

Dynamic Recruitment of the Feedforward and Recurrent Mechanism for Black–White Asymmetry in the Primary Visual Cortex

Weifeng Dai (戴伟枫),^{1*} Tian Wang (王天),^{1,2*} Yang Li (李洋),¹ Yi Yang (杨祎),¹ Yange Zhang (张艳歌),¹ Jian Kang (亢健),¹ Yujie Wu (武宇洁),¹ Hongbo Yu (俞洪波),³ and Dajun Xing (邢大军)¹

¹State Key Laboratory of Cognitive Neuroscience and Learning & IDG/McGovern Institute for Brain Research, Beijing Normal University, Beijing, 100875, China, ²College of Life Sciences, Beijing Normal University, Beijing, 100875, China, and ³School of Life Sciences, State Key Laboratory of Medical Neurobiology, Collaborative Innovation Center for Brain Science, Fudan University, Shanghai, 200438, China

Black and white information is asymmetrically distributed in natural scenes, evokes asymmetric neuronal responses, and causes asymmetric perceptions. Recognizing the universality and essentiality of black–white asymmetry in visual information processing, the neural substrates for black–white asymmetry remain unclear. To disentangle the role of the feedforward and recurrent mechanisms in the generation of cortical black–white asymmetry, we recorded the V1 laminar responses and LGN responses of anesthetized cats of both sexes. In a cortical column, we found that black–white asymmetry starts at the input layer and becomes more pronounced in the output layer. We also found distinct dynamics of black–white asymmetry between the output layer and the input layer. Specifically, black responses dominate in all layers after stimulus onset. After stimulus offset, black and white responses are balanced in the input layer, but black responses still dominate in the output layer. Compared with that in the input layer, the rebound response in the output layer is significantly suppressed. The relative suppression strength evoked by white stimuli is notably stronger and depends on the location within the ON-OFF cortical map. A model with delayed and polarity-selective cortical suppression explains black–white asymmetry in the output layer, within which prominent recurrent connections are identified by Granger causality analysis. In addition to black–white asymmetry in response strength, the interlaminar differences in spatial receptive field varied dynamically. Our findings suggest that the feedforward and recurrent mechanisms are dynamically recruited for the generation of black–white asymmetry in V1.

Key words: black–white asymmetry; cortical suppression; feedforward connection; LGN; primary visual cortex; recurrent connection

Significance Statement

Black–white asymmetry is universal and essential in visual information processing, yet the neural substrates for cortical black–white asymmetry remain unknown. Leveraging V1 laminar recordings, we provided the first laminar pattern of black–white asymmetry in cat V1 and found distinct dynamics of black–white asymmetry between the output layer and the input layer. Comparing black–white asymmetry across three visual hierarchies, the LGN, V1 input layer, and V1 output layer, we demonstrated that the feedforward and recurrent mechanisms are dynamically recruited for the generation of cortical black–white asymmetry. Our findings not only enhance our understanding of laminar processing within a cortical column but also elucidate how feedforward connections and recurrent connections interact to shape neuronal response properties.

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*W.D. and T.W. contributed equally to this work.

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Correspondence should be addressed to Dajun Xing at dajun_xing@bnu.edu.cn.

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Introduction

Black and white information is asymmetrically processed in the visual system. At the neuronal level, black and white stimuli evoke unequal neuronal responses in the visual cortex of various species: cat (Jin et al., 2008; Dai and Wang, 2012; K. Liu and Yao, 2014; Rekauszke et al., 2016; de Souza and Casanova, 2019; Jansen et al., 2019; Mazade et al., 2019; Han et al., 2022); human (Zemon et al., 1988, 1995; Olman et al., 2010; Kremkow et al., 2014); monkey (Yeh et al., 2009; Xing et al., 2010, 2014; Samonds et al., 2012; Zurawel et al., 2014; P. Li et al., 2022); ferret (Zahs

and Stryker, 1988; G. B. Smith et al., 2015); tree shrew (Veit et al., 2014; Lee et al., 2016; Khani et al., 2018); mouse (S. L. Smith and Häusser, 2010; Polack and Contreras, 2012; Tan et al., 2015; Jimenez et al., 2018; B. Williams et al., 2021; Tring et al., 2022); and mink (McConnell and LeVay, 1984). At the perceptual level, a preference for black polarity is found in a variety of tasks (Krauskopf, 1980; Chubb et al., 2004; Badcock et al., 2005; Komban et al., 2011, 2014; Lu and Sperling, 2012). This black–white asymmetry in neuronal encoding and perception is supposed to reflect the adaptation of the visual system to its environment, in which black and white features are asymmetrically distributed (Ratliff et al., 2010; Cooper and Norcia, 2015). Although the universality and essentiality of black–white asymmetry have been recognized, the neural substrates for black–white asymmetry remain unclear.

Two principal mechanisms were proposed to explain the generation of black–white asymmetry in the early visual cortex. In the first mechanism, the feedforward mechanism, black–white asymmetry is assumed to result from imbalanced feedforward contribution of ON and OFF afferents. The imbalance between the ON and OFF pathways first appears in the retina (Copenhagen et al., 1983; Burkhardt et al., 1998; Gollisch and Meister, 2008; Burkhardt, 2011; Nichols et al., 2013) and is maintained or enhanced in the LGN (Jin et al., 2008, 2011a). The second mechanism, the recurrent mechanism, underscores the role of intracortical recurrent connections. In this mechanism, black–white asymmetry emerges because the intracortical recurrent connection will selectively amplify responses elicited by the preferred stimulus polarity or selectively suppress responses elicited by the nonpreferred stimulus polarity. Recent studies in cats and monkeys suggest that white stimuli will induce stronger suppression in the primary visual cortex: cat (Taylor et al., 2018; St-Amand and Baker, 2023) and monkey (Xing et al., 2014; Yang et al., 2022). Despite intensive studies, whether both mechanisms contribute to black–white asymmetry remains to be determined. If both mechanisms are involved, how they interact is yet unknown.

To dissociate these two mechanisms, it is vital to simultaneously obtain neuronal responses in multiple stages of the visual hierarchy. The visual cortex of higher mammals consists of six interconnected layers. Neurons in different layers are arranged in a columnar structure (Mountcastle, 1957; Hubel and Wiesel, 1962, 1968) and have distinct intralaminar and interlaminar connections (Peters and Yilmaz, 1993; Boyd and Matsubara, 1996; Binzegger et al., 2004; Hirsch and Martinez, 2006). Leveraging these diverse neural circuits in columnar organization and the development of laminar recording, we aim to disentangle the involvement of the feedforward mechanism and the recurrent mechanism in the generation of cortical black–white asymmetry.

In the current study, we simultaneously recorded neuronal responses across all layers of the cat primary visual cortex and separately recorded LGN responses. Black and white squares smaller than the classical receptive field (RF) were used to determine the black–white asymmetry of each recording site. We first characterized the laminar pattern of black–white asymmetry. By comparing the population profile of black–white asymmetry among the LGN, V1 input layer, and V1 output layer, we revealed that the feedforward mechanism and the recurrent mechanism are dynamically recruited for black–white asymmetry in V1.

Materials and Methods

Animal preparation

Acute experiments were performed in adult cats of either sex (*Felis catus*, 2–4.5 kg; V1 recording: 9 animals; LGN recording: 7 animals; for 1

animal, V1 and LGN were both recorded). All procedures were in accordance with the National Institutes of Health Guidelines, and the research protocol was approved by the Biological Research Ethics Committee of Beijing Normal University (ID: IACUC (BNU)-NKLCNL 2017-06) and Fudan University (ID: 2021JS0087).

Surgical procedures were similar to those described in previous studies (Han et al., 2021b; B. Wang et al., 2021). In brief, animals were injected with dexamethasone (0.4 mg/kg, s.c.) 12 h before the surgery. At the beginning of the surgery, animals were initially anesthetized with isoflurane (5% concentration) and injected with atropine sulfate (0.05 mg/kg, s.c.). During the surgery and the electrophysiological recording, anesthesia and paralysis were maintained with propofol (2–6 mg/kg/h) and vecuronium bromide (0.1 mg/kg/h), respectively. The end-tidal CO₂ was maintained at 3.5%–4%, and the body temperature was set at 36.5°C–37.5°C. Ventilation pressure, heart rate, ECG, and blood oxygen were monitored continuously. To prevent brain edema and to reduce saliva secretions during the experiment, dexamethasone antibiotic was injected every day (0.4 mg/kg), and atropine sulfate (0.05 mg/kg) was injected every other day. To dilate the pupils, 1% atropine sulfate solution was administered. To protect the corneas and focus visual stimuli on the retina, contact lenses with appropriate refractive power (+2.0 D) were fitted onto the eyes. To reduce optical aberration, artificial pupils (3 mm in diameter) were placed in front of the eyes. Before the experiment, the optic disk was back projected onto the screen with a reversible ophthalmoscope, from which we estimated the location of the area centralis.

The animal's head was fixed on the stereotaxic instrument, and a craniotomy was performed to enable electrophysiological recording of V1 (P7–A5, L0–L5, Horsley–Clarke coordinate, both hemispheres) or LGN (centered at A9L8 with a diameter of 6 mm). After the penetration of the linear probe, 1.5%–2% agar was applied to protect the cortex.

Electrophysiological recording

A multielectrode linear array was used to record neuronal activity across all layers of the cat primary visual cortex (RF center within 20° of the area centralis) and LGN (RF center within 30°–40° of the area centralis). A 24 electrode linear probe (U-Probe, Plexon; 15 μ m in diameter and 100 μ m interelectrode distance) was used for all animals, except for 1 animal during V1 recording, which used a 64 electrode linear probe (Probe64D Sharp, IDAX Microelectronics; 50 μ m interelectrode distance). The linear probe was controlled by a microelectrode drive (NAN Instruments) to penetrate across the cortex. Electrical signals were acquired with a Cerebus 128-channel system (Blackrock Microsystems).

For V1 recording, raw data from each site were high-pass filtered (seventh-order Butterworth with 1000 Hz corner frequency), and a signal-to-noise ratio (SNR) of 5.5 was chosen as the threshold for multiunit spiking activities (MUAs). Raw data were also low-pass filtered (seventh-order Butterworth with 300 Hz corner frequency) to obtain the local field potential (LFP). Both MUA and LFP were further downsampled to 500 Hz.

From V1 recordings, we obtained 23 probe placements that had a high SNR and were perpendicular to the cortex. For some probe placements that lasted a long time, the perpendicularity can be confirmed by postmortem histology, as the track of the linear probe is clearly defined under CO staining. For the U-Probe, there are 12–19 electrodes (median: 17 electrodes) within the cortex and 2–7 electrodes within one cortical layer. For each probe placement, 2–17 electrodes (median: 11 electrodes) have a high SNR. For Probe64D Sharp, there are 32 electrodes within the cortex (27 electrodes have high SNR) and 7–9 electrodes within one cortical layer.

For LGN recordings, we had 11 probe placements that had a high SNR and were in the LGN based on the spatial RF.

Visual stimulation

Visual stimuli were generated on a PC with a Leadtek GeForce 6800 video card and were presented on a γ -calibrated CRT monitor (Dell P1230, refresh rate 100 Hz, mean luminance 32 cd/m²).

Sparse noise stimuli consisted of black and white squares presented at random positions in a 2D grid. Each square had 90% contrast from the gray background (luminance: 32 cd/m²) and was presented with

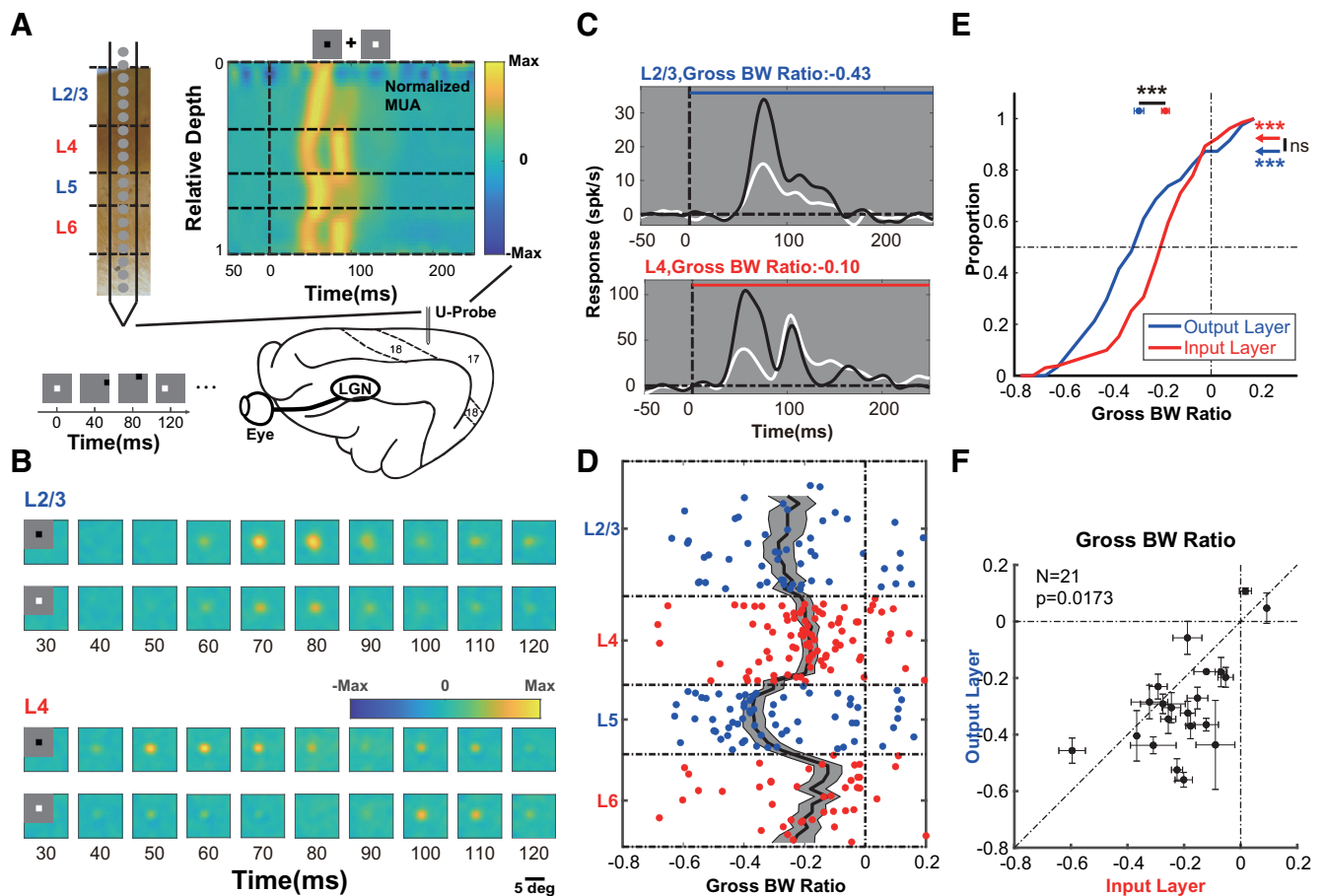


Figure 1. Laminar processing of black–white asymmetry in cat V1. **A**, Basic methods. In our study, multielectrode linear probes (U-Probe, 100 μ m interelectrode distance; or Probe64D Sharp, 50 μ m interelectrode distance) were used to record V1 laminar responses and LGN responses. V1 and LGN responses were separately recorded, except for 1 animal. Small black and white squares were rapidly presented (40 ms for each stimulus) at random positions in a reverse-correlation paradigm. The MUA response was extracted and analyzed. We used “output layer” to include L2/3 and L5 (in blue) and “input layer” to include L4 and L6 (in red). **B**, Spatiotemporal response of example sites from L2/3 (top) and L4 (bottom). Spatial RF evoked by black stimulus ensembles and white stimulus ensembles (overlaid in insets) are shown at different time delays after stimulus onset (30–120 ms). Calibration: 5 degrees. **C**, Gross BW Ratios of example sites from L2/3 (top) and L4 (bottom). The Gross BW Ratio is defined as $(R_{white} - R_{black}) / (R_{white} + R_{black})$, where R_{white} and R_{black} are the averaged temporal responses to white squares (white line) and black squares (black line). A negative value of Gross BW Ratio indicates a stronger overall response to black, and a positive value means a stronger white response. Responses from 0 to 250 ms after stimulus onset (red line and blue line above temporal responses) were averaged. Vertical dashed line indicates stimulus onset. Each dot represents data from one recording site. Blue dots represent sites belonging to the output layer, including L2/3 and L5. Red dots represent sites in the input layer, including L4 and L6. Black lines indicate the running medians of neighboring sites. Shaded error bars indicate the SEM. **E**, Cumulative distribution of Gross BW Ratio in the output layer (blue line) and the input layer (red line). Top, The median value and SEM of Gross BW Ratio for both layers. Colored arrows on the right indicate the proportion of black-prefering sites in each layer. Statistical comparisons for median values of Gross BW Ratio (on the top) and proportions of black-prefering sites (on the right) between the output layer and the input layer are also shown. **F**, Comparison of Gross BW Ratio between the output layer and the input layer in the same probe placement. For each probe placement, we obtained the median value and SEM of Gross BW Ratio across all sites in the output layer and in the input layer. Thus, each dot represents data from one probe placement. The significance for paired comparison between the output layer and the input layer is shown. Error bars indicate SEM. * $p < 0.05$. ** $p < 0.01$. *** $p < 0.001$.

40 ms in a reverse-correlation paradigm. The size of each square ranged from 1 degree of visual angle to 3 degrees, and the extent of the visual space covered ranged from 5 to 35 degrees, depending on the size of the neurons' RF (typically 1–5 degrees). For some experiments, there existed spatial overlap for neighboring squares to obtain denser sampling of neuronal response and higher SNR. The number of unique black and white squares ranged from 242 ($11 \times 11 \times 2$) to 442 ($17 \times 13 \times 2$), and each square was repeated 37–107 times. The stimuli were all monocularly presented to the eye contralateral to the recorded hemisphere.

Laminar alignment

For each probe placement of V1 recording, we assigned all sites to corresponding layers according to stimulus-evoked MUA, LFP, and spatial RF. Since the thickness varied across probe placements, we assigned a relative depth to each site based on previous studies (O'Leary, 1941; Boyd and Matsubara, 1996; Payne and Peters, 2002; Binzegger et al., 2004).

The range of relative depth was from 0 to 1, with 0 indicating the border between the cortical surface and L2/3, and 1 indicating the border between L6 and white matter.

The border between the cortical surface and L2/3 can always be identified from LFPs because the LFP traces are nearly identical for sites out of the cortex, and an abrupt change exists between neighboring sites once it enters the cortex.

The border between L6 and white matter was determined by MUA and spatial RF. The deepest site with a high SNR of MUA and consecutive spatial RF was deemed 50 μ m above this border.

We separated the cortex into four layers (L2/3, L4, L5, L6) using three other relative depths to mark the border between neighboring layers (relative depths from top to bottom are 0.35, 0.58, 0.76). These three borders were mainly determined based on the latency of the MUA response, as the latencies of L4 and L6 were obviously faster than those of L2/3 and L5 (see Fig. 1A).

Given the significant similarity in temporal dynamics observed between L2/3 and L5, as well as between L4 and L6, we further combined

data in L2/3 and L5 as in the “output layer” and those in L4 and L6 as in the “input layer” to enhance the statistical power.

Data analysis

Selection of sites. For each site, we obtained the MUA response, $R(x, y, p, t)$, to sparse noise stimuli, where x and y indicate the spatial position and p indicates the polarity of each square. t starts from 50 ms before stimulus presentation and ends at 250 ms after stimulus presentation.

We define $Var(t)$ as the variance across all spatial positions and polarities at each time point. The SNR of each site is then defined as $SNR = \frac{Var(t_{max})}{Var(T_{baseline})}$, where t_{max} is the time point with the maximum variance and $T_{baseline}$ is in the range $(-50$ to 0 ms). Only sites with SNRs > 8 and with relative depths in the range $(0, 1)$ for V1 recording were included in later analysis. As a result, 118 MUA sites in the output layer and 131 MUA sites in the input layer were further analyzed.

Temporal response averaged across valid spatial positions. For each valid site, we then selected spatial positions that elicited a strong response for further analysis. We define $R_{max}(x, y)$ as the maximum response across stimulus polarities and time for each spatial position. We then obtained the modified z score value $Z_{max}(x, y)$, and only spatial positions with $Z_{max} > 3.5$ were selected as valid spatial positions.

Temporal responses averaged across all valid spatial positions were defined as $R(B, t)$ and $R(W, t)$ for black and white stimuli, respectively. In addition, we defined $R(t)$ as the average of $R(W, t)$ and $R(B, t)$.

Onset peak time, offset peak time, and latency time. For the temporal response averaged across black and white, $R(t)$, we defined the time point that elicited the maximum response within the time range $(20-80$ ms) as the onset peak time, t_{onset} . The offset peak time, t_{offset} , is the time point with the maximum response within the time range $(60-120$ ms). If the difference between t_{offset} and t_{onset} is less than the duration for the stimulus presentation (40 ms in our study), we set t_{offset} equal to $t_{onset} + 40$.

For $R(B, t)$ and $R(W, t)$, we can define $t_{B,onset}$, $t_{B,offset}$, $t_{W,onset}$ and $t_{W,offset}$ in a similar way.

To calculate latency time, only temporal response $R(t)$ was used. Latency time was defined as the time point on the rising edge that reached half the height of the onset peak response. Latency time was used to perform laminar alignment.

Quantifying black–white asymmetry at different temporal ranges. To quantify the differences in the overall strength of black and white in stirring up a local population, we used the metric Gross BW Ratio for each site. Gross BW Ratio is based on the averaged response from 0 to 250 ms after stimulus presentation and is defined as follows:

$$\text{Gross BW Ratio} = \frac{\sum_{t=0}^{250} R(W, t) - \sum_{t=0}^{250} R(B, t)}{\sum_{t=0}^{250} R(W, t) + \sum_{t=0}^{250} R(B, t)} \quad (1)$$

The Gross BW Ratio ranges from -1 to 1 , with -1 indicating no white response (black dominance), 0 indicating equal strength of black response and white response, and 1 indicating no black response (white dominance).

Similarly, to quantify black–white asymmetry at the onset peak, we chose a short temporal window, starting 10 ms before the onset peak time and stopping 10 ms after the onset peak time, to calculate the Onset BW Ratio as follows:

$$\text{Onset BW Ratio} = \frac{R(W, T_{W,onset}) - R(B, T_{B,onset})}{R(W, T_{W,onset}) + R(B, T_{B,onset})} \quad (2)$$

A capital T is used here to indicate that we used the averaged response within the temporal window centered at the onset peak time.

Offset BW Ratio is calculated in a similar way to quantify black–white asymmetry at the offset peak as follows:

$$\text{Offset BW Ratio} = \frac{R(W, T_{W,offset}) - R(B, T_{B,offset})}{R(W, T_{W,offset}) + R(B, T_{B,offset})} \quad (3)$$

We can also define BW Ratio at each time based on the response strength to black and white at the corresponding time in a similar way.

In Extended Data Figure 2-1, we show $R(B, t)$ and $R(W, t)$ for all valid sites in the LGN, V1 input layer, and V1 output layer. All sites are sorted in ascending order of Onset BW Ratio. We further separate these sites into OFF sites and ON sites based on their Onset BW Ratio being negative or positive. Temporal responses averaged across all OFF sites and ON sites are also shown.

Quantifying rebound response to different stimulus polarities and in different pathways. To characterize the relative strength of the rebound response from the averaged response of black and white $R(t)$, we used a metric Rebound Ratio, defined as follows:

$$\text{Rebound Ratio} = \frac{R(T_{offset})}{R(T_{onset}) + R(T_{offset})} \quad (4)$$

Rebound Ratio ranges from 0 to 1, with 0 indicating no rebound response, 0.5 indicating equal onset response and rebound response, and 1 indicating no onset response.

Similarly, we used Black Rebound Ratio and White Rebound Ratio to characterize the rebound response elicited by black, $R(B, t)$ and white, $R(W, t)$, respectively.

$$\text{Black Rebound Ratio} = \frac{R(B, T_{offset})}{R(B, T_{onset}) + R(B, T_{offset})} \quad (5)$$

$$\text{White Rebound Ratio} = \frac{R(W, T_{offset})}{R(W, T_{onset}) + R(W, T_{offset})} \quad (6)$$

Moreover, to quantify the rebound response of the OFF pathway and ON pathway, we defined OFF Rebound Ratio and ON Rebound Ratio as follows:

$$\text{OFF Rebound Ratio} = \frac{R(W, T_{offset})}{R(B, T_{onset}) + R(W, T_{offset})} \quad (7)$$

$$\text{ON Rebound Ratio} = \frac{R(B, T_{offset})}{R(W, T_{onset}) + R(B, T_{offset})} \quad (8)$$

In these definitions, we assumed that the onset response to black and the offset response to white are both from the OFF pathway, whereas the onset response to white and the offset response to black are both from the ON pathway.

Categorization of the ON-OFF domain for each probe placement. A probe placement is categorized in the ON domain if all sites in L4 prefer white and in the OFF domain if all L4 sites prefer black. Otherwise, the probe placement is categorized as being on the ON-OFF border (Jin et al., 2008; Y. Wang et al., 2015). In our V1 recordings (23 probe placements), 13 probe placements are in the OFF domain, 4 probe placements are in the ON domain, and 6 probe placements are on the ON-OFF border.

To further quantify the relative location of the probe placement in the ON-OFF cortical map, we defined the Domain Center Index as the median value of Onset BW Ratios across all L4 sites, with -1 indicating the center of the OFF domain, 1 indicating the center of the ON domain, and 0 indicating the ON-OFF border.

Characterization of the spatial RF. We fitted the spatial RF from chosen stimulus ensembles at specific times with a tilted 2D Gaussian model as follows:

$$R(x, y|p, t) = Ae^{-\left(\frac{x'^2}{2\sigma_x'^2} + \frac{y'^2}{2\sigma_y'^2}\right)} + B \quad (9)$$

with

$$\begin{pmatrix} x' \\ y' \end{pmatrix} = \begin{pmatrix} \cos\theta & \sin\theta \\ -\sin\theta & \cos\theta \end{pmatrix} \begin{pmatrix} x - x_0 \\ y - y_0 \end{pmatrix} \quad (10)$$

In this model, σ_l and σ_s are radii along the long and short axes. x_0 and y_0 are the azimuth and elevation of the RF center, respectively. θ is the tilt angle. p indicates different stimulus ensembles: white stimulus ensemble, black stimulus ensemble, and combined white and black stimulus ensemble. t in the current study includes t_{onset} and t_{offset} .

We defined the RF size (σ) as the geometric mean of σ_l and σ_s as follows:

$$\sigma = \sqrt{\sigma_l \sigma_s} \quad (11)$$

Granger causality analysis. Multivariate Granger causality is calculated using the MVGC MATLAB Toolbox (Barnett and Seth, 2014). For a time series X with dimension $[E, T, N]$, where E is the electrode number, T is the trial length, and N is the trial number, we first estimated the corresponding VAR model parameters $[A_k, \Sigma]$ (tsdata_to_var.m) with a fixed order of 15 (corresponding to 30 ms; similar results can be obtained using the optimal order determined based on information criteria). We then calculated the autocovariance sequence Γ_k (var_to_autocov.m) from the VAR parameters. Finally, we obtained the time domain conditional Granger causality value (autocov_to_pwcgc.m), with dimension $[E, E]$, where the first dimension indicates the receiver of the projection (to) and the second dimension the sender of the projection (from).

Spike sorting

Spike sorting was initially performed automatically using KiloSort (Pachitariu et al., 2016) and then manually curated using Phy (Rossant et al., 2016). The quantity of each unit was quantified by the SNR of the spike waveform, which is defined as the ratio of the peak-to-peak amplitude of the mean waveform to twice the SD of the noise (Kelly et al., 2007). Any unit with a spike waveform SNR > 1.5 was classified as a single unit.

We separated all V1 single units into five classes based on a recent work studying extracellular spike waveforms of cat V1 (Sun et al., 2021). The following is a description of the pipeline.

First, for the spike waveform of each single unit, we obtained the signed max value (peak amplitude) and signed min value (trough amplitude). If the absolute value of the peak amplitude was larger than that of the trough amplitude, we classified this unit as a “positive-spiking” (PS) unit.

Then, we extracted three more features from the spike waveform:

- First peak-trough ratio: the ratio between the amplitude of the first peak before the trough and the trough amplitude;
- Trough width: full width at half the trough amplitude;
- Rising time: time from the trough to the first peak after the trough

If the first peak-trough ratio was < -0.1 , indicating a large positive peak before the trough, we classified this unit as a “triphasic-spiking” (TS) unit. A unit was classified as a “compound-spiking” (CS) unit if any one of the following criteria was met: the first peak-trough ratio is positive, the trough width is > 0.4 ms or the rising time is > 1 ms.

The remaining units were classified as “narrow-spiking” (NS) units or “broad-spiking” (BS) units based on the first principal component of the PCA combining trough width and rising time (Ardid et al., 2015). The distribution of the first principal component of the PCA was clearly bimodal. Spike waveforms for each of the five classes, along with their laminar distribution, are depicted in Figure 6A.

PS, TS, and CS units are proposed to originate from subcortical axons (Sun et al., 2021). We also found that PS/CS units are rarely located in the output layer and that TS units are almost exclusively located outside of L2/3 (see Fig. 6A). Therefore, we included BS, PS, TS, and CS units as “putative-excitatory” units and NS units as “putative-inhibitory” units. The ratio of “putative excitatory” units and “putative inhibitory” units is $\sim 3:1$ (see Fig. 6A), similar to the estimated ratio between excitatory neurons and inhibitory neurons in the cortex (Beaulieu et al., 1992).

For LGN recordings, only single-unit data were analyzed. For V1 recordings, both MUA and single-unit data were analyzed.

Model fitting and evaluation

We fitted neuronal responses evoked by both polarities in the output layer $R_{(p,t)}^{outputlayer}$ with two computational models, simulating the signal transmission process from the input layer to the output layer.

In Model I (No Suppression), neuronal responses in the input layer, $R_{(p,t)}^{inputlayer}$, are weighted and summed and then linearly convolved with a temporal kernel, giving rise to neuronal responses in the output layer, $R_{(p,t)}^{outputlayer}$ as follows:

$$R_{(p,t)}^{outputlayer} = \sum_{i=1}^N w_i R_{(p,t)}^{inputlayer,i} * K_{(t)}^{feedforward} \quad (12)$$

where w_i is the weight of neuron i in the input layer and $K_{(t)}^{feedforward}$ is the feedforward temporal kernel representing signal transmission from the input layer to the output layer with a log-normal form as follows:

$$K_{(t)}^{feedforward} = e^{-\frac{(\log(t) - \Delta t_{K,f})^2}{2\sigma_{K,f}^2}} \quad (13)$$

$\Delta t_{K,f}$ and $\sigma_{K,f}$ control the peak time and width of the temporal kernel.

In Model II (With Suppression), in addition to feedforward convergence from the input layer, neurons in the output layer receive delayed and polarity-selective suppression:

$$R_{(p,t)}^{outputlayer} = \sum_{i=1}^N w_i R_{(p,t)}^{inputlayer,i} * (K_{(t)}^{feedforward} - S_p^{recurrent} K_{(t)}^{recurrent}) \quad (14)$$

$S_p^{recurrent}$ represents the degree of suppression of the corresponding polarity, and $K_{(t)}^{recurrent}$ has a similar form as $K_{(t)}^{feedforward}$,

$$K_{(t)}^{recurrent} = e^{-\frac{(\log(t) - \Delta t_{K,r})^2}{2\sigma_{K,r}^2}} \quad (15)$$

except for a delayed peak time ($\Delta t_{K,r} > \Delta t_{K,f}$) and varied kernel widths ($\sigma_{K,r}$).

For the temporal responses of each site in the output layer, we pooled data from 20 sites in the input layer ($N = 20$ in Eqs. 12 and 14), including all sites that shared the same probe placement in the input layer, as well as a random selection of sites from the input layers of other probe placements. Therefore, the temporal responses of each site in the output layer could be fitted multiple times given different combinations of data from the input layer. We conducted 50 fittings for each site in the output layer, enabling us to statistically compare the relative suppression strength between white and black for each single site. To underscore the contribution from the same cortical column, we constrained the summed weights from sites in the same probe placements to exceed 50% of the total weight from all 20 sites.

Experimental design and statistical analysis

The mean or median values of several recording sites per layer from one probe placement are used for interlaminar comparison; and in such conditions, an error bar indicating SEM is also shown. Otherwise, each recording site is used as an independent repetition. To test whether there exists a difference between the medians of two groups, we use the Wilcoxon signed-rank test for paired groups and the Wilcoxon rank-sum test for independent groups. Unless explicitly noted, a two-sided test is used. The Kruskal–Wallis test, used for comparing medians across multiple groups, is supplemented with the Bonferroni method to adjust for multiple comparisons. To determine whether the median of a group is different from 0, we use a sign test. The χ^2 goodness-of-fit test is used to compare proportions of two groups. The Spearman correlation coefficient is used to test the correlation between two variables. The calibrated version of the Hartigan dip test is used to test for unimodality (Cheng and Hall, 1998; Henderson et al., 2008; Ardid et al., 2015). All error bars indicate the median $\pm$ SEM.

Results

In the current study, we used multielectrode linear probes to simultaneously record neuronal responses across all layers in A17 and A18 of anesthetized cats. Black and white squares, smaller than RF size, were rapidly presented (40 ms) in a reverse-correlation paradigm (Jones and Palmer, 1987) to evoke neuronal responses and to determine the relative strength of black and white for each recording site (Fig. 1A). Multiunit spiking activity (MUA), representing the response of a relatively local population (Xing et al., 2009), as well as sorted single-unit spiking activity, were extracted for each recording site. Excluding probe placements that were not perpendicular to the cortex or that did not have a high SNR, 23 probe placements remained, from which each recording site was assigned to the corresponding cortical layer based on response latency to squares in the RF. Across the study, we use the term “output layer” to refer to L2/3 and L5, which provide efferents to downstream areas, and “input layer” to include L4 and L6, which receive subcortical afferents and provide efferents to the output layer (Hirsch and Martinez, 2006). To help determine the role of subcortical feedforward afferents, we also recorded LGN responses in the same stimulus paradigm.

Black–white asymmetry starts from the input layer and becomes more pronounced in the output layer

The spatiotemporal responses of an example recording site in L2/3 and L4 are shown in Figure 1B. To effectively compare responses evoked by black and white stimuli, we selected spatial positions from which the maximum response to either black or white stimuli exceeded a given threshold (for details, see Materials and Methods). Temporal responses to black and white were obtained by averaging temporal responses evoked by these selected spatial positions and were further analyzed (Fig. 1C).

To characterize laminar processing of black–white asymmetry in V1, we averaged the temporal response from 0 to 250 ms after stimuli presentation to each polarity and then obtained the metric Gross BW Ratio. The Gross BW Ratio ranges from -1 to 1 , with 0 indicating equal black and white responses, a negative value indicating a stronger black response, and a positive value indicating a stronger white response. The Gross BW Ratios of both example sites are negative (Fig. 1C), indicating that black squares evoked stronger overall responses at both sites. The laminar pattern of the Gross BW Ratio is shown in Figure 1D. We can see that in all layers, the Gross BW Ratios of most sites are <0 , meaning that the overall response to black is stronger than that to white across all layers. We quantified this observation by showing that, in both the output layer and the input layer, the proportions of black-preferring sites are much larger than those of white-preferring sites (Fig. 1E, black-preferring sites vs white-preferring sites in the output layer: 87% vs 13% , $N = 118$, $p = 5.448 \times 10^{-16}$; in the input layer: 89% vs 11% , $N = 131$, $p = 2.275 \times 10^{-19}$; χ^2 goodness-of-fit test), and the median values of Gross BW Ratio are significantly <0 (Fig. 1E, output layer: -0.294 ± 0.020 , $N = 118$, $p = 1.567 \times 10^{-15}$; input layer: -0.186 ± 0.016 , $N = 131$, $p = 5.022 \times 10^{-19}$; sign test). We further showed that the median value of Gross BW Ratio in the output layer was significantly more negative than that in the input layer (Fig. 1E, $p = 1.263 \times 10^{-4}$, Wilcoxon rank-sum test), indicating that black–white asymmetry was more prominent in the output layer.

To determine whether black–white asymmetry is indeed more prominent in the output layer than in the input layer in the

same cortical column, we compared the Gross BW Ratio between the output layer and the input layer from the same probe placement. We first obtained the median value of Gross BW Ratio across all sites assigned to the corresponding layer for each probe placement and then directly compared these values between the output layer and the input layer for all probe placements. We found that the Gross BW Ratio was indeed more negative in the output layer than in the input layer (Fig. 1F, $N = 21$, $p = 0.0173$; Wilcoxon signed-rank test), demonstrating stronger black–white asymmetry in the output layer of the same cortical column. In addition, the black–white asymmetry between the output layer and the input layer was tightly correlated ($r = 0.5377$, $p = 0.0131$; Spearman's ρ), extending the notion of “phase columns” previously found in L4 of cat V1 (Jin et al., 2008; Y. Wang et al., 2015; Kremkow et al., 2016).

Based on the overall response, we showed that cortical black–white asymmetry first appears in the input layer and then becomes more pronounced in the output layer. The strong correlation of black–white asymmetry between the output layer and the input layer suggests the involvement of feedforward connections from the input layer to the output layer in the strengthening of black–white asymmetry within a cortical column.

The dynamics of black–white asymmetry are distinct between the output layer and the input layer

As is known, feedforward connections and recurrent connections function at different times. To help dissect these two mechanisms, we studied the temporal dynamics of black–white asymmetry and asked whether they differ between the output layer and the input layer. Concerning differences in latency time, we first aligned the temporal response of each site to the maximum response evoked by the onset of stimuli and then averaged across all sites in the output layer and in the input layer (temporal responses of all sites are shown in Extended Data Fig. 2-1). Population-averaged temporal responses to black and white in the output layer and the input layer are shown in Figure 2A and Figure 2B, respectively. From temporal dynamics in the input layer (Fig. 2B), two peaks that correspond to peak responses evoked by stimulus onset and stimulus offset are clearly evident. At the first peak, namely, the onset peak, the population-averaged response to black is stronger than that to white in both the output layer and the input layer. At the second peak, the offset peak, the population-averaged response to black remains stronger than that to white only in the output layer but becomes comparable to that to white in the input layer. These observations are confirmed when we obtained the temporal dynamics of the BW Ratio in both layers (the output layer, Fig. 2C; the input layer, Fig. 2D). At the onset peak, the BW Ratios in the output layer and the input layer are both negative, indicating a stronger black response. At the offset peak, the BW Ratio in the output layer remains negative, while the BW Ratio in the input layer becomes close to 0 , indicating comparable black and white responses. Similar results can be obtained when using the median, rather than the mean, of the population's temporal responses.

In addition to showing distinct temporal dynamics of black–white asymmetry between the output layer and the input layer, we calculated the proportion of black-preferring sites and white-preferring sites at the onset peak and at the offset peak. The output layer consistently included more black-preferring sites (Fig. 2E, black-preferring sites vs white preferring sites at the onset peak: 87% vs 13% , $N = 118$, $p = 5.448 \times 10^{-16}$; at the offset peak:

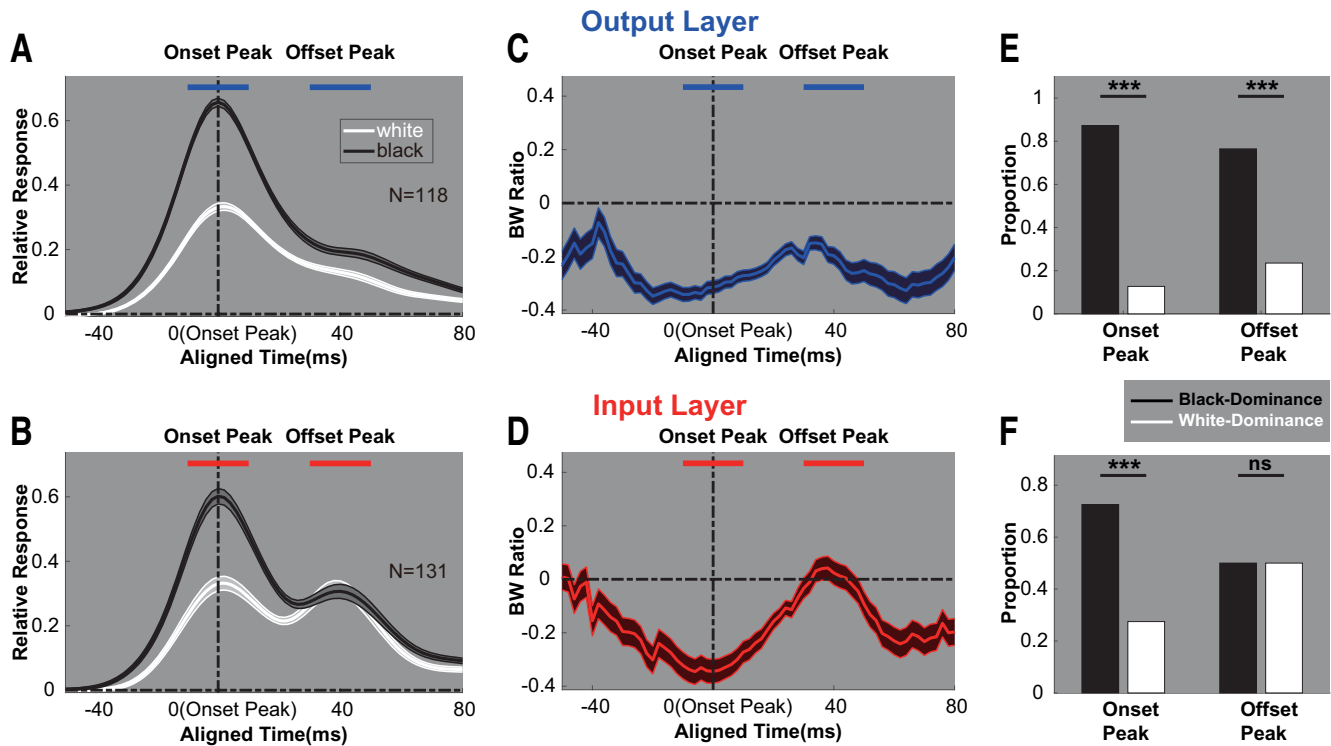


Figure 2. Distinct dynamics of black–white asymmetry in the V1 output layer and V1 input layer. **A**, Population-averaged temporal responses to black and white in the output layer. We aligned the temporal response to the onset peak for each site and then averaged them across all sites in the output layer. The black line and the white line indicate averaged temporal responses to black stimuli and white stimuli, respectively. Blue lines above the temporal responses indicate the time ranges for the onset peak and the offset peak. **B**, Population-averaged temporal responses to black and white in the input layer. Red lines above the temporal responses indicate the time ranges for the onset peak and the offset peak. **C**, Population-averaged temporal dynamics of the BW Ratio in the output layer. **D**, Population-averaged temporal dynamics of the BW Ratio in the input layer. **E**, Proportion of black-prefering sites (black bar) and white-prefering sites (white bar) at the onset peak and at the offset peak in the output layer. The onset peak response and the offset peak response were used to determine the relative strength of black and white at corresponding times. **F**, Proportion of black-prefering sites (black bar) and white-prefering sites (white bar) at the onset peak and at the offset peak in the input layer. For the aligned temporal response of all sites in LGN and V1, see Extended Data Figure 2-1.

76% vs 24%, $N = 85$, $p = 1.056 \times 10^{-6}$; χ^2 goodness-of-fit test). In the input layer, there are still more sites preferring black at the onset peak (Fig. 2F, 73% vs 27%, $N = 131$, $p = 2.538 \times 10^{-7}$; χ^2 goodness-of-fit test). Surprisingly, the number of sites preferred black and white are roughly the same at the offset peak (Fig. 2F, 50% vs 50%, $N = 130$, $p = 1$; χ^2 goodness-of-fit test).

Together, these results demonstrate that the dynamics of black–white asymmetry are distinct between the output layer and the input layer. At the onset peak, black–white asymmetry is strong in both the output layer and the input layer. At the offset peak, although the black and white responses are balanced in the input layer, black–white asymmetry remains strong in the output layer.

The feedforward mechanism alone cannot explain black–white asymmetry in the output layer

Since the population profile of black–white asymmetry across layers varied between the onset peak and the offset peak, we asked whether different mechanisms may account for black–white asymmetry at the onset peak and at the offset peak.

We first characterized the relationship of black–white asymmetry between the onset peak and the offset peak in the LGN, V1 input layer, and V1 output layer. We used the metrics Onset BW Ratio and Offset BW Ratio to quantify black–white asymmetry at the onset peak and at the offset peak, based on the onset peak response and the offset peak response, respectively. In both the LGN and V1 input layer, the Offset BW Ratio is negatively correlated with the Onset BW Ratio (LGN: Fig. 3A,

$N = 71$, $r = -0.96$, $p = 9 \times 10^{-40}$; input layer: Fig. 3B, $N = 130$, $r = -0.83$, $p = 4.34 \times 10^{-34}$; Spearman's ρ), showing the reversal of preferred polarity between the onset peak and the offset peak. In the V1 output layer, however, the Offset BW Ratio is independent of the Onset BW Ratio (Fig. 3C, $N = 85$, $r = 0.03$, $p = 0.78$; Spearman's ρ).

The similarity in the population profile between the LGN and the V1 input layer suggests that black–white asymmetry in the input layer is largely determined by the feedforward convergence of LGN neurons. The independence of the Offset BW Ratio and Onset BW Ratio in the output layer suggests that different mechanisms may be recruited at the onset peak and the offset peak in the output layer.

We then characterized the relationship of black–white asymmetry between the output layer and the input layer at the onset peak and at the offset peak. At the onset peak, although there are larger proportions of sites preferring black in the output layer than in the input layer, the median values of the output layer and the input layer are comparable (Fig. 4A, output layer: -0.3050 ± 0.0230 , $N = 118$; input layer: -0.3084 ± 0.0452 , $N = 131$; $p = 0.9221$; Wilcoxon rank-sum test). Additionally, the Onset BW Ratios of the output layer and the input layer are positively correlated (Fig. 4B, $N = 21$, $r = 0.75$, $p = 1.18 \times 10^{-4}$; Spearman's ρ), suggesting that feedforward connections from the input layer contribute to black–white asymmetry in the output layer at the onset peak. At the offset peak, in addition to a larger proportion of black-prefering sites in the output layer, the median value is more negative in the output layer than in the input layer (Fig. 4C,

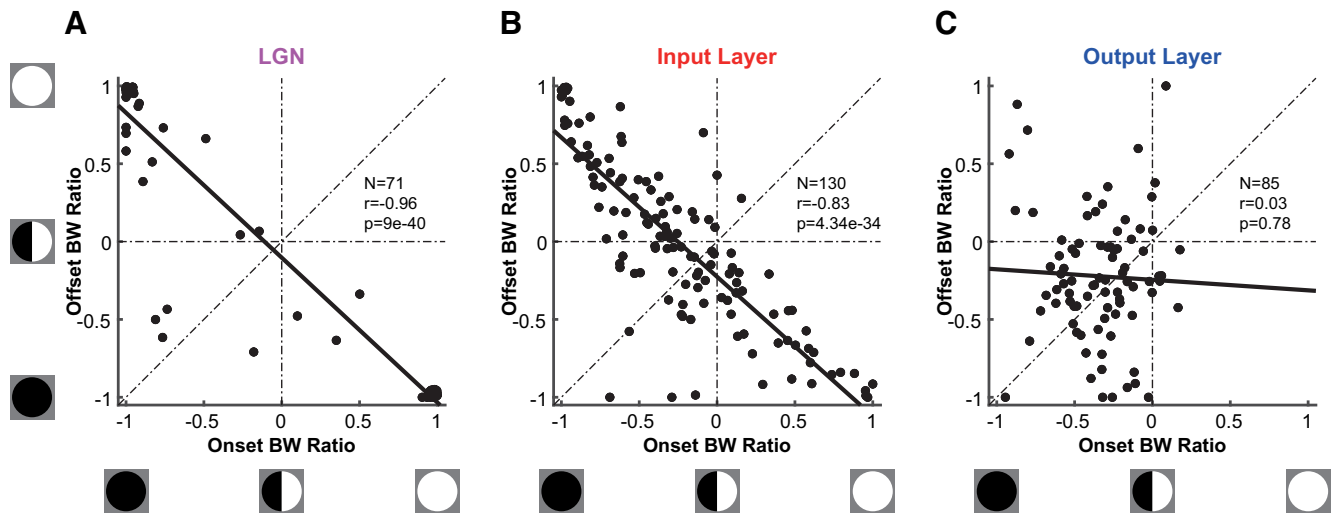


Figure 3. Black–white asymmetry at the onset peak and at the offset peak are independent in the V1 output layer. **A**, Relationship between Offset BW Ratio and Onset BW Ratio in the LGN. The Onset BW Ratio and Offset BW Ratio are calculated in the same manner as the Gross BW Ratio, except that they are based on the onset peak response and the offset peak response, respectively. Each dot represents data from one recording site. **B**, Relationship between the Offset BW Ratio and Onset BW Ratio in the V1 input layer. **C**, Relationship between the Offset BW Ratio and Onset BW Ratio in the V1 output layer.

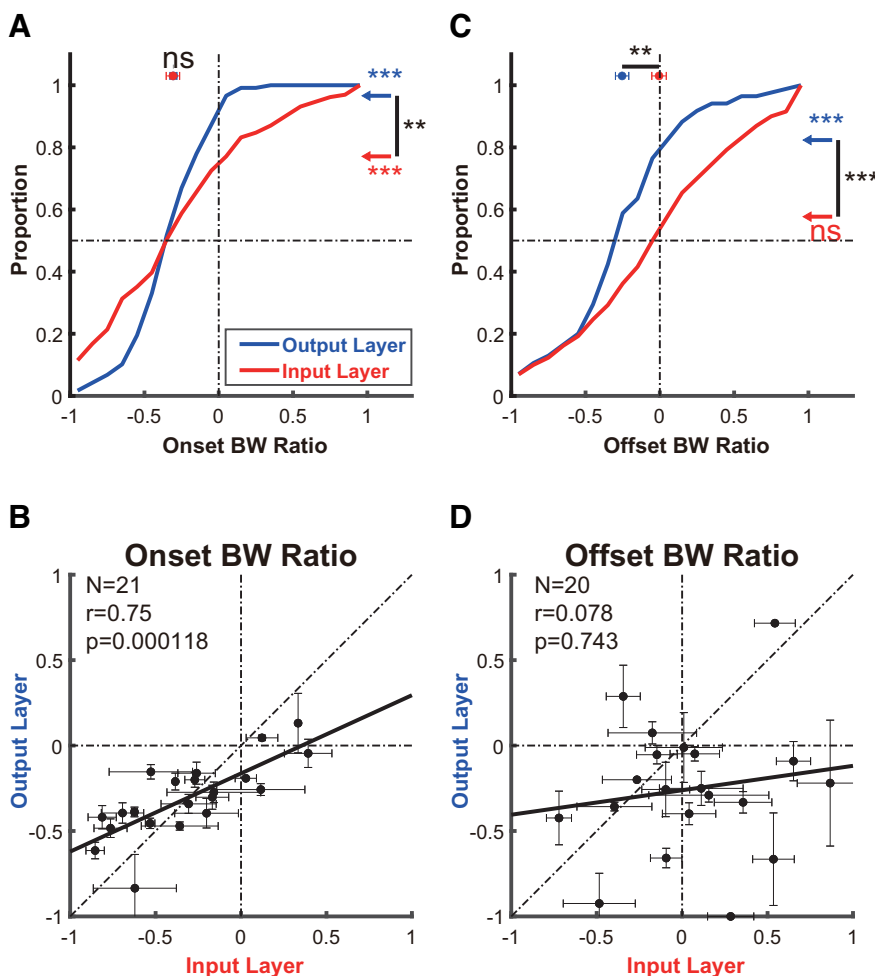


Figure 4. Black–white asymmetry between the V1 output layer and V1 input layer is independent at the offset peak. **A**, Cumulative distribution of Onset BW Ratios in the output layer (blue line) and in the input layer (red line). **B**, Relationship of Onset BW Ratios between the output layer and the input layer from the same probe placement. Each dot represents data from one probe placement. **C**, Cumulative distribution of Offset BW Ratios in the output layer (blue line) and in the input layer (red line). **D**, Relationship of Offset BW Ratios between the output layer and the input layer from the same probe placement.

output layer: -0.254 ± 0.045 , $N = 85$; input layer: -0.005 ± 0.049 , $N = 130$; $p = 0.0013$; Wilcoxon rank-sum test). Moreover, the Offset BW Ratios of the output layer and the input layer are not correlated (Fig. 4D, $N = 20$, $r = 0.078$, $p = 0.743$; Spearman's ρ), signifying that mechanisms other than the feedforward mechanism are recruited in the output layer at the offset peak.

We conclude from the above results that the feedforward mechanism contributes to black–white asymmetry in both the output layer and the input layer at the onset peak. At the offset peak, a purely feedforward mechanism cannot explain black–white asymmetry in the output layer, indicating the recruitment of other mechanisms.

The rebound response in the output layer is significantly suppressed, with the suppression strength depending on the location within the ON-OFF cortical map

As the feedforward mechanism alone cannot account for black–white asymmetry in the output layer at the offset peak, we explored the role of the recurrent mechanism.

First, we compared the population-averaged temporal response to white and black between the output layer and the input layer. Visual observation shows that, for both white (Fig. 5A) and black (Fig. 5B), the offset response is suppressed from the input layer to the output layer.

To quantify the observation of the suppressed offset response in the output layer, we calculated the relative offset peak response in relation to the onset peak response and

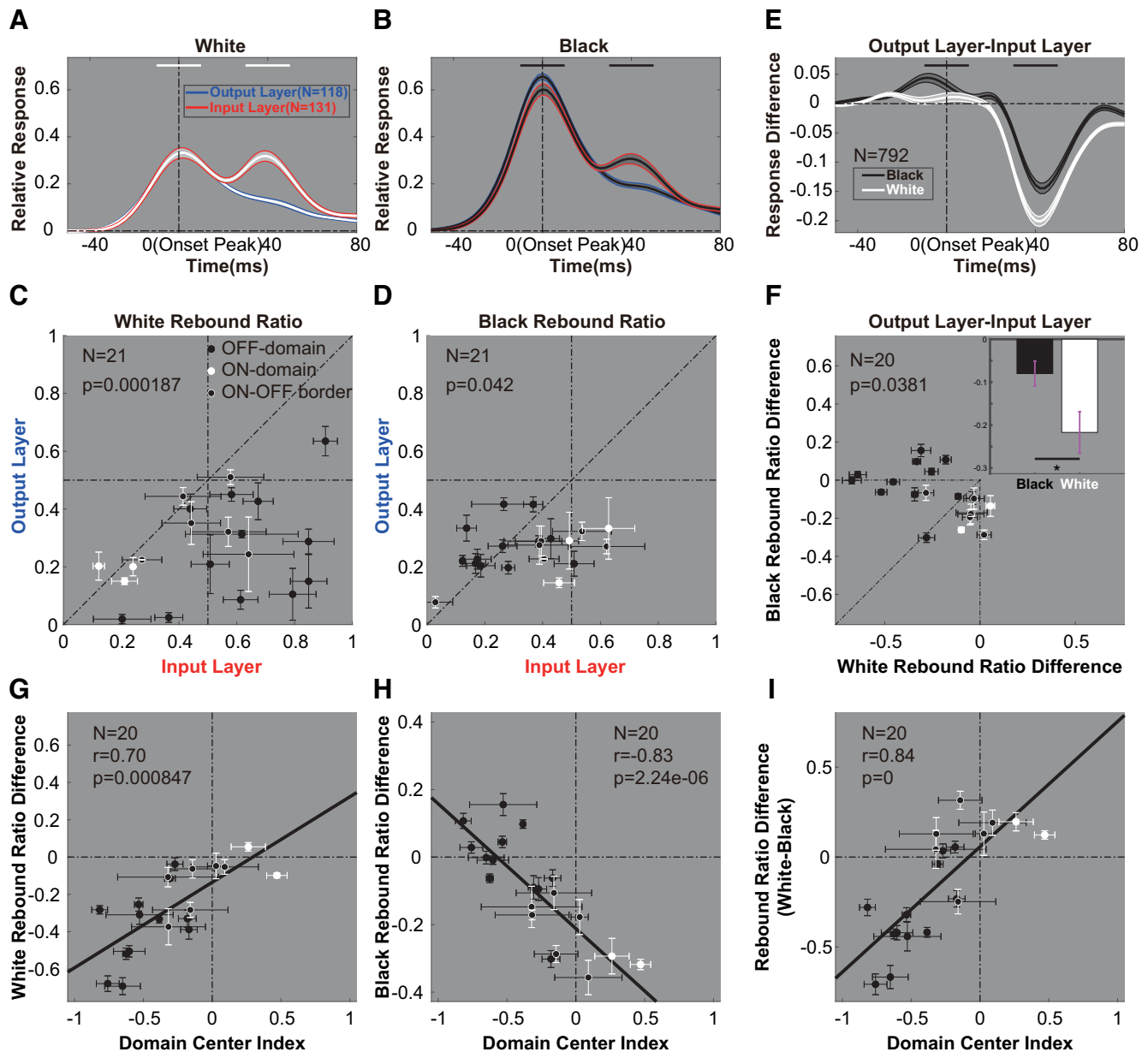


Figure 5. The rebound response is suppressed from the V1 input layer to the V1 output layer, with a dependence on the location within the ON-OFF cortical map. **A**, Population-averaged temporal response to white in the output layer (blue edge) and the input layer (red edge). **B**, Population-averaged temporal response to black in the output layer (blue edge) and the input layer (red edge). **C**, Comparison of the White Rebound Ratio between the output layer and the input layer in the same probe placement. The White Rebound Ratio is defined as $(R_{\text{white}}^{\text{offset}}) / (R_{\text{white}}^{\text{onset}} + R_{\text{white}}^{\text{offset}})$, where $R_{\text{white}}^{\text{onset}}$ is the onset peak response to white and $R_{\text{white}}^{\text{offset}}$ is the offset peak response to white. Each dot represents data from one probe placement. Solid white dots are from probe placements in the ON domain. Solid black dots indicate the OFF domain. Black dots outlined in white indicate the ON-OFF border. **D**, Comparison of the Black Rebound Ratio between the output layer and the input layer in the same probe placement. The Black Rebound Ratio is calculated in the same manner as the White Rebound Ratio, except that it is based on the onset peak response and the offset peak response to black. **E**, Population-averaged difference in temporal response between the output layer and the input layer to black (black line) and white (white line). **F**, Comparison of the Black Rebound Ratio Difference and White Rebound Ratio Difference in the same probe placement. The Black (White) Rebound Ratio in the output layer, subtracted by that in the input layer, gives rise to the Black (White) Rebound Ratio Difference. Inset, The comparison of the median value between the Black Rebound Ratio Difference and White Rebound Ratio Difference. **G**, Relationship between the White Rebound Ratio Difference and the Domain Center Index. The Domain Center Index, defined as the median of Onset BW Ratios from all L4 sites, represents the location of each probe placement within the ON-OFF domain. A value of -1 indicates an OFF domain center, 1 indicates an ON domain center, and 0 indicates the ON-OFF border. **H**, Relationship between the Black Rebound Ratio Difference and the Domain Center Index. **I**, Correlation of the difference between the White Rebound Ratio Difference and Black Rebound Ratio Difference with the Domain Center Index.

asked whether the relative offset peak response differed between the output layer and the input layer. We used the White Rebound Ratio to represent the relative strength between the offset peak response and the onset peak response to white stimuli. The White Rebound Ratio ranges from 0 to 1, with 0 indicating no rebound response, 1 indicating no onset response, and 0.5 indicating equal onset response and rebound response.

A larger value of the White Rebound Ratio means a stronger white rebound response. In Figure 5C, we show that the White Rebound Ratio was smaller in the output layer than in the input layer in the same probe placement ($N = 21$, $p = 1.87 \times 10^{-4}$; Wilcoxon signed-rank test), verifying the suppression of the white rebound response from the input layer to the output layer in the same cortical column. Likewise, we

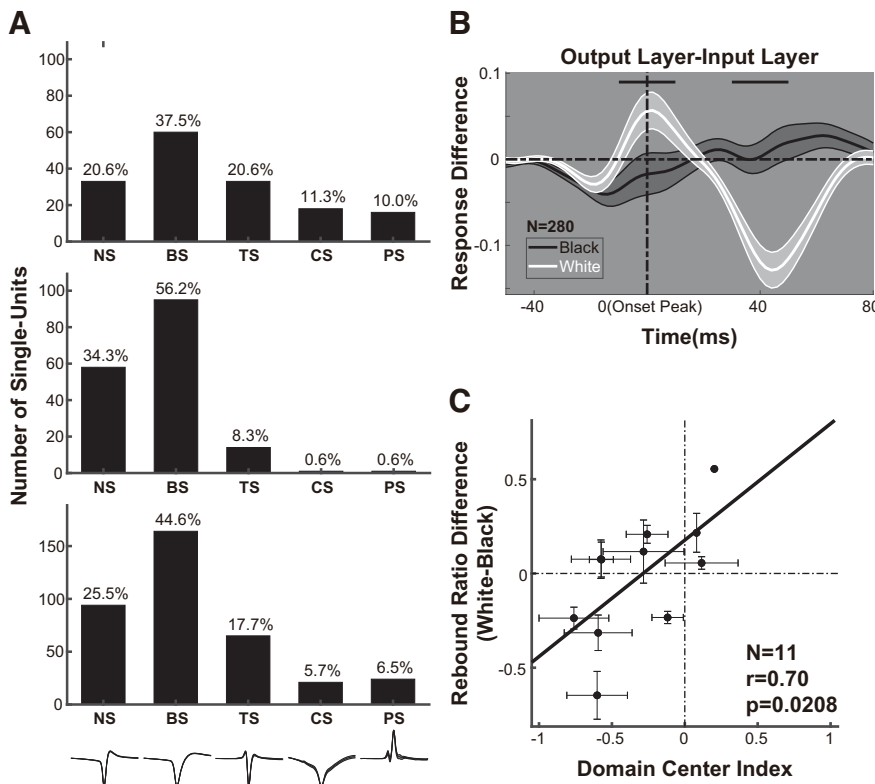


Figure 6. Suppression of rebound response in the output layer and its correlation with ON-OFF cortical map locations for putative excitatory neurons. **A**, Number and percentage of each type of single unit in the input layer (top), in the output layer (middle), and across all single units (bottom). Population-averaged spike waveforms of each type of single unit are depicted below the x axis. Units are classified as NS (narrow-spiking units), BS (broad-spiking units), TS (triphasic-spiking units), CS (compound-spiking units), and PS (positive-spiking units). In our analysis, units categorized as BS, TS, CS, and PS are grouped as putative excitatory neurons. **B**, Population-averaged difference in temporal response between the output layer and the input layer to black (black line) and white (white line) for putative excitatory neurons. **C**, Correlation of the difference between the White Rebound Ratio Difference and Black Rebound Ratio Difference with the Domain Center Index for putative excitatory neurons.

demonstrated that the black rebound response is suppressed in the output layer (Fig. 5D, $N = 21$, $p = 0.042$; Wilcoxon signed-rank test).

We next investigated whether the suppression strengths evoked by black and white were different. For either black or white, we averaged differences in temporal response between the output layer and the input layer across all probe placements. The offset response to white was evidently suppressed to a greater extent than the offset response to black (Fig. 5E). For each probe placement, we also compared the decrease in the Black Rebound Ratio (Black Rebound Ratio in the output layer minus Black Rebound Ratio in the input layer) with the decrease in the White Rebound Ratio (White Rebound Ratio in the output layer minus White Rebound Ratio in the input layer). We found that the decrease in the White Rebound Ratio was larger than the decrease in the Black Rebound Ratio (Fig. 5F, $N = 20$, $p = 0.0381$; one-sided Wilcoxon signed-rank test), suggesting stronger suppression for white than for black at the population level. A suppressed rebound response in the output layer could also be observed when considering only the signal transmission from L4 to L2/3 (data not shown) or based on the median value, rather than the mean value, of the population's temporal responses (data not shown).

Previous studies have shown an organized ON-OFF cortical map in the cat visual cortex, where neurons preferring white are

grouped in the ON domain and those favoring black are clustered in the OFF domain (Jin et al., 2008; Y. Wang et al., 2015; Kremkow et al., 2016). To evaluate whether the suppression of the rebound response depends on the location in the ON-OFF cortical map, we determined whether the probe placement was in the ON domain (Fig. 5, solid white dots), OFF domain (Fig. 5, solid black dots), or ON-OFF border (Fig. 5, black dots outlined in white) based on the consistency of Onset BW Ratios for all sites in L4 (for details, see Materials and Methods). We further defined the metric Domain Center Index to represent the location within the ON-OFF map: negative for proximity to the OFF domain and positive for proximity to the ON domain. We found that the suppression of the white rebound response was stronger in the OFF domain (Fig. 5G, $N = 20$, $r = 0.70$, $p = 0.000847$; Spearman's ρ), while the suppression of the black rebound response was stronger in the ON domain (Fig. 5H, $N = 20$, $r = -0.83$, $p = 2.24 \times 10^{-6}$; Spearman's ρ). Additionally, we found that the relative suppression strength between black and white also depends on the location of the probe placement in the ON-OFF cortical map (Fig. 5I, $N = 20$, $r = 0.84$, $p = 0$; Spearman's ρ): in the OFF domain, the white rebound response is suppressed more strongly than the black rebound response, whereas in the ON domain, the suppression strength of the rebound response tends to be stronger for black than for white.

Since the MUA signal pools responses from both excitatory and inhibitory populations (Buzsáki, 2004), we asked whether the above findings, based on the MUA signal, still hold true when only putative excitatory neurons are considered. Therefore, we conducted spiking sorting for V1 recordings and separated all single units into putative excitatory neurons and inhibitory neurons (for details, see Materials and Methods). When only putative excitatory neurons were considered, the suppression of the white rebound response was stronger (Fig. 6B), and the difference between the suppression strengths of black and white was also dependent on the location within the ON-OFF cortical map (Fig. 6C, $N = 11$, $r = 0.70$, $p = 0.0208$; Spearman's ρ).

Collectively, we demonstrated that, at the offset peak, cortical suppression is involved, weakening the offset response in the output layer. Moreover, the suppression strength depends on the location within the ON-OFF cortical map, with stronger suppression of white in the OFF domain and stronger suppression of black in the ON domain. Since the OFF domain is more prevalent in V1, suppression is stronger for white than for black at the population level, transforming a balanced black and white population response in the input layer to a stronger black population response in the output layer.

A model with cortical suppression explains black–white asymmetry in the output layer

To further test the hypothesis that cortical suppression contributes to black–white asymmetry in the output layer, we compared

the performance of two computational models. In Model I (No Suppression), neurons in the output layer only receive convergent connections from the input layer. In Model II (With Suppression), in addition to feedforward convergence from the input layer, neurons in the output layer receive delayed suppression, and the suppression strength depends on the polarity of stimuli (Fig. 7A; for details, see Materials and Methods). Adjusted goodness of fit (adjusted R^2) was used to quantify model performance. Although Model I can already explain neuronal response well, demonstrating the feedforward contribution, Model II outperforms Model I (Fig. 7B,C, $N = 118$; Model I: 0.9476 ± 0.0067 for adjusted goodness of fit; Model II: 0.9748 ± 0.0031 for adjusted goodness of fit; paired difference: 0.0264 ± 0.0041 ; $p = 4.209 \times 10^{-21}$; Wilcoxon signed-rank test), confirming the contribution of delayed suppression. Similar results can be achieved using either the Akaike information criterion or the Bayesian information criterion.

We then compared the relative suppression strength between white and black for sites that were well fitted by Model II (adjusted $R^2 > 0.8$, 117 of 118 sites, Fig. 7B, solid dots). For most sites, the relative suppression strength between white and black differed significantly (Fig. 7D, 110 of 117 sites), and sites that had stronger white suppression greatly outnumbered those that had stronger black suppression (Fig. 7E, sites with stronger white suppression vs sites with stronger black suppression: 85 vs 25), consistent with the experimental findings of stronger suppression of the white population response in the output layer (Fig. 5E,F).

Interestingly, there is a trend that sites with a stronger preference for black at the onset peak (Fig. 7F, darker blue dots) receive stronger suppression of white (above the diagonal). This observation was validated when we correlated the relative suppression strengths between white and black with the Onset BW Ratio (Fig. 7G, $N = 117$, $r = -0.5$, $p = 1.56 \times 10^{-8}$; Spearman's ρ). This correlation aligned with the experimental evidence of location-dependent relative suppression strength within the ON-OFF cortical map (Fig. 5I).

Our results suggest that, together with feedforward convergence from the input layer, cortical suppression that is delayed and polarity-selective is also recruited for black–white asymmetry in the output layer.

To further probe the possible source of this suppression, we performed Granger causality analysis on spike trains collected in the experiment and characterized the interactions within and between cortical layers in the processing of black and white information (Fig. 1A). For one example probe placement (Fig. 8A), the most evident interactions were within the output layer (within L2/3, within L5 and from L2/3 to L5). In addition to feedforward connections from L4 to L2/3 and from L4 to L5, strong recurrent interactions within the output layer were the most apparent when we averaged the Granger causality values across 19 probe placements that had at least 5 electrodes with a high SNR (Fig. 8B). The predominance of connections within the output layer (Fig. 8C, $p = 1.5000 \times 10^{-6}$, $p = 1.4204 \times 10^{-7}$ and $p = 2.2190 \times 10^{-14}$ for Granger causality values within the output layer vs within the input layer, within the output layer vs from the input layer to the output layer, within the output layer vs from the output layer to the input layer, respectively; Kruskal–Wallis test, Bonferroni-corrected) suggests that the suppression may originate from recurrent connections within the V1 output layer.

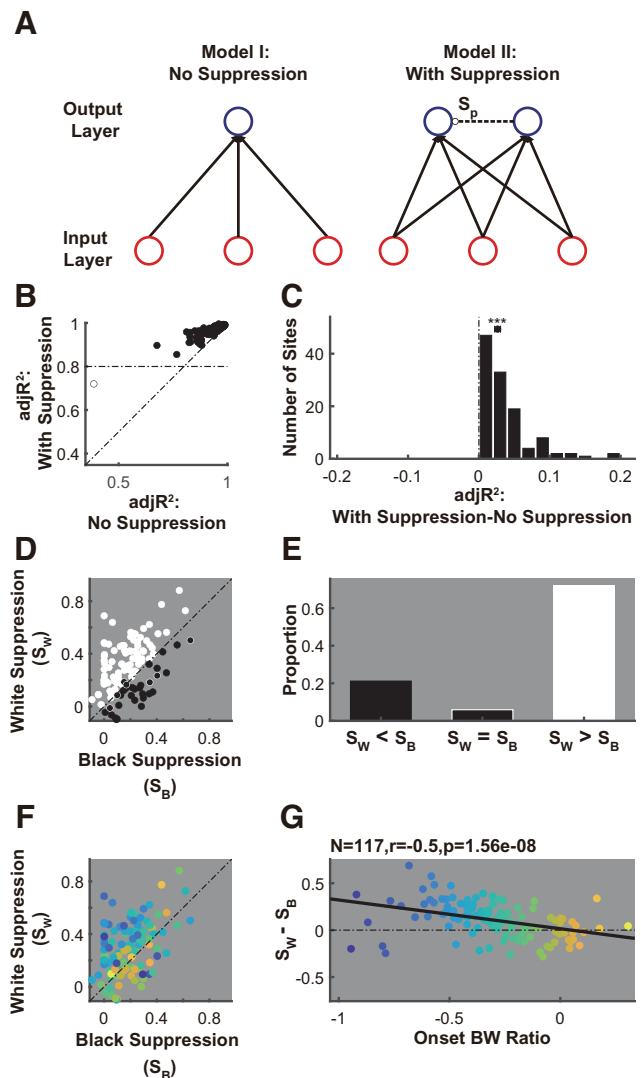


Figure 7. Delayed and polarity-selective suppression is recruited in the output layer, contributing to black–white asymmetry. **A**, Illustration of two computational models for explaining neuronal responses evoked by black and white in the output layer. In Model I (No Suppression, left), neurons in the output layer only receive feedforward connections from the input layer. In Model II (With Suppression, right), in addition to feedforward connections from the input layer, neurons in the output layer receive delayed and polarity-selective suppression (S_p). **B**, Comparison of model performance between Model II (With Suppression) and Model I (No Suppression) based on adjusted goodness of fit, which takes the number of free parameters into account. Each dot represents data from one recording site in the V1 output layer. **C**, Distribution of the difference in model performance between Model II (With Suppression) and Model I (No Suppression). **D**, Comparison of the suppression strength between white and black for all sites in the output layer. Solid black and white dots represent sites with stronger black and white suppression, respectively. Dots outlined in white represent comparable black and white suppression. **E**, Proportions of sites in the output layer that receive stronger black suppression (solid black bar), stronger white suppression (solid white bar), and similar strengths of black and white suppression (black bar, white edge). **F**, Comparison of the suppression strength between white and black for all sites in the output layer. The color of each dot represents Onset BW Ratio of corresponding site. A gradient of blue to yellow is used to denote the values, with darker blue representing a more negative Onset BW Ratio. **G**, Correlation of the relative suppression strength between white and black with the Onset BW Ratio. The color coding of each dot aligns with the schema presented in **F**.

The interlaminar differences in spatial RF also varied dynamically

In addition to black–white asymmetry in response strength, previous studies have noted black–white asymmetry in RF size: cat

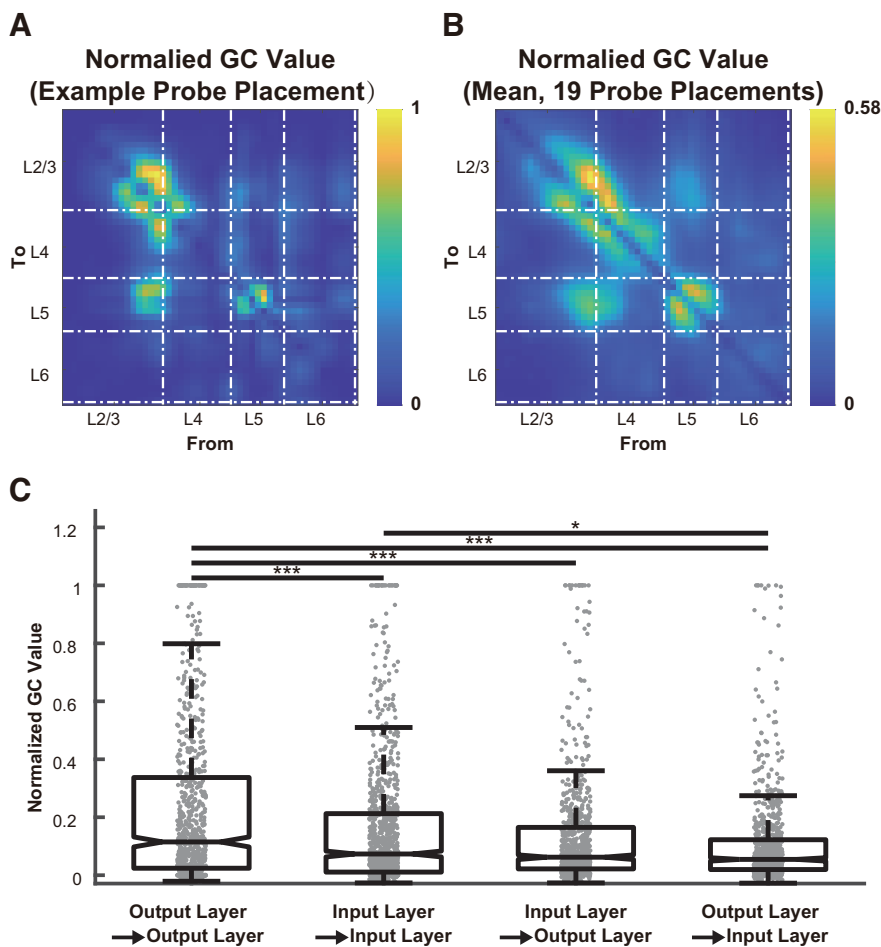


Figure 8. Strong recurrent connections within the V1 output layer. **A**, Normalized Granger causality values for an example probe placement. The source layer (sender of the projection, from) is positioned along the abscissa, and the target layer (receiver of the projection, to) is represented along the ordinate. **B**, Normalized Granger causality values averaged across 19 probe placements that have at least 5 electrodes with a high SNR. **C**, Comparison of normalized GC values among intralaminar and interlaminar pairs. On each box, the central mark indicates the median, and the bottom and top edges of the box indicate the 25th and 75th percentiles, respectively. The whiskers extend to the most extreme data points not considered outliers, and the notches represent the 95% CI (same for the following figures). Each gray dot represents a pair of projections. *x* axis labels specifying the projection's sender (source) and receiver (target). The arrow's direction indicates the receiver (target).

LGN (X. Liu et al., 2021); cat V1 (S. Liu et al., 2007; Kremkow et al., 2014; Mazade et al., 2019); and cat higher visual areas (Piché et al., 2013; de Souza and Casanova, 2019). We also wondered whether RF sizes for ON/OFF subregions vary dynamically across cortical layers. To characterize the interlaminar differences in the spatial RF, we estimated RF size for ON and OFF subregions at different times (Fig. 1B).

First, we studied the differences in RF size between OFF and ON subregions, which was achieved by comparing the RF size obtained from the black stimulus ensemble (Black Radius) and white stimulus ensemble (White Radius) at the onset peak. In both the output layer and the input layer, the Black Radius is larger than the White Radius (Fig. 9A, output layer: $N = 86$, $p = 1.01 \times 10^{-8}$; Fig. 9B, input layer: $N = 51$, $p = 0.000198$; Wilcoxon signed-rank test), in accordance with previous cat studies (but see monkey studies: Chichilnisky and Kalmar, 2002; Archer et al., 2021). Additionally, the differences between the Black Radius and White Radius are comparable between the output layer and the input layer ($(\text{WhiteRadius} - \text{BlackRadius}) / (\text{BlackRadius})$, output layer: -0.0925 ± 0.0141 , $N = 86$; input layer: -0.0721 ± 0.0292 , $N = 51$; $p = 0.9414$; Wilcoxon rank-sum test).

Subsequently, we characterized the differences in RF size between the output layer and the input layer. At the onset peak, RF size is always larger in the output layer than in the input layer, regardless of stimulus ensemble (Fig. 9C, white ensemble: $p = 0.00439$; black ensemble: $p = 0.00186$; black and white ensemble: $p = 0.000782$; Wilcoxon rank-sum test). At the offset peak, however, RF sizes are similar between the output layer and the input layer (Fig. 9D, white ensemble: $p = 0.419$; black ensemble: $p = 0.071$; black and white ensemble: $p = 0.786$; Wilcoxon rank-sum test).

Finally, we compared the RF size by combining the ON subregion and OFF subregion between the onset peak and the offset peak. In both the LGN and the V1 input layer, the RF size increases at the offset peak (LGN: Fig. 9E, $N = 63$, $p = 3.92 \times 10^{-9}$; V1 input layer: Fig. 9F, $N = 91$, $p = 3.61 \times 10^{-9}$; Wilcoxon signed-rank test). Remarkably, RF sizes at the offset peak even decreased compared with those at the onset peak in the V1 output layer (Fig. 9G, $N = 52$, $p = 0.0362$; Wilcoxon signed-rank test). Similar results as for the MUA can also be obtained when only putative excitatory neurons are considered (onset radius vs offset radius, input layer: $N = 32$, $p = 0.0397$; output layer: $N = 32$, $p = 0.304$; Wilcoxon signed-rank test).

Consistent with our findings of a suppressed rebound response in the output layer, the dynamic change in spatial RF across cortical layers also suggests that, at the offset peak, cortical suppression may come into play and reshape the RF in the output layer (Fig. 9E–G) from the enlarged RF size of the input layer.

Discussion

By comparing the population profiles of black–white asymmetry among the LGN, V1 input layer, and V1 output layer, we demonstrated the dynamic recruitment of the feedforward mechanism and the recurrent mechanism for the generation of cortical black–white asymmetry. At the onset peak, the feedforward mechanism contributes to strong black–white asymmetry in both the output layer and the input layer. At the offset peak, delayed and polarity-selective suppression further transforms balanced black and white population responses in the input layer to black-dominant population responses in the output layer.

Laminar processing of black–white asymmetry

To our knowledge, this study is the first to systematically investigate the laminar processing of black–white asymmetry in the cat primary visual cortex. Previous studies using linear probes either did not perform laminar analysis (St-Amand and Baker, 2023) or only focused on a specific layer (Jin et al., 2008; Komban et al.,

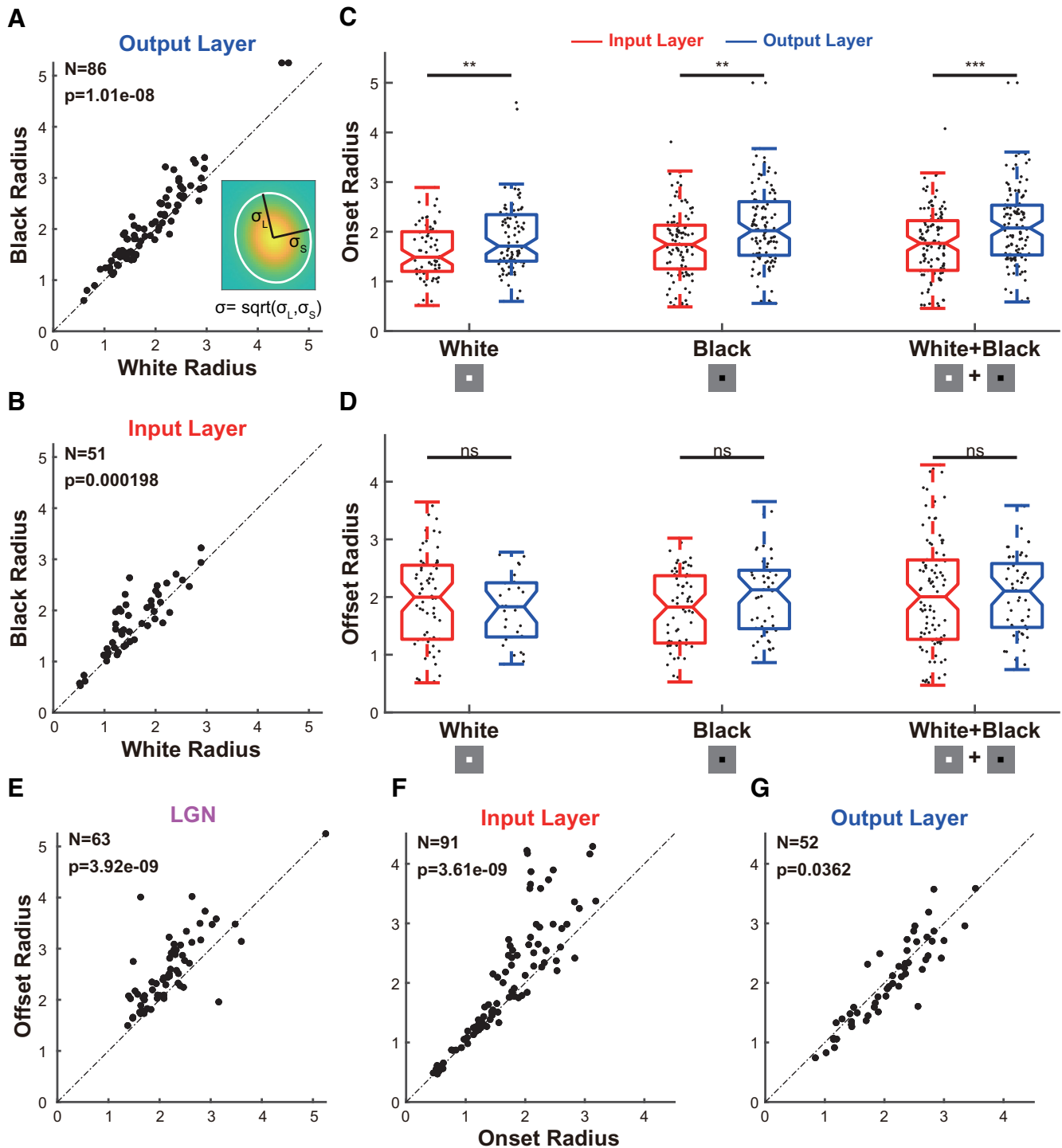


Figure 9. The RF size at the offset peak is larger than that at the onset peak in the V1 input layer but not in the V1 output layer. **A**, Comparison of the Black Radius and White Radius at the onset peak in the output layer. The Black Radius and White Radius are the RF radius from the black stimulus ensemble and from the white stimulus ensemble, respectively. Each dot represents data from one recording site. Inset, The 2D tilted Gaussian fitting of spatial RF and the demonstration of the calculation of RF radius, which is the geometric mean of the radius along the long axis and that along the short axis. **B**, Comparison of the Black Radius and White Radius at the onset peak in the input layer. **C**, Comparison of the Onset Radius between the output layer and the input layer from different stimulus ensembles. The Onset Radius is the RF radius at the onset peak. The box plots are overlaid with values from each single recording site. Red represents data from the input layer. Blue represents data from the output layer. **D**, Comparison of the Offset Radius between the output layer and the input layer in different stimulus ensembles. The Offset Radius is the RF radius at the offset peak. **E**, Comparison between the Offset Radius and Onset Radius in the LGN. The Offset (Onset) Radius is the RF radius at the offset (onset) peak combining black and white stimulus ensembles. **F**, Comparison between the Offset Radius and Onset Radius in the V1 input layer. **G**, Comparison between the Offset Radius and Onset Radius in the V1 output layer.

2014; Y. Wang et al., 2015). Additionally, imaging studies only had access to the superficial layer (Onat et al., 2011; Rekauszke et al., 2016). The earliest studies on the laminar pattern of black–white asymmetry were performed in

monkey V1 (Yeh et al., 2009; Xing et al., 2010). Focusing on the onset peak response, they also found stronger black–white asymmetry in the output layer, similar to our findings in cat V1.

In cat area 21a (an area of the cat ventral pathway) and PMLS (an area of the cat dorsal pathway), recent studies have found that black–white asymmetry is preserved (Piché et al., 2013; de Souza and Casanova, 2019). Since little is known about the black–white asymmetry in the output layer of cat V1 before the current study, our results fill in the gap in knowledge regarding the transmission of black–white asymmetry from the striate cortex to the extrastriate cortex.

Feedforward contribution to black–white asymmetry

Strong black–white asymmetry in both the output layer and the input layer at the onset peak may result from the feedforward convergence of OFF-dominant geniculate afferents, which are reported to occupy larger cortical territories (Jin et al., 2008) and make stronger thalamocortical connections (Jin et al., 2011b).

At the offset peak, we found that the preferred polarity reversed in the LGN, meaning that the white rebound response will be stronger in OFF LGNs. Theoretically, the feedforward convergence of OFF-dominant geniculate afferents should result in a stronger white rebound response in the V1 input layer. However, the black and white rebound responses are balanced in the V1 input layer. We attribute this fact to the stronger rebound of the ON pathway, which is observed in our LGN and V1 recordings (Extended Data Fig. 2-1) and has been reported previously: cat LGN (Jin et al., 2011a; H. Li et al., 2017) and cat V1 (Komban et al., 2014; Mazade et al., 2022).

Cortical suppression of rebound response in the output layer

Comparing interlaminar dynamics to black and white, we found that the rebound response is suppressed in the output layer and that the relative suppression strength between white and black depends on the location within the ON-OFF cortical map. The suppression of the rebound response in the output layer was also observed in simple cells in monkey V1 (P. E. Williams and Shapley, 2007). By modeling the dynamics of orientation selectivity, T. Wang et al. (2020) revealed two laminar subnetworks of suppression in monkey V1, with a fast suppression centered in the input layer and a slow suppression centered in the output layer. The suppression we found in the output layer is similar to their slow suppression in terms of laminar location and latency. Considering the differences in animal models (cat vs monkey) and visual stimuli (uniform squares smaller than RF size vs gratings of optimal size), clarifying whether our cortical suppression and their slow suppression have the same neural substrates is crucial to our understanding of the general principles of information processing in a cortical column.

At the population level, we found stronger suppression of the white rebound response than the black rebound response. Stronger suppression of the ON pathway after stimulus onset has been reported in cat V1 (Taylor et al., 2018; St-Amand and Baker, 2023). Our finding of stronger white suppression after stimulus offset resembles results in awake monkey V1 (Yang et al., 2022, their Figs. 5 and 6).

In the current study, the term “suppression” is used to refer to the reduction of neuronal response, but the underlying neural circuits can be either the increase of inhibition or the decrease of excitation. Our experimental results and model results suggested that the suppression is of intracortical recurrent origin and contributes to black–white asymmetry in the output layer. The underlying neural circuits and possible functional roles of the suppressed rebound response, as well as its dependence on stimulus polarity, will be fruitful research directions.

Functional role of black–white asymmetry

In correspondence with the black–white asymmetry of natural scenes (Geisler, 2008; Ratliff et al., 2010; Cooper and Norcia, 2015; Mazade et al., 2019, 2022), visual perception induced by black and white stimuli also shows asymmetry (Blackwell, 1946; Bowen et al., 1989; Chan and Tyler, 1992; Kontsevich and Tyler, 1999; Chubb and Nam, 2000; Badcock et al., 2005; Komban et al., 2011, 2014; Lu and Sperling, 2012; Buchner and Baumgartner, 2007; Luo-Li et al., 2016, 2018; Khani et al., 2018). A recent study found a neural correlate in tree shrew V1 for the perceptual difference between black and white (Khani et al., 2018). Given the observed differences in the strength and dynamics of black–white asymmetry between the output layer and the input layer, whether the strategies for encoding visual inputs vary in different layers and the relevance of different cortical layers in visual perception needs further investigation.

In addition to being selective to stimulus polarities, cortical neurons also show preferences for other visual features, such as orientation, direction, and spatial frequency. Whether a canonical neural circuit is responsible for these feature preferences is consistently of great interest for system neuroscientists. Black–white asymmetry is reportedly related to orientation selectivity, spatial frequency selectivity, and spatial resolution in the input layer of cat V1 (Kremkow et al., 2016; Kremkow and Alonso, 2018; Najafian et al., 2022; St-Amand and Baker, 2023). Recent research proposes that cortical direction selectivity is attributable to variations in timing and strength between the ON and OFF pathways (Shariati and Freeman, 2012; Luo-Li et al., 2018; Chariker et al., 2021, 2022). Since we found distinct interlaminar temporal dynamics of black and white, our next step is to study the relationship between black–white asymmetry and other feature selectivities, as well as their dependence on the intralaminar and interlaminar interactions in the primary visual cortex.

Limitations of the study

Our study is based on analyzing neuronal responses evoked by small black and white squares, whereas recent studies have shown that stimulus size modulates the relative strength of black and white (Jansen et al., 2019; Mazade et al., 2019, 2022) and influences the working status of the neuronal network (Han et al., 2021a; Y. Li et al., 2022). In addition to stimulus size, stimulus contrast, stimulus duration, luminance range, and background luminance, all influence the relative strength of black and white (Mazade et al., 2019, 2022; Rahimi-Nasrabadi et al., 2021, 2023). The dependence of laminar patterns and the neural mechanisms of black–white asymmetry on different stimulus configurations remain to be investigated in future studies.

Currently, the contributions of two principal mechanisms to black–white asymmetry are studied, but other mechanisms may certainly be involved, such as the feedback connection from the higher-order cortex (Galuske et al., 2002; Hirsch and Martinez, 2006), the direct thalamic afferents to the output layer (Binzegger et al., 2004), or the fast suppression found in cat V1 and in the input layer of monkey V1 (T. Wang et al., 2020; St-Amand and Baker, 2023).

In the current study, the animals were anesthetized. The effect of the anesthetic, propofol, on neuronal responses along the cortical column remains controversial (Redinbaugh et al., 2020; Bastos et al., 2021). Whether propofol will selectively influence the feedforward or recurrent connection is also unclear (Andrada et al., 2012; Boly et al., 2012; Sanders et al., 2018; Aggarwal et al., 2019; Weiner et al., 2023). Future studies can use awake animals, disrupt neuronal responses at different times, and test whether animal

behavior is affected to determine the perceptual correlates of the diverse interlaminar temporal dynamics we found in anesthetized animals.

We probed the feedforward and recurrent mechanisms based on comparison (Figs. 5 and 9) and correlation (Fig. 8) analyses among different cortical layers in the time domain. Previous theoretical and experimental studies have suggested that the feedforward and feedback signals are mediated by γ and α/β rhythms, respectively (Bastos et al., 2012, 2015; Van Kerkoerle et al., 2014). We also used Granger causality analysis on our dataset in the frequency domain, but we did not observe obvious oscillations in any frequency band. This might be because of the brief durations and small sizes of the stimuli in our study. To obtain more conclusive evidence for the involvement of the feedforward and recurrent/feedback mechanisms, future studies should causally manipulate neural circuits in V1 and the higher-order visual cortex, such as reversible cortical cooling (Galuske et al., 2002; Bardy et al., 2006; Carrasco et al., 2015) or GABA inactivation (Nelson et al., 1994; Hensch and Stryker, 2004; Chen et al., 2014).

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