Circuitry and the Classification of Simple and Complex Cells in V1

J. Wielaard and P. Sajda
Laboratory for Intelligent Imaging and Neural Computing, Department of Biomedical Engineering, Columbia University, New York, New York

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Wielaaard, Jim and Paul Sajda. Circuitry and the classification of simple and complex cells in V1. J Neurophysiol 96: 2739–2749, 2006. First published June 21, 2006; doi:10.1152/jn.00346.2006. Based on a large-scale neural network model of striate cortex (V1), we present a simulation study of extra- and intracellular response modulations for drifting and contrast reversal grating stimuli. Specifically, we study the dependency of these modulations on the neural circuitry. We find that the frequently used ratio of the first harmonic to the mean response to classify simple and complex cells is highly insensitive to circuitry. Limited experimental sample size for the distribution of this measure makes it unsuitable for distinguishing whether the dichotomy of simple and complex cells originates from distinct LGN axon connectivity and/or local circuitry in V1. We show that a possible useful measure in this respect is the ratio of the intracellular second-to first-harmonic response for contrast reversal gratings. This measure is highly sensitive to neural circuitry and its distribution can be sampled with sufficient accuracy from a limited amount of experimental data. Further, the distribution of this measure is qualitatively similar to that of the subfield correlation coefficient, although it is more robust and easier to obtain experimentally.

INTRODUCTION

Hubel and Wiesel (1962, 1968) postulated the existence of two distinct cell classes in the primary visual cortex (V1): cells that receive input from the lateral geniculate nucleus (LGN), designated as “simple” cells, and cells that do not receive input from the LGN, designated as “complex” cells. There seems at present little doubt that in terms of their extracellular responses (spikes), V1 cells can be sensibly divided into two categories. However, there is an ongoing debate as to whether the circuitry part of the Hubel and Wiesel hypothesis is true—that is, whether in fact there exist two V1 cell classes in terms of LGN axon connectivity and/or distinct cortical circuitry within V1 (Abbott and Chance 2002; Alonso and Martinez 1998; Alonso et al. 2001; Chance et al. 1999; Chung and Ferster 1998; Ferster and Lindstrom 1983; Gilbert 1977, 1983; Hirsch et al. 1998, 2002; Martinez and Alonso 2001; Martinez et al. 2005; Meichler and Ringach 2002; Priebe et al. 2004; Spitzer and Hochstein 1988).

Hubel and Wiesel based their hypothesis on their observation that apparently two distinct classes of ON–OFF subfields constitute the receptive fields of V1 cells. A different, but reasonably consistent (Mata and Ringach 2005), measure for simple and complex cells can be given in terms of extracellular response modulations in response to drifting grating stimuli. The distribution of $S_1/S_0$ (the “modulation index”) for spike responses (where $S_1$ is the first harmonic and $S_0$ the mean of the spike train) resulting from a drifting grating stimulus is profoundly bimodal for V1 cells (Casanova et al. 1992; Chino et al. 1994; Cumming et al. 1999; DeAngelis et al. 1994; DeValois et al. 1982; Lennie et al. 1990; Movshon et al. 1978a,b; Ohzawa et al. 1996, 1997; Sceniak et al. 1999; Skottun et al. 1991; Smith et al. 1997). Simple cells are conventionally defined as having $S_1/S_0 > 1$ and complex cells $S_1/S_0 < 1$.

There seems to be somewhat less consistency between the $S_1/S_0$ and subfield measures in alert monkeys (Kagan et al. 2003). Also, the bimodality of the $S_1/S_0$ distribution was observed to be much less profound in alert monkeys (Kagan et al. 2003), but it remains unclear whether this arises from the much larger number of complex cells than simple cells in the sample, which by itself would have a diminishing effect on a bimodality. However, in terms of subfield organization of the receptive field for spike responses, in alert monkeys two classes are also clearly distinguishable (Kagan et al. 2003).

From a more general signal processing perspective, simple and complex cells in V1, defined either by subfield or the $S_1/S_0$ criterion, also tend to have distinct properties. Simple-cell responses are approximately linear and show a linear dependency on spatial phase, whereas complex cells display a strong nonlinear behavior and are insensitive to spatial phase. Basic neural computations regarding visual perception seem to require the linearity provided by simple cells (Graham 1989; Wandell 1995). Further, neurons in other sensory cortices have linear signal processing properties that resemble those seen in V1. Examples are the primary auditory cortex (Kowalski et al. 1996) and the primary somatosensory cortex (DiCarlo and Johnson 2000). Finally, simple and complex cells have been found in the primary visual cortex of many other species of mammals, such as owl monkeys (O’Keefe et al. 1998), baboons (Kennedy et al. 1985), tree shrews (Kaufman and Somjen 1979), rats (Bume et al. 1984), mice (Drager 1975), rabbits (Glanzman 1983), and sheep (Kennedy and Martin 1983). Clearly, understanding the neural mechanisms and circuitry that lead to the creation of simple and complex cells is of fundamental importance.

It was recently suggested (Priebe et al. 2004) that evidence for the existence of two distinct circuitry classes related to the simple/complex dichotomy in V1 seems to be lacking in terms of intracellular recordings in cat. Distributions of intracellular response properties of V1 cells in response to drifting gratings, as well as of the subfield correlation coefficient based on intracellular responses, were found to be unimodal and were...
interpreted as not to provide any indication of two distinct classes of circuitry.

In contrast, recent intracellular measurements in cat (Martínez et al. 2005) from another group were interpreted as evidence in favor of two distinct classes of circuitry. In that study, distributions of different intracellular quantities such as the subfield correlation coefficient, subfield overlap, and the intracellular push–pull index were found to be clearly bimodal (Hartigan test, \( P < 0.01 \)). In addition, the data in that study are layer specific: simple cells, when defined according to the original Hubel and Wiesel criterion, were found to be exclusively located in layers 4 and 6, i.e., in the layers that receive LGN input.

In this paper we present a simulation study of extra- and intracellular response modulations of V1 neurons for drifting and contrast reversal grating stimuli. We also study the behavior of the extra- and intracellular subfield correlation coefficients. The simulations are based on a large-scale neural network model of macaque V1 (Wieland and Sajda 2005), which allows us to investigate the dependency of the distributions of response modulations on circuitry. It enables us to clarify whether and how such measures could provide insight into the question of whether there are two distinct classes of V1 cells in terms of LGN input (Hubel and Wiesel 1962, 1968; Martínez et al. 2005), in line with the original Hubel and Wiesel hypothesis, or whether LGN input arrives in V1 in a more egalitarian manner (Abbott and Chance 2002; Chance et al. 1999; Mechler and Ringach 2002; Priebe et al. 2004; Tao et al. 2004).

**METHODS**

**Model summary**

We provide here only a very brief description of the model used. For a complete description and further details of the model we refer to Wieland and Sajda (2005). Some additional background information can also be found in previous work (McLaughlin et al. 2000; Wieland et al. 2001) by one of the authors (J.W.).

The model consists of eight ocular dominance columns and 64 orientation hypercolumns (i.e., pinwheels), representing a 16-mm² area of a macaque V1 input layer 4Cα or 4Cβ. The model contains about 65,000 cortical cells and the corresponding appropriate number of LGN cells. Our cortical cells are modeled as conductance-based integrate-and-fire point neurons, of which 75% are excitatory cells and 25% are inhibitory cells. Based on circuitry, the model contains two classes of cortical cells: cells that receive LGN input and cells that do not. Our LGN cells are rectified spatiotemporal linear filters. The model is constructed with isotropic short-range cortical connections (<500 μm), realistic LGN receptive field sizes and densities, and realistic sizes of LGN axons in V1.

Dynamic variables of a cortical model cell \( i \) are its membrane potential \( v_i(t) \) and its spike train \( f_i(t) = \sum \delta(t - t_{ik}) \), where \( t \) is time and \( t_{ik} \) is its \( k \)th spike time. Membrane potential and spike train of each cell obey a set of N equations of the form

\[
\frac{dv_i}{dt} = -g_L(v_i - v_L) - g_{E,i}(t, [\mathcal{F}], \eta_i)(v_i - v_E) \\
- g_{I,i}(t, [\mathcal{F}], \eta_i)(v_i - v_I) \quad i = 1, \ldots, N
\]  

These equations are integrated numerically using a second-order Runge–Kutta method with a 0.1-ms time step. Whenever the membrane potential reaches a fixed threshold level \( v_T \) it is reset to a fixed reset level \( v_R \) and a spike is registered. The equation can be rescaled so that \( v(t) \) is dimensionless and \( C_L = 1, v_L = 0, v_E = 14/3, v_I = -2/3, v_R = 1, v_R = 0 \), and conductances (and currents) have dimension of inverse time.

The quantities \( g_{E,i}(t, [\mathcal{F}], \eta_i) \) and \( g_{I,i}(t, [\mathcal{F}], \eta_i) \) are, respectively, the excitative and inhibitory conductances of neuron \( i \). They are defined by interactions with the other cells in the network, external noise \( \eta_i \), and, in the case of \( g_{E,i} \), possibly by LGN input. The notation \( [\mathcal{F}]_E \) stands for the spike trains of all excitatory (inhibitory) cells connected to cell \( i \). Both, the excitatory and inhibitory populations consist of two subpopulations \( \mathcal{P}_E \) and \( \mathcal{P}_I \), \( k = 0, 1 \). The \( k \) = 1 populations receive LGN input and the \( k = 0 \) populations do not. In the model presented here, 30% of both the excitatory and inhibitory cell populations receive LGN input. We assume noise, cortical interactions, and LGN input act additively in contributing to the total conductance of a cell

\[
g_{E,i}(t, [\mathcal{F}], \eta_i) = \sum_{k \in \mathcal{P}_E} g_{E,i}^{\mathcal{P}_E}(t, [\mathcal{F}]) + \delta g_{E,i}^{\text{LGN}}(t) \\
g_{I,i}(t, [\mathcal{F}], \eta_i) = \sum_{k \in \mathcal{P}_I} g_{I,i}^{\mathcal{P}_I}(t, [\mathcal{F}]) + \delta g_{I,i}^{\text{LGN}}(t) \quad (2)
\]  

where \( \delta_i = \ell \) for \( i \in \mathcal{P}_E \) and \( \delta_i = 0 \). The terms \( g_{E,i}^{\mathcal{P}_E}(t, [\mathcal{F}]) \) are the contributions from the cortical excitatory (\( \mu = E \)) and inhibitory (\( \mu = I \)) neurons and include only isotropic connections

\[
g_{E,i}^{\mathcal{P}_E}(t, [\mathcal{F}]) = \sum_{k \in \mathcal{P}_E} \sum_{j \in \mathcal{P}_E} \delta_{\ell j} E_{ij} \mathbf{G} \left( \frac{x_i - x_j}{L} \right) \sigma_j \eta_j(t - s)f_i(s) \quad (3)
\]  

where \( \mu \in \mathcal{P}_E (\mu') \). Here \( \bar{x}_i \) is the spatial position (in cortex) of neuron \( i \), the functions \( G_{\mu j}(\tau) \) describe the synaptic dynamics of cortical synapses and the functions \( \mathbf{G} \left( \frac{x_i - x_j}{L} \right) \) describe the cortical spatial couplings (cortical connections). The length \( L \) of excitatory and inhibitory connections is about 200 and 100 μm, respectively.

In agreement with experimental findings, the LGN neurons are modeled as rectified center-surround linear spatiotemporal filters. A cortical cell, \( j \in \mathcal{P}_E (\mu') \), is connected to a set \( N_{\mathcal{P}_E} \) of left eye LGN cells, or to a set \( N_{\mathcal{P}_E} \) of right eye LGN cells

\[
g_{E,i}^{\text{LGN}}(t) = \sum_{k \in \mathcal{P}_E} \left[ g_{E,i}^L + g_{E,i}^R \right] \int ds \left[ \mathbf{G}^L \left( \frac{\bar{y}_i - \bar{y}_j}{L} \right) Q(T - s)f_i(s) \right] \quad (4)
\]  

where \( Q = L \) or \( R \). Here \( |x_i - x_j| = 0 \) if \( x_i \) or \( x_j \) is outside the receptive field of \( j \)th cortical cell; \( \bar{y}_i \) is the receptive field center of the \( j \)th cortical cell; \( L \) is the visual stimulus. The parameters \( g_{E,i}^L \) represent the maintained activity of LGN cells and the parameters \( g_{E,i}^R \) measure their responsiveness to visual stimuli. The LGN kernels are of the form

\[
G_{E,i}^L(\tau) = \begin{cases} 0 & \tau \leq \theta_i \\
\frac{k}{\pi \sigma_{\tau_i}^2} e^{-\tau^2/(\pi \sigma_{\tau_i}^2)} & \tau > \theta_i \end{cases}
\]  

and

\[
D_{\mu j}(\tau) = \pm \left( 1 - K_{\mu j} \right) \left\{ \frac{1}{\pi \sigma_{\tau_i}^2} e^{-\tau^2/(\pi \sigma_{\tau_i}^2)} - \frac{K_{\mu j}}{\pi \sigma_{\tau_i}^2} e^{-\tau^2/(\pi \sigma_{\tau_i}^2)} \right\}
\]  

where \( k \) is a normalization constant; \( \sigma_{\tau_i} \) and \( \sigma_{\tau_i} \) are the center and surround sizes, respectively; and \( K_{\mu j} \) is the integrated surround-center sensitivity.

The connection structure between LGN cells and cortical cells, given by the sets \( N_{L_{\mu j}} \), is made to establish ocular dominance bands and a slight orientation preference, which is organized in pinwheels (Blasdel 1992). It is further constructed under the constraint that the LGN axonal arbors sizes in V1 do not exceed the anatomically established values.

A sketch of the model’s geometry and connection structure is given in Fig. 1. Note that, contrary to the Hubel and Wiesel picture, our model can be classified as hierarchical only in terms of LGN inputs.
Stimuli

The luminance of the drifting grating stimulus used is given by \(I(\tilde{y}, t) = I_0[1 + e \cos(\omega t - k \cdot \tilde{y})]\), with average luminance \(I_0\), contrast \(e\), temporal frequency \(\omega\), and spatial wave vector \(k\). Contrast-reversal stimuli are given by \(I(\tilde{y}, t) = I_0[1 + e \cos(\omega(t + \phi))]\). All parameters are close to preferred values; response modulations for contrast reversal stimuli are averaged over the spatial phase \(\phi\). Receptive fields are mapped out using small spots (diameter \(<1/5th\) receptive field) of oscillating luminance, \(I(\tilde{y}, t) = I_0[1 + e \cos(\omega t)]\). ON and OFF responses are collected during the bright \(I(\tilde{y}, t) > I_0\) and dark \(I(\tilde{y}, t) < I_0\) parts of the cycles. We used the spatial correlation coefficient of the ON and OFF subfields

\[ r = \frac{\langle (r_{\text{ON}} - \langle r_{\text{ON}} \rangle)(r_{\text{OFF}} - \langle r_{\text{OFF}} \rangle) \rangle}{\langle (r_{\text{ON}} - \langle r_{\text{ON}} \rangle)^2 \rangle^{1/2}} \] (7)

where \(\langle \cdot \rangle\) denotes the spatial average and \(r_{\text{ON}}(r_{\text{OFF}})\) represents the amplitude of the ON (OFF) response at a particular spatial location. All stimuli are presented monocularly and at high contrast (\(e = 1\)).

RESULTS

Drifting gratings

Examples of our model’s extracellular and intracellular response modulations for a drifting grating stimulus are provided in Fig. 2. These are responses of both a simple and a complex cell for several orientations of the grating, at the cells’ preferred spatial and temporal frequencies. Notice the dominance of the first harmonic in the response of the simple cell.

The distribution of the spike train modulation index \(S1/S0\) over our cell population is shown in Fig. 3A. Strength parameters (see METHODS) have been set so that the distribution of these modulations in the spike responses is in agreement with experimental data for macaque (Ringach et al. 2002). Note that the distribution is profoundly bimodal and that our model cortex (as does macaque V1) contains about an equal number of simple and complex cells (as defined by the \(S1/S0\) criterion).

It is easy to understand how the diversity in response modulations occurs in our model. The modulations enter our model cortex by the LGN input received by 30% of the cortical cells. The phases of these LGN inputs into the different cortical cells vary randomly on \([0, 2\pi]\). This is so because of the receptive field offsets of the clusters of LGN cells connected to different cortical cells, the difference in spatial organization (e.g., symmetry) of the clusters themselves, and the diversity in temporal delays in the LGN kernels (Wielaard and Sajda 2005). A cell receives input from many other cells; thus a cell’s excitatory and inhibitory inputs will show stronger or weaker modulations depending on its specific environment in the network and whether it receives LGN input. Interplay between the strengths and phases of the modulations in these inputs and cell-specific parameters will ultimately determine the modulation in the cell’s spike and membrane potential response.
A classification into simple and complex is far from a binary distribution and is in fact a smooth. A complex cell is not "sharp." That is, the distribution in Fig. 3 shows that, despite this fact, the classification into simple and complex cells that do and cells that do not receive LGN input (METHODS). Our model, by construction, has two distinct classes of cells: cells that do and cells that do not receive LGN input (METHODS). We see that, despite this fact, the classification into simple and complex cells is not "sharp." That is, the distribution in Fig. 3A is far from a binary distribution and is in fact a smooth distribution with a "gap" at small negative values, i.e., \( V_{1}/V_{0} < -\delta \) or \( V_{1}/V_{0} > 0 \) with \( \delta \approx 2 \).

Because of the absence of the spike threshold, one may generally expect intracellular (or subthreshold) responses to be a better reflection of the synaptic inputs of a cell than extracellular responses. One may therefore expect its intracellular responses to be a better reflection of the circuitry relating to a cell than its extracellular responses. This is of course not necessarily true for all intracellular responses and all measures derived from them. Interestingly, our simulations show that this is in fact not true for the \( V_{1}/V_{0} \) measure. As shown in Fig. 3B, the minimal classification error is obtained for the class boundary \( \{ V_{1}/V_{0} \} = 2 \), i.e., “no LGN input” \( V_{1}/V_{0} < 2 \) versus “LGN input” \( V_{1}/V_{0} > 2 \). In that case we make classification errors of 14 and 5%, respectively. The minimal average classification error possible based on intracellular responses is thus again 11%, as it was for extracellular responses. Contrary to general expectations, identification of the circuitry cannot be made more accurately from the extracellular modulations \( V_{1}/V_{0} \) than from the extracellular modulations \( S1/S0 \).

The distribution of modulations in the membrane potential has not yet been observed experimentally in macaque. However, as mentioned in the introduction, intracellular data for cat were recently published (Priebe et al. 2004). Our model’s results show qualitative agreement with these data. In particular, as is shown in Fig. 4, the distributions of \( V_{0} \), \( V_{1} \), and \( V_{f} \) are also unimodal, whereas separation of simple and complex cell classes occurs only in the \( V_{1} \) distribution (and not for \( V_{0} \) and \( V_{f} \)). All potentials are measured with respect to the blank response \( v_{p} \). Note that, although the threshold potential \( v_{p} \) of our integrate-and-fire neurons is fixed and identical for each cell, it becomes cell dependent when measured with respect to the blank response; that is, \( V_{f} = v_{p} - v_{b} \).

Qualitatively, these findings can be explained from a simple rectification model (Mechler and Ringach 2002; Priebe et al. 2004) where all intracellular modulations occur with the same temporal frequency as the stimulus. If one includes the “blank” response (zero contrast) in such a model, it is straightforward to show that generally a bimodal intracellular distribution corresponds to a unimodal intracellular distribution (like the one obtained for our model), including a gap in the support at small negative values. This gap occurs when \( V_{0} \) becomes negative (with respect to the blank), the first harmonic \( V_{1} \) must then exceed \( V_{0} \) for the cell to fire. This requires the gap width \( \delta > 1 \). Here we assume that for a blank stimulus any action potentials in the network occur as a result of the fluctuations in the membrane potential (“fluctuation-driven dynamics”), rather than as a result of its mean value, which is true for practically...
Simple cells perform an approximately linear spatial summation in the model for several spatial phases. Shown are the responses of a simple and a complex cell in the model in response to a contrast reversal grating. Notice the strong phase sensitivity of the simple cell (consistent with linearity) and the phase insensitivity and frequency-doubling of the responses of the complex cell.

Contrast reversal gratings

Examples of extracellular and intracellular response modulations in our model in response to a contrast reversal grating are shown in Fig. 5. These are averaged response waveforms of spike train and membrane potential, with the grating at the preferred orientation and preferred spatial and temporal frequencies. Shown are the responses of a simple and a complex cell in the model for several spatial phases $\phi$ of the grating. Simple cells perform an approximately linear spatial summation, that is, their responses contain a dominant $S1$ component and the spatial phase dependency of their response waveform is similar to the spatial phase dependency of the stimulus. Complex cells respond nonlinearly; their response waveform is relatively insensitive to spatial phase and contains a dominant $S2$ component (frequency-doubling).

The distribution of the phase-averaged $S2/S1$ for a sample consisting of an equal number of cells with and without LGN input is shown in Fig. 6A. The distribution displays a weak bimodality, behavior that agrees with experimental data (Hawken and Parker 1987). Interestingly, this property of our model follows naturally, without any parameter adjustments, after the strength parameters have been set to achieve essentially only orientation tuning and a proper distribution of extracellular response modulations in response to a drifting grating (Fig. 3A) (see Wielaard and Sajda 2005).

The minimal classification error for extracellular classification of cells with and without LGN input occurs for a class boundary at $S2/S1 = 1$, as can be seen in Fig. 6A. In that case we make classification errors of 20 and 5% for cells with and without LGN input, respectively, so that the minimal average classification error possible based on this extracellular measure is 10%.

The distribution of the phase-averaged $S2/S1$ for a different sample, in this case consisting of an equal number of simple and complex cells (as defined by $S1/S0$), is shown in Fig. 6C. The distribution looks very similar as that in Fig. 6A. However, identification of simple and complex cells is notably less precise than identification of cells with and without LGN input: using the class boundary $S2/S1 = 1$ we make an average classification error of about 16% in classifying simple and complex cells.

It is easy to understand how the diversity in $S2/S1$ (and $V2/V1$) occurs. As explained in Wielaard et al. (2001), for a contrast reversal grating stimulus the total LGN input into a cortical cell has, in general, a dominant $S1$ component with a phase close to either 0 or $\pi$, determined by the positions of the LGN inputs into the cell.

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FIG. 5. Cycle-averaged membrane potential and spike train for a typical simple and complex cell in the model in response to a contrast reversal grating. Responses are for 8 spatial phases $\phi$ of the grating covering a range of $\pi$. Grating orientation is the equivalent of the preferred orientation of the cell. Notice the strong phase sensitivity of the simple cell (consistent with linearity) and the phase insensitivity and frequency-doubling of the responses of the complex cell.

all cells as can be seen from Fig. 4C. As mentioned earlier, we observe a gap width of about 2 in our model (Fig. 3B).

Experimental data for intracellular distributions constitute an important piece of the rather sparse body of information currently available on V1 circuitry. The absence of a bimodality in the intracellular distributions, observed experimentally in cat V1, has been interpreted (Priebe et al. 2004) as lack of evidence for the existence of two distinct cell classes, and instead as evidence for the existence of a continuum of circuitry. However, this conclusion is strictly speaking not correct: two distinct classes of circuitry can of course just as well result in a unimodal as in a bimodal distribution. Our model results are merely a concrete example of the former. Thus whether distinct circuitry is responsible for simple and complex cells remains very much an open question, which we will further address in the following sections.

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FIG. 6. Distributions of response modulations in spike train $S2/S1$ (A, C) and membrane potential $V2/V1$ (B, D) for a contrast reversal stimulus. In A and B the sample consists of 1,200 cells, with about an equal number of cells with (dashed) and without (dotted line) LGN input. In C and D the sample consists of 1,200 cells, with about an equal number of simple (dashed) and complex (dotted) cells.
The cortical excitatory and inhibitory inputs in a cell will thus have a strong S2 component because they arise from many other cells. The actual strengths of S1 and S2 components in a cell’s excitatory and inhibitory inputs thus depend on the cell’s specific environment in the network and on whether it receives LGN input. Interplay of these inputs and cell-specific parameters will determine the S2/S1 ratio in the cell’s spike response. Clearly, most cells that receive LGN input (simple) will have S2/S1 < 1 and most cells that do not receive LGN input (complex) will have S2/S1 > 1.

No experimental data are available for the distribution of V2/V1 of the membrane potential waveforms. Our model’s distribution of the phase-averaged V2/V1 is shown in Fig. 6, B and D. Our model predicts that, quite contrary to the situation for the modulation index S1/S0 and V1/V0, the (weak) bimodality of the distribution of S2/S1 for spike waveforms is not eliminated in the V2/V1 distribution for membrane potential waveforms. Rather, it becomes substantially more pronounced in the V2/V1 distribution. Finally, we see that the intracellular measure V2/V1 is indeed a better reflection of the circuitry than the extracellular measure S2/S1. The minimal classification error for intracellular classification of cells with and without LGN input occurs for a class boundary at V2/V1 = 1, as can be seen in Fig. 6B. We make minimal classification errors of 13 and 2% for cells with and without LGN input, respectively; intracellularly the minimal average classification error possible is thus 5%, an improvement by a factor of 2 with respect to the extracellular measure S2/S1.

The fact that the weak bimodality present in the S2/S1 becomes much more pronounced in the V2/V1 distribution can again be intuitively understood from the simple rectification model mentioned earlier. In this model the membrane potential waveforms are subjected to an artificial threshold to give the spike waveforms. For complex cells, both the membrane potential and spike responses will contain a strong second harmonic. Thus in this case practically all of the membrane potential waveform will be above the (artificial) threshold, so that evaluation of V2/V1 will yield about the same result as for S2/S1. This is apparent in Fig. 6: the S2/S1 > 1 and V2/V1 > 1 sections of the distributions are very similar. For simple cells, the membrane potential and spike responses will contain a dominant first harmonic and both will display about an equally small second harmonic component. Because of the rectification, the first harmonic present in the membrane potential waveform is substantially reduced in the spike waveform. Thus V2/V1 will turn out substantially smaller than S2/S1 in this case. This is again apparent in Fig. 6: the V2/V1 < 1 (simple cells) section of the distributions is shifted to the left with respect to the S2/S1 < 1 sections.

**Subfield correlation**

An example of the ON–OFF subfield organization for a simple and a complex cell in our model is shown in Fig. 7. The subfields are obtained with a small spot of oscillating (8 Hz) luminance (METHODS) and responses are collected during the bright (ON) and dark (OFF) parts of the cycle. In agreement with experimental observations, the simple cell (Fig. 7, C and D) shows ON and OFF subfields that are separated, whereas for the complex cell (Fig. 7, A and B) they largely overlap.

The distributions of the subfield correlation coefficients (r) (METHODS) based on spike and membrane potential responses are qualitatively similar to the S2/S1 and V2/V1 distributions, respectively. This is illustrated in Fig. 8. That this is so can also be understood intuitively. Cells with strongly overlapping ON and OFF subfields (r ≈ 1) will generate a dominant second harmonic and very little first-harmonic response for a contrast reversal grating (i.e., they will have large S2/S1 and V2/V1 ratios). Cells with strongly nonoverlapping subfields (r ≈ −1) will generate a dominant first harmonic and little second-harmonic response for a contrast reversal grating (i.e., they will have small S2/S1 and V2/V1 ratios). Thus one may naturally expect some similarity between the distributions of the subfield correlation coefficient and of the ratio of second and first harmonic in response to contrast reversal gratings.

Similarly as for the intracellular V2/V1 measure, it can also be seen from Fig. 8, A and B that the intracellular subfield correlation coefficient (Fig. 7B) better reflects the circuitry than does the extracellular subfield correlation coefficient (Fig. 7A). Extracellularly we obtain a minimal average classification error (for classifying cells with and without LGN input) of 10%, whereas this is reduced fivefold intracellularly to a minimal classification error of 2%. The classification of simple and complex cells is notably worse (see Fig. 8, C and D). Using r = 0 as the class boundary, we make an average extracellular classification error of 22% (Fig. 8C). Intracellularly we make an average classification error of 16% (Fig. 8D). A summary of our results for the classification utility (LGN vs. no LGN) of the different extracellular and intracellular metrics discussed is shown in Table 1.

As mentioned earlier in the INTRODUCTION, different results for the distribution of the intracellular subfield correlation coefficient were obtained by different experimental laboratories. A unimodal (or at best weakly bimodal) distribution was observed by Priebe et al. (2004); a strongly bimodal distribution was observed by Martinez et al. (2005). It must be noted, however, that the latter distribution was constructed from...
significantly fewer cells. On the other hand, the conclusion made by Priebe et al. (2004) (i.e., that their unimodal distribution would suggest a continuum of circuitry) is strictly speaking incorrect. What was noted earlier for the intracellular V1/V0 distribution is also true here: two distinct classes of circuitry can of course, in principle, just as well result in a unimodal as in a bimodal distribution (of the intracellular subfield correlation coefficient). In this case, however, as we will see in following text, our model results indeed confirm to some extent the naive intuition that a unimodal distribution of the intracellular subfield correlation coefficient suggests a continuum of circuitry.

More specifically, we have yet to address the following questions. To what extent can a strong bimodality in the intracellular V2/V1 (or subfield correlation coefficient) distribution, like the one we observe in our model, actually be interpreted as a signature of V1 circuitry? Is it correct to conclude that if intracellular experimental data would show a profoundly bimodal V2/V1 (or subfield correlation coefficient) distribution, that this is evidence for the existence of two distinct classes of circuitry in V1? Could the presence of a less-profound bimodality, or unimodality of the observed V2/V1 (or subfield correlation coefficient) distribution be evidence for a continuum of circuitry in V1? We address these questions in the next section.

**Continuous versus discrete classes of V1 circuitry**

Conductance and membrane potential waveforms (cycle average; see METHODS) for a typical model cell are shown in Fig. 9. Results shown are for a drifting grating stimulus (left column) and for a contrast reversal grating stimulus (right column). For the drifting grating (Fig. 9A) we see that the LGN input (black) is dominated by the first harmonic, whereas the cortical conductances have a large mean value with substantially smaller modulations. The situation is distinctly different for the contrast reversal stimulus (Fig. 9B). At the preferred phase, the LGN conductance still contains a dominant first harmonic, although it is phase sensitive, and the first harmonic practically vanishes at the orthogonal phase. The cortical conductances, however, are insensitive to the grating phase and clearly show a dominant second-harmonic component.

In our model (as well as in real V1 cortex; see e.g., Destexhe et al. 2003) conductances are large. As a result, there is to a good approximation a simple Ohmic relation between the cycle-averaged conductances and membrane potential (Wieland et al. 2001)

\[
\langle v_t(t) \rangle = V_t(t) = \frac{(I_{v,t}(t))}{(g_{E,t}(t))} \tag{8}
\]

where

\[
I_{v,t}(t) = g_{E,t}(t) v_e - g_{I,t}(t) v_i
\tag{9}
\]

\[
g_{v,t}(t) = g_t + g_{E,t}(t) + g_{I,t}(t) \tag{10}
\]
and \( g_{E,k} \) and \( g_{I,k} \) are the total excitatory and inhibitory conductances and \( V_E \) and \( V_I \) are the excitatory and inhibitory reversal potentials, respectively. That the Ohmic approximation (Eq. 8) is indeed highly accurate is shown in Fig. 9, E and F.

Manipulation of the relative strengths of the cortical and LGN components of the excitatory conductances changes the relative strengths of the modulations in the membrane potential (and spike train) and thus the distributions of these modulations. Together with the Ohmic approximation, this provides us with a way to predict, given results of our main simulation, the behavior of these distributions as a function of circuitry. That is, given our results for two distinct cell classes (with and without LGN input) it allows us to predict what the distributions look like for an arbitrary continuum of cell classes (with respect to LGN input) simply by interpolation.

Consider a population of \( N_0 \) cells with LGN input in our model. Their excitatory conductances can be written as \((k = 1, \ldots, N_0)\)

\[
g_{E,k}(t) = g_{E,k}^{\text{LGN}}(t) + g_{E,k}^{\text{ON}}(t) \tag{11}
\]

Note that in our model all \( g_{E,k}^{\text{LGN}}(t) \) are of roughly similar magnitude. To manipulate the membrane potential modulations we introduce the parameters \( \alpha_k(t) \) and \( \beta_k \in [0, 1] \) and a new total excitatory conductance

\[
g_{E,k}(t) = (1 - \alpha_k) g_{E,k}^{\text{LGN}}(t) + (1 - \beta_k) g_{E,k}^{\text{ON}}(t) \tag{12}
\]

where the \( \ast \) denotes convolution. We leave the inhibitory and leakage conductances unchanged for each cell in the population and compute the membrane potential modulation distributions from Eq. 8. Further, we take

\[
\alpha_k(n) = \begin{cases} -\frac{\xi \beta_k C_1}{n} & \text{for } n \geq 2 \\ -\frac{\xi \beta_k C_1}{n} & \text{else} \end{cases} \tag{13}
\]

where \( C = g_{E,k}^{\text{LGN}}(0) / g_{E,k}^{\text{ON}}(0) \) and the circumflex accent \( \hat{\alpha} \) denotes the Fourier components, e.g., \( \hat{\alpha}(n) = (\omega/2\pi) \int_0^{2\pi} \alpha_k(t)e^{-in\omega} dt \). Constructed in this way, the parameter \( \alpha_k(t) \) provides a uniform scaling factor with additional amplification of the second harmonic set by the parameter \( \xi \). The construction ensures that cells maintain reasonable firing rates because the mean of the total excitatory conductance is unaltered, i.e., \( \hat{G}_{E,k}(0) = \hat{g}_{E,k}(0) \) for arbitrary \( \beta_k \) and \( \xi \). We eliminate all LGN input and thus create a cell from the other class, i.e., without LGN input, by taking \( \beta_k = 1 \). Results of this manipulation, and \( \xi = 2, \) for a model cell are shown in Fig. 9, C–F. Notice the drastic change in the membrane potential (green); the transformation in this case obviously changes the cell from a simple cell to a complex cell.

We now return to the distributions of the membrane potential modulations V2/V1. We apply the transformation to a sample of \( N_0 = 600 \) model cells with LGN input and calibrate the transformation by fixing \( \hat{\xi} \) so that for \( \beta_k = 1, k = 1, \ldots, N_0 \) we obtain a V2/V1 distribution that approximates the V2/V1 distribution for 600 randomly selected cells without LGN input in our model. This is shown in Fig. 10, A and B. The distribution of V2/V1 for the sample with LGN input is shown in Fig. 10A. First we note that making the transformation (Eq. 12) with \( \beta_k = 0, k = 1, \ldots, N_0 \) (arbitrary \( \hat{\xi} \)), changes little because of the high accuracy of the Ohmic approximation (compare solid and dashed curves in Fig. 10A). From Fig. 10B we see that making the transformation (Eq. 12) with \( \hat{\xi} = 2, \beta_k = 1, k = 1, \ldots, N_0 \), results in a distribution of V2/V1 that approximately matches that for cells without LGN input in the model (compare solid, dotted, and dashed curves).

Keeping \( \hat{\xi} = 2 \) fixed, we can now create a sample consisting of two distinct classes of cells (with and without LGN input) from the sample consisting of only cells with LGN input, and recover the results of our full simulation. We do this by making the transformation (Eq. 12) with \( \beta_k = 0 \) for half of the cells and \( \beta_k = 1 \) for the other half in the sample. This is shown in Fig. 10C, where we see that the result (red curve) closely resembles the distribution of Fig. 6B (i.e., our full simulation result for the V2/V1 distribution for a sample consisting of an equal number of cells with and without LGN input).

We can introduce a continuum of circuitry (with LGN input) by making the transformation (Eq. 12) with \( \beta_k, k = 1, \ldots, N_0 \) drawn randomly (and independently) from a uniform distribution on [0, 1] for each cell. The result is shown in Fig. 10C (blue curve). We see that our method predicts that the profound bimodality present for two distinct classes of circuitry entirely disappears for a continuum of circuitry.

Our transformation method is not limited to a contrast reversal grating stimulus. We can apply the same transformations to the responses to the stimuli that were used to obtain the ON and OFF subfields for our model cells (METHODS). The results are shown in Fig. 11. In this case the transformation is somewhat less precise for cells with a higher subfield correlation (compare red and black curves). The reason is that higher subfield correlation implies higher overlap of the subfields and thus weaker responses to the spot stimuli used (METHODS). Figure 11 (red and black curves) thus shows that the signal-to-noise ratios of our data are somewhat too low for higher subfield overlaps for our transformation to be very accurate. Nevertheless, the results in Fig. 11 clearly demonstrate a qualitative difference between the distributions for binary and continuous circuitry. Similarly as for the V2/V1 distribution, we see that the profound bimodality present for two distinct

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**FIG. 10.** A: original distribution of V2/V1 for the sample of \( N_0 = 600 \) cells with LGN input (solid) and the Ohmic approximation (dashed). B: distribution of V2/V1 for a sample of 600 model cells without LGN input (solid) and for sample of the \( N_0 = 600 \) cells in A (with LGN input) after the transformation \( \beta_k = 1 \) (dashed). C: original distribution of V2/V1 for the cells with and without LGN input in A and B (1,200) black). Distribution after the transformation \( \beta_k = 0 \) for half of the cells in A and \( \beta_k = 1 \) for the other half (red). Distribution after the transformation with \( \beta_k \) drawn randomly (independently) from a uniform distribution on [0, 1] for the cells in A (blue).
classes of circuitry largely disappears for a continuum of circuitry, although somewhat less convincingly so than for the V2/V1 distribution.

Finally, we apply the same transformations to the drifting grating stimulus—that is, to the V1/V0 distribution. The results are shown in Fig. 12. As reference samples we once again use the samples consisting of 600 cells with and 600 cells without LGN input of Fig. 10, A and B. As was the case for contrast reversal, the result for binary circuitry practically coincides with the full simulation result (black and red curves). Further, unlike the V2/V1 distribution for contrast reversal, the V1/V0 distribution for drifting gratings changes little for a continuum circuitry. Indeed, confirmation of the experimental data was also reported for a detailed neural network model similar in spirit to ours, but with a more continuous (egalitarian) distribution of LGN inputs (Tao et al. 2004). Its insensitivity thus makes the V1/V0 distribution a poor indicator for V1 circuitry. This is particularly true given the limited quantity of experimental data attainable even in principle with current techniques. Note for instance that to truly experimentally confirm the distribution predicted by our model (i.e., including the negative branch, the gap, etc.), the sample needs to be much larger than the 100 cells for which data are currently available, from Fig. 12 we may deduce that a sample size of 1,200 is in fact still quite insufficient for this purpose.

We believe our work helps to clear up some apparent misconceptions for what concerns the interpretation of the unimodal/bimodal nature of intracellular distributions in relation to circuitry.

In general unimodal distributions can result from one, two, a continuum, or any other arrangement of classes; thus in principle one cannot conclude (Priebe et al. 2004) that generally unimodal distributions suggest continuous classes (circuitry). Our model cortex with two distinct classes (of circuitry) yields unimodal intracellular distributions for V0, V1, V1/V0, and Vf as observed experimentally. This is merely an illustration of the fact that it is incorrect to interpret the unimodal feature of these distributions as evidence for a continuum of circuitry. Similarly, our results in the case of the intracellular subfield correlation coefficient distribution are necessary to infer that a unimodal distribution may indeed be taken as evidence for a continuum of circuitry.

Further classification based on a unimodal distribution is not a priori inferior to classification based on a bimodal distribution. Our simulations also provide an example of this by means of the intracellular V1/V0 and corresponding extracellular S1/S0 distributions. As we have shown, identification of the two cell classes in the model (cells with and without LGN input) can be made just as well in terms of the core and tails of the V1/V0 distribution as in terms of the two modes of the S1/S0 distribution. Incidentally, the same seems to hold true with regard to classification of simple and complex cells on the (bimodal) S1/S0 and (unimodal) V1/V0 distributions for experimental data (Priebe et al. 2004; their Fig. 3B), as well as for a model with a continuum of LGN circuitry (Tao et al. 2004; their Fig. 6A), and for our model (not shown).

Finally, we have shown that—contrary to general expectations—the intracellular measure V1/V0 is not a better indicator of circuitry than the extracellular measure S1/S0 (Table 1). We have shown that the intracellular V1/V0 distribution is in fact highly insensitive to circuitry and not likely to be a very useful measure to distinguish between circuitry of one or another kind based on experimental data.

Our simulations show that the intracellular V2/V1 distribution for contrast reversal stimuli is highly sensitive to whether cells receive their LGN input in a continuous (egalitarian) or in a distinctly binary fashion. Our results suggest this measure can be used as an indicator of V1 circuitry. The sensitivity of this measure is explained by the fact that for contrast reversal stimuli, there is a clear qualitative difference between the phase dependency of the LGN and the collective cortical inputs into a cell. The LGN input shows a distinct phase dependency, whereas the collective cortical input is practically phase insensitive and frequency-doubled. If the LGN inputs arrives in V1 in a binary fashion, our simulations predict the distribution of V2/V1 for cells in the input layers is profoundly bimodal. If the LGN input is egalitarian, our simulations predict that this distribution is profoundly unimodal.

We have shown that the behavior of the intracellular subfield correlation coefficient as a function of circuitry is largely similar to what we see for V2/V1. This also holds true (not shown) for the subfield overlap index, a measure that is strongly correlated with the subfield correlation coefficient (Mata and Ringach 2005). Our results also suggest that the
distribution of the intracellular subfield correlation coefficient can serve as an indicator of V1 circuitry. Removal of the bimodal nature for continuous circuitry, however, is somewhat less clear for this distribution than for the V2/V1 distribution. As mentioned in the introduction, the intracellular subfield correlation coefficient distribution—unlike the V2/V1 distribution—has been observed experimentally. Naively interpreted, the experimental data so far, however, suggest conflicting pictures for the circuitry of simple and complex cells. On the one hand, the data of Priebe et al. (2004) (i.e., their data for the intracellular subfield correlation coefficient, Fig. 7 of their paper) would suggest continuum of circuitry, whereas on the other hand the data of Martinez et al. (2005) (i.e., Fig. 3 of their paper and their Fig. 4 for the push–pull index distribution) would suggest two distinct classes of circuitry. The findings presented here provide evidence that this naive interpretation is in fact correct: using numerical simulations we showed that the unimodal intracellular subfield correlation coefficient distribution of Priebe et al. (2004) is indeed likely an indication of a continuum of circuitry, whereas the bimodal intracellular subfield correlation coefficient distribution of Martinez et al. (2005) is likely an indication of two distinct classes of circuitry.

As for the reasons for the apparent discrepancy between the data reported by Priebe et al. (2004) and Martinez et al. (2005), there are several possibilities. The most obvious is the difference in sample size. The substantially smaller data set of Martinez et al. (2005) could simply lead to a “biased estimate” of the same phenomenon. Other reasons for the discrepancy could be related to the intracellular measurements of inhibition, as indicated in Hirsch and Martinez (2006). Whereas in Martinez et al. (2005) responses to light/dark spots are frequently inverse images of each other (their Fig. 1), in Priebe et al. (2004) this is quite rare (their Fig. 6; note that pronounced negative deflections are rare). This could be the result of technical differences or also of differences in layer sampling. Priebe et al. (2004) did not identify the layers of the cells recorded; perhaps only a small proportion of their cells were recorded within layer 4. Finally, there are perhaps other technical reasons, such as the fact that some of the cells from Martinez et al. (2005) were studied with QX-314.

It is important to realize that the capacity of the intracellular V2/V1 distribution, as a measure for simple/complex cell circuitry, is by no means limited to the context in which it is presented in this paper. That is, it is not limited to a situation in which the distinction between circuitry is “LGN input” and “no LGN input.” Rather, it equally well applies to a situation where all simple and complex cells would be created entirely from cortical interactions (e.g., in V1 layers that do not receive LGN input). Also it applies equally well to a (purely hypothetical) situation where all simple and complex cells would be created entirely from cortical interactions (e.g., in V1 layers that do not receive LGN input). The reason is that the behavior of V2/V1 for contrast reversal gratings is closely related to the subfield composition of a cell’s receptive field (and thus to the simple/complex cell dichotomy) and not, in principle, to whether the cell receives LGN input. Therefore for what concerns the behavior of V2/V1, it is irrelevant whether the subfield organization of simple and complex cells results entirely from LGN input, entirely from cortical interactions, or from a combination of both. Thus the phase-averaged V2/V1 distribution for contrast reversal gratings in general is quite a good indicator of whether the simple/complex dichotomy is a reflection of distinct circuitry and it is not limited to input layers. This is useful because it means that with respect to questions about “distinct” versus “continuum” of circuitry, experimental data from different layers could be pooled together to construct an overall V2/V1 distribution. This is not to say, of course, that layer-specific experimental observation of the V2/V1 distribution does not remain of great interest. The distribution could very well be different for different layers and in fact (as mentioned earlier), when so, this may be a reason for the apparent discrepancy between the data of Priebe et al. (2004) and Martinez et al. (2005).

As we have shown, unlike for the V1/V0 distribution (drifting grating), an experimental estimate of the V2/V1 distribution could be obtained for relatively small cell samples (order of hundreds of cells). The suggested V2/V1 distribution is also a robust measure: it concerns a ratio of low-order Fourier components, of a generally strong response (to contrast reversal gratings), which is furthermore averaged over phases. It is for instance much less sensitive to noise and experimental errors than the subfield correlation coefficient or overlap index. As far as we know, experimental data are not yet available, or at least not in sufficient amounts, to use this distribution as an indicator of V1 circuitry.

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