 35 differences in all. The mean of each distribution is indicated with an arrow. For the absolute phase difference the mean was 0.05 cycles, with a standard deviation of 0.05 cycles. The adapted and control absolute phase values were significantly different (paired *t*-test, $P = 2.7 \times 10^{-10}$, $t = 8.8$, $N = 35$). For the latency difference, the mean was -10.3 ms, with a standard deviation of 19.5 ms. The paired *t*-test led to a significant difference between control and adapted latencies ($P = 0.005$, $t = -3.03$, $N = 35$). At the bottom, the correlation between the absolute phase and latency differences is demonstrated, along with the regression line through the points. This line had an intercept of 0.03 cycles and a slope of 1.9 Hz, with a correlation coefficient of -0.76.

inhibitory transmitter GABA have failed to reveal any such modifications (DeBruyn & Bonds, 1986; Vidyasagar, 1990; McLean & Palmer, 1992).

The following attempt to account for the data presented above will nonetheless be based on potentiation of inhibition. This discussion therefore serves less to explain adaptation than to see how the timing properties could come about. The problem is to obtain the asymmetric effect where activity is suppressed at onset but not at offset. The path to solving this problem crosses two conditions. The asymmetry can be obtained if (1) the source of the suppressive inhibition acts at onset but is silent later in the target cell's response. A model must also apply uniformly to all cells, since there do not appear to be cells that adapt in radically different ways. Therefore, (2) the sources of inhibition must themselves be subject to inhibition early in their responses.

Simplifying to a two-cell model (illustrated in Fig. 13), the two conditions above lead to a pair of mutually inhibitory neurons that respond a half-cycle out of phase with each other. In this way, each cell fires primarily when its partner is silent. However, if the inhibition (solid curves in Fig. 13 show inhibition onto cell whose response is shown on the same axis) has a longer time course than the activity that generates it, then each cell would see an inhibitory input when it is starting to respond (Fig. 13). Adapting is thought of as potentiating this inhibitory input, creating an increased suppression at onset. Because the source of the inhibition is silent after onset, the response recovers later in the stimulus cycle.

This model has the structure of a push–pull pair, that is, antagonism between receptive fields that differ by a half-cycle (Hubel & Wiesel, 1959; Palmer & Davis, 1981; Ferster, 1986, 1988; Heggelund, 1986; Tolhurst & Dean, 1987, 1990; McLean et al., 1994). One might think intuitively that two such receptive fields have opposing response properties, but this is not the case. For instance, push–pull receptive fields prefer the same direction of motion (they share orientation preference by definition). A simple example may help to illustrate this. Suppose the two model cells each receive a single excitatory input from geniculate afferents that differ from each other by a quarter-cycle in space and in time (i.e. they are in spatiotemporal quadrature). The total input to each cell would then consist of an excitatory and an inhibitory input that are in spatiotemporal quadrature, which would render the cortical cells direction selective. The two cells would prefer the same direction, however, and would respond a half-cycle apart when stimulated in this direction (since they receive identical inputs except for the sign reversals). In the nonpreferred direction, rather than responding a half-cycle apart the two cells respond simultaneously, and through mutual inhibition suppress each other. Thus, one would expect that timing aftereffects would differ between the two directions in direction-selective cells according to this model. Unfortunately, this hypothesis is difficult to test because of the poor responses in the nonpreferred direction of direction selective cells. Intracellular recording may be required to test this aspect of the model.

The two-cell model was presented for simplicity, and has deficiencies as stated (for instance, total suppression in the nonpreferred direction is impossible). In reality many cells are involved, and the model can be scaled up to a richly interconnected cortex in several ways. The important aspect is that it predicts that the inhibition onto a cell is tuned similarly to the

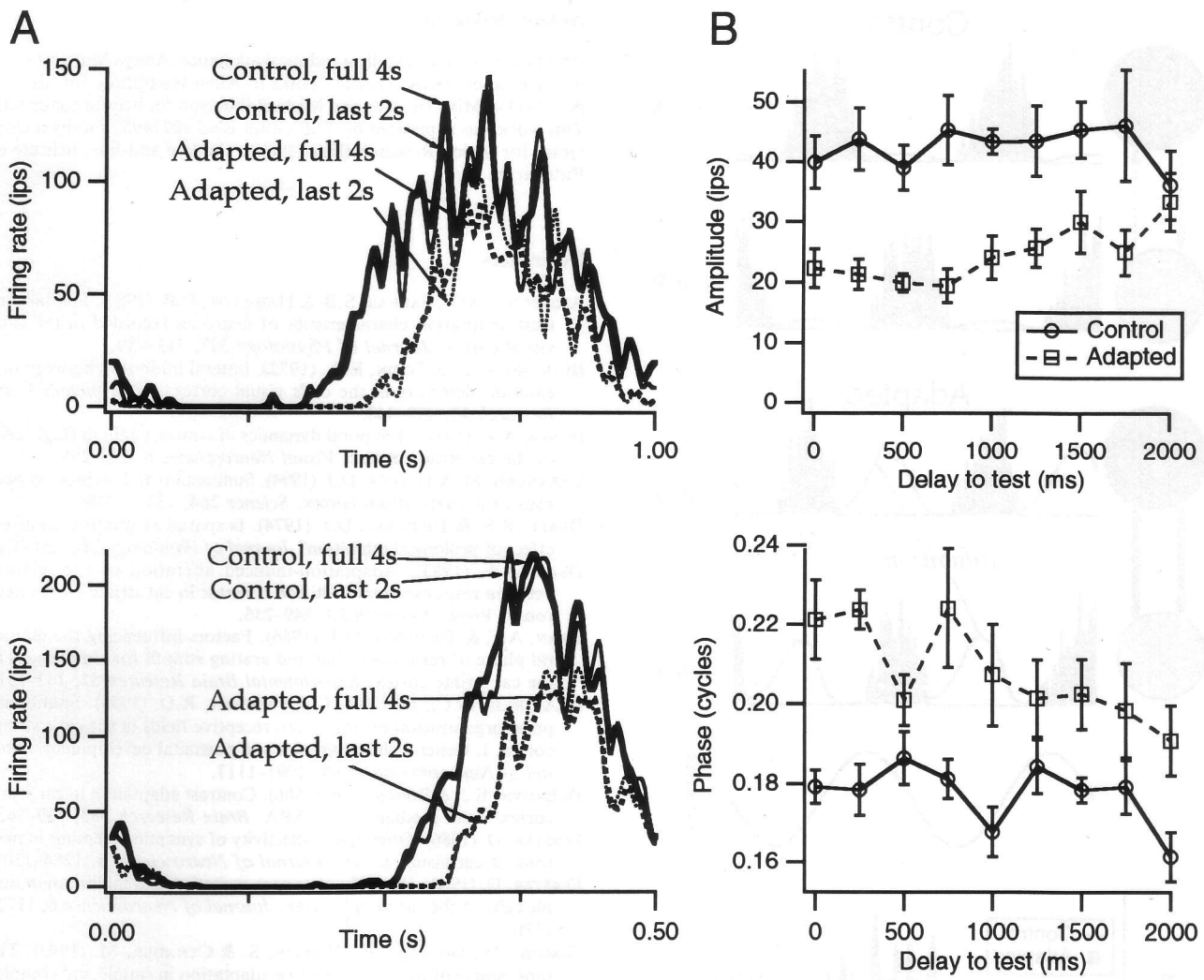

Fig. 12. Controls to rule out decaying aftereffects as the cause of timing changes. In A, data from a temporal-frequency tuning experiment show how the responses during the final 2 s of the test portion compare to the entire 4 s. These responses were obtained from nine iterations at 0.2 contrast and 1 cycles/deg in the preferred direction, following 10 s of adapting at a contrast of 0 or 0.3. The histograms from the 1- and 2-Hz test stimuli show that the onsets were delayed as much after 2 s as they were immediately following the end of adapting. In B, the persistence of aftereffects was examined in a separate experiment by delaying test stimulus onset. All gratings drifted in the preferred direction at 0.15 cycles/deg and 4 Hz. Test stimuli of 0.25 contrast were turned on at delays ranging from 0 to 2000 ms following the offset of the 8-s-long, 0.5-contrast adapting stimulus. Test stimuli were turned off 4 s after the offset of the adapting stimulus, so the number of stimulus cycles presented varied with the delay.

excitation (Blakemore & Tobin, 1972; Saul & Daniels, 1986; Ferster, 1986, 1988), but that this inhibition is shifted by a half-cycle relative to the excitation (Tolhurst & Dean, 1990). The match between response properties implies that aftereffects are tuned around the adapting stimulus, and that adaptation behaves like a tuned version of gain control or normalization. In Heeger's (1992) model, the feedback inhibition responsible for normalizing responses was assumed to be nonspecific. Wilson and Humanski (1993) show that the tuning of adaptation can arise simply from the tuning of inhibition. Because many cells contribute to the inhibitory input onto a given cell, nonspecific effects occur. However, the net tuning of the inhibitory input matches the response properties of the target cell, creating specific aftereffects. The net inhibitory activity is about a half-cycle out of phase in time with the response of the target cell, creating the specific timing changes revealed here.

The model emphasizes that the tuning of adaptation aftereffects can also arise from changes in response timing. The fact that amplitude aftereffects become stronger with increasing temporal frequency could reflect a change in the half-cycle difference between mutually inhibitory cells as a function of temporal frequency. At higher temporal frequencies, the push–pull relation probably changes (Saul & Humphrey, 1990, 1992*a*). It should be stressed that adaptation is not more powerful at high temporal frequencies; this is only true of the amplitude aftereffects (Maddess et al., 1988; Saul & Cynader, 1989*b*; Bonds,

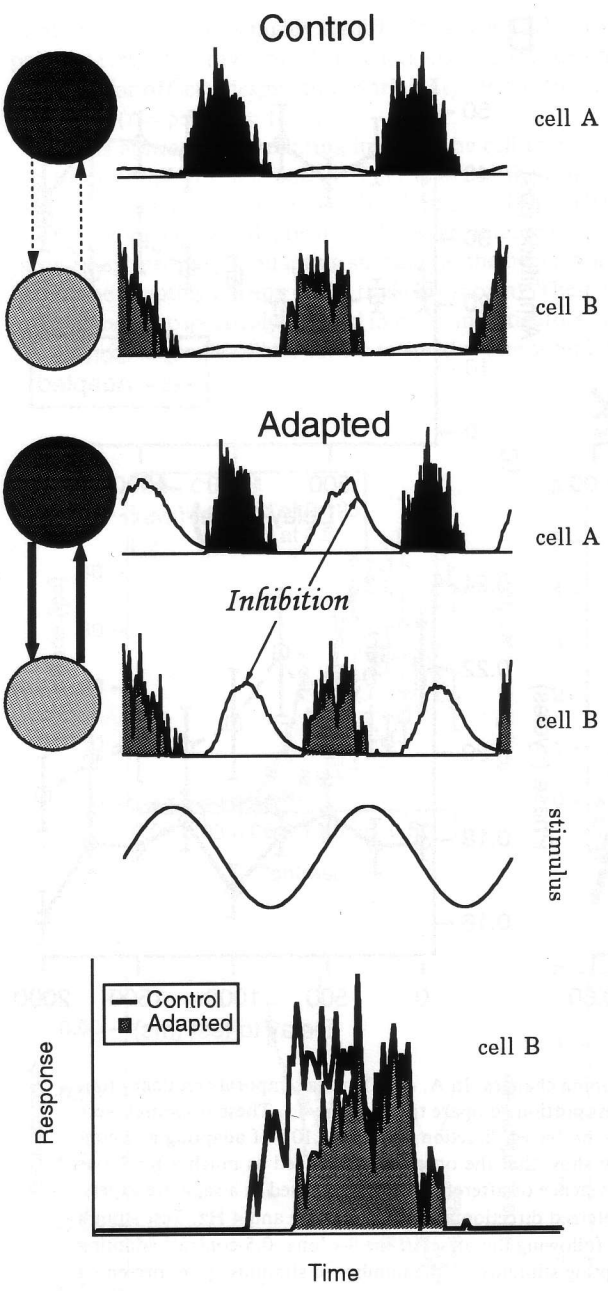

Fig. 13. Simulation results for a two-cell model for timing aftereffects. Cells A and B were given excitatory inputs that were noisy sine waves separated by a half-cycle. The response from each cell was convolved with an exponentially decaying function to low-pass filter the subtractive inhibitory input to the other cell. The simulation computed the half-wave rectified responses by an iterative feedback procedure. The inhibitory gain was increased by a factor of 10 between the control and adapted conditions shown here; otherwise the computations were identical. The histograms from the middle section of the responses of cell B are compared at the bottom. As in the real data, onsets were delayed but offsets were unaffected.

1991). At low temporal frequencies, even in the absence of a big change in response strength, one would expect the change in timing to affect behavior. Psychophysical correlates of the single-cell results might therefore be found at low temporal frequencies where amplitude aftereffects would interfere less.

Acknowledgments

Paul Baker provided excellent technical assistance. Aditya Murthy helped in some experiments. Special thanks to Allen Humphrey for his support, and to Mike Hawken and Michael Ibbotson for helpful comments. This work was supported by NSF Grant BNS 9021495, and by a Core Grant for Vision Research (EY08098) to the Eye and Ear Institute of Pittsburgh.

References

Albrecht, D.G., Farrar, S.B. & Hamilton, D.B. (1984). Spatial contrast adaptation characteristics of neurones recorded in the cat's visual cortex. *Journal of Physiology* **347**, 713–739.

Blakemore, C. & Tobin, E.A. (1972). Lateral inhibition between orientation detectors in the cat's visual cortex. *Experimental Brain Research* **15**, 439–440.

Bonds, A.B. (1991). Temporal dynamics of contrast gain in single cells of the cat striate cortex. *Visual Neuroscience* **6**, 239–255.

Carandini, M. & Heeger, D.J. (1994). Summation and division by neurons in primate visual cortex. *Science* **264**, 1333–1336.

Dealy, R.S. & Tolhurst, D.J. (1974). Is spatial adaptation an aftereffect of prolonged inhibition? *Journal of Physiology* **241**, 261–270.

Dean, A.F. (1983). Adaptation-induced alteration of the relation between response amplitude and contrast in cat striate cortex neurones. *Vision Research* **23**, 249–256.

Dean, A.F. & Tolhurst, D.J. (1986). Factors influencing the temporal phase of response to bar and grating stimuli for simple cells in the cat striate cortex. *Experimental Brain Research* **62**, 143–151.

DeAngelis, G.C., Ohzawa, I. & Freeman, R.D. (1993). Spatiotemporal organization of simple-cell receptive fields in the cat's striate cortex. I. General characteristics and postnatal development. *Journal of Neurophysiology* **69**, 1091–1117.

DeBruyn, E.J. & Bonds, A.B. (1986). Contrast adaptation in cat visual cortex is not mediated by GABA. *Brain Research* **383**, 339–342.

Ferster, D. (1986). Orientation selectivity of synaptic potentials in neurons of cat visual cortex. *Journal of Neuroscience* **6**, 1284–1301.

Ferster, D. (1988). Spatially opponent excitation and inhibition in simple cells of the cat visual cortex. *Journal of Neuroscience* **8**, 1172–1180.

Giaschi, D., Douglas, R., Marlin, S. & Cynader, M. (1993). The time course of direction-selective adaptation in simple and complex cells in cat striate cortex. *Journal of Neurophysiology* **70**, 2024–2034.

Hamilton, D.B., Albrecht, D.G. & Geisler, W. S. (1989). Visual cortical receptive fields in monkey and cat: Spatial and temporal phase transfer function. *Vision Research* **29**, 1285–1308.

Hammond, P., Mouat, G.S. & Smith, A.T. (1985). Motion aftereffects in cat striate cortex elicited by moving gratings. *Experimental Brain Research* **60**, 411–416.

Hammond, R., Mouat, G.S. & Smith, A.T. (1986). Motion aftereffects in cat striate cortex elicited by moving texture. *Vision Research* **26**, 1055–1060.

Hammond, P., Mouat, G.S. & Smith, A.T. (1988). Neural correlates of motion aftereffects in cat striate cortical neurones: Monocular adaptation. *Experimental Brain Research* **72**, 1–20.

Hammond, P. & Mouat, G.S. (1988). Neural correlates of motion aftereffects in cat striate cortical neurones: Interocular transfer. *Experimental Brain Research* **72**, 21–28.

Hammond, P., Pomfrett, C.J.D. & Ahmed, B. (1989). Neural motion aftereffects in the cat's striate cortex: Orientation selectivity. *Vision Research* **29**, 1671–1683.

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

Heggelund, P. (1986). Quantitative studies of enhancement and suppression zones in the receptive field of simple cells in cat striate cortex. *Journal of Physiology* **373**, 293–310.

Hubel, D.H. & Wiesel, T.N. (1959). Receptive fields of single neurones in cat's visual cortex. *Journal of Physiology* **160**, 106–154.

Humphrey, A.L. & Weller, R.E. (1988). Structural correlates of functionally distinct X-cells in the lateral geniculate nucleus of the cat. *Journal of Comparative Neurology* **268**, 448–468.

Kulikowski, J.J., Rao, V.M. & Vidyasagar, T.R. (1981). Effects of directional adaptation on the response profiles of simple cells in the visual cortex of cat and macaque. *Journal of Physiology* **318**, 21.

LEE, B.B., ELEPFANDT, A. & VIRSU, V. (1981). Phase of responses to sinusoidal gratings of simple cells in cat striate cortex. *Journal of Neurophysiology* **45**, 818–828.

MADDESS, T., MCCOURT, M.E., BLAKESLEE, B. & CUNNINGHAM, R.B. (1988). Factors governing the adaptation of cells in area 17 of the cat visual cortex. *Biological Cybernetics* **59**, 229–236.

MAFFEI, L., FIORENTINI, A. & BISTI, S. (1973). Neural correlate of perceptual adaptation to gratings. *Science* **182**, 1036–1038.

MAFFEI, L., BERNARDI, N. & BISTI, S. (1986). Interocular transfer of adaptation after effect in neurons of area 17 and 18 of split chiasm cats. *Journal of Neurophysiology* **55**, 966–976.

MARLIN, S.G., HASAN, S.J. & CYNADER, M. (1988). Direction-selective adaptation in simple and complex cells in cat striate cortex. *Journal of Neurophysiology* **59**, 1314–1330.

MARLIN, S.G., DOUGLAS, R.M. & CYNADER, M.S. (1991). Position-specific adaptation in simple cell receptive fields of the cat striate cortex. *Journal of Neurophysiology* **66**, 1769–1784.

MARLIN, S.G., DOUGLAS, R.M. & CYNADER, M.S. (1993). Position-specific adaptation in complex cell receptive fields of the cat striate cortex. *Journal of Neurophysiology* **69**, 2209–2221.

MCLEAN, J. & PALMER, L.A. (1992). Contrast adaptation and excitatory amino acid (EAA) receptors in striate cortex. *Investigative Ophthalmology and Visual Science* (Suppl.) **33**, 1021.

MCLEAN, J., RAAB, S. & PALMER, L.A. (1994). Contribution of linear mechanisms to the specification of local motion by simple cells in areas 17 and 18 of the cat. *Visual Neuroscience* **11**, 271–294.

MOVSHON, J.A., THOMPSON, I.D. & TOLHURST, D.J. (1978). Spatial summation in the receptive fields of simple cells in the cat's striate cortex. *Journal of Physiology* **283**, 53–77.

MOVSHON, J.A. & LENNIE, P. (1979). Pattern-selective adaptation in visual cortical neurones. *Nature* **278**, 850–852.

OHZAWA, I., SCLAR, G. & FREEMAN, R.D. (1985). Contrast gain control in the cat's visual system. *Journal of Neurophysiology* **54**, 651–667.

PALMER, L.A. & DAVIS, T.L. (1981). Receptive-field structure in cat striate cortex. *Journal of Neurophysiology* **46**, 260–276.

PETTET, M.W. & GILBERT, C.D. (1992). Dynamic changes in receptive-field size in cat primary visual cortex. *Proceedings of the National Academy of Sciences of the U.S.A.* **89**, 8366–8370.

REID, R.C., VICTOR, J.D. & SHAPLEY, R.M. (1992). Broad-band temporal stimuli decrease the integration time of neurons in cat striate cortex. *Visual Neuroscience* **9**, 39–45.

SAUL, A.B. & DANIELS, J.D. (1986). Modeling and simulation II: Specificity models for visual cortex development. *Journal of Electrophysiological Techniques* **13**, 211–231.

SAUL, A.B. & CYNADER, M.S. (1989*a*). Adaptation in single units in visual cortex: The tuning of aftereffects in the spatial domain. *Visual Neuroscience* **2**, 593–607.

SAUL, A.B. & CYNADER, M.S. (1989*b*). Adaptation in single units in visual cortex: The tuning of aftereffects in the temporal domain. *Visual Neuroscience* **2**, 609–620.

SAUL, A.B. & HUMPHREY, A.L. (1990). Spatial and temporal response properties of lagged and nonlagged cells in cat lateral geniculate nucleus. *Journal of Neurophysiology* **64**, 206–224.

SAUL, A.B. & HUMPHREY, A.L. (1992*a*). Temporal-frequency tuning of direction selectivity in cat visual cortex. *Visual Neuroscience* **8**, 365–372.

SAUL, A.B. & HUMPHREY, A.L. (1992*b*). Evidence of input from lagged cells in the lateral geniculate nucleus to simple cells in cortical area 17 of the cat. *Journal of Neurophysiology* **68**, 1190–1208.

SAUL, A.B. (1993). Adapting retards response timing in single neurons of cat visual cortex. *Society for Neuroscience Abstracts* **19**, 1575.

SHAPLEY, R.M. & VICTOR, J.D. (1981). How the contrast gain control modifies the frequency response of cat retinal ganglion cells. *Journal of Physiology* **318**, 161–179.

TOLHURST, D.J. & DEAN, A.F. (1987). Spatial summation by simple cells in the striate cortex of the cat. *Experimental Brain Research* **66**, 607–620.

TOLHURST, D.J. & DEAN, A.F. (1990). The effects of contrast on the linearity of spatial summation of simple cells in the cat's striate cortex. *Experimental Brain Research* **79**, 582–588.

VAUTIN, R.G. & BERKLEY, M.A. (1977). Responses of single cells in cat visual cortex to prolonged stimulus movement: Neural correlates of visual aftereffects. *Journal of Neurophysiology* **40**, 1051–1065.

VICTOR, J.D. (1987). The dynamics of the cat retinal X-cell centre. *Journal of Physiology* **386**, 219–246.

VICTOR, J.D. (1988). The dynamics of the cat retinal Y-cell subunit. *Journal of Physiology* **405**, 289–320.

VIDYASAGAR, T.R. (1990). Pattern adaptation in cat visual cortex is a co-operative phenomenon. *Neuroscience* **36**, 175–179.

VON DER HEYDT, R., HANNY, P. & ADORJANI, C. (1978). Movement aftereffects in the visual cortex. *Archives of Italian Biology* **116**, 248–254.

WILSON, H.R. (1975). A synaptic model for spatial-frequency adaptation. *Journal of Theoretical Biology* **50**, 327–352.

WILSON, H.R. & HUMANSKI, R. (1993). Spatial-frequency adaptation and contrast gain control. *Vision Research* **33**, 1133–1149.