Complex Cells Increase Their Phase Sensitivity at Low Contrasts and Following Adaptation

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Crowder NA, van Kleef J, Dreher B, Ibbotson MR. Complex cells increase their phase sensitivity at low contrasts and following adaptation. J Neurophysiol 98: 1155–1166, 2007. First published May 30, 2007; doi:10.1152/jn.00433.2007. One of the best-known dichotomies in neuroscience is the division of neurons in the mammalian primary visual cortex into simple and complex cells. Simple cells have receptive fields with separate ON and OFF subregions and give phase-sensitive responses to moving gratings, whereas complex cells have uniform receptive fields and are phase invariant. The phase sensitivity of a cell is calculated as the ratio of the first Fourier coefficient ($F_1$) to the mean time-average ($F_0$) of the response to moving sinusoidal gratings at 100% contrast. Cells are then classified as simple ($F_1/F_0 > 1$) or complex ($F_1/F_0 < 1$). We manipulated cell responses by changing the stimulus contrast or through adaptation. The $F_1/F_0$ ratios of cells defined as complex at 100% contrast increased at low contrasts and following adaptation. Conversely, the $F_1/F_0$ ratios remained constant for cells defined as simple at 100% contrast. The latter cell type was primarily located in thalamorecipient layers 4 and 6. Many cells initially classified as complex exhibit simple and complex. Subsequently, these cell types have been described in the cortices of many mammalian species (e.g., eutherians: Van Hooser et al. 2005; marsupials: Ibbotson and Mark 2003; Rocha-Miranda et al. 1976). Simple cells have separate ON and OFF subregions in their receptive fields, whereas complex cells have uniform receptive fields where ON and OFF stimuli generate excitatory responses regardless of where in the receptive field they are presented. These two cell types provide the main feedforward input to all subsequent layers of cortical visual processing outside the primary visual cortex, so it is important to understand the mechanisms that generate their spiking responses.

It is common practice to distinguish between simple and complex cells quantitatively by analyzing the spiking responses to moving sinusoidal gratings (cat: Movshon et al. 1978a,b; cat and monkey: Skottun et al. 1991; ferret: Baker et al. 1998; rat: Girmak et al. 1999; wallely: Ibbotson et al. 2005). When a grating of preferred spatial and temporal frequency is moved across the receptive field of a cell in the primary visual cortex there is a component of the response that is phase sensitive (i.e., the spike rate oscillates at the temporal frequency of the grating) and a component that is phase invariant. The $F_1/F_0$ ratio is then calculated by dividing the first Fourier coefficient of the response ($F_1$) by the mean time-averaged response ($F_0$). The response of a linearly summing simple cell should oscillate sinusoidally about the mean spontaneous activity of the cell. However, because most simple cells have little or no spontaneous activity the response appears as a half-wave–rectified sinusoid, thus producing $F_1/F_0$ ratios > 1 (Fig. 1A). If a simple cell behaves as a linear spatiotemporal filter followed by half-wave rectification the $F_1/F_0$ ratio would be 1.57 (Tolhurst and Dean 1990). For complex cells, the phase-invariant component of the spiking response dominates such that $F_1/F_0$ ratios are < 1 (Fig. 1B). The choice of an $F_1/F_0$ ratio of one as the dividing line between simple and complex cells is based on large data sets ($n > 1,500$) (Skottun et al. 1991). Cluster analysis has also confirmed that the dividing line between simple and complex cell populations is close to one (Ibbotson et al. 2005). Importantly, classification based on this analysis agrees well with classification based on the spatial distribution of ON and OFF subregions within cells’ receptive fields (Bardy et al. 2006; Dean and Tolhurst 1983; Mata and Ringach 2005; Priebe et al. 2004). The analysis of extracellular responses has provided evidence for the separation of cell types into simple and complex groups, but what is the mechanism that generates their differing spiking patterns? Intracellular recordings have shown that in response to moving sinusoidal gratings the membrane potentials of both simple and complex cells exhibit an oscillating response component ($V_1$) and a phase-invariant voltage depolarization ($V_0$) (Priebe et al. 2004). The phase-invariant depolarization and the amplitude of the oscillatory component both increase with increasing contrast. Furthermore, in complex cells the depolarization associated with the phase-invariant response component has a higher contrast gain than the voltage modulation (Anderson et al. 2000; Carandini and Ferster 1997, 2000). Contrast adaptation generates a phase-invariant hyperpolarization accompanied by a smaller reduction in the amplitude of the voltage modulation at the stimulus frequency (Carandini and Ferster 1997, 2000; Sanchez-Vives et al. 2000). However, neither stimulus contrast nor adaptation appears to affect the absolute spike threshold (Anderson et al. 2000; Carandini and Ferster 2000). Mecher and Ringach (2002) demonstrated that even if the $V_1/V_0$ ratio is unimodal, the $F_1/F_0$ ratio of one as the dividing line between simple and complex cells is based on large data sets ($n > 1,500$) (Skottun et al. 1991).
produces a highly phase sensitive spiking response with an $F_i/F_o$ ratio that is well above the spiking threshold ($V_m$, left column) for a simple cell (A) and complex cell (B) responding to a preferred stimulus. In these examples, the transformation is produced by a threshold-linear model (middle column), such that action potentials are fired only when the membrane potential exceeds the cell’s threshold potential. Note that the left column shows only the coarse membrane potential and no action potentials have been drawn in. For the simple cell, preferred stimulation produces a depolarization of the membrane potential with an oscillatory component centered on the cell’s spiking threshold ($V_{sp}$; A, left column), which produces a highly phase sensitive spiking response with an $F_i/F_o$ ratio [calculated by dividing the first Fourier coefficient of the response ($F_i$) by the mean time-averaged response ($F_o$)] of 1.57 (A, right column). For the complex cell, preferred stimulation produces a depolarization with a phase-locked component that rides on top of a nonoscillatory component that is well above the spiking threshold ($B$, top row). This membrane potential produces a spiking response with large oscillatory and nonoscillatory components and an $F_i/F_o$ ratio of 0.36. If the nonoscillatory component of the membrane potential decreases ($B$, gray arrow), as might occur after contrast adaptation, the membrane potential is brought closer to the spike threshold, which produces an increase in the $F_i/F_o$ ratio of the spiking response.

ratio can be bimodal because of the highly nonlinear relationship between the membrane potential and spiking output. Pribe et al. (2004) tested this hypothesis by comparing $V_i/V_0$ and $F_i/F_o$ ratios from intracellular recordings in cat cortex. They confirmed that the $V_i/V_0$ ratio was unimodal, whereas the $F_i/F_o$ ratio was bimodal. The differences between the intracellular and spiking distributions could be fully explained by the nonlinear relationship between membrane potential and firing rate.

In the present paper we test some predictions of the spike-threshold hypothesis by measuring the $F_i/F_o$ ratios of cells in the cat primary visual cortex during two experimental manipulations. First, we altered the contrast of the grating stimulus and, second, we adapted the cells using prolonged high-contrast motion stimulation. Considering both previously published intracellular recording data and the spike threshold hypothesis we predict that decreasing stimulus contrast or adapting to high contrast will act to pull the membrane potential down toward the spiking threshold (Fig. 1B, bottom row). Due to the nonlinear effect of the spike threshold, both stimulus manipulations are expected to generate an increase in the $F_i/F_o$ ratio of the spiking responses of complex cells. A far smaller effect would be expected in simple cells because the intracellular membrane potential is in a compressive range where changes in the effective spike threshold should have minimal effects (Mechler and Ringach 2002). Tolhurst and Dean (1990) measured $F_i/F_o$ ratios for five simple cells in area 17 of the cat that were stimulated by moving gratings of different contrasts and reported that $F_i/F_o$ ratios changed very little with contrast, although they did not present any complex cell data. We recorded from 205 neurons located in areas 17 and 18 of cat primary visual cortex and show that cells defined as complex at 100% contrast became more phase sensitive as contrast declined, but the phase sensitivity of cells defined as simple at 100% contrast remained unchanged across contrasts. Furthermore, based on the preceding definitions, complex but not simple cells became more phase sensitive following contrast adaptation.

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Anesthesia and surgical procedures

Nine cats of both sexes were prepared as described previously (Crowder et al. 2006; Price et al. 2006). Briefly, single-unit recordings were made from areas 17 and 18 in anesthetized and paralyzed cats. Initially, the trachea and right cephalic vein were cannulated under ketamine HCl (20 mg/kg, intramuscularly) anesthesia. Further surgery was performed with high halothane doses (1–2%). Anesthesia during unit recordings was provided by inhaled halothane (0.5%) and a 2:1 ratio of N2O and O2. The level of anesthesia was monitored by recording electrocardiograms and electroencephalograms. All methods regarding the animal preparation were approved by the animal ethics committee of the Australian National University.

Extracellular recordings and visual stimuli

Extracellular recordings were made with lacquer-coated tungsten microelectrodes (FHC, Bowdoinham, ME) driven by a piezoelectric drive (Burleigh inchworm and 6000 controller, Burleigh Instruments, Victor, NY). Extracellular signals from individual units were isolated, amplified, and filtered, then acquired with a CED1401 interface and Spike2 software sampled at 40 kHz (Cambridge Electronic Designs, Cambridge, UK).

After the dominant eye and receptive field location of each neuron had been determined, the nondominant eye was covered and testing was performed with visual stimuli produced by a VSG Series 2/5 stimulus generator (Cambridge Research Systems, Cambridge, UK) and presented on a calibrated monitor (Eizo T662-T, 100-Hz refresh, 1,024 × 768 pixels) at a viewing distance of 57 cm. Sinewave gratings were presented in a circular aperture surrounded by a gray background of mean luminance (Lum; 50 cd/m2). Sinewave Contrast is defined as: Michelson Contrast = $[(\text{Lum}_{\text{max}} - \text{Lum}_{\text{min}})/(\text{Lum}_{\text{max}} + \text{Lum}_{\text{min}})] \times 100$ where $\text{Lum}_{\text{max}}$ and $\text{Lum}_{\text{min}}$ are the maximum and minimum luminance of the grating. For all cells, the location and size of the classical receptive field (RF), as well as the preferred orientation/direction, spatial frequency (SF), and temporal frequency (TF) were determined by calculating on-line tuning functions using 100% contrast gratings. Off-line, SF and TF tuning curves were fit using a least-squares algorithm to a skewed-Gaussian function

$$R_s = A \exp \left\{ - \left( \frac{\log (x/s_0)}{B + C \log (x/s_0)} \right)^2 \right\} + R_{\text{spont}}$$
where $R_c$ is the response at TF or SF; $A$ controls the amplitude; $x_{\text{pref}}$ is the cell’s preferred TF or SF, at which the peak spiking rate $A$ occurs; $B$ is the bandwidth; $C$ controls the skew of the curve; and $R_{\text{spont}}$ is the spontaneous activity.

Receptive field size was determined in two ways: 1) a circular patch of moving grating centered on the middle of the RF was expanded in size to find the diameter that produced the largest response and 2) an annulus of moving grating was centered on the RF and the diameter of the empty center was decreased until spiking responses could just be elicited, thus indicating the edge of the excitatory RF. The first measure found the diameter at which the response saturated, whereas the second method found the outer boundary of the excitatory RF. Both measures usually agreed but, when they differed, the result from method 2 was used to set the stimulus size.

The experimental stimuli were sine-wave gratings of optimal orientation, SF, and TF presented in a circular aperture the size of the classical receptive field. Nonadapted contrast response functions were collected by presenting each contrast (4, 8, 12, 16, 24, 32, 48, 64, 82, 100%) in random order for 1- or 0.5-s tests (10 repetitions) interleaved with 4 s of mean luminance. A 3-min recovery period was allowed between collecting the data for every contrast response function. For adapted contrast response functions, an adapting stimulus was presented for 60 s followed by 0.5-s tests (aforementioned contrast levels for 10 repetitions) interleaved with 4-s-adaptation top-ups. The default contrast for the adapting stimulus was 32%, but lower (16%) or higher (100%) contrasts were used if the contrast response function produced after 32% adaptation was very compressed or changed very little, respectively.

Data analysis

$F_t/F_o$ ratios were calculated from the responses produced by the moving sine-wave grating during the 1- or 0.5-s test interval. $F_o$ values were calculated as the mean firing rate (averaged across repeats and time) above spontaneous and $F_t$ values were the first Fourier coefficient of the mean response (averaged across repeats) obtained using the FFT function in MATLAB. Due to the short test window, our analysis included only cells with optimum temporal frequencies of $\pm 2$ Hz. We were concerned that this short sampling time may have placed too much emphasis on the onset transient. Therefore we examined TF tuning curves that always used 1-s sampling windows and found that $F_t/F_o$ ratios that were calculated with a start time 100 ms after stimulus onset to exclude the onset transient were strongly correlated with $F_t/F_o$ ratios that were calculated with a start time at the stimulus onset ($r^2 = 0.85$). Based on this correlation, it is clear that including the onset transient did not systematically alter the $F_t/F_o$ ratios. Therefore to include cells with optimum TFs as low as 2 Hz in our contrast adaptation analysis, while still calculating Fourier transforms based on at least one full cycle, we chose to calculate $F_t/F_o$ ratios with the start time at the stimulus onset. For 98% of our data the presentation time was an integer multiple of the stimulus period. For the remaining 2% of cells, $F_t/F_o$ analysis was performed on a section of the recorded response that was an integer multiple of the stimulus period.

We used two independent criteria to ensure the accuracy of the $F_t/F_o$ analysis at low contrasts. The first criterion addressed whether mean stimulus-evoked spike rates statistically exceeded the spontaneous firing rate. First, spontaneous firing rates were calculated from the response to the 4 s of mean luminance interleaved between tests in the nonadapted contrast stimulus. A Poisson distribution was then calculated from this spontaneous spiking. We calculated a response threshold based on the 99% cutoff from the Poisson fit to the spontaneous rate (Fig. 2, A and C, dotted horizontal lines). $F_o$ responses that did not exceed this Poisson threshold for $\pm 20$ ms were not included in the main $F_t/F_o$ analysis (Figs. 3–7).

A second independent criterion was used to evaluate the significance of the $F_t/F_o$ ratio at lower spike counts. Each experimentally measured value of $F_t/F_o$ was compared with the distribution of $F_t/F_o$ values produced by assigning a number of spikes randomly with uniform probability across the response interval. The number of spikes was equal to the average number of spikes across experimental repeats and the $F_t/F_o$ ratios were averaged over a number of repetitions equal to the number of experimental repeats. By repeating this simulation 20,000 times we produced probability distributions of $F_t/F_o$ comparable to each experimental data point. Measured $F_t/F_o$ values that lay outside the middle 95% of their associated randomly generated distribution were considered significant. Responses to all stimuli, including evoked spike rates that did not exceed the Poisson threshold described earlier, were included in this analysis, although cells with negative $F_t/F_o$ or with an average spike count <1 were excluded.
Control experiments

Previous research has shown that the RF size and SF tuning of macaque V1 neurons can change with contrast (Sceniak et al. 1999, 2002). In our main experiment the aperture size of the stimulus was fixed across contrasts. Therefore we also wanted to determine how $F_1/F_0$ ratios change with contrast when the stimulus size as well as SF and TF of the test grating were optimized at each contrast. For a subgroup of cells, RF size and both SF and TF tuning were tested at 8, 16, and 100% contrasts. For each cell, $F_1/F_0$ ratios were then calculated from responses to two tests. The first test presented gratings in a circular aperture at 8, 16, and 100% contrasts with grating parameters (aperture size, SF, and TF) obtained using 100% contrast gratings. This stimulus had parameters identical to those of the normal experimental procedure. The second test again presented gratings in a circular aperture at 8, 16, and 100% contrasts with grating parameters (aperture size, SF, and TF) obtained using 100% contrast gratings.

![FIG. 3. Relationship between contrast and phase sensitivity, and the influence of contrast adaptation. A: relationship between contrast (abscissa) and $F_1/F_0$ ratio (ordinate) across the population for simple (triangles) and complex (circles) cells. Nonadapted $F_1/F_0$ ratios are shown as solid symbols, and $F_1/F_0$ ratios calculated following contrast adaptation are shown as empty symbols. Error bars denote SE. It is clear that the $F_1/F_0$ ratios of complex cells decrease with increasing contrast, whereas the $F_1/F_0$ ratios of simple cells are not influenced by contrast. Furthermore, contrast adaptation causes $F_1/F_0$ ratios to increase across all contrasts for complex cells but not simple cells. B: averaged normalized values of $F_1$ (empty squares) and $F_0$ (filled squares) plotted separately against contrast (abscissa) for nonadapted complex cells. C–E: plots of $F_1$ and $F_0$ values separately for nonadapted simple cells (C), adapted complex cells (D), and adapted simple cells (E). For B–E, SE error bars were almost all fully occluded by plotted symbols.](image).

![FIG. 4. Effect of stimulus contrast on $F_1/F_0$ ratios of neurons in primary visual cortex. Each scatterplot graphs $F_1/F_0$ ratios obtained at 100% contrast (abscissa) against $F_1/F_0$ ratios obtained at some lower contrast (ordinate). Simple and complex cells (classification based on the responses to 100% gratings) are shown as black triangles and gray circles, respectively. For each scatterplot, solid lines indicate the border between simple and complex cells, and the dotted line indicates equality.](image)
adaptation combined produce far higher proportions of simple cells. More simple cells are evident at lower contrasts and that low contrasts and of 1, which is the border between simple and complex responses. Note that calculated under 3 conditions: unadapted, 100% test contrast (D), unadapted, 32% test contrast (E) and cells are adapted to 32% contrast and stimulus contrast was 32% (F). Solid and empty arrows indicate the population means of complex and simple cells, respectively. Dotted lines indicate an F1/F0 ratio of 1, which is the border between simple and complex responses. Note that more simple cells are evident at lower contrasts and that low contrasts and adaptation combined produce far higher proportions of simple cells.

circular aperture at 8, 16, and 100% contrasts, but used the optimal grating parameters for each contrast. In a separate control experiment the grating’s contrast, SF, and TF were kept constant, but the stimulus size was varied in three steps between the largest and smallest RF sizes obtained for each cell. This experiment was repeated using 4, 8, and 16% contrasts. Each stimulus in these control experiments was presented for 32 repetitions.

Histology

At the end of recording sessions electrolytic lesions were placed (40 μA, 10 s, electrode positive) 2, 4, and 6 mm below the brain surface at a location displaced 3 mm medially from the recording site. This procedure generated clear lesions that could be correlated for depth with the recording tracks, which were clearly visible in all preparations. Small physical lesions were produced at the bottom of each track using the method of Crowder et al. (2006) to allow accurate localization of the deepest cell location. Lesions were not made at every recording site because this was found to greatly reduce the recording quality of the electrode. Animals were given a lethal dose of pentobarbitone sodium (100 mg/kg) and immediately perfused transcardially with saline (0.9%) followed by 10% formal saline. Brains were extracted and processed in the standard fashion (Crowder et al. 2006). Sectioned tissue was examined using light microscopy to confirm the locations of electrode tracks. Drawings of the sectioned brains were made and orientations of the electrode penetrations reconstructed (taking careful note of the deepest recording site). Cell locations were then determined by working backward from the deepest point toward the shallowest recording using shrinkage-adjusted measurements based on the recording depths noted on the piezoelectric drive. The borders of the cortical layers were identified by visual inspection. Lamination data are presented in Fig. 9. Each cell location was first converted to a percentage of the total thickness of the lamina in which it resides. This made the cells comparable from the same layer but different cats and thus different layer thicknesses. Layers were then plotted as a fraction of the total cortical thickness, also called the normalized cortical depth (see Hawken et al. 1988; Ringach et al. 2002).

FIG. 6. Phase sensitivity of complex cells is dependent on stimulus contrast and adaptation. A–C: population histograms for the same group of cells (n = 77) when F1/F0 ratios were calculated under 3 conditions: cells were unadapted and the test contrast was 100% (A); cells were unadapted and the test contrast was 12% (B); and cells were adapted to 32% contrast and the test contrast was 12% (C). D–F: population histograms for 126 cells when F1/F0 ratios were calculated under 3 conditions: unadapted, 100% test contrast (D); unadapted, 32% test contrast (E); and cells are adapted to 32% contrast and stimulus contrast was 32% (F). Solid and empty arrows indicate the population means of complex and simple cells, respectively. Dotted lines indicate an F1/F0 ratio of 1, which is the border between simple and complex responses. Note that more simple cells are evident at lower contrasts and that low contrasts and adaptation combined produce far higher proportions of simple cells.

FIG. 7. Control experiments testing phase sensitivity of complex cells. A: comparison of F1/F0 ratios obtained from 100% contrast gratings (abscissa) with F1/F0 ratios obtained from 8% (empty circles) or 16% (filled circles) gratings (ordinate) when the stimulus size, spatial frequency (SF), and temporal frequency (TF) of each stimulus grating were set to the preferences obtained using 100% gratings. Dotted line indicates equality. B: another comparison F1/F0 ratios obtained from 100% contrast gratings (abscissa) with F1/F0 ratios obtained from 8 or 16% gratings (ordinate; symbols as in A), but now the stimulus size, SF, and TF for each grating were set to the optimal obtained for that contrast. C: comparison of F1/F0 ratios obtained using a stimulus size corresponding to the largest measured receptive field size (abscissa) with F1/F0 ratios obtained using a stimulus size corresponding to the smallest measured receptive field size (empty symbols; ordinate) and an intermediate stimulus size (filled symbols). Typically, the largest receptive field sizes were obtained with low-contrast gratings (see RESULTS). Circles, squares, and triangles represent grating contrasts of 4, 8, and 16%, respectively. Stars represent centroid measures for the pooled medium (filled star) and small size (empty star) distributions. Dotted line indicates equality.
RESULTS

We recorded from 205 single units in areas 17 (n = 122) and 18 (n = 83) of cat primary visual cortex that were stimulated with sine-wave gratings inside circular apertures the size of each cell’s classical receptive field (see METHODS). Optimally oriented gratings were moved in the direction that generated the strongest response. Our electrode penetrations were tangential to the cortical surface and histological analysis revealed that all cortical layers were represented in our sample.

Simple-cell responses depend on the spatial phase (or location) of the stimulus, whereas complex cell responses are spatial-phase invariant (Movshon et al. 1978a,b). Here we classify simple and complex cells based on the ratio between the first Fourier coefficient (F_1) and mean spiking responses (F_0) to moving sine-wave gratings (Skottun et al. 1991). F_1/F_0 ratios >1 or <1 indicate simple or complex cells, respectively. We classified a cell as simple or complex based on its response to 100% contrast gratings.

F_1/F_0 ratio and stimulus contrast

Spike density functions plotting the responses of a typical simple cell to stimulation at four contrasts are shown in Fig. 2A. At all tested contrasts the cell shows highly oscillatory responses with bursts of spikes that coincide in time with the fundamental temporal frequency of the stimulus. Figure 2B shows that there is no consistent change in the F_1/F_0 ratio between contrasts, suggesting that contrast has no influence on this cell’s classification. The response of a complex cell to four contrasts is shown in Fig. 2C. This cell also shows oscillatory responses at the F_1 frequency, but at high contrasts they are small relative to the mean response (F_0). Note that as contrast decreases, the amplitude of the oscillations remains quite steady, although the relative amplitude of the F_0 component decreases. Consequently, the F_1/F_0 ratio increases with decreasing contrast, such that this particular cell had an F_1/F_0 ratio of 0.05 at maximum contrast but a ratio of 0.76 when the contrast was 8% (Fig. 2, C and D).

In this section, we assessed the responses of 22 simple and 159 complex cells using sine-wave gratings of different contrasts. The mean F_1/F_0 ratios across simple cells are shown by the solid triangles in Fig. 3A. Changes in contrast did not significantly alter the mean F_1/F_0 ratios of the simple cell population (two-way ANOVA, P > 0.92). On the contrary, the complex cell population showed a clear trend toward increased F_1/F_0 ratios at lower stimulus contrasts (Fig. 3A, solid circles). For complex cells, there was a significant relationship between contrast and F_1/F_0 ratio (two-way ANOVA, P < 0.001). F_1 and F_0 values were also examined separately for both complex and simple cells, as shown in Fig. 3, B and C, respectively. For complex cells, the average normalized F_0 values (Fig. 3B, solid squares) increased with increasing contrast in a sigmoid-like fashion, typically observed in studies of contrast adaptation (e.g., Crowder et al. 2006; Ohzawa et al. 1982, 1985). The F_1 values (open squares) for the complex cell population showed fairly small changes in amplitude with increasing contrast. The large increases in F_0 amplitude seen in complex cells, accompanied by relatively small increases in F_1 amplitude, are consistent with decreasing F_1/F_0 ratios with increasing contrast. For the simple cell population, both F_1 and F_0 values increased proportionally with increasing contrast (Fig. 3C), which is consistent with the relatively steady F_1/F_0 ratios across contrasts.

Scatterplots showing changes in the F_1/F_0 ratios of individual cells are shown in Fig. 4. This population data were used to generate the plots in Fig. 3. For complex cells, there is a clear trend toward higher F_1/F_0 ratios at lower contrasts (population migrates above the line of equality as contrast declines). The increase in F_1/F_0 ratios for the complex cell population compared with values at 100% contrast was significant for all test contrasts ≤32% (paired t-test, P < 0.01), with the remaining points being insignificant (paired t-test; 48%, P > 0.3, 64%, P > 0.21, and 82%, P > 0.87). The changes in the F_1/F_0 ratios for the simple cell population were not significant for any test contrasts (paired t-test, P > 0.3). Note that at some test contrasts a few cells that had been classified as simple at 100% contrast had an F_1/F_0 ratio <1. For all but one of these points, the reduced ratio did not fall outside the SE error bars of the other nine contrasts tested and therefore was not a significant trend.

F_1/F_0 ratio and contrast adaptation

Prolonged exposure to moving gratings generates contrast adaptation in the great majority of neurons in the primary visual cortex (Crowder et al. 2006; Ohzawa et al. 1982, 1985). This is manifest as a reduction in firing rate to most test contrasts, particularly those at low values. Perceptually, the impact of adaptation is to reduce the apparent contrast of the stimulus (Blakemore et al. 1973; Hammett et al. 1994). Given that our previous data showed that low contrasts lead to higher F_1/F_0 ratios, we examined whether contrast adaptation could increase F_1/F_0 ratios. That is, does contrast adaptation increase the phase sensitivity of cells in a similar way as lowering stimulus contrast?

Adapted contrast response functions were obtained using a top-up contrast adaptation protocol (see METHODS). The F_1/F_0 ratios of simple and complex cells following contrast adaptation are shown, respectively, as open triangles and circles in Fig. 3A. When in the adapted state, simple cells did not significantly change their F_1/F_0 ratios for any test contrast (Fig. 3A; two-way ANOVA, P > 0.22). However, complex cells showed significant decreases in their F_1/F_0 ratios following adaptation for most test contrasts (Fig. 3A; two-way ANOVA, P < 0.001). Note that for the lowest test contrast (4%) there is no increase in F_1/F_0 ratio after adaptation, suggesting a saturation effect.

F_1 and F_0 values after adaptation were plotted separately for complex and simple cells classified at 100% contrast (Fig. 3, D and E, respectively). For complex cells, both F_1 and F_0 values undergo response gain control (compression) and contrast gain control (rightward shift of the contrast response function) after contrast adaptation (Fig. 3D). Similar to the nonadapted condition, F_0 values show larger changes with contrast than F_1 values. F_1 and F_0 values are more similar in the adapted state than in the unadapted state, which matches the observed upward shift in the F_1/F_0 ratios after adaptation (Fig. 3A). For the simple cell population, both F_1 and F_0 values also undergo changes in response gain and contrast gain following contrast adaptation (Fig. 3E). However, as in the nonadapted condition F_1 and F_0 values
decreased proportionately, thereby producing no change in $F_1/F_0$ ratios following contrast adaptation.

Data from areas 17 and 18 were pooled because neurons in both brain areas show similar changes in $F_1/F_0$ ratios with changing contrast and adaptation. A four-way ANOVA using brain area, simple or complex classification at 100% contrast, contrast, and adaptation as variables revealed that neither the effect of contrast ($P > 0.99$) nor that of adaptation ($P > 0.54$) on $F_1/F_0$ ratio was statistically different between areas 17 and 18. The only significant difference between brain areas was that complex cells in area 17 had slightly higher $F_1/F_0$ ratios than those in area 18 ($P < 0.03$).

In the preceding results, simple and complex cells were classified by their $F_1/F_0$ ratios to 100% contrast. However, it is evident that the population distribution of simple and complex cells can change dramatically depending on the conditions under which the $F_1/F_0$ ratio is calculated. Figure 5A shows histograms of cell count against the $F_1/F_0$ ratio obtained using 100% contrast gratings for the 255 cells in our sample. Twenty-two cells (11%) had $F_1/F_0$ ratios > 1. Of these cells, 91 also gave significant responses at 8% contrast and these are highlighted in Fig. 5A as gray histograms. It is evident that most cells in this subgroup were classified as complex when stimulated at 100% contrast (i.e., 81 of 91). When tested at 8% contrast, 27 of the 91 cells (30%) had $F_1/F_0$ ratios > 1 (Fig. 5B). It is clear that stimulus contrast has a significant influence on the $F_1/F_0$ ratios of cells. How does adaptation influence the population data? In Fig. 6, A–C we plot histograms of cell count against $F_1/F_0$ ratio for 77 neurons from which $F_1/F_0$ ratios were calculated under three conditions: unadapted with a 100% test contrast stimulus (Fig. 6A), unadapted using a 12% test contrast stimulus (Fig. 6B), and using a test contrast of 12% after adaptation to 32% contrast (Fig. 6C). At 100% test contrast there is a clear oversampling of complex cells, but eight (10%) simple cells are evident at $F_1/F_0$ ratios > 1. When the $F_1/F_0$ ratios were calculated from responses collected with a 12% test contrast the overall distribution shifts toward higher ratios and the number of cells with $F_1/F_0$ ratios > 1 increases to 13 (17%; Fig. 6B). Finally, when the $F_1/F_0$ ratio is calculated at the same low test contrast but with neurons in an adapted state, we see a large shift toward $F_1/F_0$ ratios > 1 (34 cells, 44%). Thus when tested at relatively low contrast and in an adapted state, 26 neurons previously categorized as complex cells now have $F_1/F_0$ ratios > 1. A similar, albeit weaker, trend was evident when a 32% test contrast was used (Fig. 6, D–F, n = 126). The population shift toward more cells with $F_1/F_0$ ratios > 1 with lower contrast and with adaptation to 32% contrast is evident, even though the effect at 32% contrast is smaller than that with a 12% test contrast (compare Figs. 3 and 6).

Influence of stimulus parameters

Sceniak et al. (1999) demonstrated that the extent of spatial summation in macaque V1 neurons shrinks at high contrasts. Furthermore, although the preferred SF does not change with contrast, SF tuning bandwidth is narrower at low contrasts (Sceniak et al. 2002). In our main experiment the stimulus aperture size was fixed across contrasts. Therefore it was reasonable to ask whether $F_1/F_0$ ratios would still increase with decreasing contrasts if parameters for each test grating (aperture size, SF, TF) were optimized for that contrast.

We analyzed data from 24 area 17 neurons whose RF size, SF tuning, and TF tuning were tested at 8, 16, and 100% contrast. Consistent with the findings of Sceniak et al. (1999, 2002), the size of the classical receptive fields decreased with increasing contrast ($P < 0.021$, one-way ANOVA), and the preferred SF ($\lambda_{\text{pref}}$, see METHODS) did not vary with contrast ($P > 0.49$, one-way ANOVA). Figure 7A plots $F_1/F_0$ ratios generated by testing with 8% (filled circles) and 16% (open circles) contrast as a function of $F_1/F_0$ ratios generated using 100% contrast. For this graph, the grating parameters of aperture size, SF, and TF were constant across contrasts and were set by values obtained from 100% contrast test stimuli. Most points (65%) are above the line of equality, indicating that, similar to the main data set, $F_1/F_0$ ratios tend to increase with decreasing contrasts. The data plotted in Fig. 7B were obtained using optimal aperture sizes, SFs, and TFs for each contrast. Again, most points (71%) are above the line of equality, indicating that $F_1/F_0$ ratios tend to increase with decreasing contrasts. A two-way ANOVA was used to look at the effects of contrast and grating parameter optimization on $F_1/F_0$ ratios that had been normalized to the 100% test. This analysis revealed that $F_1/F_0$ ratios increase significantly with decreasing contrasts ($P < 0.022$), the effect of which did not depend on whether grating parameters were optimized for each contrast ($P > 0.26$).

To further examine the effect of stimulus size on $F_1/F_0$ ratio we presented each cell with gratings of constant contrast, SF, and TF, but at three different aperture sizes. Only neurons whose classical receptive field size increased monotonically with decreasing contrast were included in this analysis. Large medium, and small aperture sizes were the RF sizes obtained with 8, 16, and 100% contrasts, respectively. Figure 7C plots $F_1/F_0$ ratios calculated from firing in response to the large aperture size on the abscissa and $F_1/F_0$ ratios calculated from firing in response to the medium (solid symbols) and small (open symbols) aperture sizes on the ordinate. This experiment was repeated using three contrasts (circles: 4%; squares: 8%; triangles: 16%). Stars represent centroids of the distributions for the medium (solid) and small stimulus sizes (open), respectively. A two-way ANOVA using aperture size and contrast as variables revealed that changes in aperture size ($P < 0.93$) did not produce consistent changes in $F_1/F_0$ ratios at any contrast ($P < 0.76$). Also note that at a given contrast the increased aperture size generated increased firing rates. A two-way ANOVA using size and contrast as variables revealed that firing rate increased with both contrast ($P < 0.0003$) and aperture size ($P < 0.01$). Therefore for a particular contrast the $F_1/F_0$ ratio was stable, even if the firing rate was adjusted by changing stimulus size.

Spike count analysis

Figure 8 summarizes the results of the second independent analysis, which compared measured $F_1/F_0$ ratios with those produced by chance alone (see METHODS). Figure 8, A and B shows the spike count plotted against complex cell $F_1/F_0$ ratios.
when the stimulus gratings had contrasts of 4 and 100%, respectively. As expected, across the population, 100% contrast stimulation elicited a greater number of spikes during the stimulus period than did 4% contrast. The shaded area represents the middle 95% of the distribution of $F_1/F_0$ ratios expected from different numbers of randomly timed spikes (see METHODS) outside which $F_1/F_0$ ratios are considered significant. $F_1/F_0$ ratios that fell outside or inside the gray region at 100% are denoted by squares and × symbols, respectively, in both A and B. C: relationship between contrast (abscissa) and adapted complex (empty circles) responses that were termed significant based on the spike count analysis. Error bars denote SE. D: plots of spike count against $F_1/F_0$ ratio for complex cells tested with the control protocol where stimulus size was varied in 3 steps between the largest and smallest receptive field diameters obtained for each cell but contrast was held constant. Cells were stimulated with different contrasts 4% (white), 8% (gray), and 16% (black) contrasts at small (circles), medium (diamonds), and large (squares) stimulus sizes. As in A and B, the gray area represents the central 95% of the probability distributions of $F_1/F_0$ produced by randomly distributed spikes, but is narrower because these tests were performed for 32 repetitions.

FIG. 8. Relationship between spike count and phase sensitivity. A and B: plots of average spike counts during the stimulus period (abscissa) against $F_1/F_0$ ratios (ordinate) obtained at 4 and 100% contrasts, respectively. Shaded gray area represents the central 95% of the probability distributions of $F_1/F_0$ ratios produced by randomly distributed spikes (see METHODS) outside which $F_1/F_0$ ratios are considered significant. $F_1/F_0$ ratios that fell outside or inside the gray region at 100% are denoted by squares and × symbols, respectively, in both A and B. C: relationship between contrast (abscissa) and adapted complex (empty circles) responses that were termed significant based on the spike count analysis. Error bars denote SE. D: plots of spike count against $F_1/F_0$ ratio for complex cells tested with the control protocol where stimulus size was varied in 3 steps between the largest and smallest receptive field diameters obtained for each cell but contrast was held constant. Cells were stimulated with different contrasts 4% (white), 8% (gray), and 16% (black) contrasts at small (circles), medium (diamonds), and large (squares) stimulus sizes. As in A and B, the gray area represents the central 95% of the probability distributions of $F_1/F_0$ produced by randomly distributed spikes, but is narrower because these tests were performed for 32 repetitions.

When the stimulus gratings had contrasts of 4 and 100%, respectively. As expected, across the population, 100% contrast stimulation elicited a greater number of spikes during the stimulus period than did 4% contrast. The shaded area represents the middle 95% of the distribution of $F_1/F_0$ ratios expected from different numbers of randomly timed spikes during the stimulus interval. Interestingly, the mean value of the $F_1/F_0$ ratio is predicted to increase as the spike count decreases, even though the same random process is used to assign spikes. Thus even a random process could produce increased $F_1/F_0$ ratios as contrast (and thus the spike count) is decreased. For a real effect to be present, increases in $F_1/F_0$ at low contrasts must be larger than predicted by our stochastic simulations (we will therefore term these ratios significant). In fact, at 4% contrast 67% of cells had significant $F_1/F_0$ ratios, indicating that for most cells the increase in $F_1/F_0$ at low contrasts could not be accounted for by chance alone. At 100% contrast 54% of the total population of cells had significant $F_1/F_0$ ratios. Most (76%) cells that had significant $F_1/F_0$ ratios at 100% contrast (Fig. 8, A and B, squares) remained outside the shaded region at 4% contrast.

We then reconsidered the effects of our stimulus manipulations if we include only the significant $F_1/F_0$ ratios. Figure 8C plots the average $F_1/F_0$ ratio at different contrasts using only complex cells that were shown to have significant $F_1/F_0$ ratios. As in Fig. 3A, solid circles show average nonadapted $F_1/F_0$ ratios at different contrasts and open circles show average $F_1/F_0$ ratios following contrast adaptation. The shape of this curve is qualitatively similar to the one plotted in Fig. 3A, although it is shifted upward toward higher $F_1/F_0$ ratios. Interpretation of this result must be tempered with common sense. The responses of complex cells to high contrasts (which elicit high spike counts) are expected to be phase invariant and therefore many bona fide complex cells with insignificant $F_1$ components at high contrasts have been removed using the spike count criterion. Because of the restrictive nature of the spike count criterion we believe that it serves as a complement to, rather than a replacement for, the previous analysis.

To further show that low spike counts could not explain the higher $F_1/F_0$ ratios observed at low contrasts we reexamined our control data in which increased spike counts were produced by larger-size stimuli with the same contrast. Figure 8D plots spike count against complex cell $F_1/F_0$ ratios for contrasts of 4% (white), 8% (gray), and 16% (black) with small (circles), medium (diamonds), and large (squares) aperture sizes. Spike count was poorly correlated with $F_1/F_0$ ratio for 4% ($R^2 = 0.010$), 8% ($R^2 = 0.012$), and 16% ($R^2 = 0.15$) contrasts, which demonstrates that $F_1/F_0$ ratios have only slight dependence on spike count for a fixed contrast.

Laminar organization

We have reconstructed the locations of the recording sites for all 205 cells relative to the laminar organization of the cortex. Figure 9 plots the locations of recording sites relative to the normalized cortical depths for each layer, as derived from nine cats (for methodology, see Hawken et al. 1988; Ringach et al. 2002). When using 100% contrast gratings as stimuli 22 cells had $F_1/F_0$ ratios >1 and were therefore classified as simple cells (Fig. 9A). One of the simple cells (5% of the population) was located in layer 2, three in layer 3 (14%), eight in layer 4 (36%), and five each in layers 5 and 6 (23% each). It is also noteworthy that 17 of 21 complex cells with $F_1/F_0$ ratios >0.6 were clustered in or very close to the border of layer 4. Thus cells that are not formally classified as simple, yet have clear phase-sensitive response oscillations, are also primarily located in or very close to layer 4. Most simple cells in our population (59%) were located in layers 4 and 6.

Figure 9, B and C plots the layer distributions of a population of cells (n = 62) whose $F_1/F_0$ ratios were measured at 100% (Fig. 9B) and 4% (Fig. 9C) contrasts, respectively. For stimulation at 100% contrast, seven simple cells (11%) are evident. All of these cells are in layers 3–6 (Fig. 9B). When stimulated with 4% contrast the cell population shows a dramatic shift to higher $F_1/F_0$ ratios. That is, at low contrast 33 cells (53%) have $F_1/F_0$ ratios >1 and they reside in layers 2–6. The percentage of cells with $F_1/F_0$ ratios >1 increases by 400–500% in layers 3–6 when stimulated with a 4% contrast grating relative to a 100% contrast grating.

DISCUSSION

Here we show that cells in the primary visual cortex classified as complex when stimulated with 100% contrast gratings
COMPLEX CELLS BECOME SIMPLE-LIKE

A large fraction of cells classified as complex cells become far more phase sensitive in response to low-contrast stimuli and following contrast adaptation. When using low-contrast stimuli, many of these cells have responses that would suggest classification in the simple cell category based purely on \(F_1/F_0\) ratios. Interestingly, one relatively small group of cells have \(F_1/F_0\) ratios >1 for all tested contrasts. Using accepted definitions (Skottun et al. 1991), these latter neurons are classified as simple cells regardless of the contrast used (Tolhurst and Dean 1990). Our results suggest a strict new definition for cortical cells. To be classified as a simple cell a neuron must have an \(F_1/F_0\) ratio >1 for all stimulus contrasts that generate significant responses, when stimulated at its optimum spatial frequency. Conversely, to be classified as a complex cell a neuron must have an \(F_1/F_0\) ratio <1 at 100% contrast but can have any \(F_1/F_0\) ratio at other contrasts. It will be interesting in the future to cross-reference this strict definition with other accepted classification methods (e.g., Skottun et al. 1991).

The contrast and adaptation effects we observe can be predicted from previous intracellular recording data and the spike threshold model (Anderson et al. 2000; Carandini and Ferster 1997, 2000; Mechler and Ringach 2002; Priebe et al. 2004). Intracellular recordings have shown that the modulation ratio of the membrane potential (\(V_I/V_0\)) is unimodal, but skewed toward low \(V_I/V_0\) ratios (Priebe et al. 2004). Around 40% of cells defined as simple using extracellular \(F_1/F_0\) ratios also have \(V_I/V_0\) ratios >1. Furthermore, another 25% of cells defined as simple using \(F_1/F_0\) ratios have \(V_I/V_0\) ratios >0.6, so 65% of simple cells have highly phase sensitive membrane oscillations (Priebe et al. 2004). Conversely, from the same data set only around 5% of cells defined extracellularly as complex have \(V_I/V_0\) ratios >0.6. Thus there is a strong bias toward complex cells having only small-amplitude membrane oscillations in response to moving gratings. Consequently, the bimodal distribution of spiking modulation ratios (\(F_1/F_0\)) arises from two sources: 1) the degree to which the membrane potential oscillates in response to a moving grating, which can be manipulated by the amount of converging, spatially offset inputs (Chance et al. 1999; Hubel and Wiesel 1962; Tao et al. 2002), and 2) the bimodal distribution can arise from the nonlinear relationship between membrane potential and firing rate produced by the spike threshold (Mechler and Ringach 2002; Priebe et al. 2004). The latter is of particular importance for cells that have very low \(V_I/V_0\) ratios but have \(F_1/F_0\) ratios >1.

Importantly, the \(V_0\) values of complex cells show stronger contrast gain than the \(V_I\) and contrast adaptation preferentially decreases the \(V_0\), whereas the \(V_I\) is barely affected (Carandini and Ferster 1997, 2000; Sanchez-Vives et al. 2000). The spiking data for the complex cell in Fig. 2C (see also Fig. 3B) also indicate that decreasing contrast affects the \(F_0\) much more than the \(F_1\). Thus from both intracellular and extracellular data, it is clear that the nonoscillating component of the response (the \(V_0\), \(F_0\), or DC components) is much more sensitive to changes in contrast and adaptation than the phase-locked oscillating component (the \(V_I\) or \(F_I\)). Other stimulus parameters also change \(V_I/V_0\) and \(F_I/F_0\) ratios, notably the spatial frequency of the gratings (Movshon et al. 1978a,b; Priebe et al. 2004; Skottun et al. 1991). Complex cells have modulated responses at low spatial frequencies because bar widths are similar to the receptive field widths. On the contrary, simple cells can have phase-invariant responses at high spatial frequencies because their on and off zones are covered by many relatively narrow bright and dark bars, thus removing strongly modulated input. Thus it is important to remember that the discussion of the contrast dependence of \(V_I/V_0\) and \(F_I/F_0\) ratios is based strictly on stimulation at the optimum spatial frequency of the stimulated cell, which does not change with contrast (Sceniak et al. 1999, 2002).

The division of neurons in the primary visual cortex into simple and complex types has prompted numerous models to explain the spiking behavior of these two cell classes. In the hierarchical scheme, simple cells receive a restricted range of spatial-phase signals from the dorsal lateral geniculate nucleus (dLGN) and complex cells receive a wider range of spatial-phase information either directly from the dLGN or by simple cells (Hubel and Wiesel 1962). This differing input structure could lead to the phase dependence of simple cell responses and the spatial-phase invariance of complex cells. More recently, recurrent models have been...
proposed where simple and complex cells share the same basic cortical circuit, but have low and high levels of phase-invariant recurrent amplification, respectively (Chance et al. 1999; Tao et al. 2004). However, circuitry is not the primary concern of the present paper because both models have the net effect of pooling signals with different spatial phases. Furthermore, both models must include a transformation from membrane potential to spike rate. Instead, here we show that complex cell classification must be refined because complex $F_1/F_0$ ratios $<1$ are guaranteed only at high contrasts (the contrast-specific phase sensitivity of complex cells has functional implications, which we subsequently discuss). Moreover, it has been shown recently that phase sensitivity of complex cells in cat primary visual cortex is influenced by feedback signals from the postero-temporal visual cortex and by the stimulus encroaching into the suppressive extraclassical receptive field surround (Bardy et al. 2006). Indeed, increasing $F_1/F_0$ ratios are positively correlated with the relative strength of the silent surround suppression of responses to stimulation within the classical excitatory receptive field. Collectively, these recent findings suggest that the classification system for cells in the primary visual cortex must be modernized, as suggested earlier at the beginning of this discussion. Moreover, models of cortical function need to incorporate these new findings.

From our finding that $F_1/F_0$ ratios of complex cells increase at low contrasts and after adaptation we predict that the spatially homogeneous receptive fields (i.e., spatially overlapping ON–OFF subregions) of complex cells may develop more distinct ON and OFF subregions at low contrast and following adaptation. That is, the spatial structure of the classical receptive field of complex cells at low contrasts might more closely resemble the spatial structure of simple cells. Using sparse noise stimuli, Priebe et al. (2004) showed that cortical cells are more simple-like in their spiking responses than in their membrane potential responses. Manipulations such as lowering the contrast of the stimulus or contrast adaptation, which lower the mean membrane potential during stimulation so it is closer to the spike threshold, are expected to accentuate this effect. It will be interesting to test this prediction using reverse-correlation stimuli with low contrasts or when the cells are in an adapted state. These techniques provide a direct measure of the spatial structure of cortical cell receptive fields (e.g., Mata and Ringach 2005; Priebe et al. 2004). However, one pitfall of reverse-correlation methods such as white-noise analysis is that the low spatial correlation of the stimulus usually produces low firing rates. Lowering the contrast of these types of stimuli would lower the firing rates even further, perhaps to levels where no spikes can be recorded. It will be a challenge in the future to develop reverse-correlation stimuli that elicit responses robust enough that they can be used at low contrasts (but see Touryan et al. 2005). Intracellular recording techniques could also be used to monitor changes in the synaptic input at low contrasts and after adaptation directly (e.g., Priebe et al. 2004).

**Implications for cortical architecture**

The finding that the $F_1/F_0$ ratios of the units classified as simple cells at 100% contrast did not show any contrast or adaptation dependence suggests that these cells might form a distinct cell class. Recent data from cat cortex combining receptive field mapping and intracellular labeling techniques have conclusively shown that simple cells defined as having separate ON and OFF subregions reside in layer 4 and the upper part of layer 6 (Martinez et al. 2005). Layer 4 and its borders, along with the upper region of layer 6, receive direct thalamic input (for review see Payne and Peters 2005). Martinez et al. (2005) conclude that “simple receptive fields represent an exclusive feature of the first stages of cortical processing.” We have identified the recording sites for all cells in our population and correlated them with cortical layers and depths. Using $F_1/F_0$ ratios to classify simple and complex cells at 100% contrast, we found that around 60% of simple cells were located in layers 4 and 6. Moreover, a high percentage of simple cells in layer 5 were close to the border of layer 4 and the great majority of complex cells with high $F_1/F_0$ ratios ($>0.6$) were also found in layer 4. Thus from our data layer 4 has an overrepresentation of highly phase sensitive cells when tested using 100% contrast gratings. When stimulated at low contrasts, it is also layer 4 that shows by far the largest increase in the number of cells with high $F_1/F_0$ ratios. We see in Fig. 9 that the proportion of cells that have $F_1/F_0$ ratios $>0.6$ increases from 22% when the stimulus is at 100% contrast to 77% when the stimulus is at 4% contrast. Our results are strongly supportive of the concept that simple receptive fields and highly phase sensitive complex cells are prominent in geniculocortical layers and represent early stages of cortical processing.

How do the preceding observations correlate with the spike-threshold hypothesis, which suggests that the division of cells into two types arises from the nonlinear interaction of spike threshold with membrane potential responses? The spike-threshold hypothesis suggests a continuum of cell types at the intracellular level (Mechler and Ringach 2002). That is, $V_s/V_n$ ratios have a unimodal distribution (Priebe et al. 2004), yet this unimodal distribution becomes bimodal at the extracellular level (i.e., $F_1/F_0$ ratios) arising from the biophysical properties of the spike threshold. However, the degree of phasicity of the membrane potential responses does play an important role. In fact, Priebe et al. (2004) showed that no cells that are classified as complex based on $F_1/F_0$ ratios have $V_s/V_n$ ratios $>1$. Therefore all complex cells already have relatively low oscillatory responses in their membrane potentials, even before the nonlinearities of the spike threshold take effect. This fact suggests to us that these cells have undergone phase averaging through some mechanism and represent a “higher” level of processing than simple cells. In contrast, most simple cells have quite large $V_s/V_n$ ratios (i.e., 65% have $V_s/V_n$ ratios $>0.6$; Priebe et al. 2004). We interpret this result to mean simple cells are at a lower level of processing than complex cells. Whether this is because they receive exclusive input from the LGN (as in the classical hierarchical model; Hubel and Wiesel 1962) or because they receive weaker recurrent excitation from their neighboring cortical cells (as in the recurrent model; Chance et al. 1999), cells that have $F_1/F_0$ ratios $>1$ at all contrasts appear to form an anatomically segregated cell class whose phase sensitivity is not as malleable as complex cells. By
combining these concepts with the observation that simple cells reside in the thalamocerebellar layers of the cortex, our results provide support for the concept that there is an anatomical hierarchy, with cells in layers receiving direct thalamic input exhibiting more phasic response properties.

Functional considerations

The distribution of contrast levels in natural images peaks at low contrasts: 0–25% (Balboa and Grzywacz 2000; Chirimuuta et al. 2003; Ruderman and Bialek 1994; Tadmor and Tolhurst 2000; Vu et al. 1997). Our present results show that the phase sensitivity of complex cells increased substantially at these contrasts. Moreover, cortical cells rapidly adapt to the prevailing contrast, so under natural viewing conditions it can be expected that most neurons will be in an adapted state, which we show increases phase sensitivity even further. Therefore we predict that the primary visual cortex is dominated by cells with phase-sensitive response properties when viewing scenes containing naturalistic contrast distributions. This shift to simple-like responses may be advantageous because under certain circumstances simple cells may transmit information at faster rates and carry more edge-like or line-like information than complex cells (Mechler et al. 2002; Reich et al. 2001). However, there is also evidence that simple and complex cells do not differ greatly in their ability to discriminate spatial features (Mechler et al. 2002). Finally, it makes the most sense to consider the processing of natural visual scenes in an awake and freely behaving animal. Attention and behavioral state could strongly influence the activity of early visual cortex, thereby altering the contrast- and adaptation-dependent effects observed in the present study (Kagan et al. 2002; McAdams and Reid 2005).

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