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#### 27 Abstract:

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Perceptual decision-making is a complex process that involves sensory integration 29 30 followed by application of a cognitive threshold. Signal detection theory (SDT) provides 31 a mathematical framework for attributing the underlying neurobiological processes to 32 these distinct phases of perceptual decision-making. In particular, SDT reveals the 33 sensitivity (d') of the neuronal response distributions and the bias (c) of the decision 34 criterion, which are commonly thought to reflect sensory and cognitive processes, 35 respectively. However, neuronal representations of bias have been observed in sensory 36 areas, suggesting that some changes in bias are due to effects on sensory encoding. 37 To directly test whether sensory encoding can influence bias, we optogenetically 38 manipulated neuronal excitability in primary visual cortex (V1) during a detection task. 39 Increasing excitability in V1 significantly decreased behavioral bias, while decreasing 40 excitability had the opposite effect. To determine whether this change in bias is 41 consistent with the effects on sensory encoding, we made extracellular recordings from 42 V1 neurons in passively viewing mice. Indeed, we found that optogenetic manipulation 43 of excitability shifted the neuronal bias in the same direction as the behavioral bias, 44 despite using a fixed artificial decision criterion to predict hit and false alarm rates from 45 the neuronal firing rates. To test the generality these effects, we also manipulated the 46 guality of V1 encoding by changing stimulus contrast or inter-stimulus interval. These 47 stimulus manipulations also resulted in consistent changes in bias measured both 48 behaviorally and neuronally. Thus, changes in sensory encoding are sufficient to drive 49 changes in bias measured using SDT.

50

#### 51 Introduction:

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53 Perceptual decision-making is a multi-step process though which sensory information 54 about the external world is first transformed into a neuronal code and then used to make 55 a behavioral choice. In this process, both sensory encoding and the cognitive aspects of 56 the decision-making process are critical factors that determine the final choice (Gold

and Shadlen, 2007; Carandini and Churchland, 2013; Romo and de Lafuente, 2013;
Hanks and Summerfield, 2017).

59

Efforts to dissect the relative contribution sensory and cognitive processes to decision-60 61 making often take advantage of signal detection theory (SDT), a classical and widely 62 used method that allows inference of the underlying neuronal response distributions and 63 decision criteria from behavioral measures (Green and Swets, 1966). In particular, SDT 64 allows the use of hit and false alarm (FA) rates to extract two aspects of the perceptual 65 decision: sensitivity (d') and bias (c). Measures of sensitivity allow inference of the 66 separability of the underlying neuronal activity evoked in response to targets and 67 distractors. Thus, this measure is thought to reflect the quality of encoding in sensory circuits that provide input to the decision-making circuits (Bashinski and Bacharach, 68 69 1980; Bennett et al., 2013; Pinto et al., 2013; Luo and Maunsell, 2015; Jurjut et al., 70 2016; Ni et al., 2017). On the other hand, bias measures the overall tendency to classify 71 the stimulus as a target or distractor. Thus, it can reflect the subject's decision criterion. 72 In fact, c is often used synonymously with "criterion" and is therefore commonly thought 73 to reveal cognitive contributions to the decision-making process and involve areas 74 downstream of sensory cortex (McDonald et al., 2000; Grove et al., 2012; Jones et al., 75 2015; Crapse et al., 2017; de Gee et al., 2017; Luo and Maunsell, 2018; van Vugt et al., 76 2018).

77

78 However, neuronal correlates of bias have also been identified in sensory cortical areas. 79 Human neuroimaging experiments have found a strong correlation between the strength 80 of representation of prior information (such as expected stimulus features or locations) 81 in sensory areas and the strength of behavioral bias (White et al., 2012; Kok et al., 82 2013; Vintch and Gardner, 2014). Similarly, spontaneous fluctuations in the excitability 83 of sensory cortical areas correlate with spontaneous fluctuations in behavioral bias (lemi 84 et al., 2017). These data suggest that activity in sensory areas can influence behavioral 85 bias. However, it is not clear whether this is due to a direct effect of sensory encoding 86 on bias or the result of a bidirectional interaction between sensory and cognitive 87 systems.

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89 In fact, there is a clear mathematical explanation for how changes in sensory encoding 90 can alter behavioral bias (Witt et al., 2015). Since bias is always measured relative to 91 the optimal criterion (Figure 1a), changes in sensory encoding that shift the optimal 92 criterion have the potential to result in changes in measured bias. This happens any 93 time that changes in the responses to the target and distractor are not opposite and 94 proportional. Thus, many manipulations that alter sensory encoding, ranging from 95 adaptation to attention, might be expected to cause changes in bias in addition to 96 sensitivity, even in the absence of a cognitive contribution.

97

98 To directly test whether changes in sensory encoding are sufficient to affect bias, we 99 trained mice on an orientation discrimination task in which we could 1) measure hit and 100 FA rate to calculate bias and sensitivity and 2) control the neuronal responses to both 101 targets and distractors. Altering responses to targets and distractors through either 102 direct optogenetic manipulation of neurons in primary visual cortex (V1) or manipulation 103 of visual stimulus properties results in a reliable change in behavioral bias with relatively 104 little impact on sensitivity. Further, electrophysiological recordings from neurons in V1 105 during each of these manipulations also revealed a strong effect on bias in the same 106 direction as during behavior. Thus, changes in bias can be driven by changes in either 107 cognitive factors or sensory encoding, and the lack of a change in sensitivity does not 108 preclude a change in sensory encoding.

109

#### 110 **Results**

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To explore whether purely sensory changes can affect measured bias in perceptual decision-making, we designed an orientation discrimination task to allow measures of hit and false alarm (FA) rate (**Figure 1b**). In this task, a head-fixed mouse presses a lever to initiate trials and releases it to report a target orientation. Each trial begins with the repeated presentation of at least two (and up to nine) iso-oriented gratings ('distractors', 100 ms duration) followed by a counterclockwise change in orientation relative to the distractor ('target', range: 9-90°; **Figure 1c**). If the mouse releases the

lever within a window 200-550 ms following the onset of the target stimulus, it is considered a hit; if the mouse releases the lever within the same window following a distractor stimulus, it is considered a FA. Thus, we can use these behavioral measures to calculate sensitivity and bias using SDT (Green and Swets, 1966).

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124 In addition to being appropriate for making measurements of SDT, this task has a 125 couple of additional advantages. First, the mice can perform the task at a high level of 126 proficiency with low lapse rates (0.053±0.008; range 0.003-0.107; n=14 mice), FA rates 127 (0.048±0.004; range 0.032-0.098; n=14 mice) and threshold for orientation 128 discrimination (25.2°±1.3°; range 14.2°-32.0°; n=14 mice). Thus, there are minimal 129 concerns about changes in motivational state or arousal that could influence our 130 measures of bias. Second, we have a good idea of how neuronal activity in primary 131 visual cortex (V1) is used to perform the behavior (Jin et al., 2018). Namely, the 132 decision-making circuits sum V1 spike rates, with particular weight on the neurons that 133 prefer targets. Thus, the decision variables and decision criterion are in units of firing 134 rate, and manipulations that coincidently alter firing rates in response to distractors and 135 targets will change the optimal criterion and therefore induce a change in measured 136 bias (Figure 1a).

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# Direct suppression and activation of V1 alters both behavioral and neuronal measures of bias

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141 To directly test the contribution of sensory encoding in V1 to measures of bias, we 142 optogentically manipulated the firing rates (FR) of V1 neurons. We virally or genetically 143 expressed excitatory opsins (ChR2 or Chronos) in either inhibitory or excitatory neurons 144 using transgenic mouse lines (PV::Cre or VGAT-ChR2 and EMX1::Cre). We then used 145 blue light to suppress or excite V1 neurons specifically during presentation of targets or 146 distractors either during performance of the orientation discrimination task (Figure 1b-c) 147 or in passively viewing mice (Figure 1d-e). Indeed, extracellular recordings from V1 148 neurons reveal that optogenetic activation of inhibitory neurons significantly reduces 149 neuronal responses to both targets near the animals' discrimination threshold and

distractors (FR changes by V1 suppression: 22.5°: -6.6±1.2 Hz, p<10<sup>-9</sup>; 0°: -5.5±1.2 Hz, 150 p<10<sup>-10</sup>: n=70 cells; Wilcoxon signed rank test; an example experiment in **Figure 1e** and 151 152 all cells in Figure S1c), while activation of excitatory neurons increases visually driven responses (FR changes by V1 excitation: 22.5°: 2.6±0.4 Hz, p<10<sup>-8</sup>; 0°: 2.5±0.3 Hz, 153 154  $p < 10^{-11}$ ; n=83 cells; Wilcoxon signed rank test; an example experiment in **Figure 1e** and 155 all cells in Figure S1g). Moreover, the waveform shapes between control and 156 optogenetic manipulations remain relatively similar (correlation coefficient: control vs. 157 V1 suppression:  $0.993 \pm 0.001$ ; control vs. V1 excitation:  $0.997 \pm 0.001$ ; Figure S1b,f). 158 Importantly, these effects are largely selective for the targeted stimulus as we see little 159 to no effect on stimuli (Stim<sub>N</sub>) for which the preceding stimulus (Stim<sub>N-1</sub>) was 160 optogenetically manipulated (FR changes by V1 suppression: 22.5°: -1.2±0.6 Hz, 161 p=0.02; 0°: -0.5±0.4 Hz, p=0.50; FR changes by V1 excitation: 22.5°: -0.2±0.3 Hz, 162 p=0.58; 0°: -0.03±0.11 Hz, p=0.79; Wilcoxon signed rank test; Figure S1d,h).

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164 Consistent with activation of inhibitory interneurons reducing firing rates, and therefore 165 the decision variable, we find that optogenetic suppression of activity in V1 reduces 166 behavioral hit rate (22.5° target: V1 suppression vs. Control: p<0.005; n=4 mice; paired 167 t-test; Figure 2a) and FA rate (V1 suppression vs. Control: p<0.05; n=4 mice; paired t-168 test). These associated changes in both hit and FA rate often reflect changes in bias (c) 169 measured by SDT. Indeed, using SDT we find a significant increase in measured bias (c 170 for 22.5° target: V1 suppression vs. Control: p<0.005; paired t-test; Figure 2b) and a 171 slight decrease in sensitivity (d' for 22.5° target: V1 suppression vs. Control: p=0.05; 172 paired t-test). Conversely, optogenetic excitation of V1 increases behavioral hit rates 173 (22.5° target: V1 excitation vs. Control: p<0.01; n=4 mice; paired t-test; Figure 2a) and 174 FA rate (V1 excitation vs. Control: p<0.01; n=4 mice; paired t-test), resulting in a 175 decrease in measured bias (c for 22.5° target: V1 excitation vs. Control: p<0.005; paired 176 t-test; Figure 2b) and a slight decrease in sensitivity (d' for 22.5° target: V1 excitation 177 vs. Control: p=0.05; paired t-test).

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To test whether the changes in firing rate can qualitatively account for the changes in behavioral bias, we used the neuronal data to directly measure bias by applying an

181 artificial decision criterion. We set the criterion to optimally discriminate the 182 optogenetically suppressed distractors (0°) from targets in the control condition (22.5°) 183 in each cell, and then used the distributions of neuronal responses to calculate hit and 184 FA rate across conditions. Suppressing neuronal activity in V1 decreases the predicted hit rate (22.5° target: V1 suppression vs. Control: p<10<sup>-6</sup>; n=47 cells; Wilcoxon signed 185 rank test; Figure 2c) and FA rate (V1 suppression vs. Control:  $p<10^{-7}$ ; n=47 cells; 186 187 Wilcoxon signed rank test) leading to an increase in measured bias (c for 22.5° target: V1 suppression vs. Control:  $p<10^{-7}$ ; Wilcoxon signed rank test; Figure 2d) without 188 189 significantly changing the sensitivity (d' for 22.5° target: V1 suppression vs. Control: 190 p=0.12; Wilcoxon signed rank test). Conversely, activating neuronal activity in V1 191 increases predicted hit (22.5° target: V1 excitation vs. Control: p<0.001; n=45 cells; 192 Wilcoxon signed rank test; Figure 2c) and FA rate (V1 excitation vs. Control:  $p < 10^{-6}$ ; 193 n=45 cells; Wilcoxon signed rank test), resulting in a decrease in measured bias (c for 22.5° target: V1 excitation vs. Control:  $p<10^{-5}$ ; Wilcoxon signed rank test; Figure 2d) 194 195 and sensitivity (d' for 22.5° target: V1 excitation vs. Control: p<0.001; Wilcoxon signed 196 rank test). Thus, our electrophysiology data shows that manipulating excitability of 197 neurons in V1 is sufficient to alter bias even in the absence of a flexible decision 198 criterion. Moreover, the neuronal and behavioral changes in bias are in the same 199 direction, suggesting that the changes in sensory encoding could be responsible for the 200 changes in behavioral bias.

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#### 202 Manipulation of stimulus contrast affects measures of bias

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204 Optogenetic tools allow for the direct manipulation of firing rates, however any 205 manipulation that coincidently increases or decreases firing rates in response to targets 206 and distractors are predicted to impact measures of bias. For instance, neurons in V1 207 have monotonic contrast-response functions (Gao et al., 2010), and therefore 208 decreasing stimulus contrast should decrease firing rates in response to both targets 209 and distractors, shifting the optimal criterion to lower stimulus values. Thus, we modified 210 our orientation discrimination task to vary stimulus contrast (30%, 50% and 70%) on a 211 presentation-by-presentation basis (Figure 3a). Extracellular recordings confirm that

manipulation of contrast significantly affected firing rates in response to both targets (22.5°: FR changes from 70% to 30%: -4.5±0.7 Hz, p<10<sup>-7</sup>; n=92 cells; Friedman test (p<10<sup>-8</sup>) with post-hoc Tukey HSD test; **Figure S3a**) and distractors (0°: FR changes from 70% to 30%: -4.2±0.5 Hz, p<10<sup>-9</sup>; n=92 cells; Friedman test (p<10<sup>-25</sup>) with post-hoc Tukey HSD test; **Figure S3b**).

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218 Consistent with lower stimulus contrast driving lower firing rates, we find that decreasing 219 stimulus contrast significantly reduces the animal's hit rate (22.5° target: p<0.05; n=5 220 mice; one-way anova (p=0.05) with post-hoc Tukey HSD test; Figure 3b) and FA rate 221 (70% vs. 30%: p<0.005; n=5 mice; one-way anova (p<0.005) with post-hoc Tukey HSD 222 test). These changes in hit and FA rate drive a significant increase in bias (c for 22.5° 223 target: 70% vs. 30%: p<0.005; n=5 mice; one-way anova (p<0.005) with post-hoc Tukey 224 HSD test; Figure 3c) without a significant change in sensitivity (d' for 22.5° target: 225 p=0.81; n=5 mice; one-way anova).

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227 As with optogenetic manipulation of neuronal activity, the effects of manipulating visual 228 stimulus features on behavior are consistent with the changes in V1 activity. Lowering 229 stimulus contrasts decreases both the predicted hit rate (22.5° target: 70% vs. 30%: 230 p<0.05; Friedman test (p<0.01) with post-hoc Tukey HSD test; Figure 3e) and FA rate  $(0^{\circ}: 70\% \text{ vs. } 30\%: \text{p}<10^{-5}; \text{ Friedman test } (\text{p}<10^{-6}) \text{ with post-hoc Tukey HSD test}),$ 231 resulting in an increase in measured bias (c for 22.5° target: 70% vs. 30%: p<10<sup>-3</sup>; 232 Friedman test (p<10<sup>-3</sup>) with post-hoc Tukey HSD test; **Figure 3f**) without significantly 233 234 changing the predicted sensitivity (d' for 22.5° target: p=0.08; Friedman test). Thus, 235 changes in the quality of sensory encoding through variation of visual stimulus 236 properties can affect behavioral and neuronal measures of bias.

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### 238 Manipulation of adaptation state affects measures of bias

Varying stimulus contrast revealed that stimulus manipulations of sensory encoding can affect measured bias. In order to demonstrate the ubiquity of this phenomenon, we manipulated a different property of the task design that affects sensory encoding: interstimulus interval (ISI; 250, 500 and 750 ms; **Figure 4a**). Varying the ISI, like varying

243 contrast, alters the strength of sensory responses, where shorter ISIs drive suppressive 244 adaptation and lower firing rates (Clifford et al., 2007; Jin et al., 2018). Indeed, 245 extracellular recordings revealed that adaptation significantly decreases the neuronal 246 responses to distractors (0°: FR changes from 750 ms to 250 ms ISI: -3.9±0.8 Hz, p<10<sup>-</sup> <sup>8</sup>; n=74 cells; Friedman test (p<10<sup>-9</sup>) with post-hoc Tukey HSD test; **Figure S4b**), while 247 slightly, but not significantly, decreasing responses to targets (22.5°: FR changes from 248 249 750 ms to 250 ms ISI: -2.4±0.8 Hz, p=0.17; n=74 cells; Friedman test; Figure S4a). 250 While there is an asymmetric effect of ISI on targets and distractors (consistent with the 251 stimulus specific effects of adaptation (Müller et al., 1999; Dragoi et al., 2000)), the net 252 effect of adaptation is to reduce firing rates and this should decrease the optimal 253 criterion and therefore increase bias.

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Consistent with this prediction, decreasing the ISI decreases both hit rate (22.5° target: 750 ms vs. 250 ms: p<0.05 n=11 mice; one-way anova (p<0.05) with post-hoc Tukey HSD test; **Figure 4b**) and FA rate (750 ms vs. 250 ms: p<10<sup>-8</sup>; n=11 mice; one-way anova (p<10<sup>-8</sup>) with post-hoc Tukey HSD test). The decrease in both hit and FA rate support an increase in measured bias (c for 22.5° target: 750 ms vs. 250 ms: p<10<sup>-4</sup>; n=11 mice; one-way anova (p<10<sup>-3</sup>) with post-hoc Tukey HSD test; **Figure 4c**), without a coincident change in sensitivity (d' for 22.5° target: p=0.85; one-way anova).

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263 As with manipulating contrast, the behavioral effects of manipulating ISI are expected 264 from the observed changes in neuronal activity recorded in V1. Using a fixed artificial 265 decision criterion, the decreased responses to targets and distractors with decreasing 266 ISI results in a significant decrease in the predicted FA rate (0°: 750 ms vs. 250 ms:  $p<10^{-4}$ ; Friedman test ( $p<10^{-4}$ ) with post-hoc Tukey HSD test; Figure 4e) and a slight, 267 268 but not significant, decrease in the hit rate (22.5° target: p=0.37; Friedman test) 269 resulting in an increase in measured bias (c for 22.5° target: 750 ms vs. 250 ms: 270 p<0.005; Friedman test (p<0.005) with post-hoc Tukey HSD test; Figure 4f) without a 271 change in sensitivity (d' for 22.5° target: p=0.26; Friedman test). Thus, the effects of ISI 272 on behavioral bias are consistent with the effects of ISI on sensory encoding. Thus, we 273 have demonstrated that both direct optogenetic, and indirect stimulus-dependent,

274 manipulations of sensory encoding affect both behavioral and neuronal measures of 275 bias.

276

#### 277 **Discussion:**

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279 Signal detection theory is a standard approach for guantifying the sensory and cognitive 280 contributions to perceptual decision-making. However, we provide both behavioral and 281 neuronal evidence that measures of bias are sensitive to changes in sensory encoding. 282 Directly manipulating neuronal excitability in V1 induced predictable changes in 283 behavioral bias with comparatively little effect on sensitivity in the performance of an 284 orientation discrimination task. Moreover, by varying either stimulus contrast or 285 adaptation state, we also observed robust changes in bias. These results clearly 286 demonstrate that changes in bias are not necessarily due to cognitive mechanisms, and 287 conversely, that the lack of a change in sensitivity does not preclude effects on sensory 288 encoding.

289

290 The optogenetic and stimulus manipulations applied in this study altered the quality of 291 stimulus encoding. These manipulations each either increase or decrease neuronal 292 responses to both targets and distractors, thereby increasing or decreasing the optimal 293 criterion. Thus, the coincident change in both hit and FA rate are interpreted in SDT as 294 a change in measured bias, even in the absence of a change in decision criterion 295 (Figure 1a). Neuronal recordings in V1 confirmed that the optogenetic and stimulus 296 manipulations shifted the target and distractor response distributions in the same 297 direction, although not necessarily by the same amount. For instance, we find that V1 298 excitation increases the response to distractors slightly more than for targets 299 (Modulation index: 0° vs. 22.5°: 0.48±0.05 vs. 0.37±0.06; p=0.07, n=83 cells; Wilcoxon 300 signed rank test), likely due to the contribution of normalization circuits (Carandini and 301 Heeger, 2012; Histed, 2018). These disproportionate changes in target and distractor 302 distributions result in a change in both neuronal and behavioral sensitivity (Figure 2). 303

304 Importantly, measurements of bias from the neuronal activity clearly demonstrate that 305 there can be changes in bias without changes in the decision criterion. We recorded 306 from passively viewing mice to rule out the possibility that feedback from cognitive 307 structures might influence the sensory responses. Moreover, in these analyses, we set 308 and fix the decision criterion across conditions. While it is possible that the optogenetic 309 and stimulus manipulations affect the animals' decision criterion, we think it is unlikely. 310 First, the optogenetic and stimulus conditions were varied on a presentation-by-311 presentation basis such that the animal could not predict the upcoming condition. 312 Therefore, it is unlikely that the mouse could adjust its decision criterion on these short 313 time scales. Even if optogenetic manipulations in V1 did change the decision criterion, 314 the decision criterion would likely remain shifted for the immediately following stimulus 315 after optogenetic termination within a trial. However we did not observe any changes in 316 the behavior measures at the current stimulus when its preceding stimulus was 317 suppressed or excited (c for 22.5°: V1 Stim<sub>N-1</sub> suppression vs. Stim<sub>N-1</sub> control:  $0.9\pm0.2$ 318 vs. 0.8±0.2, p=0.51, n=4 mice; V1 Stim<sub>N-1</sub> excitation vs. Stim<sub>N-1</sub> control: 1.0±0.1 vs. 319 0.9±0.1, p=0.31, n=4 mice; paired t-test; Figure S2). Second, these manipulations do 320 not significantly affect lapse rate across conditions (control vs. V1 suppression: p=0.13, 321 n=4 mice, paired t-test; control vs. V1 excitation: p=0.18, n=4 mice, paired t-test; across 322 contrasts: p=0.32, n=5 mice, one-way anova; across ISIs: p=0.97, n=11 mice, one-way 323 anova).

324

325 However, if the animal were to compensate for the changes in sensory encoding by 326 shifting its decision criterion, this could cancel the effects of sensory encoding on bias, 327 making it seem as though there were no change in bias at all. Therefore, a lack of a 328 change in bias does not guarantee a stable decision criterion. As we have shown, 329 changes to sensory encoding that alter the target and distractor distributions in the 330 same direction are commonplace. For instance, the classic gain-change effects of both 331 spatial and feature attention on neuronal activity should drive changes in both sensitivity 332 and bias (Treue and Maunsell, 1996; Treue and Martinez-Trujillo, 1999). In contrast, 333 changes to sensory encoding that proportionally change target and distractor

distributions in opposite directions, such that the optimal criterion is stable, are lesscommon.

336

337 Notably, these manipulations are able to induce large shifts in bias in part because of 338 the strategy that the mouse is using to perform the task (Jin et al., 2018). The circuits 339 downstream of V1 are monitoring the total firing rates of a population of target-340 responsive sensory neurons. When the firing rate of this population exceeds some 341 threshold, a change is detected. This can explain why increases in contrast, ISI or 342 excitability of V1 neurons are often mistaken for target orientations and result in 343 increased hit and FA rates. However, other decoding strategies that compute the 344 estimated orientation from the population activity, for instance through a likelihood 345 function, are also sensitive to manipulations of excitability in sensory cortex due to 346 changes in certainty, and thus may also affect measured bias (Stocker and Simoncelli, 347 2006).

348

349 We find that the effects of optogenetic manipulation of neuronal activity in V1 on 350 neuronal and behavioral bias go in the same direction. However, since we do not know 351 the quantitative transform between sensory responses and behavior, these data cannot 352 determine whether all of the changes in behavioral bias can be accounted for by 353 changes in sensory encoding. Thus, while our optogenetic data is most consistent with 354 a sensory role for V1, we cannot rule out some cognitive contributions. This reveals that 355 combining optogenetics and SDT to dissociate the sensory and cognitive contributions 356 to perceptual decision-making in distinct brain circuits is not straightforward. Realizing 357 this confound, some groups have designed tasks to support the dissociation of sensory 358 and cognitive contributions through SDT analyses. One such approach is to take 359 advantage of the temporal separability between these processes. For instance, studies 360 normally use pre-stimulus cues to bias the behavioral choice, but by adding a post-361 stimulus cue design one can better dissociate the effects of cue on sensory encoding 362 and response bias (Bang and Rahnev, 2017). Other groups have taken advantage of 363 clever stimulus design. For instance, using noisy stimulus sets to generate trial-by-trial 364 variability enables experimenters to use regression-based approaches to measure

365 stimulus sensitivity across conditions, and thereby dissociate of perceptual and 366 response bias (Wyart et al., 2012; Kloosterman et al., 2018). Together, these 367 approaches can be combined with optogenetics to determine the extent to which brain 368 areas and circuits contribute to the various stages of perceptual decision-making.

369

### 370 Methods:

371 Animals. All animal procedures conformed to standards set forth by the NIH, and were 372 approved by the IACUC at Duke University. 23 mice (both sexes; 3-24 months old; 373 singly and group housed (1-4 in a cage) under a regular 12-h light/dark cycle: C57/B6J 374 (Jackson Labs #000664) was the primary background with up to 50% CBA/CaJ 375 (Jackson Labs #000654)) were used in this study. Pvalb-cre (tm1(cre)Arbr, Jackson 376 Labs #008069; n=15; PV::Cre), VGAT-ChR2-EYFP (Slc32a1-COP4\*H134R/EYFP, 377 Jackson Labs #014548; n=2) and Emx1-IRES-Cre (tm1(cre)Krj, Jackson Labs # 378 005628; n=6; EMX1::Cre) were crossed to C57/B6J mice for in vivo extracellular 379 electrophysiology (n=11) and behavior (n=14) experiments. Note two of the mice (one 380 PV::Cre and one Emx1::Cre) were used in both behavior and recording.

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382 Cranial window implant. Dexamethasone (3.2 mg/kg, s.c.) and Meloxicam (2.5 mg/kg, 383 s.c.) were administered at least 2 h before surgery. Animals were anesthetized with 384 ketamine (200 mg/kg, i.p.), xylazine (30 mg/kg, i.p.) and isoflurane (1.2-2% in 100%  $O_2$ ). 385 Using aseptic technique, a headpost was secured using cyanoacrylate glue and C&B 386 Metabond (Parkell), and a 5 mm craniotomy was made over the left hemisphere (center: 387 2.8 mm lateral, 0.5 mm anterior to lambda) allowing implantation of a glass window (an 388 8-mm coverslip bonded to two 5-mm coverslips (Warner no. 1) with refractive index-389 matched adhesive (Norland no. 71)) using Metabond.

The mice were allowed to recover for one week before habituation to head restraint. Habituation to head restraint increased in duration from 15 min to >2 h over 1-2 weeks. During habituation and electrophysiology sessions, mice were head restrained while either allowed to freely run on a circular disc (InnoWheel, VWR) or rest in a plastic tube.

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**Visual stimulation.** Visual stimuli were presented either on a 144-Hz (Asus) or 120-Hz (Samsung) LCD monitor, calibrated with an i1 Display Pro (X-rite), for electrophysiology and behavior experiments, respectively. The monitor was positioned 21 cm from the contralateral eye. Circular gabor patches containing static sine-wave gratings alternated with periods of uniform mean luminance (60 cd/m<sup>2</sup>). Visual stimuli for electrophysiology and behavior experiments were controlled with MWorks (<u>http://mworks-project.org)</u>.

402 Three visual stimulus protocols were used for electrophysiology experiments in 403 which we varied: 1) blue light (473 nm) stimulation of single stimulus presentations 404 (each trial targeted with equal probability either: the distractor two stimuli before the 405 target, the distractor before the target, the target, or no stimulation) and target 406 orientations (22.5°, 45° and 90°; n=3 mice for each excitation and inhibition; Figure 1-407 2); 2) stimulus contrast (30, 50 and 70%) and target orientation (22.5° and 90°; n=5 408 mice **Figure 3**); and 3) number of distractor presentations (two to nine), inter-stimulus 409 interval (ISI: 250, 500 and 750 ms) and target orientation (22.5°, 45° and 90°: n=4 mice: 410 Figure 4). In the case that the stimulus properties were not varied, the default was six 411 distractor presentations, a 250 ms ISI, 100% contrast. In order to maximize the contrast-412 dependence of neuronal responses, Protocol 2 used a 20° diameter gabor at a spatial 413 frequency (SF) of 0.16 cyc/deg, to limit the contribution of increasing surround 414 suppression with increasing contrast. Protocols 1 and 3 used a 30° gabor at a SF of 0.1 415 cyc/deg. All protocols had an inter-trial interval (ITI) of 4 s. All stimulus conditions that 416 were varied on a trial-by-trial or presentation-by-presentation basis were randomly 417 interleaved.

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Retinotopic mapping. Retinotopic maps generated from intrinsic autofluorescence or 419 420 cortical reflectance (for VGAT-ChR2-EYFP mice). For intrinsic autofluorescence, the 421 brain was illuminated with blue light (473 nm LED (Thorlabs) or a white light source 422 (EXFO) with a 462 ± 15 nm band pass filter (Edmund Optics)), and emitted light was 423 measured through a green and red filter (500 nm longpass); for cortical reflectance, the 424 brain was illuminated with orange light (530 nm LED (Thorlabs)), and all of the reflected 425 light was collected. Images were collected using a CCD camera (Rolera EMC-2, 426 Qimaging) at 2 Hz through a 5x air immersion objective (0.14 numerical aperture (NA).

Mitutoyo), using Micromanager acquisition software (NIH). Stimuli were presented at 4-6 positions (drifting, sinusoidal gratings at 2 Hz) for 10 s, with 10 s of mean luminance preceding each trial. Images were analyzed in ImageJ (NIH) to measure changes in fluorescence (dF/F; with F being the average of all frames) to identify primary visual cortex (V1) and the higher visual areas. Vascular landmarks were used to identify targeted sites (V1) for electrophysiology and optogenetics experiments.

433

Viral injection. We targeted V1 in PV::Cre mice (n=4) for expression of 434 435 Channelrhodopsin2 (ChR2) and in Emx1::Cre mice (n=6) for expression of Chronos. 436 Dexamethasone (3.2 mg/kg, s.c.) was administered at least 2 h before surgery and 437 animals were anesthetized with isoflurane (1.2-2% in 100% O<sub>2</sub>). The coverslip was sterilized with 70% ethanol and the cranial window removed. A glass micropipette was 438 439 filled with virus (AAV5.EF1.dFloxed.hChR2.YFP (UPenn CS0384) or 440 AAV9.hSyn.FLEX.rc.Chronos.GFP (Addgene 59056)), mounted on a Hamilton syringe, 441 and lowered into the brain. 50 nL of virus were injected at 250 and 500 µm below the 442 pia (30 nL/min); the pipette was left in the brain for an additional 10 minutes to allow the 443 virus to infuse into the tissue. Following injection, a new coverslip was sealed in place, 444 and an optical cannula (400 µm diameter; Doric Lenses) was attached to the cranial 445 site. Optogenetic window above the injection behavioral experiments and 446 electrophysiology experiments were conducted at least two weeks following injection to 447 allow for sufficient expression.

448

449 **Extracellular electrophysiology.** Electrophysiological signals were acquired with a 32-450 site polytrode acute probe (either A4x8-5mm-100-400-177-A32 (4 shanks, 8 site/shank 451 at 100 µm spacing) or A1x32-Poly2-5mm-50s-177-A32, (1 shank, 32 sites, 25 µm 452 spacing), NeuroNexus) through an A32-OM32 adaptor connected to a Cereplex digital 453 headstage (Blackrock Microsystems). Unfiltered signals were digitized at 30 kHz at the 454 headstage and recorded by a Cerebus multichannel data acquisition system (Blackrock 455 Microsystems). Visual stimulation synchronization signals were also acquired through 456 the same system via a photodiode directly monitoring LCD output.

457 On the day of recording, the cranial window was removed, and a small durotomy 458 performed to allow insertion of the electrode into V1. A ground wire was connected via a 459 gold pin cemented in a burrhole in the anterior portion of the brain. The probe was 460 slowly lowered into the brain (over the course of 15 min with travel length of around 800 461 µm) until the most superficial recording site was in the brain and allowed to stabilize for 462 45 - 60 min before beginning recordings. For optogenetic stimulation in protocol 1, the 463 optic fiber was held in place via an articulated arm (Flexbar, SKU: 14830) to allow light 464 delivery (473 nm LED, Thorlabs) to the recording site. For V1 suppression, the mean 465 light power was 0.28±0.02 mW (range: 0.1-0.4 mW); and for V1 excitation, the mean light power was 0.05±0.003 mW (range: 0.03-0.06 mW), matching the ranges that were 466 467 used in the behavioral tests.

468 Of the 11 mice that were used for extracellular electrophysiology, 3 were 469 previously trained in the orientation discrimination task, 3 were trained in a contrast 470 discrimination task, and 5 were naïve.

471

472 Behavioral task. Animals were water scheduled and trained to discriminate orientations 473 in visual stimuli by manipulating a lever. The behavior training and testing occurred 474 during the light cycle. We first trained mice to detect full-field, 90° orientation difference 475 (target) from a static grating. Most mice (n=12) were trained with a 0° distractor; 476 however, 2 mice were trained with a 45° distractor. On the initial days of training, mice 477 were rewarded for holding the lever for at least 400 ms (required hold time) but no more 478 than 20 s (maximum hold time). At the end of the required hold time, the grating 479 changed orientation and remained horizontal until the mouse released the lever (or the 480 maximum hold time expired). Typically, within two weeks of training, the mice began 481 releasing the lever as soon as the target orientation appears. Once the animals began 482 reliably responding to the target orientation, we added a random delay between lever 483 press and target stimulus to discourage adoption of a timing strategy. Over the course 484 of the next few weeks, the task was made harder by (in roughly chronological order): 1) 485 increasing the random delay, 2) decreasing the target stimulus duration and reaction 486 time window, 3) removing the stimulus during the ITI, 4) shrinking and moving the 487 stimuli to more eccentric positions, 5) adding a mean-luminance ISI to mask the motion

488 signal in the orientation change, and finally 6) introducing hard targets (range: 9-90°).
489 Delays after errors were also added to discourage lapses and early releases.

490 In the final form of the task, each trial was initiated when the ITI (3s) had elapsed 491 and the mouse had pressed the lever. Trial start triggered the presentation of a 100 ms 492 static sinusoidal, gabor patch (30° in diameter, SF of 0.1 cycle/deg, positioned at an 493 eccentricity of  $30^{\circ}$  -  $40^{\circ}$  in azimuth and  $0^{\circ}$  -  $10^{\circ}$  in elevation) followed by an ISI randomly 494 selected on a presentation-by-presentation basis (250, 500 or 750 ms). For a subset of 495 mice (n=5, Figure 3), the contrast of each presentation was also randomized 496 (Michelson contrast: 30%, 50% and 70%); in these experiments the stimulus size was 497 reduced to 20° and the SF increased to 0.16 cycle/deg, at 5°-15° in azimuth and 10° in 498 elevation to 1) reduce the surround suppression and 2) compensate for the difficulty 499 induced by low contrast and small size of the stimuli. The target orientation occurred 500 with a random delay (flat distribution) after the first two presentations on each trial and 501 the target orientation was randomly selected from a fixed set of values around each 502 animal's threshold. Mice received water reward if they released the lever within 100-650 503 ms (sometimes extended to 1000 ms) after a target occurred. However, for calculating 504 hit and false alarm (FA) rate, we use a narrower reaction window (200-550 ms) to 505 ensure that the majority of the releases in this window are due to stimulus driven 506 responses and have independent reaction windows for adjacent stimuli with short ISIs.

507 For optogenetic stimulation (Figure 1-2), we delivered blue light to the brain 508 though the cannula from a 473 nm LED (Thorlabs) or a 450 nm laser (Optoengine) and 509 calibrated the total light intensity at the entrance to the cannula. The light power is 510 titrated so that it does not induce significant changes in the lapse rate for both V1 511 suppression (lapse rate: control vs. V1 suppression: 0.08±0.01 vs. 0.10±0.02; p=0.13, 512 n=4 mice, paired t-test) and V1 excitation (control vs. V1 excitation: 0.12±0.06 vs. 513 0.06±0.03; p=0.18, n=4 mice, paired t-test). For V1 suppression, the mean light power 514 was 0.27±0.07 mW (range: 0.07-0.4 mW); and for V1 excitation, the mean light power 515 was 0.06±0.02 mW (range: 0.02-0.1 mW, Figure 2a-b). On each trial, a single stimulus 516 (either the distractor two stimuli before the target, the distractor before the target, the 517 target, or the distractor after the target) was targeted with equal probability. The light 518 was turned on around 30ms before the time of visual presentation onset for the duration

519 of the stimulus (100 ms). Behavioral control was done with MWorks, and custom 520 software in MATLAB (MathWorks).

Notably, there are overlapping animals in dataset of the optogenetic (**Figure 1-2**), contrast (**Figure 3**) and ISI manipulations (**Figure 4**). Below, we provided a table (**Table 1**) that describes the mice overlap and difference in time in collecting these datasets. Numbers (1-3) indicate the time sequence of the tasks that were tested and data was collected for each mouse, while 0 reflects no training on that task. Four mice were trained in a single task, 9 mice were trained on two tasks thus belonged to two datasets, and only 1 mouse was included in all datasets.

- 528
- 529

#### Table 1| Mice overlap and timeline among three datasets

Mouse ID#	Genotype	Optogenetics	Contrast	ISI
а	EMX1::Cre	1	0	0
b	EMX1::Cre	1	2	0
С	VGAT-ChR2	1	2	0
d	EMX1::Cre	2	0	1
е	EMX1::Cre	2	0	1
f	PV::Cre	2	0	1
g	VGAT-ChR2	2	0	1
h	PV::Cre	3	2	1
i	PV::Cre	0	2	1
j	PV::Cre	0	2	1
k	PV::Cre	0	2	1
I	PV::Cre	0	0	1
m	PV::Cre	0	0	1
n	PV::Cre	0	0	1

530

### 531 Data processing

*Electrophysiology processing and analysis.* Individual single units were isolated using the SpyKing CIRCUS package (<u>http://spyking-circus.readthedocs.io/en/latest/</u>). Raw data were first high pass filtered (> 500 Hz) and spikes were detected when a filtered voltage trace crossed threshold (9-13 median absolute deviations computed on each 536 channel). A combination of density-based clustering and template matching algorithms 537 were used to automatically cluster the spikes. The resulting clusters were then 538 inspected and adjusted manually using a MATLAB GUI. Clusters with refractory period 539 violations (< 2 ms, >1% violation) in the auto-correlogram and that were not stable 540 across the whole recording session were discarded from the dataset. Clusters were 541 combined if they met each of three criteria by inspection: 1) similar waveforms; 2) 542 coordinated refractory periods in the cross-correlogram; 3) similar inter-spike interval 543 distribution shape. Unit position with respect to the recording sites was calculated as the 544 average of all site positions weighted by the waveform amplitude of each site. For V1-545 suppression or excitation experiments, we also quantified the similarity of the 546 waveforms between control and optogenetic conditions using correlation coefficient (r) 547 values. Because for majority of the cells, V1 suppression strongly reduce firing rate 548 (Figure S1c) rendering few or even no spikes for analyzing waveforms, we extended 549 the window starting from 200 ms before visual onset, end with 250 ms after visual 550 offset. Signal and noise ratio of the trough value of the waveform shape was calculated 551 as mean divided by SD across spikes. All of the subsequent analysis was performed in 552 MATLAB.

553 Visually-evoked responses of each unit in V1 were measured based on average 554 peri-stimulus time histograms (PSTHs, bin size: 20 ms) over repeated presentations 555 (>25 trials) of the same stimulus. Response amplitudes were measured on a trial-by-trial 556 basis: by subtracting the firing rate at the time of the visual stimulus onset from the 557 value at the peak of the average PSTH within a window of 0-100 ms after the visual 558 onset. However, in the case of V1 excitation, responses were measured by subtracting 559 the baseline firing rate (value at visual onset, bin 0 ms, multiplied by 6) from the number 560 of spikes during the visual presentation window (0-100ms, 6 bins). This is because the 561 peak response latencies after V1 excitation were often shorter than the latencies of the 562 visual responses in the control condition. "Responsive cells" were chosen as having 563 statistically significant visually-evoked responses using a paired t-test to compare 564 baseline responses (averaged over 0-100 ms before the visual onset) with visually-565 evoked responses (averaged over 0-100 ms after the visual onset; this analysis window 566 excluded off-responsive units from analysis). For all protocols, we included cells that

were significantly driven by either the first distractor stimulus or any of the target orientations. For V1 suppression experiments, we excluded cells that were significantly driven by the light stimulation. For protocol 2, this test was only performed for the highest contrast stimuli. Thus, we included 70/110 cells for V1 suppression; and 83/109 cells for V1 excitation; for protocol 2, we included 92/151 cells and for protocol 3, 74/100 cells were included; Modulation index (MI) of V1 excitation on neuronal responses (R) is calculated as:

$$MI = \frac{R_{excite} - R_{control}}{|R_{excite}| + |R_{control}|}$$

574 For calculation of predicted hit rate and FA rate: the distribution of single trial 575 responses to the 22.5° target was compared to the distribution of responses to the distractor (0°, 3<sup>rd</sup>-6<sup>th</sup> stimulus). For protocol 1 - V1 suppression, the artificial decision 576 577 criterion for each cell was fixed as the mean of the responses to the suppressed 578 distractor and the target in control. For protocol 1 - V1 excitation, the artificial decision 579 criterion for each cell was fixed as the mean of the responses to the distractor in control 580 conditions and the excited target. For protocol 2, the artificial decision criterion was fixed 581 across all contrasts for each cell as the mean of the responses to the lowest contrast 582 distractor (0°-30%) and the highest contrast target (22.5°-70%). For protocol 3, the 583 artificial decision criterion was fixed across all ISIs for each cell as the mean of the 584 responses to the most adapted distractor (0°-250ms ISI) and the most recovered target 585 (22.5°-750 ms ISI). Thus, hit rate or FA rate across all conditions (either contrasts, ISIs or V1 suppression/excitation) were calculated as percentage of trials of the target or 586 587 distractor responses that is higher than the artificial decision criterion, respectively.

588 Signal detection theory (Green and Swets, 1966) was applied to measure 589 neuronal sensitivity (d') and bias (c). For the extreme values of 0 and 1 for the predicted 590 hit rate and FA rate, it is adjusted as follows to allow calculate sensitivity (d') and bias 591 (c): rates of 0 was replaced with 0.5/n, and rates of 1 was replaced with (n-0.5)/n, where 592 n is the number of target or distractor trials (Macmillan and Kaplan, 1985; Stanislaw and 593 Todorov, 1999). d' and c were then calculated as follows:

d' = Z(hit rate) - Z(FA rate) $c = -\frac{Z(hit rate) + Z(FA rate)}{2}$ 

where Z is the inverse of the cumulative distribution function of the normal Gaussian distribution. To avoid confounds of directionality (since an increase in a positive d' and a decrease in a negative d' are both increases in sensitivity), only cells that had a positive d' in the control condition (V1 suppression- 47/70; V1 excitation- 45/83), or across contrasts (19/92) and ISIs (21/74 cells) were included.

599

600 Behavior processing and analysis.

601 All behavioral processing and analysis were performed in MATLAB. All trials were 602 categorized as either an early release, hit, or miss based on the time of release relative 603 to target onset: responses occurring earlier than 100 ms after the target stimulus were 604 considered early releases; responses occurring between 200 and 550 ms after the 605 target were considered hits; failures to respond before 550 ms after the target were 606 considered misses. Behavioral sessions were manually cropped to include only stable 607 periods of performance and were further selected based on the following criteria: for 608 protocol 1: 1) at least 40% of trials were hits; and 2) less than 50% of trials were early 609 releases; for protocols 2&3: 1) at least 50% of trials were hits; and 2) less than 35% of 610 trials were early releases. Based on these criteria, the data in Figure 2 - V1 611 **suppression** included  $16 \pm 3$  (range: 8-19) sessions for each mouse with  $4793 \pm 706$ 612 trials (range: 3408-6695); Figure 2 - V1 excitation included 29 ± 13 (range: 3-58) 613 sessions for each mouse with 8416 ± 3981 trials (range: 1551-18102); the data in Figure 3 included 34 ± 13 (range: 11-75) sessions for each mouse with 8975 ± 3519 614 615 trials (range: 1017-23181), respectively; the data in **Figure 4** included 17± 3 sessions 616 (range: 5-46) for each mouse with an average of  $6348 \pm 815$  trials per mouse (range: 617 2593-11857).

618 Hit rate was computed from the number of hits and misses for each stimulus 619 type:

# $Hit \, rate = \frac{hit}{hit + miss}$

All distractor stimulus presentations were categorized as either a CR or a FA: responses occurring between 200 and 550 ms after a distractor stimulus were considered FAs; presentations where the mouse held the lever for at least 550 ms after

623 the distractor stimulus were considered CRs. FA rate was computed from the total 624 number of FAs and CRs in the session:

$$FA \, rate = \frac{FA}{FA + CR}$$

Hit and FA rate were used calculate behavioral d' and c the same equations as were used to calculate d' and c for the neuronal data. Since the detection threshold varies across mice and not all the mice have been sampled at exactly the same orientations such as 22.5°, the hit rate for 22.5° is extrapolated based on a Weibull function fitted from the psychometric curve for each mouse.

630

#### 631 **Statistical analysis.**

632 Data were tested for normality using a Lilliefors test. While behavioral measures were 633 normally distributed, electrophysiological measures of spike rates were not. Therefore, 634 behavioral data were compared with either a t-test or ANOVA with post hoc Tukey HSD 635 test for datasets with two and multiple groups, respectively. However, for the neuronal 636 activity we used only non-parametric tests (Wilcoxon signed rank test and Friedman test 637 with post hoc Tukey HSD test to compare two and multiple groups, respectively). 638 Sample sizes were not predetermined by statistical methods, but are similar to other 639 studies. Data collection and analysis were not performed blind to experimental 640 conditions, but all visual presentation conditions in extracellular recording and behavior 641 experiments are randomized.

642

#### 643 **Data and code availability.**

644 All relevant data and code are available from the corresponding author upon reasonable 645 request.

646

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  109:3593–3598.
- 743
- 744 **Figure Legends**

# Figure 1 - Optogenetically suppressing or exciting V1 decreases or increases both signal and noise distributions in an orientation discrimination task.

747 (a) Schematic of effect of shifting signal and noise distributions on bias measured using 748 signal detection theory. Top: distributions of target (22.5°, solid black) and distractor (0°, 749 solid gray) responses. Note that bias (c) is measured as the distance between the 750 actual (black vertical line) and optimal (c=0, gray vertical line) criterion. Bottom: 751 manipulations that decrease both the target and distractor distributions shift the optimal 752 criterion to the left, and therefore result in an increase in bias. (b) Schematic of behavior 753 setup and trial progression. Blue light is turned on for a single target or distractor 754 presentation on each trial. V1 suppression (blue) and excitation (red) is achieved via 755 optogenetically driving PV+ or VGAT+ neurons and Emx1+ neurons respectively. (c) Hit 756 rate and FA rate (inset) for control (black) and V1 suppression (blue, left) or excitation 757 (red, right) for one example mouse each. Hit rates are fit with a Weibull function; vertical 758 dotted lines are threshold, error is 95% confidence interval. (d) Schematic of 759 extracellular recording setup. Stimuli are presented as in b. (e) Distributions of spikes 760 summed across a simultaneously recorded population in response to distractor  $(0^\circ,$ 761 open bars) and target (22.5°, filled bars) stimuli on control trials (black) and during V1 762 suppression (blue, n=17 cells, left) or excitation (red, n=16 cells, right) for one example 763 experiment each. Triangles show the mean of the distribution.

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### Figure S1 – related to Figure 1 - Optogenetically suppressing or exciting V1 decreases or increases neuronal responses to both targets and distractors.

768 (a) Left: an example cell's responses to 22.5° target (top) and 0° distractor (bottom) for 769 control (black) and V1 suppression (blue). Shaded areas are SEM across trials. Right: 770 mean waveform shapes for control and V1 suppression for the same cell in the left. 771 Shaded areas are SD across spikes. Correlation coefficient (r) is shown to reveal the 772 similarity in the waveform shapes between control and V1 suppression. Signal-to-noise 773 ratio (SNR, mean/SD) of the trough value of the waveform is also shown. (b) Histogram 774 of the correlation coefficient (r, top) and SNR values across all the cells (n=70 cells). (c) 775 Comparison of neuronal responses (FR in Hz) to the 22.5° target (left) and 0° distractor

(right) between control and V1 suppression (blue) on the current stimulus (Stim<sub>N</sub>). Light colors are individual cells and dark colors are the mean of the populations. Error bars are SEM across 70 cells (3 mice). (d) Comparison of neuronal responses to the 22.5° target (left) and 0° distractor (right) on Stim<sub>N</sub> when the previous stimulus (Stim<sub>N-1</sub>) was suppressed vs. control. (e-h) Same as a-d, for V1 excitation (red, n=83 cells, 3 mice).

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### Figure 2 - Suppressing or exciting V1 increases or decreases behavioral and neuronal bias.

785 (a) Comparison of the hit (22.5°, left) and FA rate (0°, right) between control and V1 786 suppression (blue, n=4 mice) or excitation (red, n=4 mice). Light colors are individual 787 mice and dark colors are the mean of the population. Error bars are SEM across mice. 788 (b) Same as a, for bias (left) and sensitivity (right) at 22.5°. (c) Same as a, for predicted 789 hit (22.5°, left) and FA rate (0°, right) from neuronal responses using a fixed criterion for 790 each cell (see Methods). (d) Predicted bias (left) and sensitivity (right) using the 791 predicted hit and FA rate in c. Extreme values of hit and FA rate were corrected (see 792 Methods). Error bars are SEM across cells (V1 suppression-blue: n=47 cells, 3 mice; V1 793 excitation-red, n=45 cells, 3 mice).

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### Figure S2 – related to Figure 2 - Lack of effects of $Stim_{N-1}$ suppression or excitation on behavior measures at $Stim_N$ .

(a) Comparison of hit rate (22.5°, left) and FA rate (0°, right) on Stim<sub>N</sub> when the previous
stimulus (Stim<sub>N-1</sub>) was suppressed (blue) vs. control. Light colors are individual mice and
dark colors are the mean of the populations. Error bars are SEM across mice (n=4
mice). (b) Same as a, for bias (left) and sensitivity (right) measures for 22.5° target. (cd) Same as a-b, for V1 excitation (red, n=4 mice).

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Figure 3 - Decreasing stimulus contrast decreases both hit and FA rate and
 increases behavioral and neuronal bias.

807 (a) Left: schematic of behavioral setup. Stimulus contrast is varied (30% (light grav), 50% (dark gray) or 70% (black)) on each stimulus presentation. Right: hit rate and FA 808 809 rate (inset) for each contrast for an example mouse. Hit rates are fit with a Weibull 810 function; vertical dotted lines are threshold, error is 95% confidence interval. (b) 811 Comparison of hit (left, 22.5° target) and FA rate (right, 0° distractor) between two 812 contrasts (70% vs 30%). Gray circles are individual mice and black circle is the mean of 813 the population. Error bars are SEM across 5 mice. (c) Same as b, for bias (left) and 814 sensitivity (right) at 22.5°. (d) Left: schematic of extracellular recording setup. Right: 815 response distributions to distractor (0°, open bars) and target (22.5°, filled bars) stimuli 816 of 30% (light gray) and 70% (black) contrast in an example cell. Triangles are the mean 817 of the distribution. The criterion (vertical red line; see Methods) was determined for each 818 cell and used to predict neuronal hit and false alarm rates for all contrasts. (e-f) Same 819 as b-c, for predicted (e) hit and FA rate and (f) bias and sensitivity from the neuronal 820 data (n = 19 cells, 4 mice).

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# Figure S3 - related to Figure 3 - Reducing stimulus contrast reduces neuronal responses to both targets and distractors.

(a) Comparison of neuronal responses (FR in Hz) to the 22.5° target between 30% and
70% contrasts. Gray circles are individual cells and black circle is the mean of the
population. Error bars are SEM across 92 cells (4 mice). (b) Same as a, for responses
to the 0° distractor.

829 830

# Figure 4 - Adaptation decreases both hit and FA rate and increases behavioral and neuronal bias.

(a) Left: schematic of behavioral setup. Inter-stimulus interval (ISI) is varied (250 ms
(light gray), 500 ms (dark gray) or 750 ms (black)) on each stimulus presentation. Right:
hit rate and FA rate (inset) for each ISI for an example mouse. Hit rates are fit with a
Weibull function; vertical dotted lines are threshold, error is 95% confidence interval. (b)
Comparison of hit (left, 22.5° target) and FA rate (right, 0° distractor) between two ISIs

838 (750 vs. 250 ms). Gray circles are individual mice and black circle is the mean of the 839 population. Error bars are SEM across 11 mice. (c) Same as b, for bias (left) and 840 sensitivity (right) at 22.5°. (d) Left: schematic of extracellular recording setup. Right: 841 response distributions to distractor (0°, open bars) and target (22.5°, filled bars) stimuli 842 following 250 (gray) or 750 ms (black) ISI for an example cell. Triangles show the mean 843 of the distribution. The criterion (vertical red line: see Methods) was determined for each 844 cell and used to predict neuronal hit and false alarm rates for all ISIs. (e-f) Same as b-c, 845 for predicted (e) hit and FA rate and (f) bias and sensitivity from the neuronal data (n =846 21 cells, 4 mice).

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### Figure S4 - related to Figure 4 - Adaptation reduces neuronal responses to both targets and distractors.

(a) Comparison of neuronal responses (FR in Hz) to the 22.5° target after 750 or 250

ms ISIs. Gray circles are individual cells and black circle is the mean of the population.

853 Error bars are SEM across 74 cells (4 mice). (**b**) Same as **a**, for responses to the 0° 854 distractor.



**Optogenetically suppressing or exciting V1 decreases or increases both signal and noise distributions in an orientation discrimination task.** (a) Schematic of effect of shifting signal and noise distributions on bias measured using signal detection theory. Top: distributions of target (22.5°, solid black) and distractor (0°, solid gray) responses. Note that bias (c) is measured as the distance between the actual (black vertical line) and optimal (c=0, gray vertical line) criterion. Bottom: manipulations that decrease both the target and distractor distributions shift the optimal criterion to the left, and therefore result in an increase in bias. (b) Schematic of behavior setup and trial progression. Blue light is turned on for a single target or distractor presentation on each trial. V1 suppression (blue) and excitation (red) is achieved via optogenetically driving PV+ or VGAT+ neurons and Emx1+ neurons respectively. (c) Hit rate and FA rate (inset) for control (black) and V1 suppression (blue, left) or excitation (red, right) for one example mouse each. Hit rates are fit with a Weibull function; vertical dotted lines are threshold, error is 95% confidence interval. (d) Schematic of extracellular recording setup. Stimuli are presented as in **b**. (e) Distributions of spikes summed across a simultaneously recorded populations in response to distractor (0°, open bars) and target (22.5°, filled bars) stimuli on control trials (black) and during V1 suppression (blue, n=17 cells, left) or excitation (red, n=16 cells, right) for one example experiment each. Triangles show the mean of the distribution.



**Optogenetically suppressing or exciting V1 decreases or increases neuronal responses to both targets and distractors.** (a) Left: an example cell's responses to 22.5° target (top) and 0° distractor (bottom) for control (black) and V1 suppression (blue). Shaded areas are SEM across trials. Right: mean waveform shapes for control and V1 suppression for the same cell in the left. Shaded areas are SD across spikes. Correlation coefficient (r) is shown to reveal the similarity in the waveform shapes between control and V1 suppression. Signal-to-noise ratio (SNR, mean/SD) of the trough value of the waveform is also shown. (b) Histogram of the correlation coefficient (r, top) and SNR values across all the cells (n=70 cells). (c) Comparison of neuronal responses (FR in Hz) to the 22.5° target (left) and 0° distractor (right) between control and V1 suppression (blue) on the current stimulus (Stim<sub>N</sub>). Light colors are individual cells and dark colors are the mean of the populations. Error bars are SEM across 70 cells (3 mice). (d) Comparison of neuronal responses (FR in Hz) to the 22.5° target (left) and 0° distractor (right) on Stim<sub>N</sub> when the previous stimulus (Stim<sub>N-1</sub>) was suppressed vs. control. (**e-h**) Same as **a-d**, for V1 excitation (red, n=83 cells, 3 mice).



**Suppressing or exciting V1 increases or decreases behavioral and neuronal bias.** (a) Comparison of the hit (22.5°, left) and FA rate (0°, right) between control and V1 suppression (blue, n=4 mice) or excitation (red, n=4 mice). Light colors are individual mice and dark colors are the mean of the population. Error bars are SEM across mice. (b) Same as a, for bias (left) and sensitivity (right) at 22.5°. (c) Same as **a**, for predicted hit (22.5°, left) and FA rate (0°, right) from neuronal responses using a fixed criterion for each cell (see Methods). (d) Predicted bias (left) and sensitivity (right) using the predicted hit and FA rate in **c**. Extreme values of hit and FA rate were corrected (see Methods). Error bars are SEM across cells (V1 suppression-blue: n=47 cells, 3 mice; V1 excitation-red, n=45 cells, 3 mice).





Lack of effects of  $Stim_{N-1}$  suppression or excitation on behavior measures at  $Stim_{N-1}$  (a) Comparison of hit rate (22.5°, left) and FA rate (0°, right) at  $Stim_{N}$  when  $Stim_{N-1}$  was suppressed (blue) vs. control. Light colors are individual mice and dark colors are the mean of the populations. Error bars are SEM across mice (n=4 mice). (b) Same as **a**, for bias (left) and sensitivity (right) measures for 22.5° target. (**c-d**) Same as **a-b**, for V1 excitation (red, n=4 mice).



**Decreasing stimulus contrast decreases both hit and FA rate and increases behavioral and neuronal bias.** (a) Left: schematic of behavioral setup. Stimulus contrast is varied (30% (light gray), 50% (dark gray) or 70% (black)) on each stimulus presentation. Right: hit rate and FA rate (inset) for each contrast for an example mouse. Hit rates are fit with a Weibull function; vertical dotted lines are threshold, error is 95% confidence interval. (b) Comparison of hit (left, 22.5° target) and FA rate (right, 0° distractor) between two contrasts (70% vs 30%). Gray circles are individual mice and black circle is the mean of the population. Error bars are SEM across 5 mice. (c) Same as b, for bias (left) and sensitivity (right) at 22.5°. (d) Left: schematic of extracellular recording setup. Right: response distributions to distractor (0°, open bars) and target (22.5°, filled bars) stimuli of 30% (light gray) and 70% (black) contrast in an example cell. Triangles are the mean of the distribution. The criterion (vertical red line; see Methods) was determined for each cell and used to predict neuronal hit and false alarm rates for all contrasts. (e-f) Same as b-c, for predicted (e) hit and FA rate and (f) bias and sensitivity from the neuronal data (n = 19 cells, 4 mice).



**Reducing stimulus contrast reduces neuronal responses to both targets and distractors.** (a) Comparison of neuronal responses (FR in Hz) to the 22.5° target between 30% and 70% contrasts. Gray circles are individual cells and black circle is the mean of the population. Error bars are SEM across 92 cells (4 mice). (b) Same as a, for responses to the 0° distractor.



Adaptation decreases both hit and FA rate and increases behavioral and neuronal bias. (a) Left: schematic of behavioral setup. Inter-stimulus interval (ISI) is varied (250 ms (light gray), 500 ms (dark gray) or 750 ms (black)) on each stimulus presentation. Right: hit rate and FA rate (inset) for each ISI for an example mouse. Hit rates are fit with a Weibull function; vertical dotted lines are threshold, error is 95% confidence interval. (b) Comparison of hit (left, 22.5° target) and FA rate (right, 0° distractor) between two ISIs (750 vs. 250 ms). Gray circles are individual mice and black circle is the mean of the population. Error bars are SEM across 11 mice. (c) Same as b, for bias (left) and sensitivity (right) at 22.5°. (d) Left: schematic of extracellular recording setup. Right: response distributions to distractor (0°, open bars) and target (22.5°, filled bars) stimuli following 250 (gray) or 750 ms (black) ISI for an example cell. Triangles show the mean of the distribution. The criterion (vertical red line; see Methods) was determined for each cell and used to predict neuronal hit and false alarm rates for all ISIs. (e-f) Same as b-c, for predicted (e) hit and FA rate and (f) bias and sensitivity from the neuronal data (n = 21 cells, 4 mice).



Adaptation reduces neuronal responses to both targets and distractors. (a) Comparison of neuronal responses (FR in Hz) to the 22.5° target after 750 or 250 ms ISIs. Gray circles are individual cells and black circle is the mean of the population. Error bars are SEM across 74 cells (4 mice). (b) Same as a, for responses to the 0° distractor.