

On the Division of Cortical Cells Into Simple and Complex Types: A Comparative Viewpoint

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Ibbotson, M. R., N.S.C. Price, and N. A. Crowder. On the division of cortical cells into simple and complex types: a comparative viewpoint. *J Neurophysiol* 93: 3699–3702, 2005. First published January 19, 2005; doi:10.1152/jn.01159.2004. Hubel and Weisel introduced the concept of cells in cat primary visual cortex being partitioned into two categories: simple and complex. Subsequent authors have developed a quantitative measure to distinguish the two cell types based on the ratio between modulated responses at the stimulus frequency (F_1) and unmodulated (F_0) components of the spiking responses to drifting sinusoidal gratings. It has been shown that cells in anesthetized cat and monkey cortex have bimodal distributions of F_1/F_0 ratios. A clear local minimum or dip exists in the distribution at a ratio close to unity. Here we present a comparison of the distributions of the F_1/F_0 ratios between cells in the primary visual cortex of the eutherian cat and marsupial Tammar wallaby, *Macropus eugenii*. This is the first quantitative description of any marsupial cortex using the F_1/F_0 ratio and follows earlier papers showing that cells in wallaby cortex are tightly oriented and spatial frequency tuned. The results reveal a bimodal distribution in the wallaby F_1/F_0 ratios that is very similar to that found in the rat, cat, and monkey. Discussion focuses on the mechanisms that could lead to such similar cell distributions in animals with diverse behaviors and phylogenies.

INTRODUCTION

Hubel and Weisel (1962) first categorized cells in the primary visual cortices of cats into two distinct cell types: simple and complex. The distinction was based on the spiking responses of cells during four visual tests. Simple cells 1) have spatially segregated ON and OFF regions within their receptive fields; 2) show summation within each subregion; 3) have antagonistic ON and OFF subregions; and 4) have responses that can be predicted based on the organization of their receptive field (RF) subregions. Cells that did not meet all or any of these criteria were classified as complex. Since the pioneering observations of Hubel and Weisel, a method was developed to quantify the simple and complex categories based on the spiking responses of the cells to moving sinusoidal gratings (De Valois et al. 1982; Movshon et al. 1978a,b; for review, Skottun et al. 1991). The method calculates the mean response of the cells above spontaneous rate during the period of motion (F_0) and the amplitude of oscillations at the fundamental temporal frequency of the stimulus (F_1). An F_1/F_0 ratio is then calculated. Skottun et al. (1991) showed that, when the ratios were plotted for a large population of cells in cat and monkey V1, the neurons fell into a bimodal distribution with peaks at ratios of 1.7 and 0.2–0.3. There was a clear minimum or dip close to an F_1/F_0 ratio of unity. Separating the neuron types

based on those with F_1/F_0 ratios >1 or <1 produced a distribution that correlated well with the classifications based on the qualitative measures suggested by Hubel and Weisel (1962). Cells with ratios below unity were classed as complex cells and the others as simple cells.

We know that mammals originated from reptile-like therians in the cretaceous period (e.g., Ibbotson and Mark 2003; Mark and Marotte 1992). Approximately 135 million years ago, the therians split into two major radiations: the metatherians (marsupials) and eutherians (placentals). The majority of what we know about cortical physiology is based on recordings from eutherians (primarily cats and monkeys). Using qualitative methods, cells with simple and complex-like properties have been reported in two nocturnal marsupials: an American opossum, *Didelphis aurita* (Rocha-Miranda et al. 1976), and an Australian possum, *Trichosaurus vulpecula* (Crewther et al. 1984). Simple and complex cells have also been identified qualitatively in a highly visual, day-and-night active marsupial, the Tammar wallaby, *Macropus eugenii* (Ibbotson and Mark 2003; Vidyasagar et al. 1992). These studies showed that cortical neurons in the wallaby are highly tuned for orientation, spatial, and temporal frequency in much the same way as cortical cells in rats, cats, and monkeys (e.g., Girman et al. 1999). Given that the two main mammalian radiations split so long ago, it is of interest to further compare the physiology of the marsupial primary visual cortex with eutherian mammals in more detail. Here we provide the first quantitative evidence for the existence of simple and complex cells at the extracellular level in the cortex of the Tammar wallaby and compare the data with that from the cat.

METHODS

Five wallabies were prepared as described previously (Ibbotson and Mark 2003). Briefly, animals were anesthetized using intravenous infusion of 1 mg/kg/h of pentobarbital sodium (Boehringer-Ingelheim), paralyzed using suxamethonium chloride (4.2 mg/kg/h; Glaxo), and artificially respired with oxygen and N_2O . After extracellular isolation of individual units in primary visual cortex (area 17), direction tuning and locations of ON and OFF regions were qualitatively tested using hand-driven light bars. Optimal direction, spatial frequency, temporal frequency, and classical receptive field size were determined quantitatively with computer-driven monochromatic sinusoidal gratings (frame rate, 100 Hz; mean luminance, 45 cd/m²). F_1/F_0 ratios were calculated from gratings with contrasts $>32\%$ moving in the neuron's preferred direction, spatial frequency, and temporal frequency. Test gratings were presented for 6 s in most cases (8–32 repeats), interleaved with a uniform gray of mean luminance for 10 s.

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In a proportion of cells that were lost before completing all tests, F_1/F_0 ratios were calculated using data from the initial spatial/temporal frequency tests, which were 2 s in duration. These data were only used if the optimum temporal frequency (TF) was ≥ 2 Hz, thus giving several full response cycles to calculate the F_1/F_0 ratio. The F_1 component of the response was calculated using Fourier analysis. The first cycle of each response was excluded from the analysis to prevent onset transients influencing either the F_1 or F_0 components. Spontaneous activity was subtracted from responses before calculation of the F_1 or F_0 components. All procedures were approved by the animal ethics committee of the Australian National University.

RESULTS

F_1/F_0 ratios were calculated for 123 area 17 neurons. This data set represents a reanalysis of data presented in Ibbotson and Mark (2003), as well as previously unpublished data. All neurons used in this analysis showed orientation or direction tuning, and there was no systematic relationship between orientation tuning and F_1/F_0 ratio. Nondirectional cells were excluded from the data set, and all ratios were calculated using responses elicited by motion in the preferred direction.

Figure 1 shows responses from two neurons in the primary visual cortex of the wallaby when stimulated by optimally oriented sine-wave gratings drifting in the preferred direction. The neuron in Fig. 1A was highly orientation-tuned and direction-selective (see *inset*). It shows a highly oscillatory response

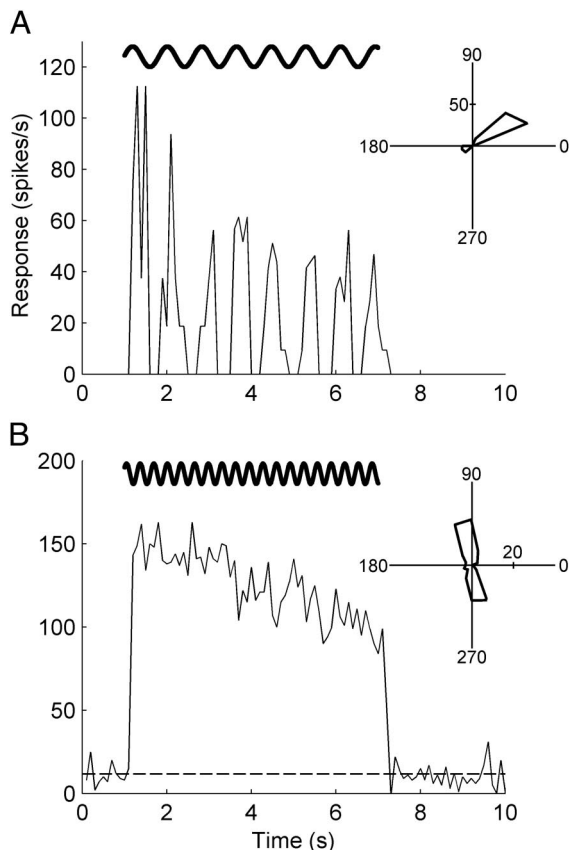


FIG. 1. Peristimulus time histograms showing the responses generated by sine-wave gratings moving in the preferred direction for 2 neurons in the wallaby primary visual cortex. A and B: simple and complex cell, respectively. Sine-waves at the top of each graph show the stimulus profile in time, and dashed lines indicate the spontaneous firing rate. *Inset*: polar plots show direction tuning for each neuron.

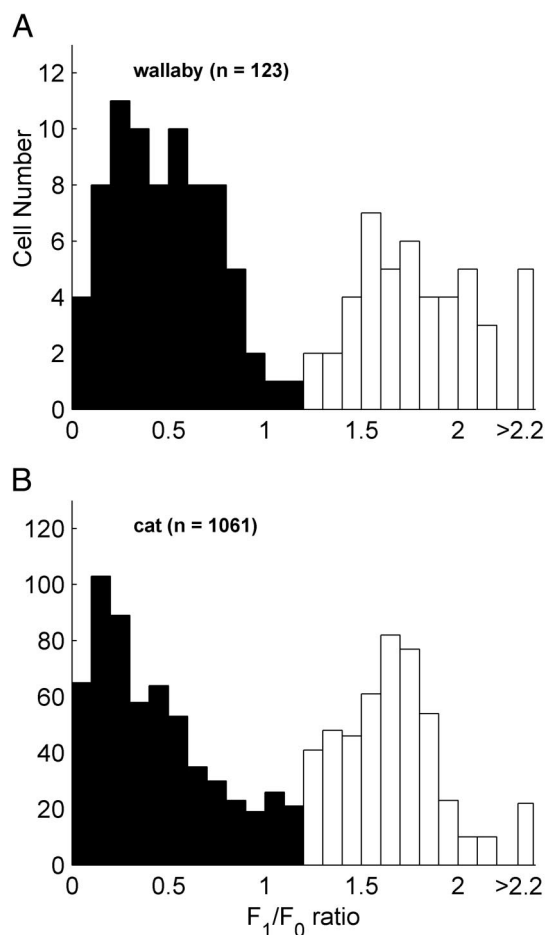


FIG. 2. A: F_1/F_0 ratios for the wallaby. Black and white columns represent complex and simple cells classified by cluster analysis, respectively. B: F_1/F_0 ratios from 1,061 neurons in cat cortex, as presented by Skottun et al. (1991). In all histograms, F_1/F_0 ratios >2.2 are presented in the right bar.

waveform at the same frequency as the grating drift rate (1.22 Hz) during preferred direction motion. This cell was classed as a simple cell using both the F_1/F_0 ratio and more traditional tests using hand-driven light bars. During preferred direction motion, the neuron in Fig. 1B shows no obvious oscillations at the fundamental stimulus frequency (3.1 Hz), but instead, has a large steady spiking output. This cell was classified quantitatively and qualitatively as a complex cell. It showed clear orientation tuning but was approximately equally responsive to motion in either direction along its preferred motion axis (Fig. 1B, *inset*).

It is normally accepted that cells with F_1/F_0 ratios above unity are simple cells and those below are complex cells. Figure 2A shows a histogram of the F_1/F_0 ratios for 123 wallaby neurons. We used the centroid method of cluster analysis to divide the cells into two groups. The population formed a clear bimodal distribution, separated at an F_1/F_0 ratio of 1.2. The cluster analysis confirms that the dividing line between simple and complex cells is close to unity. Based on the dividing line given by the cluster analysis, we identified 48 simple cells (white bars, peak F_1/F_0 ratio = 1.5) and 75 complex cells (black bars, peak F_1/F_0 ratio = 0.3). Only a small number of cells, which all had ratios between 0.8 and 1.3, showed differences between their classification as simple or complex using the F_1/F_0 ratio and qualitative receptive field

tests. Neurons classified as simple and complex had mean spontaneous rates of 2.61 ± 3.12 (SD) and 10.16 ± 4.87 , respectively.

For comparison, in Fig. 2B we present the summed results from six laboratories that have recorded from cat cortex (Skottun et al. 1991). The same cluster analysis was used to divide this population into two groups. Because we did not have access to the raw F_1/F_0 ratios, the cluster analysis was conducted by uniformly distributing the F_1/F_0 ratios for the cells in each column between the values at the extreme of each column. The dividing line between the populations for the cumulative cat data occurs at an F_1/F_0 ratio of 1.2.

Hartigan's dip statistic (Hartigan and Hartigan 1985) revealed that the distributions of F_1/F_0 ratios in both wallaby and cat are significantly different from unimodality ($P < 0.05$). Using the same test separately on the simple and complex cell populations shows unimodal distributions ($P > 0.8$), revealing that, as a whole, both populations are bimodal. Wilcoxon rank-sum tests showed a difference of $P < 0.03$ between the medians of the cat and wallaby simple cells and $P < 0.06$ between the medians of the cat and wallaby complex cells. Wilcoxon rank-sum tests showed highly significant differences ($P \ll 0.01$) when simple and complex medians were compared.

The wallaby cortex does not have large sulci (Vidyasagar et al. 1992), so penetrations were typically perpendicular to the cell layers, thus ensuring that the electrode traveled through all layers (Fig. 3A). Complex cells were reasonably evenly distributed throughout the cortical layers, whereas simple cells were more common in layers 4–6 (Fig. 3B).

DISCUSSION

The oscillatory nature of spiking responses to sine-wave gratings has been used to quantitatively classify cat and monkey V1 neurons into simple and complex groups with high concordance to more qualitative methods using hand-driven

light bars (Skottun et al. 1991). Our results show that neurons in the primary visual cortex of the marsupial Tamar wallaby can also be classified as simple or complex cells based on F_1/F_0 ratios. The dips between simple and complex populations in rat (Girman et al. 1999), cat, monkey, and wallaby are all close to unity. The quantitative findings from the wallaby confirm earlier qualitative reports that its cortical cells can be divided into those with or without distinct ON and OFF zones in their receptive fields (Ibbotson and Mark 2003; Vidyasagar et al. 1992). Based on this data, we are confident that neurons in the wallaby cortex can be divided into simple and complex types.

Many have considered the bimodal distribution of the F_1/F_0 ratio as an indication of two different mechanisms at work in the cortex (for reviews, Mechler and Ringach 2002; Skottun et al. 1991). However, Mechler and Ringach (2002) showed through modeling that the underlying membrane potential modulation can be similar in simple and complex cells and that it is only the nonlinear spike-generating mechanism that leads to a bimodal F_1/F_0 ratio. The V_1/V_0 ratio is the intracellular equivalent of the F_1/F_0 ratio, with V_0 being the mean depolarization of the membrane potential from the cell's resting potential and V_1 being the modulation in the membrane potential. Intracellular recordings from the cat cortex have revealed that the underlying membrane oscillations produce V_1/V_0 ratios with a unimodal distribution peaking around 0.1, whereas the F_1/F_0 ratios have a bimodal distribution peaking at 0.3 and 1.7 (Priebe et al. 2004). These results imply that the nonlinear spiking mechanism contributes significantly to the generation of simple and complex categories. Importantly, the spiking component of the cortical cell responses is essential from a functional standpoint because only the information contained in the spike trains is transmitted along the axon to higher-order visual areas (Abbott and Chance 2002). It is common for the response patterns derived from the spiking output of cells to be quite different from the intracellular membrane activity. For example, the orientation tuning functions of neurons in cat cortex are wider when measured using membrane potential fluctuations instead of spiking responses (Carandini and Ferster 2000).

Further support that the same basic cortical circuit generates simple and complex responses comes from experiments showing that cells in cat areas 17/18 can be converted from simple into complex by blocking the action of GABA, an inhibitory neurotransmitter (Borg-Graham et al. 1998; Chance et al. 1999; Frégnac and Shulz 1999; Pernberg et al. 1998). It is conjectured that inhibitory interneurons normally hyperpolarize simple cell membrane potentials well below spiking threshold. Removal of the inhibition depolarizes the resting membrane potential, thus making it easier for the cell to spike. Kagan et al. (2002) have shown that there are fewer simple cells in awake behaving monkeys than in anesthetized animals, perhaps indicating state-dependent modulation of cortical circuitry.

Similarities in the anatomical connections of the geniculostriate pathways in monkeys, cats, and wallabies suggest that the cortical circuitry has a common design (e.g., Henry and Mark 1992; Mark and Marotte 1992; Sheng et al. 1990, 1991; Tyler et al. 1998; Vidyasagar et al. 1992; Wimborne et al. 1999). Given this similarity, the presence of simple and complex cells in wallaby might be expected. Furthermore, due to

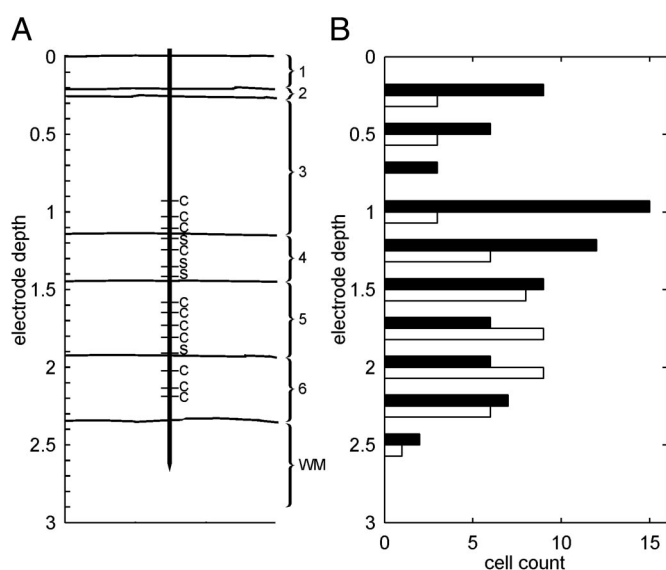


FIG. 3. A: reconstruction of an electrode track indicating the depths of simple (S) and complex (C) cells. Cortical layer numbers and white matter (WM) are noted on the right. B: cell counts for various electrode depths with white and black bars representing simple and complex cells, respectively. Electrode depth is shown on the ordinate.

general similarities in the connectivity of the geniculo-striate pathway in mammals, between-species variations in visual response properties may be based more on visual ecology than phylogenetic distance between species (Ibbotson and Mark 2003). For example, both cats and wallabies are day and night active species with good spatial acuity (Hemmi and Mark 1998) and have been shown here to have similar F_1/F_0 ratios. However, visual ecology is unlikely to be the only determining factor of F_1/F_0 ratios, because the rat, which is not regarded as a highly visual animal, also has a similar F_1/F_0 distribution (Girman et al. 1999). It is a goal for future comparative studies to find if bimodal F_1/F_0 distributions occur in all visual mammals or only those with highly orientation selective visual cortices. Our findings add to the argument of Mark and Marotte (1992) that the wallaby is a valid animal model to study vision, but with the added benefit that early development can be studied more easily due to slow embryonic development and access to developing pouch young. The comparative use of the wallaby is now further reinforced by the recent initiation of the kangaroo genome project, of which the wallaby forms the experimental model (Wakefield and Graves 2003).

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GRANTS

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