Title: Premature vision drives aberrant development of response properties in primary visual cortex

Abbreviated Title: Premature vision drives aberrant development

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ABSTRACT:

Development of the mammalian visual system is thought to proceed in two stages. In the first stage, before birth in primates and before eye opening in altricial mammals, spontaneous activity generated by the retina and cortex shapes visual brain circuits in an activity-dependent but experience-independent manner. In the second stage, visual activity generated by sensory experience refines receptive fields. Here we investigated the consequences of altering this sequence of events by prematurely opening one or both eyes of ferrets and examining visual receptive fields in monocular cortex after the closure of the critical period for ocular dominance plasticity. We observed that many cells in animals with prematurely-opened eyes exhibited low-pass temporal frequency tuning and increased temporal frequency bandwidths, and these cells showed slightly increased orientation and direction selectivity index values. Spontaneous activity was greatly elevated in both hemispheres following the premature opening of one or both eyes, suggesting a global change in circuit excitability that was not restricted to cells that viewed the world through the prematurely opened eye. No major changes were noted in spatial frequency tuning. These results suggest that premature visual experience alters circuit excitability and visual receptive fields, in particular with respect to temporal processing. We speculate that closed lids in altricial mammals serve to prevent visual experience until circuits are initially established and are ready to be refined by visual experience.

INTRODUCTION

The proper development of visual cortical circuits depends on both experience-independent (Katz and Shatz 1996, Wong 1999) and experience-dependent (Huberman et al 2008, Wang et al., 2010) processes. Classically, these mechanisms have been divided into two sequential stages: an early stage, before the onset of visual experience, in which molecular cues and spontaneous activity in retina and cortex guide initial circuit formation (Katz and Shatz 1996, Wong 1999), followed by a period in which activity driven by visual experience refines circuit function (Huberman et al 2008, Li et al,. 2006, Wang et al., 2010). The sequential nature of these two phases presumably ensures a developmental trajectory in which circuits achieve a state of maturation that provides proper support for the onset of experience-driven mechanisms that finalize the construction process.

Given the sequential nature of visual development, it is interesting to ask if there are any positive or negative consequences of violating this sequence by introducing patterned visual stimulation at earlier time points. Are there significant changes that cannot be reversed even with subsequent visual experience? These questions are especially important to address in light of the rising population of human infants born very prematurely (Crump et al., 2019), who receive visual stimulation during what is typically a presensory period (Colonnese et al. 2010).

To address these questions, we have examined the impact of premature visual experience on receptive fields in visual cortex of the ferret. Ferrets undergo a long postnatal developmental period and have a history of foundational developmental studies in vision. Ferrets are born with their eyes closed – a condition that is maintained for 30-35 days (Issa et al., 1999) – making it possible to introduce inappropriately early visual experience by opening the lids with forceps,

without introducing factors related to immature birth. We opened zero, one, or both eyes early, and evaluated receptive fields in primary visual cortex electrophysiologically after the closure of the critical periods for direction selectivity and ocular dominance. We studied monocular receptive fields only, so that we could be sure of the developmental condition of the eye, necessarily the contralateral eye, that was driving the receptive field properties we observed.

We observed substantial changes in temporal frequency tuning in monocular cells that observed the world through an early-opened eye. These cells, on average, exhibited strikingly broad tuning for temporal frequency with markedly enhanced responses at low temporal frequencies. These major alterations in visual selectivity were not present in all receptive field properties, as orientation and direction tuning in these cells were only slightly altered. By contrast, we observed substantial changes in spontaneous firing rates in both hemispheres after either or both eyes were opened early, suggesting that premature vision has a more global impact on the establishment of a firing rate set point in cortex (Turrigiano and Nelson, 2004; Hengen et al. 2013).

In all, these results suggest that premature visual experience causes lasting changes in temporal processing and in the baseline tone of cortical circuits. The changes in temporal frequency tuning are likely to have an impact on motion perception. To perceive a moving object, an animal must have knowledge of the object's direction and speed. The ratio of the temporal frequency of a stimulus to its spatial frequency is its speed, so temporal frequency tuning provides critical information about stimulus speed. Human babies that are born very prematurely are a heterogenous group with a wide variety of visual deficits (Kozeis 2010, Dutton 2013, Sakki et al., 2018), but even when one excludes cases of known brain or retinal damage,

very premature babies exhibit increased thresholds for motion perception later in life (Taylor et al., 2009, Hou et al., 2011). Our results in ferret raise the possibility that inappropriately early visual experience could be an important factor that contributes to lasting motion processing deficits in humans born very prematurely.

Part of this work appeared as the PhD thesis of SVG (Griswold, 2024).

METHODS

All experimental procedures were approved by the Brandeis University's Institutional Animal Care and Use Committee (IACUC) and performed in compliance with National Institutes of Health guidelines.

Animal source and housing: Ferrets (*Mustelo putorius furo*) were obtained from Marshall Bio-Resources. Litters of 4 or more kits arrived with a jill between postnatal days (P) 12-21. Animals were housed in a room with timed lights (12 h on, 12 h off) in a custom stainless-steel cage (60 cm × 60 cm × 35 cm) with a hammock and small toys. For the entire study, a total of 27 female ferrets were used and all experimental procedures were carried out between postnatal days P55–68. Female ferrets were used because housing mature male ferrets in the same room with mature female ferrets causes stress to the female ferrets.

Facilitating premature visual experience: We divided animals into three experimental groups. The first group of animals had one of their eyes gently opened with forceps at P25, while the other eye was left closed to open naturally, and time of natural eye opening was noted. We used the label early Eye Opening One Contralateral (henceforth EO1contra) to indicate neurons in the monocular visual cortex that viewed the world through the (contralateral) eye that was opened

111 early, and early Eye Opening 1 Ipsilateral (henceforth EO1ipsi) to indicate neurons in the
112 monocular visual cortex that viewed the world through the eye that opened on time. In the
113 second group of animals, both eyes were opened at P25, and neurons from the monocular visual
114 cortex that viewed the world through either of these eyes were labeled early Eye Opening 2
115 (henceforth EO2). Finally, the third group of animals were two eye controls, and were allowed to
116 open both eyes normally, with time of natural eye opening noted. Ferrets frequently open one
117 eye up to a day before the other, and any disparity in the time of opening between the eyes was
118 noted. Ferret kits in laboratory housing receive limited visual stimulation through their closed
119 lids, as the mother actively keeps the kits in their relatively dark nest. In order to ensure that
120 animals with early-opened eyes actually had patterned visual experience (and animals with
121 closed lids had the same stimulation filtered through the lids), animals were brought to the lab
122 for 2 hours a day for 4 consecutive days beginning at P25. These ferret kits were placed in a rat
123 cage atop a heating pad, and gently manipulated to maintain wakefulness during this natural,
124 unguided viewing. We studied 17 animals that had one eye prematurely opened, 4 animals that
125 had both eyes were opened, and 11 control.

126 *Surgical preparation for terminal physiology experiments P55-68*: The ferret was sedated with
127 ketamine (20 mg kg−1 im). Atropine (0.16–0.8 mg kg−1 im) and dexamethasone (0.5 mg kg−1
128 im) were administered to reduce bronchial and salivary secretion and to reduce inflammation,
129 respectively. The animal was next anesthetized with a mixture of isoflurane, oxygen, and nitrous
130 oxide through a mask and a tracheostomy was performed. The animal was then ventilated with
131 1.5–3% isoflurane in a 2:1 mixture of nitrous oxide and oxygen. A cannula was inserted into the
132 intraperitoneal (ip) cavity for delivery of neuromuscular blockers and Ringer solution (3 ml kg−1
133 h−1), and the animal was inserted in a custom stereotaxic frame that did not obstruct vision. All

134 wound margins were infused with bupivacaine. A suture was made in the scalp and the skin
135 resected over the posterior half of the skull. A small opening in the cranium was drilled over V1
136 with a dental drill (Medidenta). The dura covering the brain at the craniotomy site was removed
137 over a 1 mm × 1 mm area to allow for electrode placement. Craniotomies were made over V1 of
138 each hemisphere. The eyelids were sutured open, and contact lenses were placed on the eyes to
139 prevent corneal damage. Before visual stimulation commenced, the ferret was paralyzed with the
140 neuromuscular blocker gallamine triethiodide (10–30 mg kg^{-1} h^{-1}) through the ip cannula to
141 suppress spontaneous eye movements, and the nitrous oxide oxygen mixture was adjusted to 1:1.
142 The animal's ECG was continuously monitored to ensure adequate anesthesia, and the
143 percentage of isoflurane was increased if the ECG indicated any distress. Body temperature was
144 maintained at 37 °C. At the conclusion of the experiment, the animal was killed with an overdose
145 of sodium pentobarbitol (200 mg/kg, IP) and transcardially perfused to retrieve the brain for
146 histology.

147 *Electrophysiological recordings*: 32 channel electrodes (Plexon S probes, 50um inter-tetrode
148 spacing; 50um intra-tetrode spacing) were used for all recordings. The signal was amplified
149 using the RHD2000 amplifying/ digitizing chip and USB interface board (Intan Technologies).
150 Stimulus timing information was acquired using a Micro1401 acquisition board and Spike2
151 software (Cambridge Electronic Design). Spike sorting was performed off-line using JRClust
152 running in Matlab (Jun et al., 2017). An electrode was inserted into the brain using a Sutter
153 Instruments MP-285 manipulator. To reduce sampling bias, we recorded from any site that had a
154 signal-to- noise ratio sufficient for isolation and had a response that appeared to be modulated by
155 the presentation of drifting gratings. Data are reported from all units that are responsive enough
156 to be included in analysis (see below). After finishing the recording at one site, the electrode was

157 lowered at least 640 microns before attempting to identify a suitable subsequent recording site.
158 The experiment was concluded when successful recordings were made from one or both
159 hemispheres.

160 *Locating Monocular Neurons*: After placing the electrode at a minimum depth of 200 μm in the
161 brain, entering the brain at an angle of 30-45 degrees, the search for monocular neurons
162 commenced. The electrode was driven into the brain until monocular neurons were discovered.
163 A population of neurons was deemed monocular if their receptive fields were in the periphery of
164 the eye contralateral to the recording hemisphere. Monocularity was ensured by determining
165 whether movement in the central visual and ipsilateral visual fields evoked a response; any such
166 responses indicated binocularity. If no purely monocular cells were found in a given penetration,
167 the electrode was removed and placed and another penetration was made elsewhere in the brain.

168 *Locating the Optic Disk*: An indirect ophthalmoscope (Heine Omega 600) and handheld 78 or
169 90D lens (Volk) were used to locate the optic disk and determine the orientation of the eye. This
170 was necessary as the orientation of the eye is necessary for determining the true eccentricity of
171 receptive fields. When one investigator had the optic disk in the center of view of the indirect
172 ophthalmoscope, another investigator introduced a wooden rod into the line of sight and moved
173 it until the end of the rod was centered on the image of the optic disk (also the center of view).
174 The position of the end of the rod was then measured in X, Y, and Z relative to the animal's eye
175 to make the optic disk direction.

176 *Visual Stimuli*: Visual stimuli were created in MATLAB (MathWorks) using the Psychophysics
177 Toolbox (Brainard 1997, Pelli 1997) and displayed on a 21-inch flat face CRT monitor (GDM-
178 520, Sony) with a resolution of 800 × 600 and a refresh rate of 100 Hz. We manually mapped

receptive fields by displaying circular patches of drifting sinusoidal gratings at different positions and moving the monitor to accommodate different eccentricities while listening to the responses on a loudspeaker.

Drifting grating stimuli were full-field, drifting sinusoidal gratings (4 s duration; 3.5 s interstimulus interval) presented pseudorandomly, with direction of motion (in steps of 45°) in either of the two directions orthogonal to the axis of orientation. Each individual grating stimulus was full screen and had a single set of parameters (direction, spatial frequency, temporal frequency), and was separated from the other stimuli by a gray screen interstimulus interval. We ran two sets of stimuli where multiple grating parameters were covaried in order to sample a wide variety of receptive field properties in our multi-neuron recordings. In the first set, orientation (angles 0°/horizontal, 45°, 90°/vertical, 135°) was co-varied with 8 different spatial frequencies (0.04, 0.08, 0.16, 0.24, 0.32, 0.64, 0.90, and 1.25), and 6 different contrasts (0.04, 0.08, 0.16, 0.32, 0.64, and 1), while temporal frequency was held constant at 4 Hz. In this first set of stimuli, gratings drifted back and forth every 4 cycles; for example, horizontal stimuli drifted upward and then downward. In a second set of stimuli, direction (0°/up, 45°, 90°/right, 135°, 180°/down, 225°, 270°/left, 315°) was co-varied with stimuli of 7 different temporal frequencies (0.5, 1, 2, 4, 8, 16, and 32 Hz) at 100% contrast and a fixed spatial frequency of 0.1 cycles/° visual angle. In this second set of stimuli, gratings drifted in a single direction and did not move back and forth. Each stimulus set had a blank, control stimulus that was the same duration as the other stimuli where the screen did not change. The first set of stimuli was repeated 5 times, and the second set 7 times.

Data analysis: Responses were determined by examining either the mean response during the entire stimulus or by taking the F1 component of the response. The same analysis (mean, or F1 at the temporal frequency of the stimulus of interest) was performed for the closest blank (control) stimulus and the response to the control stimulus was subtracted to yield the stimulus-driven response. For each tuning curve for orientation, direction, and spatial frequency analyses, we examined whether the mean or the F1 response was higher, and used those responses for analysis and fits. For temporal frequency analysis, we only used mean responses because we found a profound response suppression in many cells. Inclusion/exclusion: For each stimulus type, we examined the set of all responses to visual stimuli and blanks with an ANOVA test to evaluate the null hypothesis that the mean response to all of these stimuli were the same; cells with a $p<0.05$ to this visual responsiveness test were included in fits and analyses, and cells with $p>0.05$ were excluded.

Orientation selectivity was examined in the first set of stimuli at the preferred spatial frequency for each cell. Circular variance was calculated in orientation space (Ringach et al., 2002, Mazurek et al., 2014) with the equation $V = 1 - |R|$, where R is the resultant calculated as:

$$R = \frac{\sum_k r_k e^{i2\theta_k}}{\sum_k r_k}$$

Where rk was the mean spike rate in response to a grating drifting with angle θk.

Tuning curves from cells that showed significant variation across orientation stimuli and blank (ANOVA test, (Mazurek et al., 2014)) were fit with a double gaussian to obtain the angle preference.

Direction selectivity was examined in the second set of stimuli for the preferred temporal frequency of each cell (unless noted). Circular variance was calculated in direction space with the following equation:

$$1 - DirCirVar = \left| \frac{\sum_k R(\theta_k)\exp(i\theta_k)}{\sum_k R(\theta_k)} \right|$$

Preferred spatial frequency was determined by responses to the first stimulus battery at the preferred orientation at 100% contrast. Preferred temporal frequency was determined by responses to the second stimulus battery at the preferred direction. Each was fitted with a model due to Movshon et al. 2005: $R(f) = k * \exp\left(-\left(\frac{f}{fc}\right)^2\right)/[1 + (\frac{fh}{f})^{\beta}]$.

Low frequency cut-offs were determined by following the fit from its peak to lower frequencies until the first frequency where the response dropped to half its maximum (L50); high frequency cut-offs (H50) were determined by the same procedure, except that the fit was followed from the peak towards higher frequencies (Moore et al. 2005, Heimel et al., 2005). If the response never dropped below half its maximum, then the low frequency cut off was said to be 0 or the high frequency cut off was said to be infinity. Temporal frequency tuning bandwidth was defined as log2(H50/L50).

We defined a low pass index as the response to the lowest temporal frequency tested (in this case 0.5 Hz) to the maximum response obtained to the set of temporal frequencies shown. LPI = $\frac{R(TF=0.5\ Hz)}{\max\ (R(TF=0.5Hz),R(TF=1Hz),\ldots,R(TF=32Hz))}$. If a cell exhibited the highest firing for a temporal frequency of 0.5 Hz, then it would have an low pass index of 1. If it exhibited a similar firing rate in response to a temporal frequency of 0.5 Hz even if the preferred temporal frequency were higher, then the low pass index would still be near 1. If the cell responded poorly at a temporal frequency of 0.5 Hz, then it would have a low pass index near 0.

Contrast responses were fit with Naka-Rushton functions as described in (Peirce 2007) and sensitivity determined by the reciprocal of the contrast for which the response exceeds 5 standard deviations of the response to a blank screen. The Naka-Rushton function is defined as:

$$R = R_{\max} \frac{c^n}{c^n_{50} + c^n} + B$$

Where Rmax is the maximum response of the neuron, c50 is the contrast at which the response is halfway between baseline and maximum, c is the contrast of the stimulus presented to the neuron, and B is the baseline response of the neuron. n is a factor simply referred to as the exponent.

Statistics: Index values were examined with linear mixed effects models in Matlab (function: fitlme), where treatment condition (control, EO1contra, EO1ipsi, EO2) were fixed effects and animal identities were random effects.

254 *Immunohistochemistry*: Upon completion of experiments, an electrode coated in the fluorescent
255 dye DiI (DiCarlo et al., 1996) was inserted at the location and depth and left in place for 20
256 minutes. Animals were then transcardially perfused and the brain was placed in 4%
257 paraformaldehyde in 0.1M PBS at 4°C for 24 hours and then moved to 10% sucrose in PBS for
258 24-48 h. This was followed by placement in 30% sucrose in PBS at 4°C until sectioning. The
259 brain was sectioned sagittally into 100 μm sections using a sliding microtome (Leica SM2010R).
260 We washed sections in 0.1M PBS 3×5 min and permeabilized in 0.3% Triton-X 100 diluted in
261 PBS for 2 hours at room temperature on a shaker. Then slices were incubated in fluorophore-
262 conjugated anti-NeuN antibody (Alexa Fluor 488 Rabbit anti NeuN, Millipore ABN78A4) at a
263 1:300 dilution overnight (>12 hours) at room temperature on a shaker. Sections were then
264 washed 3×5 min in PBS and mounted on slides and allowed to air dry. Slides were then cover-
265 slipped with Fluoromount-G media (Electron Microscopy Sciences, Ft. Washington, PA) and
266 edges were sealed using nail polish. Histological sections were viewed using a fluorescent
267 microscope (Keyence BX-Z 710) and electrode tracks were reconstructed using DiI dye traces.

268 **RESULTS**

269 Our primary goal was to explore the influence of premature vision on the parameters of
270 receptive fields in V1. We reared ferrets under three conditions in order to examine the impact of
271 premature vision through one or both eyes in comparison with controls (**Figure 1**): in one group,
272 we opened one eye early; in a second group, we opened both eyes early; and a third, control
273 group were allowed to open their eyes naturally. Animals in both of the premature eye opening
274 groups experienced early vision beginning on postnatal day 25, a developmental timepoint when
275 retinal waves are still occurring (Meister et al., 1991, Wong et al., 1993), yet V1 is also

276 responsive to visual input through the closed lids (Krug et al., 2001, Akerman et al., 2002). This
277 ensured interaction between spontaneous, endogenously generated activity and patterned visual
278 input. We hypothesized that this interaction may drive aberrant development of cortical receptive
279 fields, as it is known that visual input is capable of initiating retinal waves through the closed lids
280 (Tiriac et al., 2018). Following premature eye opening, animals were brought to the lab for 2
281 hours a day of unguided visual exposure over 4 days, for a total of 8 hours of visual exposure.
282 Visual exposure consisted of gentle handling to prevent the young kits from sleeping thus
283 ensuring a sufficient amount of visual experience through the prematurely opened eye(s).
284 Animals received no other intervention between the end of visual stimulus training on P28 and
285 terminal electrophysiology experiments which occurred between P55-68.

286 We made multichannel recordings at a developmental timepoint when past studies have
287 shown that V1 receptive fields are largely mature. By postnatal day 42, contrast sensitivity (Li et
288 al., 2006), orientation (Chapman and Stryker 1993), direction, temporal frequency, and spatial
289 frequency (Li et al., 2006) tuning have reached adult-like levels and ocular dominance plasticity
290 is greatly reduced (Issa 1999). Thus, if premature vision causes permanent changes to receptive
291 field properties, we ought to be able to see them at P55-68.

292 We recorded responses to long batteries of visual stimulation with sinusoidal gratings
293 where multiple parameters were co-varied in order to assess a wide variety of possible receptive
294 field differences between control animals and animals that had their eyes opened prematurely. In
295 this study, all recordings were performed in the monocular visual cortex in order to simplify the
296 interpretation of these changes without needing to consider interactions between the two eyes.
297 We labeled cells as EO1contra (monocular neurons contralateral to a single early-opened eye),

298 EO1ipsi (monocular neurons ipsilateral to a single early-opened eye), E02 (monocular neurons
299 contralateral to an early opened eye where both eyes were opened early), and control (monocular
300 neurons in control animals). EO1contra and E02 cells observed the world through early-opened
301 eyes, while EO1ipsi neurons observed the world through eyes that opened on time but were
302 ipsilateral to early-opened eyes.

303 **Orientation and direction tuning index values are slightly increased by premature**
304 **experience**

305 Cells in all animals exhibited some degree of orientation and direction selectivity.
306 Orientation selectivity was assessed for stimuli that moved back and forth in two opposite
307 directions at each cell's preferred spatial frequency. Direction selectivity was assessed at the
308 neuron's optimal temporal frequency and a spatial frequency of 0.1. Example responses for each
309 group are shown in Fig. 2A-H. Control animals exhibited a baseline average orientation index
310 value (1-CV) of 0.42, and this value was not significantly elevated in EO1ipsi neurons (0.45,
311 $p<0.54$, Linear Mixed Effects Model). However, orientation selectivity was slightly elevated in
312 EO1contra neurons (0.52, $p<0.024$) and E02 neurons (0.54, $p<0.016$, LMEM). Direction
313 selectivity as assessed by 1-DCV was slightly reduced in EO1ipsi neurons (0.24, $p<0.027$,
314 LMEM) as compared to control values (0.29), and 1-DCV values were not significantly different
315 in EO1contra neurons (0.29, $p< 0.296$) or E02 neurons (0.33, $p<0.169$, LMEM) . The overall
316 distribution of direction preferences in 45° bins did not significantly differ across the groups
317 (chi-square test, $p = 0.11$), nor did the distribution of orientation angle preferences in 45° bins
318 (chi-square test, 5.3 x 10-2). Therefore, we observed only minor long-term changes in orientation
319 and direction tuning between animals with premature vision and control animals.

320 **Temporal frequency tuning is aberrant in animals with premature visual experience**

321 We were struck by the unusual temporal frequency tuning curves that we observed in
322 animals whose eyes were opened prematurely. Many EO1contra cells exhibited strong responses
323 at the lowest temporal frequency tested (Fig. 3A), and we observed a trend for this in EO2 cells
324 as well (Fig. 3B). Further, several cells also showed evidence of a suppression of the response
325 below baseline. Tuning curves from E0IPS cells (Fig. 3C) superficially looked more like curves
326 from control animals (Fig. 3D), although quantitative analyses uncovered small differences.
327 Most cell types exhibited similar peak temporal frequency values (Fig. 3E), except that EO1ipsi
328 cells exhibited slightly higher temporal frequency preferences ($p<0.021$, LMEM). To quantify
329 the response to the lowest temporal frequency tested, we calculated a low pass index, defined as
330 the ratio of the response to the lowest temporal frequency tested to the largest temporal
331 frequency response observed (Fig. 3F). Temporal frequency low pass index values of control
332 cells were 0.20 on average, while EO1contra cells showed low pass index values that averaged
333 0.35 ($p< 0.039$, LMEM) and EO2 cells showed empirically elevated values of 0.33 that were not
334 significantly different from control ($p< 0.142$, LMEM). High pass index values, determined by
335 calculating the response at the highest temporal frequency tested divided by the maximum
336 response, did not differ across these animals (Fig. 3G).

337 In order to assess tuning bandwidth, we calculated low- and high-frequency cut off values
338 by identifying the low and high frequency values where the response dropped below half the
339 maximum response value. If this never occurred, the cell was considered to be low-pass (if this
340 never occurred on the low frequency side) or high-pass (if this never occurred on the high
341 frequency side). We then calculated the bandwidth between this low and high value in octaves. If

342 a cell was low-pass or high-pass or both, the cell was said to have infinite bandwidth. In Fig. 3H,
343 we show bandwidth computed from rectified responses, and saw a empirically elevated
344 bandwidths in EO1contra cells (2.33 octaves, $p< 0.07$) and E02 cells (2.33 octaves, $p<0.08$)
345 compared to control cells (1.95 octaves) or EO1ipsi cells (1.91 octaves, $p<.937$). Many cells
346 exhibited suppression, where the response fell below the response to a control stimulus, and we
347 took the absolute value of the response in calculating the absolute bandwidth so that both
348 positive and negative responses were considered. The median absolute bandwidth (Fig. 3I) of
349 control cells (4.1 octaves) was narrower than any of the cells in animals whose eyes were opened
350 early, including EO1ipsi cells (4.7 octaves, $p<0.0013$), EO1contra cells (4.8 octaves, $p<0.002$),
351 and EO2 cells (5.1 octaves, $p<0.00015$, LMEM). These changes in bandwidth were related to
352 changes in low- and high-cut-off values (**Figure 3-Figure Supplement 1**).

353 **Spatial frequency tuning is relatively unaffected by premature visual experience**

354 Spatial frequency tuning was hardly influenced by early eye opening. We assessed spatial
355 frequency at a cell's preferred orientation, as determined by responses to drifting gratings that
356 moved back and forth in opposite directions. Example tuning curves are shown in Fig 4A-D.

357 In linear mixed effect modeling, no significant differences were observed in peak spatial
358 frequency preferences across these groups (control: 0.031 cpd; EO1ipsi: 0.045 cpd, $p<0.19$;
359 EO1contra: 0.031 cpd, $p<0.949$; EO2: 0.042 cpd, $p<0.362$, LMEM). Similarly, median spatial
360 frequency low pass index values were very similar, with a slightly significant change noted for
361 EO1ipsi animals (control: 0.86; EO1ipsi: 0.76, $p<0.0499$; EO1contra: 0.85, $p<0.928$; EO2: 0.79,
362 $p<0.390$, LMEM). We observed slightly higher spatial frequency high pass index values in EO2

363 cells, but effects were modest: (control: 0.02; EO1ipsi: 0.02, $p<0.857$; EO1contra: 0.04, $p<0.090$;
364 EO2: 0.06, $p<0.0323$, LMEM).

365 We observed no significant effects with respect to spatial frequency bandwidth, either
366 when measured with responses that were greater than 0 or measuring the absolute response (that
367 is, interpreting responses below baseline as positive responses). Bandwidths of individual cells
368 were often infinite, given the large preponderance of low-pass cells, and so we analyzed the data
369 in rank order instead of the raw values. Median values for both positive-only responses and
370 absolute responses were always above the ranks of cells with finite bandwidths, indicating that
371 the typical cell in all groups had infinite bandwidth. Differences from control were not
372 significant for positive-only responses (EO1ipsi: $p<0.310$, EO1contra: 0.622, EO2: $p<0.898$,
373 LMEM) or absolute responses (EO1ipsi: $p<0.06$, EO1contra: $p<0.597$, EO2: $p<0.385$, LMEM).

374 In short, we found very little evidence of substantial changes to spatial frequency tuning
375 in these monocularly-driven cells.

376 **Spontaneous firing rates and response suppression are increased in animals that have had**
377 **premature visual experience**

378 Hebbian and homeostatic mechanisms are active early in development (Turrigiano and
379 Nelson, 2004), and may be critical for setting response gains and the background excitability of
380 neural circuits (Roy et al., 2018; Roy et al. 2020a). To examine whether response gains or
381 excitability were impacted by premature vision, we quantified maximum firing rates in response
382 to visual stimuli, response suppression, and background firing rates.

383 The peak mean responses of neurons to visual stimuli (Fig. 5A) did not differ among the
384 experimental groups. Control neurons exhibited average peak responses of 7.0 Hz; EO1ipsi
385 neurons did not differ significantly (6.4 Hz, $P<0.600$), nor did EO1contra neurons (10.1 Hz,
386 $p<0.518$) or EO2 neurons (10.5 Hz, $p<0.295$).

387 In contrast to peak responses, response suppression below background levels was
388 pronounced in animals with prematurely opened eyes (Fig. 5B). We calculated all responses by
389 subtracting the background rate measured during control stimuli (gray screen), and took response
390 suppression for each cell to be the maximum amount of suppression below background rates for
391 the average response to any visual stimulus. Suppression was rarely observed in control cells
392 (average: 2.1 Hz), but was substantially elevated in EO1ipsi cells (7.0 Hz, $p<1.59e-9$) and
393 slightly elevated in EO1contra cells (3.4 Hz, $p<0.022$) and EO2 cells (2.8 Hz, $p<0.035$).

394 Finally, background firing rates were significantly higher in animals whose eyes were
395 opened early (Fig. 5C). Spontaneous firing rates were low in control animals (2.6 Hz), and were
396 markedly increased in EO1ipsi hemispheres (11.1 Hz, $p<1.09e-4$), EO1contra hemispheres (6.6
397 Hz, $p<0.0132$) and EO2 hemispheres (6.6 Hz, $p<0.0248$). Therefore, early opening produced a
398 long-lasting effect on spontaneous firing rates after the critical period.

399 In all, early eye opening induced changes in response suppression and background firing
400 rates that were still evident at the time of our measurements several weeks later. We observed
401 these changes in both hemispheres, which indicates that the differences in direct visual drive to
402 visual receptive fields are not underlying these differences but instead are the result of some
403 more global process. These results are consistent with the idea that early eye opening induces

long-term changes to circuit-level excitability that are not corrected during the remainder of development.

DISCUSSION

We explored the impact of premature vision on the development of a number of V1 RF properties in ferret. We found small increases in direction and orientation tuning in cells that viewed the world through prematurely-opened eyes. We observed profound changes in temporal frequency tuning: cells recorded from animals that had their eyes opened prematurely exhibited more low-pass temporal frequency tuning curves and broader temporal frequency bandwidths compared to controls. Spatial frequency preferences were not substantially altered. Finally, cells in either hemisphere in animals with prematurely-opened eyes had higher spontaneous firing rates and exhibited marked suppression below this spontaneous firing rate in response to some visual stimuli.

A novel temporal frequency tuning deficit with possible implications for motion processing

We found that ferrets with premature visual experience exhibited a pronounced broadening of temporal frequency tuning curves and increases in the fraction of low- pass neurons. The alterations in temporal frequency tuning identified in ferrets following premature eye opening are strongly suggestive of a deficit in motion processing. The broadening of temporal frequency tuning curves and increase in the proportion of low pass cells in V1 could translate to a decrease in the animal's ability to distinguish the temporal frequency (and perhaps the speed) of a moving visual stimulus.

Altered rearing has been shown to influence the subsequent development of motion processing in various ways. Dark-reared cats and ferrets exhibit poor direction selectivity (Imbert and Buisseret 1975, Li et al., 2006), but dark-reared ferrets do not show strong deficits in temporal frequency processing. Overall responses after dark-rearing are reduced, but temporal frequency tuning is only slightly narrowed (Li et al., 2006). Cats raised in a strobe-light environment (mostly after eye opening) exhibited strong changes in subsequent direction selectivity (Kennedy and Orban 1983; Humphrey and Saul 1998) and behavioral sensitivity to motion (Pasternak et al., 1981; Pasternak et al., 1985) that partially recovers with motion detection training. However, temporal frequency tuning of these animals has not been reported in detail. Pasternak et al (1981) reported that strobe-reared ferrets exhibited greater difficulty in distinguishing slow moving stimuli from static stimuli compared to controls, an ability that slightly improved with practice, suggesting possible temporal frequency deficits. Kennedy and Orban (1983) report a reduction in high-pass velocity-tuned cells, but not an increase in low-pass cells; Humphrey and Saul (1998) do not report temporal frequency tuning across their population but their example cell does appear to be broadly tuned and low-pass. Temporal frequency tuning is not subject to rapid modification shortly after eye opening, as Ritter and colleagues demonstrated that providing ferrets that had just opened their eyes naturally with 6-9 hours of visual stimulation of a single temporal frequency did not elicit a shift in temporal frequency tuning (Ritter et al., 2017). The same stimulation causes a dramatic increase in direction selectivity (Ritter et al., 2017) that normally develops in the first week to 10 days after eye opening and requires visual experience (Li et al., 2006, Li et al., 2008, Van Hooser et al., 2012). The only manipulation we know of in the literature that has been shown to modify temporal frequency properties of developing animals is prey capture: mice that learned to hunt crickets in

447 the critical period for ocular dominance plasticity exhibit lower low-pass index values (Bissen et
448 al. 2025).

449 In sum, the deficits in temporal frequency tuning we observed are unlike those reported
450 previously. Premature vision produces permanent alteration of temporal frequency tuning curves,
451 while dark-rearing does not and comparable results from strobe rearing are not available.

452 **Biology of early development in mustelids**

453 In the wild, mustelids raise their young in nests in the ground, in cavities such as holes in
454 trees or caves, or in areas of dense vegetation (Ruggiero et al. 1994). They may move the young
455 from one nest to another as they grow, but otherwise the young are primarily in the relatively
456 dark nest. It is highly likely that some light penetrates and that information about the 24-hour
457 cycle is available, but the light is likely to be dim and unlikely to provide a basis for high
458 luminance, high contrast stimulation through the closed lids. The animals begin to spend
459 substantial time outside the nest after eye opening.

460 The ferret is a domesticated strain of the European polecat. In laboratory settings, ferret
461 jills give birth and keep their kits in a nest box. A laboratory typically maintains a 24-hour cycle
462 with 12 or 14 hours of light, and the light reaching the closed lids must first pass through the
463 cage, the nest box, and the nesting material. Therefore, developing ferrets have an obvious
464 circadian light signal but the light available for image formation is likely dim and of low
465 contrast.

466 Although the light that reaches the close lids in developing ferrets is likely to be
467 relatively dim, and any image-forming signal passing through the closed lids would be highly

468 filtered in luminance, spatial frequency, and contrast, it is important to remember that visual
469 input before natural eye opening (through the closed lids) can drive activity in retina, LGN, and
470 cortex (Huttenlocher 1967, Chapman and Stryker 1993, Krug et al., 2001, Akerman et al., 2002,
471 Akerman et al., 2004). Further, orientation selectivity can be observed through the closed lids
472 (Krug et al., 2001), indicating that some coarse image-forming information does make it through
473 the closed lids.

474 **Mechanisms underlying altered receptive fields**

475 One way that premature patterned vision could alter the development of the brain is by
476 altering the character of retinal waves. The low resolution visual input before natural eye
477 opening is capable of driving activity in the visual circuit (Huttenlocher 1967, Chapman and
478 Stryker 1993, Krug et al., 2001, Akerman et al., 2002, Akerman et al., 2004), and evidence
479 shows that this early form of low resolution visual experience plays a role in the development of
480 ON-OFF segregation in dLGN (Akerman et al., 2002) and the initiation of retinal waves (Tiriac
481 et al., 2018). Propagation of high luminance, high contrast, and high spatial frequency input
482 through the developing retina may alter or disrupt the typical retinal wave formation and
483 propagation, and thus may have deleterious effects on developmental processes driven by
484 endogenous activity. Alternatively, high contrast signals may not interrupt retinal waves but may
485 contribute independent activity that, through experience-dependent plasticity mechanisms,
486 produces the alterations in receptive field properties that we observed.

487 Several other basic mechanistic questions remain unanswered. It is unclear where in the
488 visual circuit cascade these deficits first arise. Does the lateral geniculate nucleus or retina
489 exhibit altered temporal frequency tuning? Is the influence of the patterned visual stimulation

490 instructive, so that if one provided premature stimulation with only certain temporal frequencies,
491 one would see selectivity for those temporal frequencies, or would tuning always be broad?
492 Other questions remain concerning the top-down influence on V1 from "higher" motion areas
493 such as MT (monkeys) or PSS (ferret); MT exhibits mature neural markers earlier than V1
494 (Bourne and Rosa, 2006), and suppression of PSS impacts motion selectivity in V1 (Lempel and
495 Nielsen, 2021). Finally, our recordings were performed in monocular cortex so that we could be
496 sure of the developmental condition of the eye that drove the classic responses. It is interesting to
497 speculate about what might occur more centrally in binocular visual cortex. Ocular dominance
498 shifts are not induced when one eye is opened prematurely (Issa et al 1999), indicating that
499 ocular dominance plasticity is not engaged at this early stage, but one might imagine that the
500 impacts on temporal frequency and spontaneous firing rates would still be present. Future studies
501 will be needed to address these questions.

502 We introduced premature patterned vision at a time when cortical inhibition is
503 undergoing substantial changes. GABAergic signaling has already undergone its switch (Ben-
504 Ari, 2002) from providing primarily depolarizing input to hyperpolarizing input by P21-23
505 (Mulholland et al., 2021). In the days prior to eye opening, inhibitory cells exhibit activity that is
506 closely associated with the emerging functional modules that will reflect orientation columns
507 (Mulholland et al., 2021), but do not yet exhibit selectivity to orientation, in contrast to
508 excitatory neurons, which do exhibit selectivity to orientation at that time (Chang and
509 Fitzpatrick, 2022).

510 The broad tuning in temporal frequency and elevated spontaneous firing rates that we
511 observed could reflect a deficit in cortical inhibition in animals that experienced premature

512 vision. Yet selectivity was not entirely destroyed, as neurons still exhibited selectivity for
513 orientation and direction. Selectivity can be achieved with a combination of amplification of
514 appropriate excitatory signals and inhibitory suppression that is either selective or broad (Ben-
515 Yishai et al., 1995, Rubin et al., 2015, Somers et al., 1995, Troyer et al., 1998), so it is unclear
516 how the circuit has changed. The amount and timing of inhibition, whether feed-forward or
517 feedback, could be altered.

518 **Alterations in ipsilateral receptive fields**

519 One of our most surprising findings was a difference in the receptive fields and firing
520 properties of cells that were ipsilateral to the early opened eye. It is straightforward to imagine
521 how Hebbian mechanisms might influence monocular cells that are contralateral to the early-
522 opened eye, but one would have to imagine different and possibly more global mechanisms to
523 explain changes in monocular cells that view the world through the eye that opened naturally.

524 Homeostatic mechanisms such as synaptic scaling (Desai et al., 2008, Turrigiano et al.,
525 1998), and regulation of intrinsic excitability (Desai et al., 1998, Lambo and Turrigiano, 2013)
526 operate during the critical period for ocular dominance plasticity and serve to keep ongoing
527 firing rates within a cell-defined range (Hengen et al., 2013, Hengen et al., 2016). It is possible
528 that these homeostatic mechanisms are not yet operating in the presensory period, and that the
529 extra activity causes an increase in excitatory forces (whether synaptic or intrinsic) relative to
530 inhibitory forces.

531 Alternatively, opening a single eye early may still influence feed-forward activity in the
532 ipsilateral hemisphere. Work in ferrets and rats suggests a role for retinal waves in the

533 development of interhemispheric connectivity; bilateral enucleation of ferrets induces anomalies
534 in the distribution of callosal cells in primary visual cortex (Bock et al., 2012), and results in
535 callosal projections connecting topographically mismatched loci in VC in P4-6 rats (Olavarria
536 and Hiroi 2003). Further, retinal waves demonstrate coordinated activity between both
537 hemispheres in mice and ferrets (Weliky and Katz 1999, Ackman et al., 2012). Recent findings
538 describe a transient retina to retina connection in mice and ferret, which exists during the period
539 of retinal waves (Murcia-Belmonte et al., 2019). This connection provides a plausible
540 mechanism for the theorized inter- retinal coordination of waves thought to be necessary to drive
541 development of bilateral topographic maps (Adams and Horton 2003, Murcia-Belmonte et al.,
542 2019). Given that light is capable of initiating retinal waves (Tiriac et al., 2018), it is feasible that
543 exposure to light through a single, prematurely opened eye would initiate retinal waves capable
544 of propagating to the closed eye. Given the qualitative differences between vision through a
545 closed lid vs open eye, initiation and propagation of retinal waves would be both asymmetric and
546 mutually influential between retinas, potentially accounting for the differences in RFs observed
547 between EO1ipsi and control hemispheres.

548 **Comparison with prior studies**

549 There have been only a few animal studies that have sought to introduce inappropriately
550 early vision. Lichliter and colleagues (2018) prematurely opened the shells of bobwhite quail
551 eggs and provided visual experience to the chick, and found a subsequent loss of visual
552 selectivity to bobwhite hens vs. hens of another species (Sleigh and Lickliter 1995). Further, they
553 demonstrated multi-modal impacts on auditory processing after premature visual experience, in
554 that animals failed to eventually become responsive to cross-species hen calls. In behavioral

555 studies of rats whose eyes were prematurely opened 7 days early, investigators found that
556 opening a single eye (but not opening both eyes early) caused a deficit in pivoting locomotor
557 reactions on the side of the early-opened eye; that is, rats pivoted more frequently towards
558 stimuli viewed through the eye that opened on time (Foreman and Altaha 1991). To our
559 knowledge, the present work is the first to study cortical receptive fields after premature sensory
560 experience. All of these studies, including our own, have noted deficits after premature
561 experience.

562 **Premature vision as a risk factor for visual disfunction**

563 Very premature human babies exhibit a variety of visual deficits later in life that are not
564 explained by the condition of the eye, broadly termed Cortical/Cerebral Visual Impairment
565 (CVI) (Kozeis 2010, Dutton 2013, Sakki et al., 2018). These very premature babies are a
566 heterogenous population. Some of these infants have suffered clear brain injuries (Slidsborg et
567 al., 2012, Dutton 2013) of varies types, such as hypoxia, brain bleeding, or periventricular
568 leukomalacia (Gallo and Lennerstrand 1991, Hokken and Krabbendam 2023, Kozeis 2010), and
569 these injuries clearly have a direct impact on subsequent visual deficits that go beyond any
570 influence of early experience. But, studies that have excluded individuals with known brain
571 damage or retinal problems (or analyzed these populations separately) have also found that
572 extreme prematurity itself has an impact on later vision, particularly on motion perception
573 (Atkinson and Braddick, 2007, Benassi et al., 2018, Guzzetta et al., 2009, Hou et al., 2011,
574 MacKay et al., 2005) and sometimes lowered visual acuity (Jain et al. 2022). Previous
575 investigators have speculated that inappropriately early visual stimulation may contribute to
576 these deficits, as in Taylor et al (2009): "Why the dorsal stream should be particularly vulnerable

in this population is not completely understood. One possibility is that the unusually early visual stimulation that very premature infants are exposed to may, in itself, have a differential effect on the functional development of the dorsal and ventral streams". Our data are consistent with the idea that inappropriately early visual stimulation contributes to deficits in motion processing. A moving object has both a speed and direction, and temporal frequency is critical to determine an object's speed. The major temporal frequency tuning deficits we have observed in receptive fields are consistent with a motion deficit.

Premature vision as a cause of visual plasticity

Regardless of whether premature patterned vision has a clinically relevant role for human vision, the experiments here demonstrate clearly that premature patterned vision has a long-lasting impact on the development of receptive fields in the visual cortex. The results suggest that the evolved late eye opening of many rodents and carnivores, and the prolonged prenatal period of primates, may help to protect the visual system from exposure to high luminance, high contrast, and high spatial frequency stimulation until the visual system is ready for this type of stimulation. This shielding of the developing visual system is not found in all vertebrates, as tadpoles and zebrafish have transparent eyelids that permit patterned vision from very early stages (Avitan et al., 2017, Demas et al., 2012). By altering premature patterned vision, it may be possible to uncover the plasticity rules that are at play in the developing mammalian visual system before the natural onset of vision.

596 **Figure 1: Recording schematics, experimental timeline, and electrode tract reconstructions.**
597 A: Recording schematics: EO1contra cells were those recorded in monocular cortex contralateral
598 to a single prematurely-opened eye. EO1ipsi cells were those recorded in monocular cortex
599 ipsilateral to a single prematurely-opened eye. Dots schematize ocular dominance columns. B:
600 EO2 cells were those recorded in monocular cortex after both eyes were opened prematurely. C:
601 Control cells were those recorded in monocular cortex after both eyes were allowed to open
602 naturally. D: Experimental timeline. Animals that experienced premature vision had one eye or
603 both eyes opened on P25. All animals experienced a period outside of the nest in the form of daily
604 2 hour handling sessions beginning on P25 and ending on P28, allowing unguided viewing of the
605 laboratory environment through prematurely opened eyes or low resolution experience through
606 closed lids. Electrophysiological recording took place between P55-68, at a time when the critical
607 period for ocular dominance was closing or closed (Issa et al. 1999). E: Electrode track
608 reconstructions showing penetrations (bright spots at right/posterior) along the posterior cortical
609 surface, in monocular V1 (Law et al., 1988; White et al. 1999). Following recording, the recording
610 electrode was removed and replaced with a marking electrode coated in DiI.

611 **Figure 2: Early eye opening produced only minor changes in orientation and direction**
612 **selectivity index values:** A: Example direction tuning curves of individual EO1contra cells
613 measured after the close of the critical period. Direction tuning curves are shown for stimulation
614 at the optimal temporal frequency. Direction tuning curves look coarsely normal. Vertical scale
615 bar represents 10 spikes per second (standard indicated in italics) unless otherwise indicated.
616 Dashed line shows mean response to blank / control stimuli. Number indicates 1-DCV value. B:
617 Same, for EO2 cells C: Same, for EO1ipsi cells: D: Same, for control cells E: Orientation tuning
618 curves of individual EO1contra cells, measured in different epochs and in some different animals
619 than the direction tuning curves. Temporal frequency was 2 Hz, and the spatial frequency
620 optimal for each cell. Numbers indicate orientation selectivity index values 1-CV. F: EO2 cells
621 G: EO1ipsi cells H: control cells I: Results of a linear mixed effects analysis of orientation
622 selectivity index values (1-CV) for all cells and conditions in the study. Each small column
623 shows the cells for an individual animal. Yellow lines indicate random effect values for each
624 animal. Gray lines indicate condition means and standard errors of the mean from the linear
625 mixed effect model. Animals within a group have been sorted by mean index value. Condition
626 coefficients that differ significantly from 0 are indicated with * ($p<0.05$), and conditions
627 compared are indicated by comparison bars. See text for P values. J: Same for direction
628 selectivity index values, as assessed by (1-DCV). EO1contra and E02 cells exhibited slightly
629 higher orientation selectivity index values than control animals, while EO1ipsi cells exhibited
630 slightly lower direction selectivity values than other conditions.

631 **Figure 3: Premature eye opening altered temporal frequency tuning after maturity:**
632 Representative temporal frequency tuning curves recorded from single cells: A: EO1contra: cells
633 contralateral to a single prematurely opened eye. Several cells exhibited strong responses at the
634 lowest temporal frequency tested (that is, several exhibited low-pass tuning). Temporal
635 frequency reported at each cell's overall preferred direction (assessed over all temporal
636 frequencies). Number indicates bandwidth in octaves. -∞ is low pass. Vertical scale bar indicates
637 firing rate (20 spikes/sec standard in italics unless otherwise noted). B: EO2: cells recorded in an
638 animal with both eyes prematurely opened. Again, many cells exhibited low-pass responses. C:
639 EO1ipsi: cells ipsilateral to a single prematurely opened eye. D: Control: cells recorded in
640 animals that opened both eyes naturally. E: Linear mixed effects model plot of median temporal
641 frequency preference; linear mixed effects plotted as in **Figure 2**. Median temporal frequency
642 preference was slightly higher in EO1ipsi cells than other cells. F: Temporal frequency low pass
643 index values were significantly elevated in EO1contra cells, indicating stronger responses to the
644 lowest temporal frequency tested. G: No differences were observed in high pass index values. H.
645 Bandwidth of the rectified response. I: Bandwidth of the absolute value of responses. Cells in
646 animals that experienced early eye opening exhibited wider bandwidths (less selectivity) than
647 control animals. See text for numbers and p-values.

648 **Figure 3 – figure supplement 1. Premature eye opening alters L50 and H50 values. A)**
649 Temporal frequency L50 values across the experimental conditions. E01contra cells exhibited
650 significantly lower L50 values values than control animals ($p<0.002$, LMEM). **B)** EO2 cells, by
651 contrast, exhibited widened bandwidths by showing increased H50 values ($p<0.004$, LMEM). **C)**
652 Considering the absolute value of the temporal frequency response (where deviations above or
653 below background firing rates contributed to response), EO1contra cells again exhibited
654 significantly lower L50 values compared to control cells ($p<0.00029$, LMEM). EO1ipsi cells
655 exhibited a slight increase in L50 values ($p<0.0148$, LMEM). **D)** EO1ipsi cells showed a
656 substantial increase in absolute H50 cut off values ($p<0.00169$, LMEM).

Figure 4: Premature eye opening had very small impacts on spatial frequency tuning. A: Example spatial frequency tuning curves in EO1contra cells. B: Same for EO2 cells. C: Same for EO1ipsi cells. D: Same for control cells. E: Spatial frequency peak preferences for all cells, animals, and experimental groups (same linear mixed effect model plot layout as Fig. 2). F: Spatial frequency low pass index values. EO1ipsi cells exhibit a slightly significant ($p<0.499$) decrease in low pass index but differences across groups were small. G: High pass index values for spatial frequency; differences were modest across groups although cells with strong high-pass responses were more common in E02 cells. H: Spatial frequency bandwidth, in octaves. Most cells exhibited low-pass profiles and had infinite bandwidth, and no differences were noted across the groups. I: Spatial frequency bandwidth for absolute response.

667 **Figure 5: Premature eye opening altered response suppression below baseline and**
668 **spontaneous activity of V1 neurons:** A: Maximum firing rates of cells to visual stimulation
669 were unchanged across experimental conditions. B: Response suppression rates, defined as the
670 largest reduction in responses to visual stimulation below background firing rates, were
671 substantially bigger in EO1ipsi, EO1contra, and EO2 cells, indicating that responses below
672 baseline were features of the stimulus response in many of these cells. C: Background firing
673 rates. Responses of cells during presentation of control stimuli, where the screen remained gray
674 for the same duration as our typical visual stimuli. EO1ipsi, EO1contra, and EO2 cells showed
675 greatly and significantly elevated firing rates compared to controls. See text for numbers.

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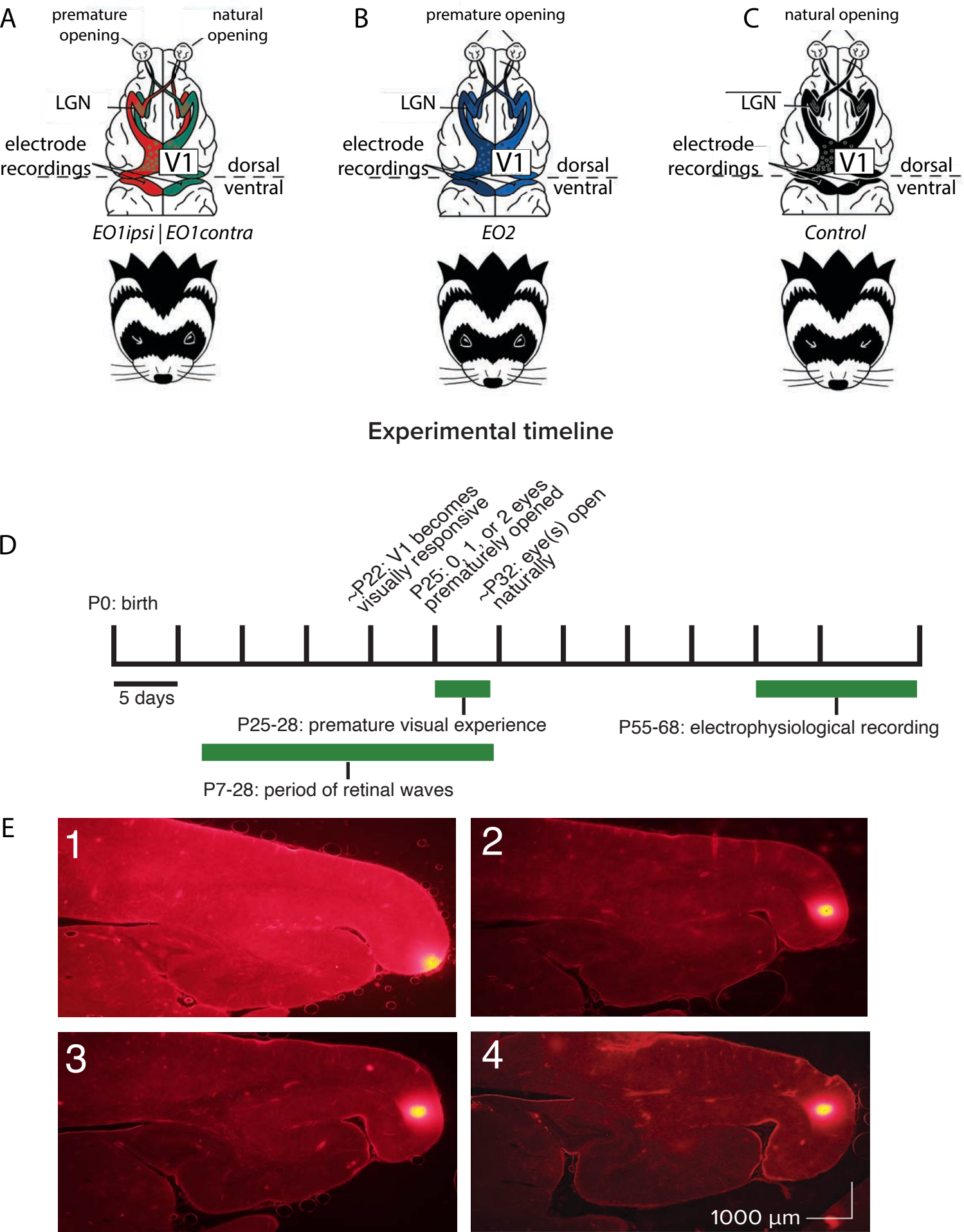
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LGN
electrode recordings
V1
dorsal
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B
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electrode recordings
V1
dorsal
ventral
EO2
C
natural opening
LGN
electrode recordings
V1
dorsal
ventral
Control
Experimental timeline
D
P0: birth
~P22: V1 becomes visually responsive
P25: 0, 1, or 2 eyes prematurely opened
~P32: eye(s) open naturally
5 days
P25-28: premature visual experience
P55-68: electrophysiological recording
P7-28: period of retinal waves
E
1
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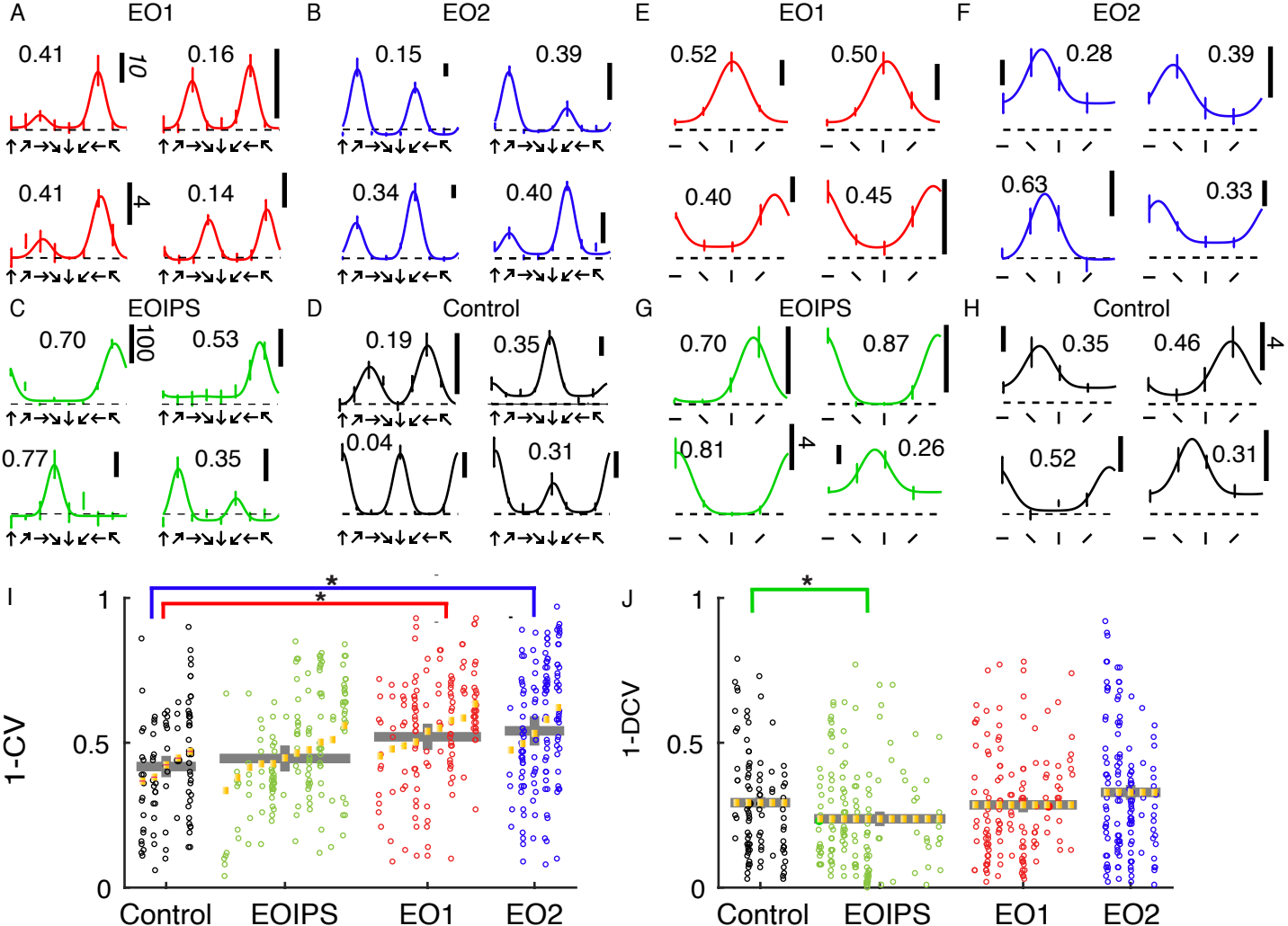
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0.41
4
0.14
B
EO2
0.15
0.39
0.34
0.40
E
EO1
0.52
0.50
0.40
0.45
F
EO2
0.28
0.39
0.63
0.33
C
EOIPS
0.70
100
0.53
0.77
0.35
D
Control
0.19
0.35
0.04
0.31
G
EOIPS
0.70
0.87
0.81
4
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H
Control
0.35
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I
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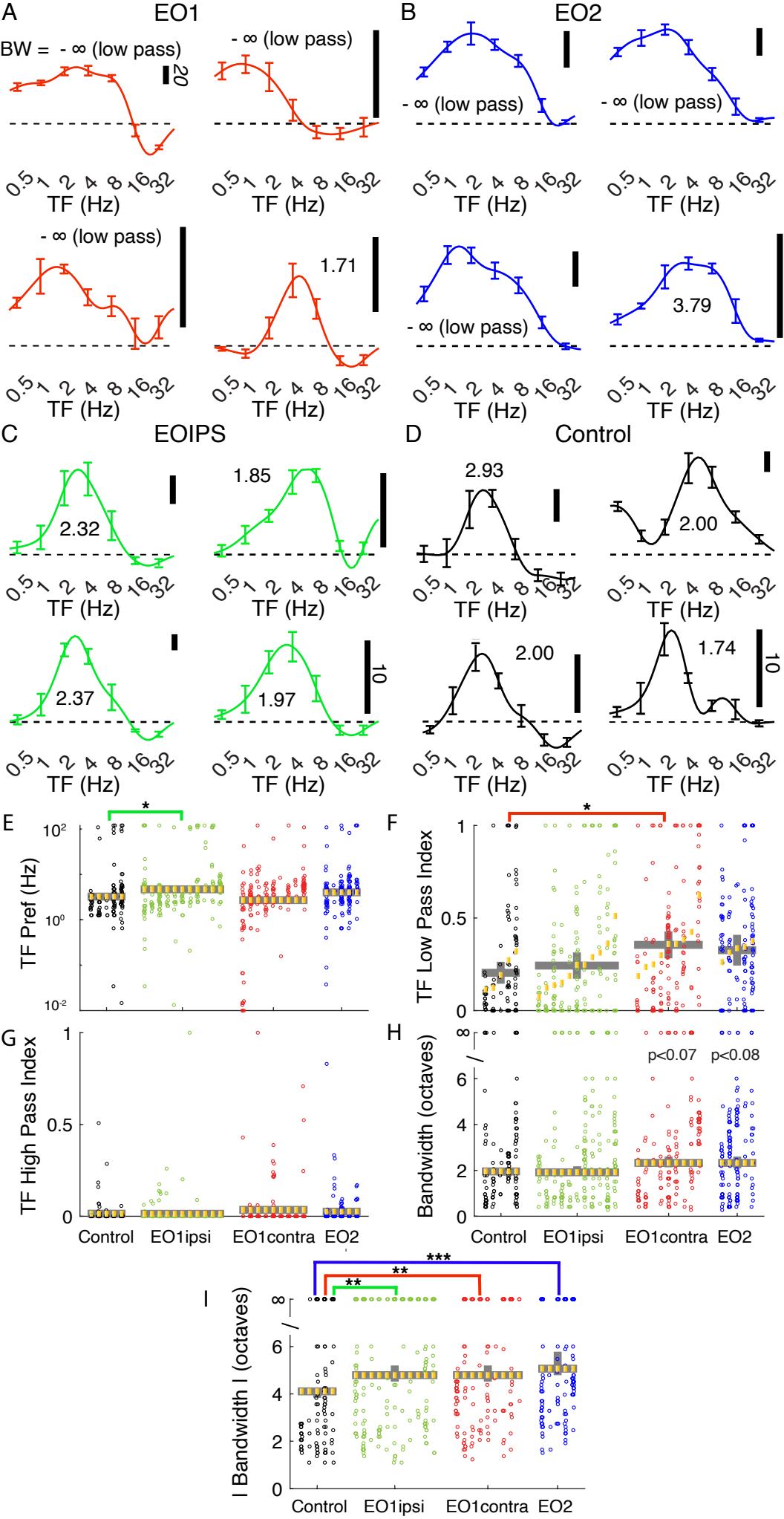
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BW = - ∞ (low pass)
- ∞ (low pass)
20
B
EO2
- ∞ (low pass)
- ∞ (low pass)
- ∞ (low pass)
1.71
- ∞ (low pass)
3.79
C
EOIPS
2.32
1.85
2.37
1.97
10
D
Control
2.93
2.00
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10
0.5 1 2 4 8 16 32
TF (Hz)
E
TF Pref (Hz)
F
TF Low Pass Index
G
TF High Pass Index
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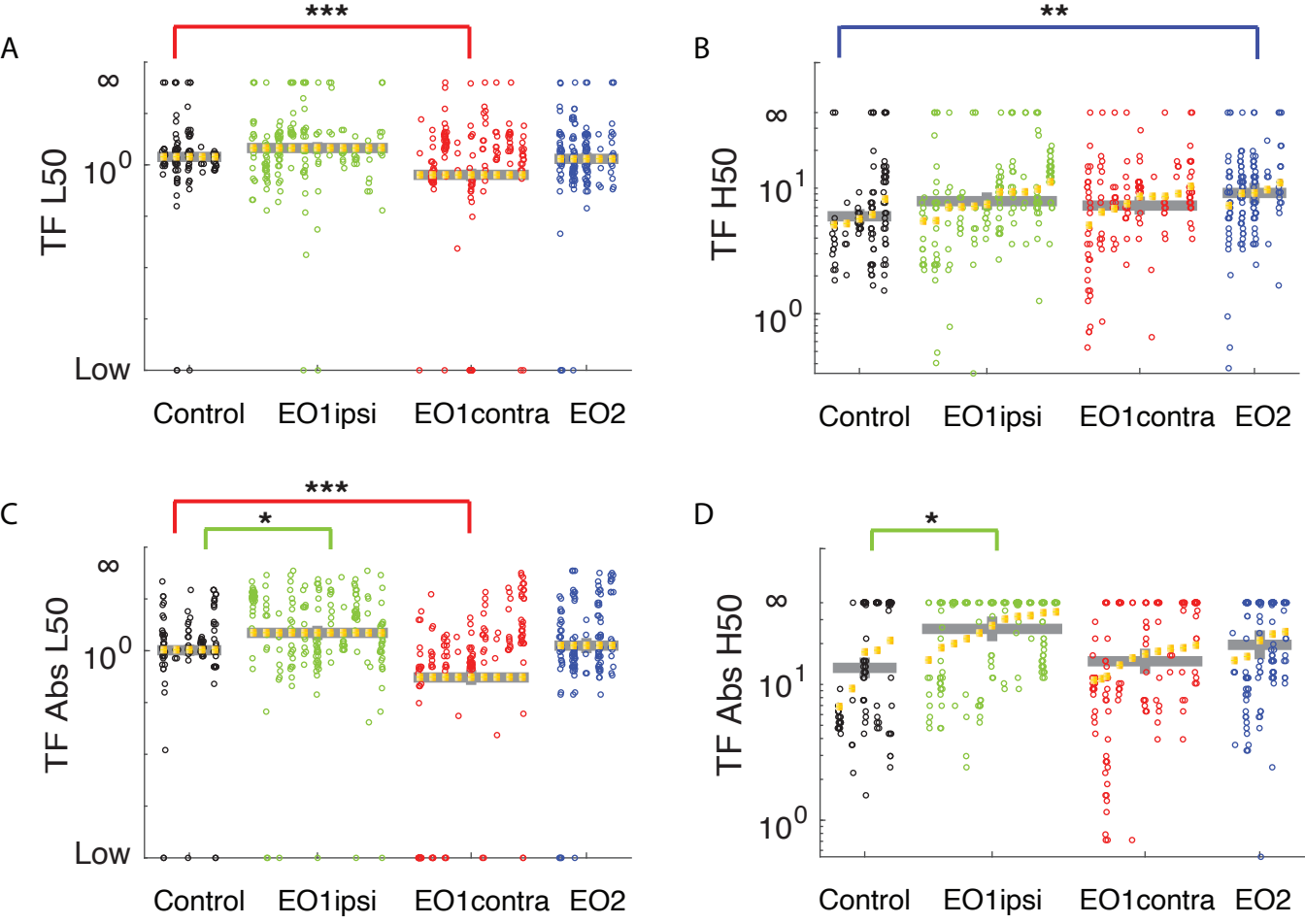
A
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Low
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Control
EO1ipsi
EO1contra
EO2
C
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TF Abs L50
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EO1ipsi
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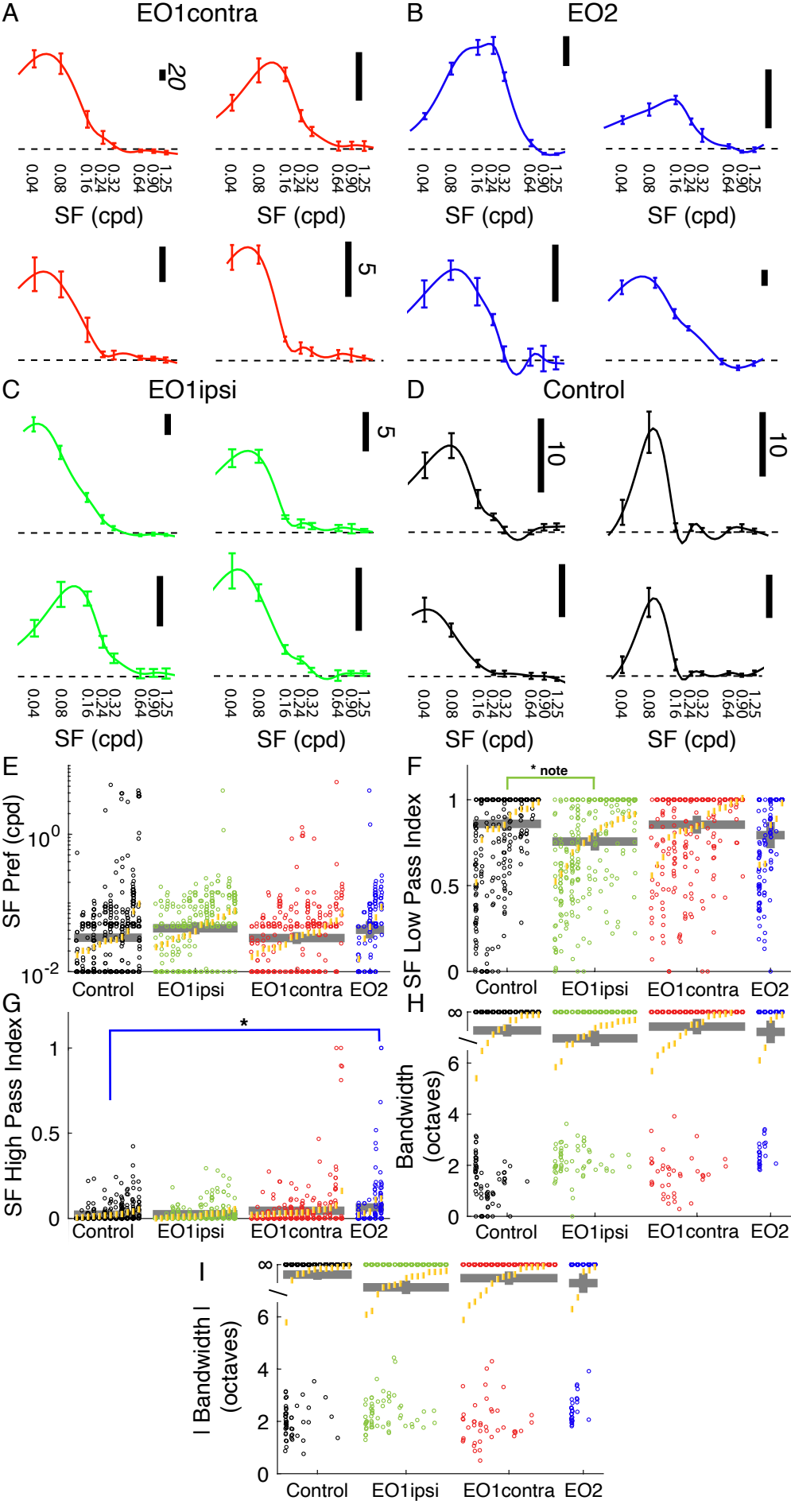
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0.90
1.25
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SF Pref (cpd)
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Control
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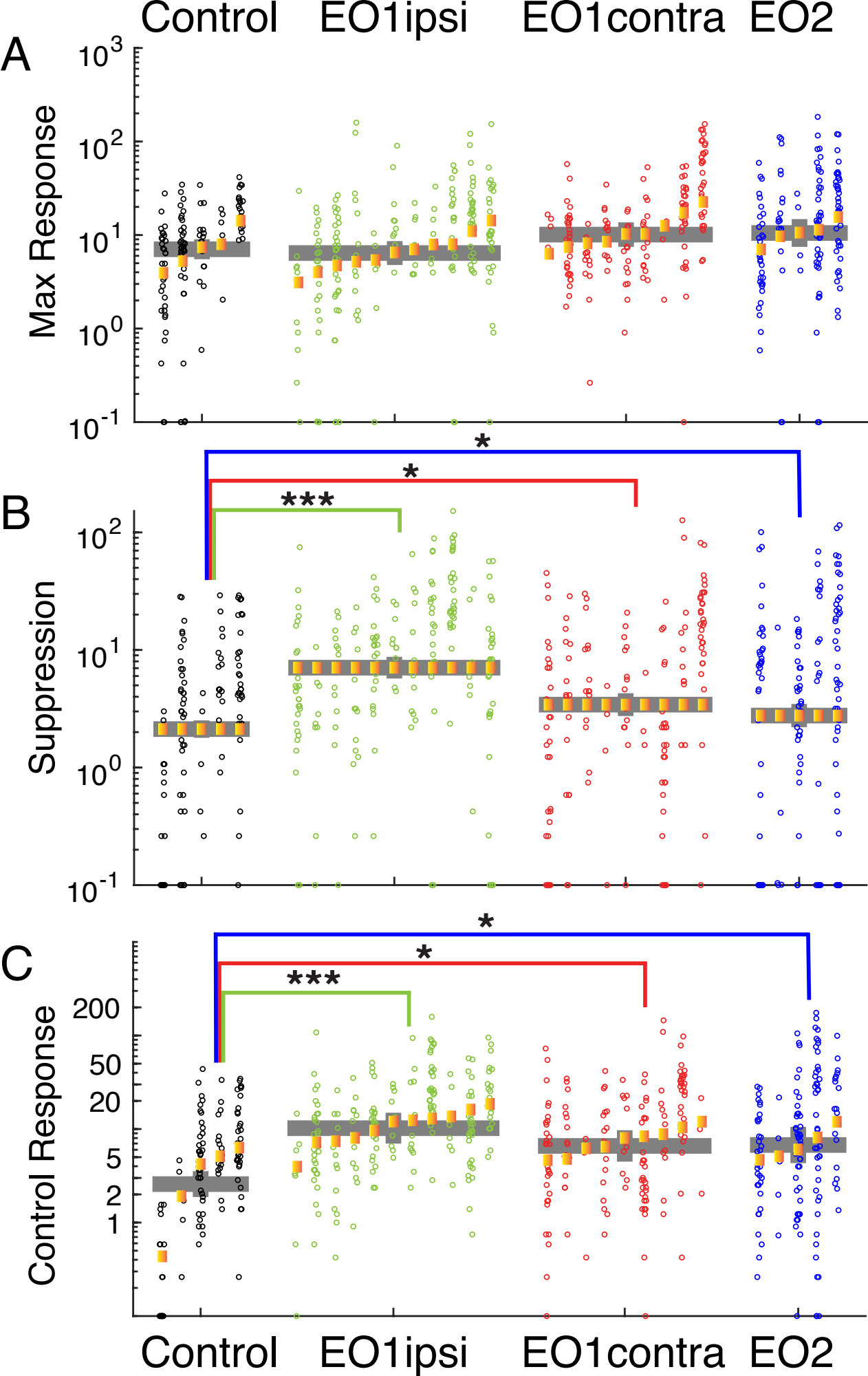
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Max Response
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10^2
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Control Response
200
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