**Cortical adaptation to acoustic contrast predicts perception of signals in noise.**

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**Abstract**

The responses of sensory neurons adapt to stimuli with persistent statistical properties. In many cases, this adaptation is efficient, resulting in neural codes that maximize information about the stimulus. Contrast gain control is a form of efficient adaptation in the auditory cortex and is believed to be crucial for enhancing the detection of signals embedded in background noise. However, it is unclear whether and how the dynamics of contrast gain control inform behavioral perception in noisy environments. Here, we trained mice to detect a target presented in background noise shortly after a change in the contrast of the background. The observed changes in cortical gain and detection behavior followed the predictions of a normative model of efficient contrast gain control; specifically, target detection and sensitivity to target level improved in low contrast backgrounds relative to high contrast backgrounds. Additionally, the time course of target detectability adapted asymmetrically depending on contrast, decreasing rapidly after a transition to high contrast, and increasing slowly after a transition to low contrast. Auditory cortex was required for detection of targets in background noise and cortical neuronal responses exhibited the patterns of target detectability observed during behavior and in the normative model. Furthermore, variability in cortical gain predicted behavioral performance beyond the effect of stimulus-driven gain control. Combined, our results demonstrate that dynamic gain changes in auditory cortex predict behavioral performance in a signal in background detection task.

**Introduction**

As we perceive the world around us, the statistics of the environment can change dramatically. In order to maintain stable percepts, it is crucial for the nervous system to adapt to persistent statistical properties of sensory inputs. The efficient coding hypothesis postulates that the nervous system accomplishes this by matching the limited dynamic range of individual neurons to the statistics of incoming sensory signals1, allowing them to encode information within many types of environments2–4. Indeed, adaptation to environmental statistics has been found in many sensory modalities and species5–13. In the auditory system, neurons exhibit contrast gain control, adapting the gain of their response function to match the variability in level (contrast) of the incoming sounds14–19. Yet, it is unknown whether and how the dynamics of contrast gain control in the auditory system inform behavior, as the dynamics of neuronal adaptation has not previously been measured simultaneously with behavior. The goal of our study was to test whether the dynamics of contrast gain control in auditory cortex predict changes in the perceptions of targets embedded in noise.

Contrast gain control is thought to create sensory representations of sounds that are invariant to background noise20. In the ferret auditory pathway, representations of sounds become more noise-tolerant in higher auditory areas, and the amount of noise-tolerance correlates with the strength of adaptation to the stimulus statistics, suggesting that level adaptation and gain control enhance the encoding of stimuli embedded in stationary noise16. Additionally, recent psychophysical studies suggest that perception in noise is altered by efficient adaptation to stimulus statistics. In humans, target level discriminability is greater in low contrast than in high contrast, an effect consistent with gain control observed in primary auditory cortex19. Similar relationships between gain control and behavioral percepts of sound location have also been found in ferrets10 and guinea pigs21. However, in these previous studies, the measurement of psychophysical performance and neuronal gain control were performed separately in human and animal subjects, respectively, so it remains unclear how variability in adaptation over sessions or subjects relates to behavioral performance. Additionally, these previous studies focus primarily on behavioral performance after complete adaptation to stimulus contrast, while recent work has highlighted the dynamical nature of efficient adaptation22,23. In the current study, we aimed to assess whether and how the dynamics of contrast gain control predicted behavioral performance across subjects.

First, we established a normative framework to model the neuronal dynamics of gain control and predict how contrast adaptation should affect the detection of signals in noise. We then derived a novel procedure for estimating moment-to-moment changes in neuronal gain based on generalized linear models (GLM) and found the dynamics of gain control in auditory cortex were asymmetric, as predicted by the normative model. Next, to test the role of contrast gain control in auditory behavior, we trained mice to detect targets after a change in background contrast. We found that contrast-induced changes in behavioral target detection threshold, sensitivity, and adaptation dynamics followed the normative model predictions. Furthermore, we found that auditory cortex was necessary for detection in the presence of a background, but not for detection in silence, suggesting a distinct role of auditory cortex in separating targets from the background. Building on this finding, we found that the dynamics of cortical encoding of targets resembled the normative model predictions and observed behavioral adaptation, and that population activity in auditory cortex predicted individual variability in task performance. Finally, we estimated cortical gain during the task, finding that variability in neural gain predicted variability in task performance. Combined, our results identify a predictive relationship between gain control and behavioral detection of signals in noise, and provide a normative framework to predict the dynamics of behavioral performance in changing sensory environments.

**Results**

*A novel target-in-background detection task and normative model for task predictions.*

To assess how perceptual performance is impacted by stimulus contrast, we devised a GO/NO-GO task in which mice were trained to detect targets embedded in low and high contrast backgrounds. During each trial, the mouse was presented with dynamic random chords (DRCs) of one contrast, which switched after 3 s to the other contrast. At variable delays after the contrast switch, broad-band target chords were superimposed on the background chords, and mice were trained to lick for a water reward upon hearing the target (henceforth, we refer to high-to-low contrast trials as “low contrast” and low-to-high contrast trials as “high contrast”, referring to the contrast where mice detected targets). Target trials were interleaved with background-only trials, during which the mouse was trained to withhold licking, but would receive a 7s timeout for licking after the contrast switch (Figure 1a,b). To assess behavioral sensitivity to targets, we parametrically varied target level in each contrast and to assess behavioral adaptation, we parametrically varied target timing (Figure 1c). This stimulus design allowed us to quantitatively test whether and how the dynamics of adaptation to background contrast affect behavioral performance.

To predict the optimal time course of contrast gain control and its impact on target detection behavior, we developed a normative model of task performance constrained by efficient neural coding. In this model, we simulated a neuron designed to encode stimuli with minimal error. To efficiently exploit its finite dynamic range, the model neuron estimated the contrast of the recent stimuli, and adjusted the gain of its nonlinearity to minimize the error in estimated contrast (Figure 1d, panels 1-3; *Online Methods*)22,23. Adding targets at different levels and times relative to contrast transitions allowed us to probe the sensitivity of the model neuron to targets of varying strength over the time course of adaptation (Extended Data Figure 1c,d). When varying target strength and measuring model psychometric performance (*Online Methods*), we found decreased detection thresholds and steeper slopes in low contrast relative to high contrast (Figure 1e). When varying target timing, two factors affected target discriminability: 1) A change in the stimulus distribution after the contrast switch; 2) The effect of gain adaptation on responses to the background (Figure 1f,g; Extended Data Figure 1c,d). These dynamics were well characterized by a single effective timescale, which we quantified by fitting an exponential function to each transition. The normative model presented three primary predictions: When adapted to low contrast, 1) target detection thresholds will be lower and 2) model psychometric functions will have steeper slopes; 3) Discriminability over time will be asymmetric: rapidly decreasing after a switch to high contrast, and slowly increasing after a switch to low contrast (Figure 1h).

*Estimated cortical gain dynamics follow normative model predictions.*

Previous work on contrast gain control used static models of contrast gain control, measuring steady-state gain after the neuron fully adapted to the new stimulus14,16,17,19, but see15,24. To measure the dynamics of gain control, we developed a Poisson GLM to estimate the gain of neurons in auditory cortex over time following a contrast transition. This model was fit to data recorded from the auditory cortex of a naive mouse (n = 97 neurons) presented with 3 s alternations of low and high contrast DRCs (Figure 2a,b).

The inference model is a GLM with dynamic gain control (GC-GLM) that decomposes the relationship between spiking activity () and the presented sounds into a stimulus component (), contrast component (), and an interaction between the stimulus and the contrast (, where is an arbitrary constant, defined as the contrast at which the gain is 1: see *Online Methods*). We calculated a gain index () from the fitted model parameters (Figure 2b) which quantified whether gain control estimated by the model was optimal given the background contrast levels. For the contrast levels used in this study, = 1.5 indicates an optimal increase in gain during low contrast, = 0.5 indicates an optimal decrease in gain during high contrast, and = 1.0 indicates no gain control (*Online Methods*). To validate the model and gain index, we simulated neurons with defined temporal trajectories of gain control, and found that the model estimates of gain () accurately predicted the ground truth gain in the simulations (*Extended Data Figure 2*; *Supplementary Information*). For comparison, we also fit previously described linear-nonlinear (LN) models to each neuron14,16,17,19, one with a static output nonlinearity (static-LN), and one with a contrast-dependent, or gain-controlled output nonlinearity (GC-LN, Figure 2c; representative neuron: Figure 2d-g). In this neuron, the fits of the GC-LN model and GC-GLM demonstrated contrast gain control, characterized by high gain in low contrast and low gain in high contrast (Figure 2f and g, respectively), suggesting that both models capture similar contrast-driven changes in cortical gain.

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| **Figure 1. Target in background detection task and normative model predictions.**  **a,** Experimental setup. **b,** GO/NO-GO task design. Spectrograms are plotted for example NO-GO and GO trials with transitions from low to high contrast (top row) and high to low contrast (bottom row), with waveforms plotted below each spectrogram (color bar indicates the sound level). Scale bar indicates 1s. Below the example trials, the timing of the response window, schematic licks, and responses to licks are plotted. For NO-GO trials, licks in the response window received a timeout. For GO trials, licks in the response window were rewarded with 5uL of water. **c,** Example target parameters. *Top*: varied target levels, with level in dB SNR indicated by the color bar. *Bottom*: varied target times, where each arrow indicates a potential target delay. **d,** Normative model of efficient gain control. Target and background distributions for each contrast are indicated in the left panel. (1) Target stimuli are indicated with circles, while the background stimulus is indicated by a line. The stimulus response in a given time window is transformed by an adapting nonlinearity to generate spikes. (2) The spiking responses are decoded to update an estimate of the stimulus variance. (3) The gain of the nonlinearity is adjusted to optimally predict the variance of the next timestep. *Inset*: Example spike distributions of the model neuron in low and high contrast for targets (dark histograms), and background (light histograms). **e,** Model target from background discriminability as a function of contrast and target level. Circles indicate model performance overlaid with logistic function fits and thresholds. **f,** Model discriminability over time in low and high contrast. Circles indicate model performance overlaid with exponential function fits. **g,** Model gain dynamics over time in each contrast. **h,** From top to bottom: model predictions for target detection thresholds, slopes and adaptation time constants in each contrast. |

Qualitatively, the GC-GLM outperformed standard LN models, primarily by capturing the adaptation dynamics after the transition (Figure 2d, middle panel), allowing us to analyze the gain control index as a function of time, (Figure 2d, bottom panel; Figure 2g). To test whether the GC-GLM could better account for the data than standard models, we compared cross-validated correlations of the model predictions with the trial-averaged PSTH for each neuron, finding a significant effect of model type on the correlations (n = 97 neurons; Kruskal-Wallis test: *H*(2) = 93.61, p = 6.70e-21). Post-hoc Wilcoxon Sign-Rank tests showed that the GC-GLM correlation was significantly higher (Median (*Mdn*) = 0.75, Inter-Quartile Range (*IQR*) = 0.24) than the GC-LN model (*Mdn* = 0.54, *IQR* = 0.49, *p* = 4.41e-6) and the static-LN model (*Mdn* = 0.25, *IQR* = 0.73, *p* = 9.56e-10). Consistent with previous studies, we also found that the GC-LN model outperformed the static-LN model (*p* = 3.50e-6, Figure 2h).

We next quantified whether the GC-GLM detected significant levels of gain control in the population. Here, we defined steady-state gain control by calculating the change in between high () and low contrast () after the gain has stabilized (1 s after the contrast switch). Based on our definition of , if gain control is optimal (*Online Methods*). Across all neurons, we found significant gain control (*Mdn*: -0.10, *IQR*: 0.35, Wilcoxon sign-rank test: *rank* = 233, *Z* = -2.90, *p* = 0.004; Figure 2i). To further validate the GLM estimates of gain, we compared the GC-GLM gain control indices at steady-state to those of the GC-LN model and found a significant relationship (linear regression: *F*(1,95) = 12.20, *p* = 7.33e-4, *R2* = 0.11; Figure 2j). Together, these results demonstrate that the GC-GLM model better accounts for the neural data by incorporating the dynamics of gain control and conclude that this method captures a similar estimate of steady-state gain control when compared to standard models.

Next, we analyzed the dynamics of gain control by fitting after each contrast switch with an exponential function (Figure 2g). In neurons with gain control ( at steady state), the average time course of was asymmetric across contrast transition types, rapidly decreasing after a switch to high contrast, and slowly increasing after a switch to low contrast (n = 45 neurons; Figure 2k). Within this same population, we quantified the timescale of adaptation to each contrast using the time constant () of each exponential fit, finding significantly longer time constants in low contrast (*Mdn* = 0.29, *IQR* = .39) relative to high contrast (*Mdn* = 0.048, *IQR* = 0.094; Wilcoxon sign-rank test: *rank* = 918, *Z*  = 4.52, *p* = 6.16e-6; Figure 2l). This asymmetry in gain adaptation agreed with the predictions of the normative model (Figure 1g) and with previously described behavior of optimal variance estimators25.

*Mouse behavioral detection is modulated by background contrast.*

We next tested whether the asymmetry in gain control observed in cortex was reflected in behavioral sensitivity to targets in background noise. Mice were initially trained in a simple version of the GO/NO-GO task where they were required to lick in response to a target and withhold licks on trials without a target (Figure 1b, 3a). Out of the 25 mice trained, 24 mice learned this task reliably, typically reaching criterion performance of 80% correct within 2-3 weeks in either contrast (Figure 3b). False alarm rates were significantly larger in high contrast than in low contrast (Extended Data Figure 3a), suggesting that detection is more difficult in high contrast, which we discuss next.

By varying the level of presented targets, we collected psychometric curves for each mouse in each contrast. To assess the effects of stimulus contrast on psychometric performance, we included sessions from mice that were exposed to similar target levels in low and high contrast (n = 11 mice; Figure 3c; see Extended Data Figure 3 and Supplementary Results for results using different target ranges). In this cohort, we found that targets were easier to detect in low contrast, observing significantly lower detection thresholds in low contrast (Mean (*M*)= 8.79, standard deviation (*std*) *=* 3.13) compared to high contrast (*M =* 15.39, *std =* 3.27; paired t-test: *t(10)* = -4.20, *p* = 0.0057, Figure 3d). Furthermore, we observed significantly steeper psychometric slopes in low contrast (*M* = 0.040, *std =* 0.0048) compared to high contrast (*M =* 0.036, *std =* 0.0026; paired t-test: *t(10)* = 3.037, *p* = 0.023; Figure 3e). Combined, these results demonstrate that targets were easier to detect and discriminate in low contrast, as predicted from the normative model presented in Figure 1.

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| **Figure 2. Cortical adaptation to sound contrast is asymmetric.**  **a,** Schematic of acute recordings from auditory cortex. **b,** Schematic of the linear-nonlinear (LN) model, with a static (grey) or gain-controlled (blue, red) nonlinearity. **c,** A Poisson GLM for estimating gain dynamics. The model decomposed the spiking response, , of the neuron into a stimulus component, , a contrast component, , and an interaction between the stimulus and contrast, which determined the gain estimate. **d**, *Top*:Spike raster for a representative unit. Blue and red horizontal bars indicate low and high contrast periods of the trial, respectively. *Middle*: the spike rate of the neuron is overlaid with the predictions from a static LN model, LN model with gain control, or GLM with gain control. Colors are indicated in the legend. *Bottom*: gain index, , estimated from the GLM parameters (*Methods*). Dashed black lines indicate gain index values for optimal gain control and grey dashed lines indicate gain index values for no gain control. Orange trace indicates the gain dynamics of the representative neuron. **e,** Spectro-temporal receptive field (STRF) fit to this neuron. Color bar indicates the strength of the filter response. **f**, Nonlinearities fit to the STRF prediction in low and high contrast. **g**, Dashed blue and red lines indicate the gain index of the example cell in low and high contrast. The overlaid solid lines are exponential fits to the data. **h,** Pearson correlation coefficients between the trial averaged model predictions and spike rates for each model (colors as in **d**). Errorbars indicate 95th percentiles around the median. Asterisks indicate the results of Wilcoxon sign-rank tests. **i,** Distribution of gain control estimated by the GLM. Orange line indicates the median. Asterisks indicate the results of a Wilcoxon sign-rank test. **j,** Gain control estimates for each neuron from the GC-GLM or the GC-LN model (black dots) overlaid with the best linear fit and 95% confidence interval of the fit. Asterisks indicate whether the linear model was significantly different from a constant model. **k,** Gain index for all of the neurons with gain control (n = 45). Light lines are the average ±SEM, while the dark lines are exponential fits to the average. **l,** Adaptation time constants from gain-controlled neurons after a switch to low (blue dots) and high contrast (red dots). Asterisks indicate the results of a Wilcoxon sign-rank test. In all plots: ns, not significant; †p<0.1; \*p<0.05; \*\*p<0.01; \*\*\*p<0.001; \*\*\*\*p<0.0001. |

To assess behavioral adaptation to the background contrast, we presented targets at threshold level at variable delays following the contrast transition. We observed behavioral time courses consistent with the normative model and with gain measured in auditory cortex: after a switch to high contrast detection rates decreased quickly over time, but after a switch to low contrast detection rates increased slowly over time (Figure 3f). In high contrast, the first significant drop in performance occurred between the first two time points, while in low contrast the first significant increase in performance occurred between the first and third time points (Figure 3f, Extended Data Table 1). Indeed, fitting exponential functions to performance over time revealed that behavioral adaptation was significantly faster in high contrast (median and interquartile range of time constant: *Mdn* = 0.023, *IQR* = 0.082) compared to low contrast (*Mdn =* 0.13, *IQR* = 0.13; Wilcoxon Rank-Sum test (n = 21): *Z* = 2.75, *p* = 0.0060; Figure 3g).

To directly compare the predictions of the normative model presented in Figure 1 to behavioral performance, we computed a contrast modulation index for the behavioral and model parameters (CMI, *Methods*). To assess whether the model prediction was within the range of expected behavioral values, we computed the 95% confidence intervals of the behavioral CMI values using a bootstrap procedure. We found that the CMI values of the normative predictions fell within the range of expected CMI values for behavioral thresholds and adaptation times. As observed in behavior, the model predicted a decrease in slope in high contrast, however, the magnitude of the predicted decrease was larger than the range of observed slope CMI values (Figure 3h). Taken together, these behavioral results qualitatively confirm the three predictions from the normative model (Figure 1h): 1) Detection thresholds are lower in low contrast; 2) Psychometric slopes are higher in low contrast; 3) Performance decreases rapidly in high contrast and increases gradually in low contrast.

*Auditory cortex is necessary for detection in background noise.*

Whereas gain control is present in many areas along the auditory pathway, it is strongest in auditory cortex16,19. As such, we hypothesized that auditory cortex supports the detection of sounds in the presence of background noise. To test whether auditory cortex is required for task performance, we inactivated auditory cortex using the GABA-A receptor agonist muscimol. We validated that muscimol disrupts cortical coding of target sounds by applying muscimol topically to the cortical surface during passive playback of the behavioral stimuli, finding near complete suppression of target responses (Extended Data Figure 4a-f, *Supplementary Information*).

To test whether inactivation of auditory cortex affects behavioral performance, we repeated the same experiments in behaving mice, administering muscimol or saline bilaterally through chronically implanted cannulae (n = 44 sessions from 4 mice; Figure 4a). We found a profound decrease in the response rates to targets and background in both contrasts (Figure 4b). We quantified these effects on the psychometric curve using a three-way ANOVA with cortical intervention (muscimol or saline), contrast, and target level as factors. We found significant main effects of cortical intervention (*F*(1,307) = 278.63, *p* = 3.83e-44), contrast (*F*(1,307) = 4.39, *p* = 0.037) and level (*F*(6,307) = 40.90, *p =* 7.54e-36). Post-hoc tests showed that muscimol application significantly decreased hit rates in both contrasts by 31.45% (95% CI: [27.76, 35.14], *p* = 1.060e-10), whereas an increase in background contrast significantly decreased hit rates in both intervention conditions by 3.95% (95% CI: [2.57, 7.64], *p* = 0.036). Furthermore, we observed significant interactions between target level and cortical intervention (*F*(6,307) = 14.11, *p* = 4.47e-14), and between target level and contrast (*F*(6,307) = 2.97, *p* = 7.87e-3), but we did not observe a significant interaction between contrast and cortical intervention, suggesting that muscimol has the same effect in low and high contrast. To quantify the effects of muscimol on psychometric performance, we extracted response rates to the maximum target level, false alarm rates, thresholds, and slopes of psychometric functions fit to each session, and found that muscimol significantly reduced every measure of psychometric performance, with the exception of behavioral threshold (Figure 4c, Extended Data Table 1). From these results, we can conclude that auditory cortex is necessary for detecting targets in background, regardless of background contrast.

A potential alternative effect of muscimol is a general loss of function that is not specific to hearing target sounds. To control for this, we devised an alternative to the detection in background task where mice detected targets in silence (Figure 4d). To ensure equivalency between the two tasks, we took the highest-level target trials in the target-in-background task (25dB SNR in high contrast) and removed the background noise during the target detection period (Figure 4e, bottom). Thus, mice were presented with the exact same targets as in the previous task, but without the background DRCs, allowing us to test whether auditory cortex is specifically required for detection in the presence of a background (*Online Methods*).

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| **Figure 3. Target detection performance is consistent with the normative model predictions.**  **a,** Schematic of the behavioral setup and task outcomes. **b,** Performance as a function of task exposure. Individual traces indicate performance of mice first trained to detect targets in low contrast (blue) or high contrast (red). Thick lines are a 7 day running average across mice in each training group. The dashed red trace near 0.5 was the performance of a mouse who failed to learn the task in high contrast, and was excluded from further analysis. **c,** Individual psychometric curves in low and high contrast, overlaid with psychometric fits to the average. Dashed vertical lines indicate detection thresholds. **d,** Detection thresholds from the data plotted in **c**. **e,** Slopes of the psychometric functions plotted in **c**. In **d, e** asterisks indicate the significance of paired t-tests. **f,** Detection performance of threshold level targets presented at different delays from the contrast switch (circles indicate mean ±SEM). Performance is overlaid with exponential fits in each contrast. Horizontal lines above the plot indicate significant Wilcoxon sign-rank tests after false-discovery correction. **g,** Adaptation time constants from exponential functions fit to individual mice. Asterisks indicate the result of a Wilcoxon sign-rank test. **h,** Comparison of normative model predictions (grey) to the data (black) for psychometric thresholds, slopes and adaptation time. The y-axis is the contrast modulation index (CMI, *Methods*) of the value in each plot, with error bars indicating the 95% confidence interval of the data determined via bootstrap. In all plots: ns, not significant; †p<0.1; \*p<0.05; \*\*p<0.01; \*\*\*p<0.001; \*\*\*\*p<0.0001. |

To assess psychometric performance in this new task, we modulated detection difficulty by attenuating the level of each target. As observed previously, inactivation of auditory cortex impaired detection in high contrast (Figure 4e, top). However, cortical inactivation had little effect on psychometric performance in silence (Figure 4e, bottom). We quantified these effects on psychometric performance using a three-way ANOVA with cortical intervention (muscimol or saline), task (detection in background or silence), and target level as factors (n = 26 sessions from 2 mice). We found significant main effects of intervention (*F*(1,181) = 62.83, *p* = 3.62e-13), task (*F*(1,181) = 6.82, *p* = 9.86e-3), and level (*F*(6,181) = 46.16, *p* = 1.69e-32). Post-hoc tests showed that muscimol significantly reduced hit rates by 20.2% (95% CI: [15.19, 25.17], *p* = 1.060e-10). Hit rates for targets presented in silence were significantly elevated by 6.65% relative to targets presented in background (95% CI: [1.65, 11.64], *p* = 0.0090). Furthermore, we found significant interactions between cortical intervention and task type (*F*(1,181) = 6.36, *p* = 0.013), intervention and level (*F*(6,181) = 3.47, *p* = 2.98e-3), and level and task type (*F*(6,181) = 8.47, *p* = 5.43e-8). As before, we parameterized psychometric performance by fitting each session with a psychometric curve, and we extracted the response rates to the maximum target level, false alarm rates, response rates at threshold level, and slopes of psychometric functions. During the target-in-background task, we found significant effects of muscimol on the response rates at maximum level and threshold, a moderate effect on psychometric slope, and no effect on false alarm rate. However, muscimol application had no significant effect on any of these measures in the target-in-silence task (Figure 4f, Extended Data Table 1). Taken together, these results show that while both cortical inactivation and the presence or absence of background noise affected behavioral performance, these effects interacted: muscimol had a larger effect on performance when background noise was present.

Combined, our findings demonstrate that the auditory cortex is specifically required for detection in the presence of background noise, but not in silence. Our next goal was to test whether neuronal activity in AC is predictive of behavioral performance.

*Cortical codes predict individual behavioral performance.*

To better understand how representations in auditory cortex could give rise to behavior, we chronically recorded from populations of neurons in auditory cortex of 12 mice while they performed the psychometric task (Figure 5a). In microdrives with drivable tetrodes, we lowered the tetrodes a small distance at the end of each session to record from new populations of cells. In the 242 sessions analyzed, we recorded from 18±15 neurons simultaneously (mean±standard deviation), with a maximum of 73 and minimum of 3 neurons simultaneously recorded. For all of the following analyses, we only included neurons with spike rates greater than 1Hz, realistic spike waveforms (*Methods*), and with significant responses to targets, which we defined as a cell whose AUC value was significantly greater than 0.5 at two or more levels (Figure 5b, inset; *Methods*). Following these selection criteria, 12±9 neurons were included in analysis for each session.

To quantify the representations of targets and background in the neural population (example responses in Figure 5b,c), we adapted a population vector approach26 to generate a discriminability metric using population activity (*Online Methods*). This method allowed us to project trial distributions in -dimensional neural space along a single dimension which separated target and background trials (Figure 5d, left panel). We then estimated the criterion projection value that best predicted whether each trial contained a target or just background27 (Figure 5d, right).

This population decoding method allowed us to estimate neurometric functions to directly compare to psychometric functions for each mouse (Figure 5e). On average, neurometric and psychometric functions were qualitatively similar (Figure 5f). To quantify the relationship between neurometric and psychometric thresholds, while controlling for the effect of contrast, we fit a mixed-effects model using contrast and neurometric threshold as fixed effects, mouse identity as a random effect and psychometric threshold as the dependent variable (Extended Data Table 1). We tested the significance of each predictor by comparing the full model fit to null models excluding neurometric thresholds or contrast. We found that both the neurometric threshold (Likelihood Ratio Test: (1) = 5.89, *p* = 0.015) and contrast (Likelihood Ratio Test: (1) = 4.70, *p* = 0.030) significantly improved the model fit (Figure 5g), demonstrating that behavioral thresholds were predicted both by individual variation in neurometric thresholds and by contrast. Furthermore, we found that the effect of contrast on neurometric and psychometric thresholds was consistent with the predictions of the normative model, such that thresholds increased by 2.83±1.14 dB SNR between low to high contrast (mean±standard error of the contrast coefficient; Extended Data Table 1). Together, these results demonstrate that population thresholds in auditory cortex are predictive of behavioral thresholds in individual mice, and both psychometric and neurometric thresholds are modulated by contrast as predicted by a normative account of gain control.

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| **Figure 4. Inactivation of auditory cortex selectively disrupts detection of targets in background sounds.**  **a,** Schematic of chronic muscimol and saline application in behaving mice. Legend indicates the three potential background conditions in the task. **b,** Psychometric performance on individual sessions (light traces) as a function of contrast (red, blue) and muscimol or saline application (dashed and solid lines, respectively). -Inf indicates performance on background-only trials. Dots indicate the average performance across mice and sessions ±SEM, overlaid with logistic fits to the data. **c,** Effects of muscimol and contrast on multiple behavioral measures. Bars indicate the mean performance, while dots indicate performance on individual sessions. Asterisks indicate the significance of Wilcoxon rank-sum tests. **d,** Example spectrograms and waveforms with a target presented in high contrast (top) and the same stimulus when the target was presented in silence (bottom). Color bar indicates the sound level, with black indicating silence. **e,** Psychometric performance in high contrast (top) and in silence (bottom). Formatting as in **b**. **f,** The effect of muscimol on multiple behavioral measures when targets were presented in high contrast (red bars) or in silence (black bars). Formatting as in **c**. In all plots: ns, not significant; †p<0.1; \*p<0.05; \*\*p<0.01; \*\*\*p<0.001; \*\*\*\*p<0.0001. |

We applied the same statistical analysis to neurometric and psychometric slopes. Previously, we found that the range of target levels presented had significant effects on the slope of psychometric curves (*Supplementary Results*, Extended Data Figure 3d-h). As such, we restricted our analysis to sessions with the same range of target levels (117/242 sessions from 6/12 mice). In this cohort, we found that neurometric slopes were a weak predictor of psychometric slopes (Likelihood Ratio Test: (1) = 2.67, *p* = 0.10) while contrast was a significant predictor of psychometric slopes (Likelihood Ratio Test: (1) = 7.98, *p* = 0.0047). As expected, the effect of contrast matched the predictions of the normative model, such that slopes decreased by -0.0095±0.0026 PC/dB SNR from low to high contrast (Figure 5h, Extended Data Table 1). Thus far, we found that contrast, but not individual variability in neurometric slope, significantly predicted psychometric performance, which differed from our previous analysis of psychometric thresholds. However, when we included all 12 mice, we found that neurometric slopes were significant predictors of psychometric slopes (Likelihood Ratio Test: (1) = 9.78, *p* = 0.0018; Extended Data Figure 5a), suggesting that our previous analysis was underpowered. Overall, these findings were consistent with our behavioral findings (Figure 3e), demonstrating that, when target levels are matched, an increase in contrast reduced neurometric and psychometric slopes and that neurometric slope is predictive of psychometric slope on a mouse-to-mouse basis.

Combined, we found that parameters of neurometric and psychometric functions are affected by contrast as predicted by a normative model of gain control. We also find that individual variation in psychometric performance is predicted by population activity in auditory cortex, independently of the effect of contrast, which further supports the role of auditory cortex in the detection of signals in noise.

*Dynamics of target detection during adaptation.*

We next measured how cortical discriminability evolved as a function of time and contrast in sessions where mice were presented with targets at threshold level at different offsets relative to the contrast switch. In line with our behavioral results (Figure 3f), we found that in high contrast the first significant drop in cortical discriminability occurred between the first two target times, while in low contrast the first significant drop occurred between the first and third target times (n = 43 recording sessions; Extended Data Table 1; Figure 5i).To quantify the speed of neural adaptation, we fit the average neural discrimination time course for each mouse with an exponential function (n = 8 mice). Consistent with the normative model (Figure 1f-h), gain control dynamics estimated from cortical activity (Figure 2k,l) and behavior (Figure 3f,g), we found asymmetric adaptation in the neural responses, with larger adaptation time constants in low contrast (*Mdn* = 0.14, *IQR* = 0.21) relative to high contrast (*Mdn* = 0.033, *IQR =* 0.16;Wilcoxon sign-rank test (n = 8): *rank*  = 28, *p* = 0.016; Figure 5j).

*Cortical gain predicts behavioral performance.*

Our results so far provide strong evidence that gain control in the auditory system shapes behavioral performance. To assess the role of cortical gain in behavior, we leveraged the design of the background sounds to estimate spectrotemporal receptive fields (STRFs) and nonlinearities of neurons recorded during task performance. For each neuron, we fit a model with a static nonlinearity (static-LN) or a model with gain control (GC-LN; Figure 6a-d). We then pooled the neurons recorded across sessions, and included only neurons with strong stimulus responses in both contrasts (*Online Methods*). First, we compared the cross-validated performance of the static-LN model versus the GC-LN model, finding higher correlations using the GC-LN model (*Mdn* = 0.82, *IQR* = 0.17) relative to the static-LN model (*Mdn* = 0.67, *IQR* = 0.12; Wilcoxon sign-rank test (n = 2,792 neurons): *rank* = 3.85e5, *Z* = -36.74, *p* = 1.88e-295; Extended Data Figure 5h). We also found significantly higher gain in low contrast (*Mdn* = 0.10, *IQR* = 0.13) than in high contrast (*Mdn* = 0.041, *IQR* = 0.023; Wilcoxon sign-rank test: *rank* = 3.57e6, *Z* = 37.92, *p* = 1.070e-314; Figure 6e, inset). These results demonstrate that LN models can more accurately predict cortical activity when incorporating contrast gain control, and confirm previous reports of robust gain control in mouse auditory cortex17–19.

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| **Figure 5. Cortical responses to targets predict behavioral performance and exhibit contrast adaptation.**  **a,** Schematic of chronic recordings during behavior. **b,** Spike raster from a neuron recorded during the task. Trials are sorted by target level, as indicated in the legend. Below is the average spike rate in each condition, smoothed with a 5ms gaussian window. Inset is the area under the ROC curve (AUC) as a function of level, with error bars indicating bootstrapped 95% confidence intervals. **c,** Neurograms of populations of simultaneously recorded neurons for a low contrast (left) and high contrast (right) behavioral session.Color bars indicate the difference in firing rate between the noise-only condition and each target level on the x-axis for each cell on the y-axis. The arrow indicates the cell in **b**. **d,** *Upper left*: schematic for estimating the direction (CD) that best separates population responses to targets (blue dots) and noise (grey dots). *Lower right*: probability distributions of population projections for noise-only trials (grey) and the highest level target trials (blue). The vertical red line indicates the criterion for the population decoder. **e,** Neurometric performance compared to behavioral performance in representative low contrast (left) and high contrast (right) sessions. In both plots, dark dots indicate the decoder performance, while light dots indicate behavioral performance on the same session, overlaid by logistic function fits. The arrow in the left panel is the decoder performance for the distributions plotted in **d**. **f,** Average psychometric and neurometric performance ±SEM over all trials. Solid lines indicate logistic fits to the average. As in **c**, light shades indicate psychometric performance and dark shades indicate neurometric performance. **g,** Predictive relationship between neural and behavioral thresholds. Each dot indicates a mouse, and the color indicates whether targets were presented in high or low contrast. Grey line is the best linear fit. The black asterisk indicates a significant relationship between neural and behavioral thresholds, and the magenta asterisks indicate whether contrast significantly modulated the behavioral and neural thresholds. **h,** as in **g**, but for slopes. **i,** Neurometric performance ±SEM as a function of target delay. Formatting and statistical tests are the same as Figure 3f. **j,** Adaptation time constants of the neurometric response for n = 8 mice. Asterisk indicates a significant Wilcoxon rank-sum test. In all plots: ns, not significant; †p<0.1; \*p<0.05; \*\*p<0.01; \*\*\*p<0.001; \*\*\*\*p<0.0001. |

Based on our previous results, we expected that the amount of gain control in auditory cortex would predict target detectability. When fitting the GC-LN model, we separately estimated neural gain during the adaptation period of the trial and the target period of the trial (defined as the time periods before and after the contrast switch, respectively; Figure 6b). To quantify the effects of contrast and trial period on gain, we performed a two-way ANOVA, with gain as the dependent variable, and contrast, trial period, and their interaction as factors (n = 2,262 neurons, after excluding outliers, see *Online Methods*). As expected, we found a significant main effect of contrast (*F*(1,4523) = 431.03, *p* = 1.60e-91). Furthermore, there was a significant main effect of trial period (*F*(1,4523) = 35.79, *p* = 2.36e-9) and a significant interaction between contrast and trial period (*F*(1,4523) = 77.91, *p* = 1.51e-18). Post-hoc tests revealed that, in low contrast, gain during the target period significantly increased (0.032, 95% CI: [0.024, 0.040], *p* = 3.77e-9), but did not significantly change in high contrast (0.0062, 95% CI: [-0.017, 0.014], *p* = 0.18; Figure 6e). These findings indicate that neural gain is not only sensitive to stimulus contrast, but also increases during the target period of the trial, specifically in low contrast.

To visualize the gross relationship between gain and psychometric performance, we first averaged the gain of stimulus-responsive neurons during the target period of the trial in each session (n = 168 sessions across 13 mice). We then selected only low contrast sessions and split the data by the median gain in the target period, computing the average psychometric curves for sessions in the bottom versus the top 50th percentile (Figure 6f, inset). We observed that sessions with high gain had steeper slopes and lower thresholds than sessions with low gain (Figure 6f). To quantify the relationship between gain and task performance, we fit a mixed-effects model using contrast and gain during the target period as fixed effects, mouse identity as a random effect and either psychometric slopes or thresholds as the dependent variable. This approach allowed us to separate the neuronal and behavioral impact of contrast gain control from effect of session-to-session fluctuations in gain. We tested whether gain and contrast were significant predictors of behavioral performance by comparing the full model to null models excluding either gain or contrast. We found that the model including gain was a better predictor of behavioral threshold than was the null model (Likelihood Ratio Test: (1) = 5.82, *p* = 0.016), indicating that thresholds decreased by about 3.046 dB SNR ±1.24 (standard error) for every 10% increase in gain. Using a similar procedure, we found that contrast was also a significant predictor of behavioral threshold (Likelihood Ratio Test: (1) = 5.84, *p* = 0.038), with the step from high to low contrast inducing a decrease in behavioral thresholds of 3.27 dB SNR ±1.33 (Figure 6g).

We applied the same analysis to test the effects of contrast and gain on psychometric slope (Figure 6f), again finding that gain significantly predicted psychometric slopes (Likelihood Ratio Test: (1) = 6.96, *p* = 0.0083), such that the psychometric slope increased by 0.16 dB/PC ±0.060 for every 100% increase in gain. However, contrast did not significantly improve the fit of this model (Likelihood Ratio Test: (1) = 2.28, *p* = 0.13; Figure 6h). This result is not entirely unexpected, given that we observed no effect of contrast on psychometric slopes when comparing across sessions with different target distributions (Extended Data Figure 2b), which is true of the sessions used in this analysis.

Our findings suggest that the relationship between gain and psychometric performance is shaped by two sources: contrast-induced gain control and fluctuations in gain from session to session. To further disentangle the relationship between these two sources of behavioral modulation, we repeated the mixed effects models, this time using gain during the adaptation period as the predictor of interest. We hypothesized that gain in this period should not be predictive of behavioral performance, as there were no targets presented during this portion of the trial. We found that this was the case; we did not observe any predictive relationship between gain estimated in this period and behavioral performance (Extended Data Figure 5i-k; Extended Data Table 1). In summary, we found that cortical gain was modulated by both stimulus contrast and trial period, increasing when contrast is low and when mice were detecting targets. Furthermore, we found that psychometric performance was predicted by both the stimulus contrast and by session-to-session changes in cortical gain during target detection.

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| **Figure 6. Cortical gain predicts session-to-session variability in behavioral performance.**  **a,** Schematic of the LN model fit to neural responses during the behavioral task. **b,** Spike raster of a representative unit recorded during the behavioral task, sorted by the background scene presented in each trial. Below is the average spike rate (black trace) overlaid with the LN model fit with a static (grey) or gain-controlled nonlinearity (green). **c,** STRF for the representative cell. **d,** The fitted nonlinearities in low and high contrast periods of the trials. **e,** Gain distributions across all recorded neurons as a function of contrast (indicated by the color) and whether the gain was estimated during the adaptation period (A) or the target period (T) of the trial (see labels in **b**). Inset: the average gain in low and high contrast for all cells, dashed lines indicate the median of each distribution. Asterisks indicate the results of Wilcoxon rank-sum tests. **f,** Psychometric curves split by the median gain. Light colored dots indicate performance across sessions with low gain, dark colored dots indicate performance on sessions with high gain. Error bars indicate ±SEM. *Inset*: the distribution of gain values on the same sessions. The dashed red line indicates the median used to split the data. **g,** Relationship between session to session changes in gain and behavioral thresholds. Each dot is a session, with the color indicating the contrast in which targets were presented. The grey line is the linear best fit. Black asterisks indicate whether gain is a significant predictor of the psychometric threshold, while magenta asterisks indicate whether contrast was a significant predictor of behavioral thresholds. **h,** Same formatting as **g**, but plotting the relationship between gain and psychometric slope. In all plots: ns, not significant; †p<0.1; \*p<0.05; \*\*p<0.01; \*\*\*p<0.001; \*\*\*\*p<0.0001. |

**Discussion**

Our auditory surroundings are characterized by different statistical properties that change over time. Changes in the dynamic range, or contrast, of acoustic inputs poses a challenge to the auditory system, which is composed of neurons with limited dynamic range. The efficient coding hypothesis predicts that as stimulus contrast changes, neurons should adjust their gain in order to match their limited dynamic range to that of the stimulus distribution1. Multiple studies have demonstrated that neurons throughout the auditory pathway exhibit such contrast gain control14,16,19. Additionally, contrast gain control is theoretically beneficial for separating signals from background noise16,20, implicating that this phenomenon should underly perception in noisy environments. Whereas recent work has demonstrated a link between contrast gain control and changes in human psychophysical performance19,21, it is unclear how cortical gain directly relates to behavior, as neuronal responses and behavior were not observed simultaneously. Finally, recent work has highlighted the dynamic nature of efficient neural codes22,23, and it is unclear how these neural dynamics affect behavior.

Our study addressed these open questions by developing a normative framework to predict how gain adaptation should affect behavior, then tested those predictions using a combination of behavior, chronic recordings, and cortical manipulations. First, we developed a normative model based on efficient coding22,23 which predicted that: 1) Detection thresholds of targets should be lower in low contrast than in high contrast; 2) Sensitivity to changes in target level should be greater in low contrast relative to high contrast; and 3) Detection should adapt asymmetrically: increasing slowly after a switch to low contrast, but decreasing rapidly after a switch to high contrast (Figure 1). Then, we used a novel form of Poisson GLM to confirm that gain control dynamics in auditory cortex are indeed asymmetric (Figure 2). To behaviorally test the predictions of the normative model and GLM, we trained mice to detect a target embedded in dynamic random chords while manipulating the contrast of the background between high and low contrast. As predicted by the normative model, mice had lower detection thresholds and were more sensitive to changes in target level in low contrast. Behavioral adaptation was also asymmetric, decreasing rapidly after a switch to high contrast, and increasing slowly after a switch to low contrast, in agreement with our model (Figure 3). Furthermore, we found that AC is necessary for this detection-in-background task (Figure 4). When recording in AC, we found that the parameters of neurometric functions were predictive of psychometric functions on a mouse-to-mouse basis, and we also showed that target discriminability adapted asymmetrically, as predicted (Figure 5). Finally, we found that we could predict behavioral performance from cortical gain on a session-to-session basis, independently of the effect of contrast (Figure 6). Taken together, these results support our hypothesis that gain control in auditory cortex shapes auditory behavior.

*The role of cortex in behavior.*

The role of auditory cortex in behavior has been subject of debate. A number of prior studies found that auditory cortex was not required for relatively simple behavioral tasks such as frequency discrimination or detection28,29. Rather, many studies found that auditory cortex is primarily involved in more complex behaviors, such those requiring temporal expectation30, localization31, or discrimination of more complex sounds32–34. Consistent with previous findings35, we found that AC inactivation selectively impaired detection of targets in a noisy background, but did not impair detection of targets in silence (Figure 4). Furthermore, neuronal activity in AC predicted variability in behavioral performance (Figures 5, 6). This set of results establishes that AC is necessary for the detection of targets in background noise and supports the more general notion that AC is required for more difficult auditory tasks.

While the previous work demonstrates the necessity of auditory cortex in behavioral performance, the brain areas and mechanisms supporting the transformation from stimulus to decision are an active field of study36,37. By recording during the task, we were able to leverage behavioral variability to show that task performance covaried with representations of targets within small neural populations (Figure 5), and with cortical gain (Figure 6). There is a large body of literature relating cortical codes to behavioral variability: early studies in the visual system suggested that information from relatively small numbers of neurons was sufficient to match or outperform animal behavior in psychophysical tasks38–40 and that behavioral choice can be predicted from activity in sensory areas27,40. These accounts suggested that variability in bottom-up sensory encoding drives the variability in behavioral output. However, more recent work suggests that variability in sensory areas is driven by top-down influences41–44, which are modulated by attention and learning45–48. A recent study imaging tens of thousands of neurons in the visual cortex supports this notion, finding that cortical representations had higher acuity than behaving mice, yet did not correlate with behavioral performance, suggesting that perceptual discrimination depends on post-sensory brain regions49.

Our results suggest that bottom-up adaptation to stimulus statistics shapes behavioral output: We observed asymmetric time courses of target discrimination following a change in contrast (Figure 3). The asymmetric adaptation in behavioral performance was consistent with predictions derived from a normative account of contrast gain control (Figure 1), resembled contrast gain adaptation in auditory cortex in the absence of behavior (Figure 2), and was also reflected by patterns of target-driven activity in auditory cortex during task performance (Figure 5). Indeed, there have been other studies demonstrating that individual differences in sensory-guided behaviors are reflected in cortical activity50,51, are bidirectionally modulated by cortical manipulation52,53, and can be predicted from tuning properties in auditory cortex54,55. While our results cannot rule out top-down input as the causal driver of sensory decisions, they do support the notion that the sensory information upon which decisions are made is shaped by neuronal adaptation, which thereby affects behavioral outcomes.

*Roles of gain in the auditory system.*

Neurons throughout the auditory system adapt to the statistics of the acoustic environment, including the frequency of stimuli over time56,57, more complex sound patterns24,58, and task-related or rewarded stimuli59–64. Inspired by the latter studies, we intentionally designed our stimuli using unbiased white-noise backgrounds, which allowed us to fit encoding models to our data. Using these methods, we focused on contrast gain control as a fundamental statistical adaptation that relates to efficient coding14,17–19. Previous work identified that contrast gain control was asymmetric14, supporting theoretical work on optimal variance estimators25. In this study, we developed a novel application of Poisson GLM that allowed us to quantify gain dynamics directly from responses to DRC stimuli. This approach allowed us to verify that gain adaptation in auditory cortex is asymmetric (Figure 2), as predicted from a normative account of contrast gain control (Figure 1). this form of GLM65,6667,6869–72

Additionally, previous studies found that contrast gain control was predictive of behavioral performance10,19. Here, we extended these findings by examining the dynamics of this process, and found that behavioral detection of targets also adapted asymmetrically (Figure 3). In addition to confirming previously reported effects of contrast on psychometric curves, these results suggest that the dynamics of contrast gain control influenced task performance. Pursuing this further, we estimated cortical gain as mice performed the task, and discovered a predictive relationship between stimulus contrast, gain in auditory cortex, and psychometric performance (Figure 6). These results suggest two sources of cortical gain modulation: 1) Bottom-up adaptation to stimulus contrast (ie. contrast gain control), and 2) session-to-session modulation of gain. Previous studies have demonstrated this latter phenomenon, suggesting that top-down gain modulation underlies attention41,42,73 and the maintenance of optimal behavioral states67,68. Our results suggest that both contrast gain control and session-to-session fluctuations in gain modulate behavior, providing a starting point for dissecting the neural mechanisms underlying these two forms of gain modulation.

*Cellular mechanisms of gain control.*

While this work and other studies have established contrast gain control as a fundamental property of the auditory system, the neuronal mechanisms driving gain adaptation at a cellular level remain unclear. Previous work theorized that cortical feedback was responsible for contrast gain control in early areas16,20, but recent experiments disproved this hypothesis19. In the current study, we have likely recorded from a mixed population of excitatory and inhibitory neurons, the latter of which exhibit specific roles in adaptation74,75. While specific inhibitory neuronal subtypes facilitate divisive or subtractive control of excitatory responses in visual69,70 and auditory cortex71,72, the role of these interneurons in contrast gain control has been inconclusive18. Additionally, our results highlight the distinction between stimulus driven gain control and stimulus-invariant gain control which covaried with behavior from session to session (Figure 6). Whether these two forms of gain control share common neural substrates is unclear. By combining cell-specific optogenetic methods with behavioral tasks, future studies may explore and test the specific role of local circuits and top-down modulation in gain control and behavior.

*The missing link between efficient coding and behavior.*

Combined, our results develop a framework and provide support for the role of contrast gain control in behavior. The efficient coding hypothesis has emerged as one of the leading principles in computational neuroscience that has shaped our understanding of neuronal coding, architecture and evolution1,76–79 and prior research found that human behavior follows principles of efficiency19,80. Here, we focused on a well-studied form of efficient coding, contrast gain control, and developed a framework to link principles of efficient neuronal coding with behavioral performance. While the mechanisms of contrast gain control in auditory cortex remain unclear, this study highlights distinct top-down and bottom-up influences on cortical gain, which may or may not share common neural substrates. We believe that the theoretical frameworks and modelling methods presented here will be broadly applicable in future studies of neural gain control, a fundamental function of the nervous system.

**Online Methods**

*Animals*.

All experiments were performed in adult male (n = 19) and female (n = 19) C57BL/6 (Stock No. 000664) or B6.CAST-*Cdh23­Ahl+* (Stock No. 002756) mice (The Jackson Laboratory; age 12-15 weeks; weight 20-30g). Some of the mice used in these experiments were crossed with other cell-type specific -cre lines, as detailed in Extended Data Table 2. All mice were housed with, at most, five mice per cage, at 28°C on a 12-h light:dark cycle with food provided ad libitum, and a restricted water schedule (see *Water restriction*). All experiments were performed during the animals’ dark cycle. All experimental procedures were in accordance with NIH guidelines and approved by the Institutional Animal Care and Use Committee at the University of Pennsylvania.

*Data availability.*

All data including spike times from electrophysiological recordings will be made available on Dryad upon publication. The reviewers of this manuscript may access the data at the following link: <https://doi.org/10.5061/dryad.6djh9w120>.

*Surgery*.

Mice were anesthetized under isoflurane (1-3%). Prior to implantation, all mice were administered subcutaneous doses of buprenorphine (Buprenex, 0.05-0.1 mg/kg) for analgesia, dexamethasone (0.2 mg/kg) to reduce brain swelling, and bupivicane (2 mg/kg) for local anesthesia. In mice implanted with microdrives, two ground screws attached to ground wires were implanted in the left frontal lobe and right cerebellum, with an additional skull screw implanted over the left cerebellum to provide additional support. A small craniotomy was performed over the target stereotactic coordinates relative to bregma, -2.6mm anterior, -4.3mm lateral. Either custom 16-channel microdrives, 32-, or 64-channel shuttle drives (cite) holding tetrode bundles of polyimide-coated nichrome wires were chronically implanted over auditory cortex, and tetrodes were lowered 800um below the pial surface. The exposed tetrodes were covered with GelFoam (Pfizer) or sterile silicone lubricant and sealed with Kwik-Cast (World Precision Instruments). The plastic body of the microdrive and a custom stainless-steel headplate were secured to the skull using dental cement (C&B Metabond) and acrylic (Lang Dental). Mice undergoing only behavioral experiments were implanted with two skull screws in the cerebellum, and a headplate was mounted on the skull as previously described. An antibiotic (Baytril, 5mg/kg) and analgesic (Meloxicam, 5mg/kg) were administered daily (for 3 days) during recovery.

*Water restriction*.

Following surgical recovery (3 days post-operation), each mouse’s weight was monitored for three additional days to establish a baseline weight. Over the next seven days, mice were water deprived, beginning with a daily ration of 120uL/g and gradually decreasing their ration to 40-50uL/g. During the task, if mice did not receive their full ration, the remainder of their ration was provided in their home cage. Mouse weight relative to baseline was monitored during all stages of water restriction. Additional health signs were used to determine a health score and subsequent treatment plan if a mouse lost more than 20% of baseline weight, as described by previously published methods81 and approved by the Institutional Animal Care and Use Committee at the University of Pennsylvania.

*Behavioral apparatus*.

During the GO/NO-GO task, the mouse was head-fixed in a custom-built, acoustically isolated chamber. A capacitive touch sensor (AT42QT1010, SparkFun) soldered to a lick spout monitored lick activity. Water rewards were dispensed from a gravity fed reservoir, controlled by a solenoid valve (161T011, Neptune Research) calibrated to deliver approximately 4-5uL of water per reward82. Low-level task logic – such as lick detection, reward and timeout delivery, and task timing intervals – was directly controlled by an Arduino Uno microprocessor running custom, low-latency software routines. High-level task logic, such as trial randomization, stimulus buffering and presentation, and online data collection and analysis were controlled by custom MATLAB (Mathworks) software communicating with the Arduino over a USB serial port. Acoustic waveforms were generated in MATLAB and converted to analog signals via a soundcard (Lynx E44, Lynx Studio Technology, Inc.) or a National Instruments card (NI PCIe-6353) and delivered through an ultrasonic transducer (MCPCT-G5100-4139, Multicomp). The transducer was calibrated to have a flat frequency response between 3 kHz and 80 kHz using a 1/4-inch condenser microphone (Brüel & Kjær) positioned at the expected location of the mouse’s ear, as described previously83,84. During electrophysiological recording sessions, licks were detected using an optical interrupt sensor (EE-SX771, Omron Automation), to prevent lick-related electrical artifacts introduced by contact with a capacitive sensor.

*Behavioral timeline*.

Each mouse underwent four stages in the behavioral task: 1) water restriction and habituation, 2) behavioral training, 3) psychometric testing, and, 4) offset testing. During the induction of water restriction, mice were habituated to head-fixation in the behavioral chambers and received water through the lick spout, getting a drop of water for licks separated by more than 2 s. After the mouse began to receive its entire ration by licking in the booth, behavioral training was initiated (typically after 1 week). Each mouse was initially trained and tested in one contrast condition (see *Stimuli*), with the initial training condition counterbalanced across mice. Behavioral performance was monitored during training, and mice were considered trained after completing at least three consecutive sessions with over 80% percent correct. After completing training, behavioral thresholds were measured during at least three sessions in which psychometric stimuli were presented (see *Stimuli*). After estimating the behavioral threshold for each mouse, offset stimulus sets were generated using threshold-level targets. After completion of at least three sessions in the offset task, each mouse was then retrained on the remaining contrast condition. Upon reaching the training criterion of 80% in the new contrast condition, mice were then tested in the psychometric and offset tasks as previously described. For mice in electrophysiological experiments, this sequence of training and testing was continued until the recording site yielded less than three units, or until the mouse stopped performing in the task.

*Stimuli*.

All stimuli were created in MATLAB and sampled at 192 kHz or 200 kHz and 32-bit resolution. A set of dynamic random chords (DRCs) were created with different contrasts, similarly to those described in previous studies14,17,19. To construct a DRC, amplitude modulated pure tones were generated at multiple frequencies and then superimposed to create a chord. In some experiments, 34 frequencies were sampled between 4 and ~40kHz in 1/10 octave steps, in the remaining experiments, 33 frequencies were sampled between 4 and 64kHz in 1/8 octave steps. The amplitude envelope of each tone was generated as follows: every 25 ms, amplitudes for each frequency were sampled from a uniform distribution with a mean of 50 dB and a width of ±5 dB in low contrast or ±15 dB in high contrast. Between each 20 ms chord, the amplitude envelope of each frequency band was linearly ramped over 5 ms to the amplitude value for the next chord, such that the total duration of each chord and its ramp was 25 ms. To synthesize the stimuli, amplitude envelopes were multiplied by a sine wave of their respective frequencies, and summed to produce the final waveform. Each time a set of DRCs was generated, 5 unique random number generator seeds were used to restrict the background noise to 5 distinct scenes (see raster in Figure 6 for an example of spike-locking to the repeated scenes).

In all stages of behavioral training and testing, stimuli created for each trial consisted of a DRC background containing a change in contrast, and the presence or lack of a target at a delay after the change in contrast. Each trial began with 3 seconds of DRC background from one contrast, followed by a switch to the other contrast. Targets consisted of a fixed chord composed of 17 frequencies pseudo-randomly sampled from the frequencies contained in the DRC background, such that the target frequencies were uniformly distributed across the frequency range of the background. To add targets to the background noise, the target amplitude at each target frequency was simply added to a single chord in the amplitude envelope of the background, and ramped as described previously: this procedure ensured that target timing was perfectly aligned to changes in the background noise, removing asynchronous timing cues that could be used to detect the target. Target amplitudes are described in values of signal-to-noise ratio (SNR) relative to the average level of the background noise (ie. a 50 dB target embedded in 50 dB background would have an SNR of 0 dB). See Extended Data Table 3 for SNRs used for each mouse. In all trials, targets were embedded after a change in the background contrast, with a delay and level dependent on the current training or testing stage.

*Efficient coding model.*

We simulated a model neuron that encodes incoming stimuli via an adapting neural nonlinearity. Stimuli were drawn from a Gaussian distribution whose mean was fixed over time but whose standard deviation could switch over time between a low and a high value ( and , respectively). At each time , a stimulus was drawn from the distribution , transformed via a saturating nonlinearity of the form , distorted by Gaussian noise with variance , and finally discretized into discrete levels to generate a response . This discrete response was linearly decoded to extract an estimate of the current stimulus: . The recent history of stimulus estimates was used to update an estimate of the underlying standard deviation: . The estimate was then used to select the parameters of the encoder () and the decoder () on the next timestep. The encoding and decoding parameters were chosen to minimize the expected error in decoding stimuli given the neuron’s current estimate of the underlying standard deviation: 22,23.

The parameters of the encoder and decoder were adapted based on a background stimulus with a mean that was fixed over time and a standard deviation that switched between low and high values and , respectively. We used this adapting nonlinearity to determine how well this model neuron could discriminate target stimuli from this background. Target stimuli were sampled from a Gaussian distribution with a fixed mean and with a variance that was scaled in proportion to the variance of the background ( and , respectively). At each timestep, we computed the Bhattacharyya coefficient () of the response distributions produced by background versus target stimuli: . We used as our measure of discriminability.

We simulated the behavior of this model using a background “probe” stimulus whose standard deviation switched every timesteps. We simulated cycles of this probe stimulus, where each cycle consisted of timesteps in the low state, followed by timesteps in the high state. This yielded timeseries of the gain and offset of the adapting nonlinearity, as well as distributions of the neural response to the background and target stimuli at each timepoint following a switch in standard deviation. We averaged the gain and offset across cycles to obtain the average properties of the encoder at each timepoint following a switch. We used the distribution of responses to target and background stimuli, measured across cycles, to compute the discriminability at each timepoint following a switch. All simulations were performed with the following values: , ,, 0 to 3 in 0.25 steps, , ,,,. For Figure 1g, model discriminability in each contrast was fit with a logistic function to estimate the sensitivity and threshold of the model. To approximate the stimulus conditions used in the offset task, the target thresholds for each contrast were then used to select target levels to plot discriminability over time (, ; Figure 1f).

*Behavioral task*.

We employed a GO/NO-GO task to measure the detectability of targets in background. In this task, each trial consisted of a noise background with a contrast shift, along with the presence or absence of a target after the change in contrast. Mice were trained to lick when they detected a target (hit), or to withhold licking in the absence of a target (correct reject). This behavior was reinforced by providing a 4-5 uL water reward when the mouse licked correctly (hit), and by initiating a 7-10 s timeout when the mouse licked in the absence of a target (false alarm). Any licks detected during the timeout period resulted in the timeout being reset. In a subset of mice, we introduced an additional trial abort period coincident with the first part of the contrast background, before the contrast switch. Any licks detected in this abort period resulted in the trial being repeated after a 7-10 s timeout, until the mouse withheld from licking during this period. In this task, misses and correct rejects were not rewarded or punished. Trials were separated by a minimum 1.5s inter-trial-interval (ITI). To discourage spontaneous licking, licks were monitored during this period, and if any licks occurred the ITI timer was reset.

To prevent mice from predicting target time, we varied the timing of the target relative to the contrast shift. This required a method for estimating hit rates and false alarm rates at different times during each trial, and to reward and punish the animal during these times in an unbiased manner. To approach this issue, we considered licks only during a 1 s response window after a target presentation (eg. if a target was presented 500 ms post-contrast-switch, the response window persisted from 500 to 1500 ms post-contrast-switch). To apply this method to background-only trials, in which no targets were presented, we considered background trials to be target trials containing infinitely small target amplitudes. For each background trial, we assigned a response window with equiprobable delay matched to the target conditions and considered only licks within those “target” response windows. Thus, over the course of a session, we randomly sampled lick probabilities in background trials during the same temporal windows as those considered during target trials. Using this scheme, we treated target and background-only trials identically, and estimated hit rates and false alarm rates over time in an unbiased manner.

Each mouse performed three stages in the behavioral task: training, psychometric testing, and offset testing. During the training task, trials consisted of two types, background-only trials or target trials presented with equal probability. To facilitate learning, we selected target SNRs at the highest end of the range described previously: in low contrast training sessions, targets were 16 dB SNR, and in high contrast training sessions, targets were 20 dB SNR. To prevent response bias as a function of target timing, we randomly varied the target delay between 250, 500, 750 and 1000 ms after the contrast change in each trial. During the psychometric testing task, there were 7 trial types consisting of background-only trials and target trials spanning six different SNRs (Extended Data Table 3). Based on behavioral piloting, we presented high SNR trials with a greater probability, to ensure that mice were consistently rewarded during the task. In low and high contrast psychometric sessions, the probability of a background trial was 0.4, the probability of the four lowest target SNRs was 0.05 each, and the probability of the two highest target SNRs was 0.2 each. As in training, target timing was varied randomly between 250, 500, 750 and 1000 ms after the contrast change in each trial. After completing at least three sessions of the psychometric task, stimuli were generated for the offset testing task. This task consisted of 15 unique trial types: 3 target levels (background trials, threshold target trials, and high SNR target trials), and 5 target delays relative to the contrast change (25, 75, 225, 475, 975 ms delay). Threshold target amplitudes were determined individually for each mouse by fitting performance averaged over several sessions with a psychometric function, and extracting the level at which the slope of the psychometric curve was steepest. Based on behavioral piloting, background trials, threshold target trials, and high SNR target trials were presented with probabilities of 0.4, 0.2, and 0.4, respectively. Target delay on each trial was selected with equal probability. In all behavioral stages, trial order was pseudorandomly generated, such that there were no more than three target or background trials in a row.

A subset of mice (n = 2), were presented targets in silence (Figure 4). To generate this stimulus set without changing the basic structure of the task or stimuli, we simply took the spectrograms of all stimuli containing 25 dB SNR targets from the low-to-high contrast stimulus sessions, and set the stimulus power flanking each target to zero. This manipulation was only performed in the target period, and the low contrast adaptation period of the trials remained the same. Thus, the targets and adaptation periods were identical to those presented in the target-in-background task. To vary the difficulty of the task, the level of the target was attenuated using the following values: -75, -60, -45, -30, -15, and 0 dB attenuation relative to the 25 dB SNR target. Mice were previously trained in the target-in-background task prior to performing the target in silence task. Before psychometrically varying the target attenuation, mice were trained in the new task to criterion performance. Mice generalized very rapidly to the new task, reaching 97% and 94% training accuracy on the first day of exposure to targets in silence (mice CA124 and CA125, respectively).

*Chronic muscimol application*.

A separate cohort of mice (n = 4) were bilaterally implanted with 26 GA guide cannulae (PlasticsOne, C315GMN-SPC mini, cut 5 mm below pedestal) in auditory cortex. The surgery was performed as described previously with the following modifications. After the skull was leveled using a stereotax, two small craniotomies were performed -2.6 mm anterior, ±4.3 mm lateral from bregma, over auditory cortex. The guide cannulae and dummy infusion cannulae (PlasticsOne, C315DCMN-SPC mini, cut to fit 5 mm C315GMN with a 0.5 mm projection depth) were sterilized in an autoclave. The dummy cannulae were partially screwed into the guide cannulae and placed in a stereotaxic clamp. After zeroing the tip of the guide cannula to the brain surface, the cannula was lowered to 500 μm below the cortical surface. This depth was chosen because the infusion cannulae (PlasticsOne, C315LIMN-SPC mini) project 500 μm from the end of the guide cannulae when completely inserted, leading to a final depth of 1000 μm – the location of auditory cortex. The dummy cannulae were then fully inserted and this procedure was repeated for the next cortical hemisphere.

Prior to injecting, two injection syringes (Hamilton Syringe, 10μL Gaslight #1701) and tubing (C313CT tubing 023x050 PE50) were backfilled with mineral oil. Sterilized infusion cannulae were then attached to each syringe and ~500nL of muscimol (diluted with 1x PBS to .25 mg/mL; Sigma Aldrich, M1523) or 0.9% sterile saline was drawn up into the injection cannulae using a dual injector (Harvard Apparatus, Pump 11 Pico Plus Elite). The mouse was then headfixed and the dummy cannulae were removed and sterilized. The loaded infusion cannulae were then screwed all the way into the guide cannulae and 400 nL of muscimol or saline was infused bilaterally at a rate of 250 nL/minute. The infusion cannulae were then replaced with the dummy cannulae and the mouse rested in its home cage for 30-45 minutes before beginning the behavioral session.

*Acute electrophysiological recordings.*

For acute recordings used to fit the GC-GLM model (Figure 2), neuronal signals were recorded from n = 1 awake, untrained mouse. Prior to the recording session, the mouse was anesthetized and a headpost and ground pin were implanted on the skull (see *Surgery*). On the day of the recording, the mouse was briefly anesthetized with 3% isoflurane and a small craniotomy was performed over auditory cortex using a dental drill or scalpel (~1 mm x 1 mm craniotomy centered approximately 1.25 mm anterior to the lambdoid suture along caudal end of the squamosal suture). A 32 channel silicon probe (Neuronexus) was then positioned perpendicularly to the cortical surface and lowered at a rate of 1-2 μm/s to a final depth of 800-1200 μm. As the probe was lowered, trains of brief noise bursts were repeated, and if stimulus locked responses to the noise bursts were observed, the probe was determined to be in auditory cortex. The probe was then allowed to settle for up to 30 minutes before starting the recording. Neuronal signals were amplified and digitized with an Intan headstage (RHD 32ch) and recorded by an openEphys acquisition board85 at a rate of 30 kHz.

For this experiment, the mouse was presented with 3 s DRCs alternating between low and high contrast (uniform distribution with a mean of 50 dB and a width of ±5 dB in low contrast or ±15 dB in high contrast at a chord rate of 25 ms, as described in *Stimuli*). In order to accurately fit the GLM in an unbiased manner, these stimuli were highly random, composed of 100 unique chord patterns for each contrast (Extended Data Figure 2i,j**)**. For each of the two recording sites, 5 repeats of this stimulus set were played.

*Behavioral electrophysiological recordings*.

Neural signals were acquired from awake, behaving mice as they performed the psychometric and offset testing tasks described previously. Chronically implanted, 16-, 32-, or 64-channel microdrives85,86 were connected to one or two 32 channel Intan amplifier headstages. Amplified signals were recorded at 30 kHz using an openEphys acquisition board via an SPI cable, where the signals were digitized.

For all recordings, broadband signals were filtered between 500 and 6000 Hz, offset corrected, and re-referenced to the median across all active channels. The preprocessed data was then sorted using KiloSort87 or KiloSort2 and the resulting clustering was manually corrected in phy2 according to community-developed guidelines. The resulting units were labelled as single units if they exhibited a clear refractory period and did not need to be split. Splitting assessments were made through manual examination of principle component features for the two best channels of a cluster. If two noticeable clusters in feature space were evident in a unit, the unit was either manually split, or classified as a multiunit.

*Generalized linear model.*

To justify the form of GLM used here, we discuss a how a model neuron could implement gain control in the simplest terms, and then structure our inference model to extract the parameters of this model neuron. We will assume that the activity of the model neuron is driven by three sources: 1) stimulus drive, 2) stimulus contrast, and 3) the multiplicative interaction between the two, which we use to define the gain (for a formal definition of this forward model and the inference model, see *Supplementary Information*).

As discussed previously, the stimulus used in our experiments is composed of many frequencies that change in loudness in discrete time steps:

where is the stimulus spectrogram that varies as a function of time and frequency . Each time and frequency bin of is sampled from a uniform distribution defined by an average value and contrast .

We assume that the hypothetical neuron responds selectively at some frequency and time lag, defined by a filter, or STRF with history and frequency components. Given , we can define the stimulus drive as

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|  |  | (1) |

where at each time , is a row vector of size frequencies times lags (ie. the “unrolled” lagged stimulus spectrogram) and is the STRF unrolled to a single column vector of the same size.

In the spirit of efficient coding theory, and as shown in previous work, we assume that the gain of the neuron should be inversely proportional to the contrast, such that (ie. when contrast is low gain should be high, and vice-versa). We also define “neutral” gain to be the average of the gain of the neuron in low and high contrast. Putting these two features together, we can summarize the gain of the neuron as

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| --- | --- | --- |
|  |  | (2) |

where is the harmonic mean of the contrast in the low and high conditions (see *Supplementary Information*). In the case of a 3-fold change in contrast, this function constrains the gain of the neuron between 0.5 and 1.5, with a neutral value of 1. As mentioned previously, we consider gain to be the multiplicative interaction between the stimulus drive and the contrast, such that the contribution of gain control to the response of the neuron is related to .

To summarize, we considered a hypothetical neuron driven by the stimulus according to a STRF and by the interaction between the stimulus drive and the contrast . To infer the relative weights of each of these components of the neural response, we defined a Poisson GLM with an intercept term and the following predictors:

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|  |  | (3) |

In other words, the model is composed of a stimulus predictor , a contrast predictor , and their interaction. Therefore, the GLM models the firing rate at time as a Poisson distribution with the following mean:

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|  |  | (4) |

where are the parameters to be inferred. Based on our behavioral data (Figure 3) and the predictions of the efficient coding model (Figure 1), we expected the influence of contrast on neural gain to be asymmetric and smooth. To enable the GLM to capture both of these qualities, we first defined the contrast predictors from a set of cubic B-spline temporal basis functions, then defined separate contrast predictors for transitions to low and high contrast. Incorporating these changes, we can redefine equation 4 above as

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|  |  | (5) |

where denotes element-by-element “broadcasting” multiplication and is a matrix of contrast predictors convolved with a set of basis functions and separated by contrast transitions (see *Supplementary Information*). For the sake of clarity, note that in the expression above, is a number, is a column vector of length , is a number, is a -by- matrix, and and are column vectors of length , where is the number of splines.

So far, we outlined a hypothetical neuron which implements gain control, and a GLM with which we can approximate the behavior of this neuron. Next, we describe how to use the fitted parameters to quantify the gain of the neuron. Conceptually, an increase or decrease in the gain of the neuron is analogous to more or less sensitivity to small changes in the stimulus. Based on this intuition, we focused on how the response of the neuron (as modelled by a fitted GLM) is expected to change between conditions where the gain is expected to contribute (ie. in the presence of gain control) and where it is not (ie. in the absence of gain control, where gain is “neutral”). Following this logic, we derived a definition for gain as the ratio between the sensitivity of the fitted model with changes in contrast, compared to the sensitivity of the same model when the contrast is at a reference value, which we defined previously as :

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|  |  | (6) |

where is the estimated gain at time , and is a reference contrast design matrix identical to except that all non-zero elements are set to 1 (see *Supplementary Information* for full derivation of ).

To fit the model, we implemented a two-step procedure. In the first step, the STRF of the neuron was estimated according to the model

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|  |  | (7) |

For the second step, we calculated the stimulus drive as described in equation 1, and then fit equation 5 to the data for each neuron using in MATLAB. This entire fitting procedure was 10-fold cross-validated with folds stratified across trials of each contrast. In the first step, we fit the STRF with frequency bins according to the stimulus spectrogram ( = 33 or 34, see *Stimuli*) and a history window of 300 ms ( = 12). When fitting the full model, we defined the contrast design matrix to capture 1000 ms of contrast history around each transition ( = 40), convolved with a set of B-spline temporal basis functions88 (here, we used B-splines with a degree of 3 and 3 equally-spaced knots, constrained to go smoothly to zero at the longest lag, which implied that = 4).

To validate the model, we first simulated neurons according to the forward model outlined above (Extended Data Figure 2a) while varying the amount of gain control and the temporal trajectory of gain in different simulation runs. We found that the GLM accurately predicted the STRF shape, spike rates and gain trajectories across a variety of simulation parameters (Extended Data Figure 2c, e-h). For a detailed description and discussion of the simulation results, see *Supplementary Information* and Extended Data Table 4.

*Behavioral and neural detection performance.*

To calculate performance in the target-in-background detection task we adopted commonly used signal detection theory methods38,89 to estimate the ability of an ideal observer to discriminate between two sensory distributions: in our case, a distribution for target trials and a distribution for background trials. When analyzing behavior, we computed the percent correct performance of an ideal observer90 as a function of the probability of hits and false alarms:

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|  |  | (8) |

where is cumulative probability of the normal distribution ( in MATLAB), is the inverse of the normal distribution (ie. the z-score, in MATLAB), is the hit rate, and is the false alarm rate. For psychophysical performance, hit rates and false alarm rates near 0 and 1 were adjusted using the log-linear rule91, to reduce biases in performance estimation resulting from low numbers of trials.

To calculate neural performance in the same reference frame as the behavior, we employed similar ideal observer techniques. First, neuronal responses (either spike rates of single units, or population projection values), were averaged in a 100ms window post target onset (for background trials, this window was randomly chosen on each trial to coincide with target presentation times on target trials). Then, using the distributions of responses during target and background trials, we computed receiver-operating-characteristic curves and took the area under the curve (AUC) as the percent correct of an ideal observer discriminating between the target and background distributions. To determine whether the AUC value for a given set of trial distributions was significantly different from chance, we performed a bootstrap procedure where we sampled from all the trials with replacement 500 times and recomputed AUC for each sample. If the 95% confidence intervals for this bootstrapped distribution did not include chance (.5), we defined that AUC value as significant. For population analyses which generated single-trial predictions, neural hit and false alarm rates were transformed to percent correct as described above.

To characterize performance, psychometric curves were fit with a logistic function:

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|  |  | (9) |

where is the x-offset of the function, determined the sensitivity of the function, determined the guess rate (lower bound), determined the lapse rate (upper bound) and was stimulus level. determined the threshold of this function, defined as the level corresponding to the steepest part of the curve. This function was fit to behavioral or neural performance using constrained gradient descent ( in MATLAB) initialized with a 10x10 grid-search of parameters and .

To characterize adaptation time constants, adaptation curves were fit with an exponential function

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|  |  | (10) |

where determined the y-offset of the function, was a multiplicative scaling factor, and was the time constant of the exponential in units of time . This function was fit to behavioral or neural responses using constrained gradient descent initialized with a 10x10x10 grid search across all three parameters.

To measure the effect of stimulus contrast on parameters of interest, we computed a contrast modulation index (CMI), which measured the relative change in the parameter between low and high contrast:

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|  |  | (11) |

where ­ is the parameter in question and subscripts and denote the value of that parameter in high and low contrast, respectively. The resulting index is 0 if there is no change, 1 if is two times larger than , and is -0.5 if is two times .

*Population response metrics.*

On sessions where three or more neurons were simultaneously recorded, we used a population vector technique26 to estimate the ability of neural populations to discriminate targets from background. First, spike rates in each trial were averaged in a 100ms window post-target onset. Then, using a leave-one-out procedure, we computed a trial averaged population vector for target trials, , and a separate average population vector for background trials, . We then estimated the coding direction in high dimensional neural space that best separated the target and background responses: The held out trial was then projected along this dimension, by taking the population response vector on that trial and projecting it along the estimated coding direction using the dot product: . This procedure was repeated holding out each trial, and estimating the coding direction from the remaining trials. For psychometric testing sessions, the target responses from the two loudest target levels were used to estimate coding direction, and in offset testing sessions the target responses from the high SNR target trials were used. After computing projections for every trial, the resulting matrix was normalized between 0 and 1.

*Population classifier*.

Based on previously described methods27, we used a criterion-based decision rule to estimate how a hypothetical down-stream neuron may read out the neural activity of a population of neurons. As before, trial distributions of neural responses to targets or background were created from the average activity in a 100ms window post-target. Then, we sampled 100 criterion values between the minimum and maximum response, and for each criterion estimated the proportion of correct trials under two decision rules: 1) report target present if the response is greater than the criterion, or, 2) report target present if the response is less than the criterion. By assessing these two decision rules, neurons that were suppressed by target presence were treated equally to neurons that were enhanced by target presence. Finally, we chose the criterion and decision rule that yielded the highest proportion of correct trials, and computed neural hit rates and false alarm rates for each target level, and background-only trials. These hit rates and false alarm rates were then transformed to percent correct according to Equation 8.

*Linear-nonlinear model*.

First, we selected only neurons in the dataset which had reliable responses to stimulus repeats. To determine response reliability, we computed a noise ratio (NR) for each neuron, which describes the amount of variability in the response due to noise versus the amount of variability in the response driven by the stimulus92,93. Values approaching 0 indicate increasingly reliable responses to the stimulus, so for the remaining analyses, we included neurons with NR < 100.

The linear nonlinear model was composed of a spectrotemporal receptive field (STRF) and a set of rectifying nonlinearities. The STRF was fit using normalized reverse correlation

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|  |  | (11) |

where is the stimulus design matrix defined in equation 1 and is the spike count in each 25 ms bin of the DRC stimulus. When defining , we used a history window of 300 ms ( = 12) and frequency bins corresponding to the frequencies composing the dynamic random chords (see *Stimuli*). After fitting the STRF, we fit the nonlinearities of the neuron. This two-step fitting procedure was repeated using 10 fold cross-validation, as described below.

For each fold, we selected 90% of the trials for training, leaving the remaining 10% to be held out for testing. Within each trial, we excluded neuronal responses around transitions from silence, or transitions in contrast, to prevent the model from overfitting strong transients in the neural response. Additionally, we excluded neural responses within a 50ms window after target presentation, to prevent overfitting of target responses. Given these exclusion criteria, we calculated the duration of stimulus sampled in the target period for each trial, and, for each trial, sampled the same duration of stimulus within the adaptation period. This procedure ensured that the model was fit to the same amount of high and low contrast stimulation per trial, to minimize overfitting to one contrast condition. Then, a stimulus design matrix was defined using these stimulus periods, and the STRF was fit using equation 11. During an initial pilot experiment, we tested whether STRF properties were affected by stimulus contrast, and found STRFs to be largely stable when estimated separately for each contrast (*Supplementary Information* and Extended Data Figure 5b-g). Therefore, we used both periods of contrast to estimate .

Using the STRF fit to the training data, we computed the linear drive by convolving the STRF with the lagged spectrogram of the training stimulus (equation 1). For the GC-LN model we separated the linear predictions into low and high contrast periods, while for the static-LN model all matched time points were used. We generated a histogram of the linear prediction values (50 bins), and for each bin, computed the mean spike rate of the neuron when the linear prediction fell within those bin edges (Figure 6d, scatter points). The resulting set of linear prediction values and average spike rates were fit with an exponential function:

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| --- | --- | --- |
|  |  | (12) |

where determined the minimum firing rate, was a multiplicative scaling factor, determined the gain of the exponent, and determined the x-offset, or firing threshold of the neuron. This function was fit to each cell using constrained gradient descent ( in MATLAB), using a 10x10 grid search for parameters and . The gain for each neuron was defined as . This entire process was repeated for each cross-validation fold, and the final parameter estimates for the STRF and nonlinearities were taken as the average over the 10 runs.

To determine the relationship between neuronal gain and behavioral performance, we computed the average neural gain across all noise responsive neurons (NR < 100) in each session for the adaptation and target periods in the trial. We then compared the session-averaged gain values to the fitted thresholds and slopes of the psychometric curve across sessions using the mixed-effects linear models outlined in the main text.

*Inclusion criteria*.

Unless otherwise noted, behavioral sessions in which the false alarm rate exceeded 50% were discarded from analysis. One mouse (ID: CA122) had consistently high false alarm rates in the high contrast condition, so we excluded high contrast sessions from this mouse from all analyses. For Figures 5 and 6, we removed neurons with low spike rates (<1Hz) and noise-like or inverted (ie. upward inflected) spike waveforms. To determine waveform quality, we computed the width of each waveform at half of the minimum value (FWHM) and its correlation with the average waveform over all neurons. Neurons whose waveforms had outlier FWHM values ( in MATLAB), negative correlations, or were not significantly correlated with the average (Bonferoni corrected *p* > 5.85e-6) were removed from further analysis. For Figure 5g-i, sessions with stable population decoding performance were included (defined as sessions where more than half of the target levels or times elicited significant population AUC values, as determined by the bootstrap procedure described previously). For Figure 6e-h, only neurons with noise ratios less than 100 were included in all analyses.

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**Supplementary Information**

**Supplemental Experimental Procedures**

*Acute electrophysiological recordings with muscimol or saline.*

Neural signals were recorded from n = 2 awake, untrained mice. Prior to the recording session, each mouse was anesthetized and a headpost and ground pin were implanted on the skull (see *Surgery* in the main text). On the day of the recording, the mouse was briefly anesthetized with 3% isoflurane and a small craniotomy was performed over auditory cortex using a dental drill or scalpel (~1mm x 1mm craniotomy centered approximately 1.25mm anterior to the lambdoid suture along caudal end of the squamosal suture). A 32-channel silicon probe (Neuronexus) was then positioned perpendicularly to the cortical surface and lowered at a rate of 1-2μm/s to a final depth of 800-1200μm. As the probe was lowered, trains of brief noise bursts were repeated, and if stimulus locked responses to the noise bursts were observed, the probe was determined to be in auditory cortex. The probe was then allowed to settle for up to 30 minutes before starting the recording.

For the muscimol and saline recordings (Extended DataFigure 3), a durotomy was performed over the injection site and baseline neural responses to the behavioral stimuli were recorded. Then, 2.5μL of .25mg/mL muscimol or 0.9% sterile saline solution was topically applied to the surface of auditory cortex and allowed 30 minutes to penetrate the tissue. The same stimuli were then recorded again after the elapsed time. In these recordings, the same targets and DRC background presented during behavior were presented. Neural signals from n = 2 mice (1 mouse for muscimol application, 1 mouse for saline application) were amplified and digitized using a Cheetah Digital LYNX system (Neuralynx) at a rate of 32kHz.

*Acute electrophysiological recordings for Extended Data Figure 5b-g*

Neural signals were recorded from n = 9 awake, untrained mice of several -cre strains (somatostatin-cre, n = 5; parvalbumin-cre, n = 2; VGAT-cre, n = 2). These mice were implanted with a headplate and groundpin, as described in *Surgery*. Additionally, each mouse was bilaterally injected with 700 µL of Flex-ChR2 during the initial surgery in auditory cortex, then bilaterally implanted with opto-cannulae which projected 500 um below the brain surface above auditory cortex. During the recordings, mice were presented with dynamic random chord stimuli (DRC) which changed contrast every 3 s. At each time step, the chords were randomly drawn from a uniform distribution with a center of 50 dB SPL and a spread of either 7.5 dB SPL or 15 dB SPL in low and high contrast respectively. Each chord was presented for 4 ms with a 1 ms linear ramp between each chord. Chords were composed of 25 frequencies between 1 and 64 kHz, spaced 0.25 octaves apart. On a subset of trials, 470 nm LED or laser light was continuously shone or pulsed at 25 Hz through the opto-cannulae for the duration of the 3 s of contrast period (power measured at the fiber tip ~2-5 mW). For the purposes of this study, we discarded all trials with light presentation.

**Supplemental Results**

*The range of presented target levels shapes psychometric performance curves.*

In the experiments presented here, we utilized several sets of target levels to assess psychometric performance (for a summary of the target levels used, see Extended Data Table 3). When computing psychometric curves across all of the target conditions for each mouse (n = 25; Extended Data Figure 3b), we found that detection thresholds were lower in low contrast (Mean dB SNR (*M*) = 8.56, standard deviation (*std*) *=* 1.81) compared to high contrast (*M =* 14.23, *std =* 2.57; paired t-test: *t(23)* = -8.19, *p* = 2.88e-8, Extended Data Figure 3c). From our normative model, we expected psychometric slopes to decrease in high contrast. Instead, when combining sessions with different target levels, we found a significant increase in slope during high contrast (*M* = 0.056, *std =* 0.018) when compared to low contrast (*M =* 0.045, *std =* 0.0052; paired t-test: *t(23)* = -3.42, *p* = 0.0024, Extended Data Figure 3d). We hypothesized that psychometric performance was sensitive to the range of targets presented. To test this, we split the data by the range of target levels used in each session, finding that targets drawn from a narrow range resulted in steeper psychometric slopes than targets drawn from a wide range, regardless of the background contrast (Extended Data Figure 3e-h). Therefore, we concluded that the paradoxical increase in psychometric slope was due to the narrow range of targets selected for many high contrast sessions. To control for these effects and thus isolate the effect of background contrast on psychometric slope, we considered only sessions with identical ranges of targets in low and high contrast and found that slopes did indeed decrease in high contrast (Figure 3).

*Muscimol application disrupts cortical encoding of targets.*

In n = 2 awake, naïve mice, we first recorded baseline responses to the stimuli used in the psychometric task, then topically applied muscimol or saline, waited 30 minutes, and recorded stimulus responses again. After muscimol application, there was a marked decrease in neural responses to targets compared to the baseline recordings (Extended DataFigure 1b, left). Notably, in our saline control, we observed little to no change in neural responses after saline application (Extended DataFigure 4b, right). We next compared how contrast, level and muscimol or saline application changed the responses during the pre- and post-application periods, finding that muscimol significantly reduced the firing rates between pre- and post-application periods, while saline significantly increased firing rates (Extended DataFigure 4c,d, Extended Data Table 1). We speculate that the small increase in firing rate between pre- and post-saline application was due to changes in recording quality or due to neural drift over the ~1 hour recording session, and note that the effect size of saline pre-post application is very small (*η2* = 0.0046) compared to the effect size of muscimol (*η2* = 0.38). We then used a three-way ANOVA to compare the effects of muscimol, contrast, and target level on target responses in the saline and muscimol recording sessions. We found a significant main effect of muscimol (*F*(1) = 322.65, *p* = 4.88e-67) and level (*F*(6) = 15.48, *p* = 1.98e-17), but no main effect of contrast (*F*(1) = 0.39, *p* = 0.53), indicating nearly complete suppression of responses to both targets and background in high and low contrast (Extended DataFigure 4e,f). These results confirmed that muscimol effectively disrupts the cortical coding of our behavioral stimuli.

*Muscimol application does not prevent licking.*

An additional alternative effect of muscimol is a general loss of the ability to lick. To assess this, we monitored the lick probability of the mice throughout the trial duration, and found that muscimol specifically reduced licking responses during the period where targets were presented (Wilcoxon rank-sum test: *T* = 337, *z* = -4.23, *p* = 2.34e-5; Extended DataFigure 4g, right panel of Extended DataFigure 4h). Mice also tended to lick immediately after the trial onset (Extended DataFigure 4i, green trace), but we found that the lick rates under muscimol and saline conditions were identical during this period (Wilcoxon rank-sum test: *T* = 528, *z* = 0.23, *p* = 0.81; Extended DataFigure 4h, left panel). These results suggest that muscimol does not impair the mouse’s ability to lick in general, but results in a specific deficit in licking in response to targets.

*STRF are stable across contrasts.*

Based on a pilot study of neuronal data acutely recorded from auditory cortex, we tested whether STRF properties were affected by stimulus contrast. We recorded spiking activity in response to DRCs that changed contrast every 3 seconds. Out of the 700 units identified from n = 9 mice, we selected the subset of neurons with noise ratios (NR) below 100 for further analysis (n = 129). For each neuron, we computed the spectrotemporal receptive field (STRF) using a spike triggered average in each contrast (Extended DataFigure 5b), then computed 100 “random” STRFs by shuffling the stimulus in time within each contrast. For each shuffle, we computed the correlation of the true low contrast STRF with the shuffled high contrast STRFs to generate a null distribution of low-high contrast STRF correlations. We then compared the true correlations of the low and high contrast STRF with this null distribution, defining them as significantly correlated if the true correlation fell outside the 99th percentile of the null distribution. We found that nearly all of the low and high contrast STRFs were significantly correlated (124/129 neurons, 96%), suggesting that contrast doesn’t change the overall structure of the STRF (Extended DataFigure 5d).

To further quantify these results, we tested whether more concrete STRF properties such as best frequency (BF), lag, and max value were affected by contrast. First, we de-noised each STRF by determining the significance of each pixel. To do this, we compared the value of each pixel to the distribution of shuffled values for that pixel, and retained only pixels greater than three standard deviations of the shuffled value. Based on the de-noised STRFs, we computed frequency and temporal components by averaging over each STRF dimension (Extended DataFigure 5c). We then estimated the BF and lag as the max of these components, and determined the max STRF value by finding the max value over all pixels. Next, we compared each measure across STRFs from low and high contrast. We found that the maximum pixel value was significantly greater in high contrast (Median (*Mdn*) = 1.33, inter-quartile range (*IQR*) = 1.28) than in low contrast (*Mdn* = 0.56, *IQR* = 0.62; Wilcoxon signed-rank test: *z* = -9.78, *rank* = 0, *p* = 1.39e-22; Extended DataFigure 5e, e). On the other hand, we found a non-significant trend towards lower BFs in low contrast (*Mdn* = 19.03 kHz, *IQR* = 35.74 kHz) compared to high contrast (*Mdn* = 22.63 kHz, *IQR* = 47.09 kHz; Wilcoxon signed-rank test: *z* = 1.78, *rank* = 1761, *p* = 0.076; Extended DataFigure 5f), and no significant change in lag (Wilcoxon signed-rank test: *z* = -0.93, *rank* = 1776, *p* = 0.35; Extended DataFigure 5g). Taken together, these results demonstrate that the frequency and temporal modulation of sound responses are consistent across contrasts, supporting previously published findings.

**Generalized linear model of contrast gain control dynamics**

A primary goal of the current study was to estimate the influence of stimulus contrast on neural gain dynamics, for instance, after a switch from one contrast to another. To approach this problem, we first define a model neuron with dynamic gain control.

*Forward model*

To best approximate the stimuli used in our experiments, we define the stimulus environment of our model as an -dimensional signal that evolves in discrete time steps:

,

where is a stimulus spectrogram that varies as a function of time and frequency . Each time and frequency bin of is sampled from a normal distribution defined by an average value and contrast at time .

To approximate the behavior of real neurons, we define a model neuron that has a two-dimensional linear filter (representing the STRF of the neuron):

,

where stimulus filter is defined as a two-dimensional gaussian distribution evaluated at lag and frequency . The filter location in frequency-history space is defined by its mean and covariance matrix . The stimulus drive of the neuron at each time step, , is then computed as the convolution of the stimulus matrix and the linear filter:

|  |  |  |
| --- | --- | --- |
|  |  | (13) |

where at each time is a row vector of length (ie. the unrolled stimulus spectrogram lagged by lags) and is the filter, unrolled as a column vector of the same length.

The model neuron has a firing rate that depends only on the stimulus drive and the contrast at time . We then assume that the number of spikes emitted by the neuron at each time step follow a Poisson distribution:

where is the firing rate at time , given by

|  |  |  |
| --- | --- | --- |
|  |  | (14) |

where is a gain control function, and , , and are parameters of the model. The parameter represents the baseline response of the neuron, is a scaling factor of the stimulus drive, and represents the operating point of the gain. We remove the obvious degeneracy in the definition of *g* and *b* (only their product matters) by requiring that *g* be adimensional and such that

|  |  |  |
| --- | --- | --- |
|  |  | (15) |

where and are the high and low contrast values. This constraint forces the neutral value of the gain, to be the midpoint between gain in the high and low contrast conditions.

*Optimal gain control*

In the spirit of the efficient coding principle, we derived a form for that will guarantee that, under certain conditions, the dynamic range of the neuron will be approximately conserved under changes in contrast. To do this, we define the dynamic range as

|  |  |  |
| --- | --- | --- |
|  |  | (16) |

which can be rewritten using equation 2 as

|  |  |  |
| --- | --- | --- |
|  | . | (17) |

If the argument of the exponentials is not too large, we can linearize this expression to obtain

|  |  |  |
| --- | --- | --- |
|  |  | (18) |

and that is approximately independent of provided that . So, for our model, we set

|  |  |  |
| --- | --- | --- |
|  |  | (19) |

where is the harmonic mean of and :

|  |  |  |
| --- | --- | --- |
|  |  | (20) |

Finally, to validate that our fitting methods are sensitive to real world neurons, which do not necessarily adjust their gain to account for changes in contrast according to the model just described, we consider an interpolation scheme that smoothly transforms a model with positive gain control to a similar model without gain control, or with “anti” gain control. To do this, we redefine as follows:

|  |  |  |
| --- | --- | --- |
|  |  | (21) |

so that by changing we can control whether gain control is optimal (), non-existant (), or “anti” ().

Putting everything together, the final expression for the firing rate of the forward model is

|  |  |  |
| --- | --- | --- |
|  |  | (10) |

*Generalized linear model*

The forward model developed in the previous section provides a simple approximation of the relationship between the stimulus, stimulus contrast and neuronal responses. We also note that the form of the forward model lends itself to estimation using a Poisson GLM, provided that the predictors are chosen appropriately. As such, we define the inference model as a Poisson GLM with an intercept term and the following predictors:

In other words, the model is composed of a stimulus predictor (), a contrast predictor (), and their interaction. Therefore, the GLM models the data at time as a Poisson distribution with the following mean:

|  |  |  |
| --- | --- | --- |
|  |  | (22) |

where are the parameters to be inferred, and, as defined previously, is the stimulus drive of the neuron determined by its STRF.

*Model fitting*

To fit the model, we took a two-step approach. First we found the best-fit filter (STRF) for the neuron. Then, we fit the full GLM to determine how the linear drive determined by the STRF is modulated by contrast. In the first step, the linear drive is obtained by fitting the model

|  |  |  |
| --- | --- | --- |
|  |  | (23) |

where is a design matrix defined as a function of frequency bins and history lags , and is the fitted STRF. Stimulus drive is then computed as in equation 1**.**

We then define the full model according toequation 11,

|  |  |  |
| --- | --- | --- |
|  |  | (24) |

where and is a set of cubic B-spline temporal basis functions. By defining a matrix as follows

|  |  |  |
| --- | --- | --- |
|  |  | (25) |

we can rewrite equation 13 in a more compact form:

|  |  |  |
| --- | --- | --- |
|  |  | (26) |

where denotes element-by-element “broadcasting” multiplication.

To fit asymmetric changes in firing rate after transitions to low or high contrast, we took the simple approach of defining separate sets of contrast predictors for each transition type. This amounted to modifying by masking transitions to high contrast or transitions to low contrast with zeros, such that the model fit a window of 40 time bins around each contrast transition. To do so, we created a new matrix by duplicating column-wise. Then, we define the first columns as predictors for the transition to low contrast by masking a 1 second period around each transition to high contrast with zeros. This same procedure was repeated for the remaining columns in , instead masking out the transition to low contrast. Substituting this into equation 15, we obtain

|  |  |  |
| --- | --- | --- |
|  |  | (27) |

For the sake of clarity, note that in the expression above, is a number, is a column vector of length , is a number, is a -by- matrix, and and are column vectors of length .

*Defining gain*

We have outlined a forward model for simulating neural activity according to efficient coding of stimulus contrast, and described an inference model (a Poisson GLM) for estimating the influence of the stimulus, stimulus contrast, and their interaction. In this section, we describe how to use the fitted parameters to quantify the amount of gain control in the neuron.

Conceptually, an increase or decrease in the gain of a system is analogous to more or less sensitivity to small changes in the stimulus, dependent what is modulating the gain (in our case, the recent history of the contrast). Based on this intuition, we focus on how the response of the neuron (as modeled by a fitted GLM) is expected to change between conditions where the gain is expected to contribute (i.e. in the presence of gain control) and where it is not (ie. in the absence of gain control, where gain is “neutral”).

To do this, we start by considering the gradient of the link function (the log rate) at time with respect to :

|  |  |  |
| --- | --- | --- |
|  |  | (28) |

We can immediately read equation 17 as “the STRF of the model is modulated by a factor of at time ”, and define the gain based on this intuition, but we will take a slightly longer and more formal route to get to the same result.

The gradient is a vector with the same dimensionality of and , and it encapsulates all information about the sensitivity of the link function to small changes in at a given time. Because is not a scalar (it has components), these changes can happen along many dimensions, and the sensitivity can be different in different directions. We can define the gain based on the sensitivity to changes in a specific direction (assuming for concreteness that , although this is not necessary for the derivation below). If , where is some scalar, then

|  |  |  |
| --- | --- | --- |
|  |  | (29) |

by definition of the gradient. We can then define the gain along direction as the ratio between the sensitivity of the log rate to changes along and the sensitivity one would have if the contrast was at some reference value where we define by construction. If we do so, we obtain

|  |  |  |
| --- | --- | --- |
|  |  | (30) |

Note that this definition does not depend on the initial choice of , or even on the specifics of the choice of basis functions used to define . In conclusion, by reasoning about the sensitivity of the response of the fitted GLM, we define a value which captures the relationship between the true gain and the stimulus contrast .

*Simulations*

To validate our inference model, we simulated neural activity according to the generative model defined in the *Forward Model* section (Extended DataFigure 2a). We were interested in capturing several dimensions upon which the generative model could vary, namely, the amount of gain control in the simulated neurons , and the dynamics of the gain function .

To parametrically control the evolution of gain over time, we simulated different temporal trajectories of gain control, by modifying as follows

|  |  |  |
| --- | --- | --- |
|  |  | (31) |

where the gain ­­ after a switch to contrast transitions from the gain in the previous contrast to the gain in the current contrast according to an exponential function with time constant . Note that could vary between the two contrasts to simulate asymmetric dynamics.

For each neuron, we first generated a STRF and linear drive according to equation 1(Extended DataFigure 2b,d). For different sets of simulated neurons, we parametrically varied the amount of gain control between -1 and 1, and varied the gain time courses to simulate three types of gain adaptation dynamics: 1) Slow transitions to low contrast with fast transitions to high contrast, 2) Fast, symmetric transitions to each contrast, 3) Fast transitions to low contrast and slow transitions to high contrast (Extended DataFigure 2f).

We simulated 100 neurons for each combination of and , with other simulation parameters held constant (Extended DataTable 4). Extended DataFigure 2e plots the average firing rates and overlaid model fits for three sets of simulations with optimal gain control () while varying . Importantly, the model flexibly captured the gain dynamics in the three simulated adaptation conditions, with the gain estimate following the true gain trajectory (Extended DataFigure 2f). For additional values of , the model accurately predicted the firing rates (Extended DataFigure 2g) and gain trajectories (Extended DataFigure 2h). We observed that some combinations of and elicited large firing rate transients, particularly in the cases where simulated gain slowly adapted after a switch to high contrast (bottom panels in Extended DataFigure 2e, f, g, h). This behavior is expected, as gain remains relatively high for a longer period after the switch, causing large fluctuations in firing rate as the stimulus drive during high contrast is increased. These large firing rate transients seemed to reduce the accuracy of gain estimate , but we observed that the predicted time courses still captured the overall asymmetries present in the underlying model.

During our behavioral recordings, we used a limited number of background noise scenes (n = 5) to reduce the overall size of the stimulus set. However, it became clear that our model required a larger sample of stimulus space to accurately estimate gain. To demonstrate this, we plotted the simulation results when neurons were exposed to 100 unique background scenes (Extended DataFigure 2i) compared to simulations where neurons were only exposed to 5 unique background scenes, as in our behavioral recordings (Extended DataFigure 2j). We observed that with 100 scenes, estimates of were very close to the true gain values, but were consistently underestimated in the case of 5 background scenes, even in the case of perfect gain control. Therefore, when analyzing our behavioral recordings, we used a standard linear-nonlinear model to estimate neural gain (Figure 5), as we previously found that gain estimates from the GLM were highly correlated with gain estimated from the LN model (Figure 2i).

**Extended Data Table 1:** Statistical Comparisons.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Comparison** | **Figure** | **Center** | **Spread** | **N** | **Test** | **Statistic** | **Effect Size** | **p-value** |
| Behavior percent correct, low contrast: time 1 vs. time 2 | 2g | T1: 0.68  T2: 0.70  (median) | T1: 0.10  T2: 0.15  (IQR) | 21 mice | Two-tailed Wilcoxon sign-rank test (FDR corrected94 for multiple comparisons) | Z = -1.93  Rank: 60 | = -0.42 | 0.054 |
| Behavior percent correct, low contrast: time 1 vs. time 3 | T1: 0.68  T3: 0.82  (median) | T1: 0.10  T3: 0.092  (IQR) | Z = -4.01  Rank: 0 | = -0.88 | 5.96e-5 |
| Behavior percent correct, low contrast: time 1 vs. time 4 | T1: 0.68  T4: 0.87  (median) | T1: 0.10  T4: 0.190  (IQR) | Z = -4.01  Rank: 0 | = -0.88 | 5.96e-5 |
| Behavior percent correct, low contrast: time 1 vs. time 5 | T1: 0.68  T5: 0.91  (median) | T1: 0.10  T5: 0.11  (IQR) | Z = -4.01  Rank: 0 | = -0.88 | 5.96e-5 |
| Behavior percent correct, high contrast: time 1 vs. time 2 | T1: 0.82  T2: 0.77  (median) | T1: 0.083  T2: 0.19  (IQR) | Z = 2.84  Rank: 181 | = 0.62 | 0.0045 |
| Behavior percent correct, high contrast: time 1 vs. time 3 | T1: 0.82  T3: 0.77  (median) | T1: 0.083  T3: 0.14  (IQR) | Z = 2.17  Rank: 163 | = 0.47 | 0.030 |
| Behavior percent correct, high contrast: time 1 vs. time 4 | T1: 0.82  T4: 0.78  (median) | T1: 0.083  T4: 0.16  (IQR) | Z = 3.36  Rank: 195 | = 0.73 | 7.80e-4 |
| Behavior percent correct, high contrast: time 1 vs. time 5 | T1: 0.82  T5: 0.79  (median) | T1: 0.083  T5: 0.12  (IQR) | Z = 1.94  Rank: 157 | = 0.42 | 0.052 |
| ANOVA for effects of pre-post muscimol application, contrast, and level on firing rate in ACtx | S4c | n/a | n/a | 42 neurons | three-way ANOVA | Fpre-post(1) = 812.54  Fcontrast(1) = 22.64  Flevel(6) = 21.70 | η2 = 0.38  η2 = 0.011  η2 = 0.061 | 4.48e-136  2.19e06  2.77e-24 |
| ANOVA for effects of pre-post saline application, contrast, and level on firing rate in ACtx | S4d | n/a | n/a | 104 neurons | three-way ANOVA | Fpre-post(1) = 15.40  Fcontrast(1) = 0.43  Flevel(6) = 76.067 | η2 = 0.0046  η2 = 1.29e-4  η2 = 0.14 | 8.89-5  0.51  1.76e-88 |
| Percent correct max dB SNR, low contrast: muscimol vs. saline | 3c | Musc.: 0.10  Saline: 0.85  (median) | Musc.: 0.67  Saline: 0.27  (IQR) | 10 musc. sessions, 10 saline sessions (4 mice) | Two-tailed Wilcoxon rank-sum test | Z = -2.76  Rank: 68 | = -0.62 | 0.0058 |
| Threshold (dB SNR), low contrast: muscimol vs. saline | Musc.: 14.78  Saline: 9.66  (median) | Musc.: 18.46  Saline: 6.88  (IQR) | Z = 0.72  Rank: 115 | = 0.16 | 0.47 |
| FA rate, low contrast: muscimol vs. saline | Musc.: 0.026  Saline: 0.132  (median) | Musc.: 0.10  Saline: 0.85  (IQR) | Z = -2.91  Rank: 66 | = -0.65 | 0.0036 |
| Max slope (PC/dB), low contrast: muscimol vs. saline | Musc.: 0.026  Saline: 0.072  (median) | Musc.: 0.056  Saline: 0.030  (IQR) | Z: -2.68  Rank: 69 | = -0.60 | 0.0073 |
| Percent correct max dB SNR, high contrast: muscimol vs. saline | Musc.: 0.06  Saline: 0.80  (median) | Musc.: 0.10  Saline: 0.85  (IQR) | 13 musc. sessions, 10 saline sessions  (4 mice) | Z = -4.06  Rank: 92 | = -0.83 | 4.96e-5 |
| Threshold (dB SNR), high contrast: muscimol vs. saline | Musc.: 16.77  Saline: 18.80  (median) | Musc.: 21.33  Saline: 5.89  (IQR) | Z = -0.35  Rank: 156 | = -0.071 | 0.73 |
| FA rate, low contrast: muscimol vs. saline | Musc.: 0.027  Saline: 0.213  (median) | Musc.: 0.10  Saline: 0.85  (IQR) | Z = -3.19  Rank: 107 | = -0.65 | 0.0014 |
| Max slope (PC/dB), high contrast: muscimol vs. saline | Musc.: 0.012  Saline: 0.058  (median) | Musc.: 0.024  Saline: 0.018  (IQR) | Z = -3.77  Rank: 97 | = -0.77 | 1.66e-4 |
| Percent correct max dB SNR, target in high contrast : muscimol vs. saline | 3f | Musc.: 0.07  Saline: 0.82  (median) | Musc.: 0.51  Saline: 0.095  (IQR) | 5 musc. sessions, 5 saline sessions  (2 mice) | Two-tailed Wilcoxon rank-sum test | Z = nan  Rank: 15 | = nan | 0.0079 |
| Percent correct at threshold, target in high contrast: muscimol vs. saline | Musc.: 0.03  Saline: 0.53  (median) | Musc.: 0.35  Saline: 0.11  (IQR) | Z = nan  Rank: 17 | = nan | 0.032 |
| FA rate, target in high contrast : muscimol vs. saline | Musc.: 0.12  Saline: 0.23  (median) | Musc.: 0.22  Saline: 0.11  (IQR) | Z = nan  Rank: 21 | = nan | 0.22 |
| Max slope (PC/dB), target in high contrast : muscimol vs. saline | Musc.: 0.038  Saline: 0.057  (median) | Musc.: 0.046  Saline: 0.012  (IQR) | Z = nan  Rank: 19 | = nan | 0.095 |
| Percent correct max dB SNR, target in silence: muscimol vs. saline | Musc.: 0.85  Saline: 0.92  (median) | Musc.: 0.23  Saline: 0.15  (IQR) | 8 musc. sessions, 8 saline sessions  (2 mice) | Z = nan  Rank: 53 | = nan | 0.13 |
| Percent correct at threshold, target in silence : muscimol vs. saline | Musc.: 0.11  Saline: 0.22  (median) | Musc.: 0.28  Saline: 0.22  (IQR) | Z = nan  Rank: 55 | = nan | 0.20 |
| FA rate, target in silence : muscimol vs. saline | Musc.: 0.029  Saline: 0.041  (median) | Musc.: 0.038  Saline: 0.11  (IQR) | Z = nan  Rank: 60 | = nan | 0.44 |
| Max slope (PC/dB), target in silence : muscimol vs. saline | Musc.: 0.028  Saline: 0.031  (median) | Musc.: 0.015  Saline: 0.0048  (IQR) | Z = nan  Rank: 63 | = nan | 0.65 |
| Mixed-effects model:  behavioral\_threshold ~ neural\_threshold + contrast + (contrast-1|mouse) | 5g | **Model Coefficients**  Estimate ± standard error  [tstat(df), p-value] | | 12 mice | Likelihood ratio test against model without neural threshold:  beh\_thresh ~ contrast + (contrast-1|mouse) | (1) = 5.89 |  | 0.015 |
| Intercept: 0.23±1.21  t(16) = 0.19, p = 0.85  Neural threshold: 0.48±0.18  t(16) = 2.63, p = 0.018  Contrast: 2.83±1.14  t(16)= 2.48, p = 0.025 | |
| Likelihood ratio test against model without contrast:  beh\_thresh ~ neur\_thresh + (contrast-1|mouse) | (1) = 4.68 |  | 0.030 |
| Mixed effects model (for mice presented the same range of targets):  behavioral\_slope ~ neural\_slope + contrast + (contrast-1|mouse) | 5h | Intercept: 0.041±0.013  t(8) = 3.26, p = 0.011  Neural slope: 0.51±0.29  t(8) = 1.78, p = 0.11  Contrast: -0.0095±0.0026  t(8)= -3.60, p = 0.0070 | | 6 mice | Likelihood ratio test against model without neural slope:  beh\_thresh ~ contrast + (contrast-1|mouse) | (1) = 2.67 |  | 0.10 |
| Likelihood ratio test against model without contrast:  beh\_slope ~ neur\_slope + (contrast-1|mouse) | (1) = 7.98 |  | 0.0047 |
| Mixed-effects model:  behavioral\_slope ~ neural\_slope + contrast + (contrast-1|mouse) | S5a | Intercept: 0.023±0.0069  t(16) = 3.34, p = 0.0042  Neural slope: 0.58±0.16  t(16) = 3.58, p = 0.0025  Contrast: 0.0096±0.0052  t(16)= 1.85, p = 0.082 | | 12 mice | Likelihood ratio test against model without neural slope:  beh\_thresh ~ contrast + (contrast-1|mouse) | (1) = 9.78 |  | 0.0018 |
| Likelihood ratio test against model without contrast:  beh\_slope ~ neur\_slope + (contrast-1|mouse) | (1) = 3.10 |  | 0.078 |
| Neural percent correct, low contrast: time 1 vs. time 2 | 5i | T1: 0.79  T2: 0.83  (median) | T1: 0.15  T2: 0.22  (IQR) | 43 sessions | Two-tailed Wilcoxon sign-rank test (FDR corrected94 for multiple comparisons) | Z = -1.12  Rank: 418 | = -0.17 | 0.26 |
| Neural percent correct, low contrast: time 1 vs. time 3 | T1: 0.79  T3: 0.85  (median) | T1: 0.15  T3: 0.15  (IQR) | Z = -3.61  Rank: 198 | = -0.56 | 0.00031 |
| Neural percent correct, low contrast: time 1 vs. time 4 | T1: 0.79  T4: 0.92  (median) | T1: 0.15  T4: 0.20  (IQR) | Z = -4.68  Rank: 103 | = -0.72 | 2.89e-6 |
| Neural percent correct, low contrast: time 1 vs. time 5 | T1: 0.79  T5: 0.91  (median) | T1: 0.15  T5: 0.16  (IQR) | Z = -5.34  Rank: 31 | = -0.82 | 9.44e-8 |
| Neural percent correct, high contrast: time 1 vs. time 2 | T1: 0.78  T2: 0.74  (median) | T1: 0.15  T2: 0.12  (IQR) | Z = 2.62  Rank: 690 | = 0.40 | 0.0088 |
| Neural percent correct, high contrast: time 1 vs. time 3 | T1: 0.78  T3: 0.76  (median) | T1: 0.15  T3: 0.13  (IQR) | Z = 1.45  Rank: 593 | = 0.22 | 0.15 |
| Neural percent correct, high contrast: time 1 vs. time 4 | T1: 0.78  T4: 0.83  (median) | T1: 0.15  T4: 0.20  (IQR) | Z = -0.24  Rank: 453 | = -0.037 | 0.81 |
| Neural percent correct, high contrast: time 1 vs. time 5 | T1: 0.78  T5: 0.83  (median) | T1: 0.15  T5: 0.16  (IQR) | Z = -2.00  Rank: 307 | = -0.31 | 0.045 |
| Mixed-effects model:  threshold ~ gain\_target + contrast + (contrast-1|mouse) | 6g | **Model Coefficients**  Estimate ± standard error  [tstat(df), p-value] | | 168 sessions | Likelihood ratio test against model without gain:  threshold ~ contrast + (contrast-1|mouse) | (1) = 5.82 |  | 0.016 |
| Intercept: 10.97±1.33  t(120) = 8.27, p = 2.059e-13  Target gain: -30.46±12.45  t(120) = -2.45, p = 0.016  Contrast: 3.27±1.55  t(120)= 2.10, p = 0.038 | |
| Likelihood ratio test against model without contrast:  threshold ~ gain\_target + (contrast-1|mouse) | (1) = 3.71 |  | 0.054 |
| Mixed-effects model:  slope ~ gain\_target + contrast + (contrast-1|mouse) | 6h | Intercept: 0.039±0.0064  t(120) = 6.23, p = 7.14e-9  Target gain: 0.16±0.060  t(120) = 2.67, p = 0.0085  Contrast: 0.0094±0.062  t(120)= 1.52, p = 0.13 | | 168 sessions | Likelihood ratio test against model without gain:  slope ~ contrast + (contrast-1|mouse) | (1) = 6.96 |  | 0.0083 |
| Likelihood ratio test against model without contrast:  slope ~ gain\_target + (contrast-1|mouse) | (1) = 2.28 |  | 0.13 |
| Mixed-effects model:  thresh ~ gain\_adapt + contrast + (contrast-1|mouse) | S5m | Intercept: 5.33±1.64  t(120) = 3.26, p = 0.0015  Adaptation gain: 56.66±35.62  t(120) = 1.59, p = 0.11  Contrast: 2.77±1.92  t(120)= 1.44, p = 0.15 | | 168 sessions | Likelihood ratio test against model without gain:  thresh ~ contrast + (contrast-1|mouse) | (1) = 2.51 |  | 0.11 |
| Likelihood ratio test against model without contrast:  thresh ~ gain\_adapt + (contrast-1|mouse) | (1) = 2.020 |  | 0.16 |
| Mixed-effects model:  slope ~ gain\_adapt + contrast + (contrast-1|mouse) | S5n | Intercept: 0.062±0.0078  t(120) = 7.98, p = 9.63e-13  Adaptation gain: -0.14±0.17  t(120) = -0.80, p = 0.43  Contrast: 0.0049±0.0084  t(120)= 0.58, p = 0.57 | | 168 sessions | Likelihood ratio test against model without gain:  slope ~ contrast + (contrast-1|mouse) | (1) = 0.64 |  | 0.43 |
| Likelihood ratio test against model without contrast:  slope ~ gain\_adapt + (contrast-1|mouse) | (1) = 0.33 |  | 0.57 |

**Extended Data Table 2:** Mouse strains and genders.

|  |  |  |  |
| --- | --- | --- | --- |
| **Experiment** | **Figures** | **Strain** | **N [female, male]** |
| Acute ACtx recordings | Figure 2 | CDH23 | 1 [M] |
| Behavior (no microdrive) | Figure 3 | C57BL/6 x CamKII-cre | 1 [F], 4 [M] |
| C57BL/6 x PV-cre | 1 [F] |
| CDH23 x SOM-cre | 1 [F], 1 [M] |
| Behavior (microdrive) | Figure 3, Figure 5, Figure 6 | CDH23 | 4 [F], 4 [M] |
| C57BL/6 x PV-cre | 1 [F] |
| C57BL/6 x SOM-cre | 1 [F] |
| CDH23 x SOM-cre | 1 [F], 2 [M] |
| CDH23 x CamKII-cre | 1 [F] |
| Muscimol (behavior) | Figure 4 | CDH23 | 2 [F], 2 [M] |
| Muscimol (acute recording) | Supplemental Figure 4 | CDH23 x CamKII-cre | 1 [M] |
| CDH23 | 1 [M] |
| Acute ACtx recordings | Supplemental Figure 5 | CDH23 x SOM-cre | 3 [F], 2 [M] |
| CDH23 x PV-cre | 1 [F], 1 [M] |
| CDH23 x VGAT | 2 [F] |
| **Total:** | | | 19 [F], 19 [M] |

**Extended Data Table 3:** Target SNRs used during psychometric testing.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Target Levels**  **[range]** | **[n]: Mouse IDs** | **n Sessions (total)** | **n High-Low Contrast Sessions** | **n Low-High Contrast Sessions** |
| 0, 5, 10, 15, 20, 25 dB SNR  [25] | [12]: CA102, CA104, CA106, CA107, CA118, CA119, CA121, CA122, CA123, CA124, CA125, CA126 | 214 | 111 | 103 |
| -5, 0, 5, 10, 15, 20 dB SNR  [25] | [8]: CA102, CA104, CA106, CA107, CA118, CA119, CA121, CA122 | 31 | 31 | 0 |
| 0, 4, 8, 12, 16, 20 dB SNR  [20] | [1]: CA046 | 1 | 0 | 1 |
| 5, 8, 11, 14, 17, 20 dB SNR  [15] | [4]: CA118, CA119, CA121, CA122 | 68 | 52 | 16 |
| 8, 10.4, 12.8, 15.2, 17.6, 20 dB SNR  [12] | [15]: CA046, CA047, CA048, CA049, CA051, CA052, CA055, CA061, CA070, CA072, CA073, CA074, CA075, CA104, CA107 | 111 | 0 | 111 |
| -4, 0, 4, 8, 12, 16 dB SNR  [20] | [11]: CA051, CA052, CA055, CA061, CA070, CA072, CA073, CA074, CA075, CA102, CA106 | 91 | 91 | 0 |
| -5, -1, 3, 7, 11, 15 dB SNR  [20] | [5]: CA046, CA047, CA048, CA049, CA051 | 19 | 19 | 0 |
| -75, -60, -45, -30, -15, 0  dB attenuation rel. 25dB SNR | [2]: CA124, CA125 | 20 | n/a | n/a |

**Extended Data Table 4:** GLM Simulation Parameters

|  |  |
| --- | --- |
| **Parameter** | **Value** |
|  |  |
|  |  |
| centroid (frequency bin , history bin ) |  |
| covariance matrix |  |
| dimensions () |  |
| Baseline rate |  |
| Stimulus scaling |  |
| Gain operating point |  |
| Gain control |  |
| Adaptation time constants |  |
| Simulated background scenes |  |
| Contrast history |  |
| B-spline degree, knots |  |

A screenshot of a video game

Description automatically generated with medium confidence

**Extended Data Figure 1 (related to Figure 1). Normative model responses, predictions, and example response distributions.**

**a,** The firing rate of the simulated neuron as a function of time. Traces shaded in blue or red indicate the firing rate to periods of low or high contrast background noise, respectively. The green trace indicates the model response to overlaid targets. **b,** The true contrast (labelled as variance) of the stimulus (blue, red, and dashed gray lines) along with the average model estimate of the contrast (solid black line) over time. **c,** Discriminability as a function of time and contrast, with the trace color indicating the contrast after the switch. The dashed vertical line indicates the time of the contrast switch. Open circles indicate time samples used to plot the distributions in **d**. **d,** Target (green) and background (blue or red) distributions as a function of time and contrast. The top row includes responses to targets and background in low contrast. Each column denotes a different time step relative to the change in contrast, as indicated by the column title. The bottom row is the same, but for high contrast. Arrows between **c** and **d** indicate distributions which yielded the indicated value of discriminability in the trace.

**A screen shot of a computer

Description automatically generated with low confidenceExtended Data Figure 2 (related to Figure 2). Simulation results to validate the GC-GLM.**

**a,** Schematic of simulated neurons in the forward model. Each neuron received broadband noise inputs which changed contrast every 2s (). A STRF modelled by a 2D-gaussian function with added noise filtered the stimulus to generate a linear response. This filter response was then modulated by a gain control function, which controlled the amount and time-course of gain control based on the stimulus contrast. This gain modulated output was then exponentiated and stochastic spikes were generated using a Poisson process. **b,** Example STRF from one simulated neuron. Colorbar indicates STRF magnitude. **c,** Model estimate of the STRF averaged across 100 simulated neurons. **d,** Example linear drive for one simulated neuron over 500 trials (ie. the filter response of the STRF convolved with the stimulus). **e,** Each panel plots the average firing rates of 100 simulated neurons (solid teal lines) and corresponding GC-GLM fits (dashed black lines) when simulating perfect gain control (GC = 1.0). Each row corresponds to 100 simulations of different gain time courses, with the top row depicting a slow transition to low contrast, with a fast transition to high contrast. The middle row plots simulations were both transitions were fast. The bottom row plots simulations where the transition to low contrast was fast, with a slow transition to high contrast. The corresponding rows of panels **f**, **g**, and **h**, are the results of simulations with the same gain time courses. **f,** Average gain time-course of the simulated neurons (solid teal lines) and the corresponding GC-GLM estimate of the gain, , averaged over 100 simulations (black dashed lines). Insets of each panel depict the contrast kernels (dashed lines) and gain kernels (solid lines) estimated for each contrast. Blue lines indicate kernels after a switch to low contrast and red lines indicate kernels after a switch to high contrast. **g,** Average log firing rate for simulations with different gain time-courses and different degrees of gain control (GC value; the legend in the lower right indicates the color-GC value mapping). Each plotted line indicates the average firing rate/prediction for 100 simulations. **h,** Average gain time-course of all simulations (solid colored lines) and the average estimates of (dashed gray lines). **i,** Simulations with 100 unique stimulus scenes, repeated 5 times each. Left panel plots the average firing rates and model fits. Right panel plots the true gain time-course (solid lines) and the average model gain estimate, (dashed lines). The shaded areas indicate 2.5 and 97.5 percentiles of the gain estimates. **j,** Simulations with 5 unique stimulus scenes, repeated 100 times each. Formatting as in **i**. For panels **e-j**, the GC value colors and line formatting are indicated in the legend on the bottom right.

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| **level**  Psychometric curves for all mice (n = 25). Thin traces are curves of individual mice, overlaid with psychometric fits to the entire dataset.**c,** thresholdsfor the curves plotted in **b**, formatted as in **a**.**d**Slope of the psychometric curves plotted in **b**, formatted as in **a**. **e,** **f**An4.48015steeper5513942**ghf**An7.001.307steeper slopes in068015036070 |

Graphical user interface, Teams

Description automatically generated

**Extended Data Figure 4 (related to Figure 4). Confirmation of cortical inactivation with muscimol.**

**a,** Setup schematic for acute muscimol recordings in ACtx. **b,** Example spike rasters from two different neurons pre- and post-muscimol or saline application. On top of the raster is the timeline for each recording. Rasters are sorted by contrast and target level, with color indicating low or high contrast backgrounds, color shade indicating target level, and gray indicating background-only trials (-Inf). *Left panel:* spike raster of a representative neuron recorded prior to muscimol application, followed by the raster for the same neuron 30 minutes after muscimol application. *Insets:* Mean firing rate for each condition. Shade indicates target level and the scale bar indicates the firing rate. Error bars are ±SEM across trials. *Right panel:* Example neuron before and after application of saline. Formatting as in left panels. **c,** Firing rates before and after muscimol application as a function of target level and contrast. Dark dashed lines indicate spike rates recorded pre-muscimol application and light dashed lines indicate the responses post-application. **d,** Firing rates before and after saline application. As in **c**, dark lines are responses recorded prior to saline application and light lines indicate responses recorded after saline application. In **c** and **d**, blue and red plots indicate responses during low contrast and high contrast, respectively, and the circles not connected by a line and labelled “-Inf” are responses to background alone. **e,** Area under the ROC curve (AUC) averaged across neurons after drug application in muscimol and saline recording sessions in low contrast. Filled circles and solid lines are responses after saline was applied while open circles and dashed lines are responses after muscimol was applied. Error bars indicate ±SEM across neurons. **f,** Same as **e**, but for high contrast. **g,** Lick probability over time during muscimol or saline sessions. Dashed vertical lines indicate trial onset (0 s) and the contrast switch (3 s). Green traces are muscimol sessions and black traces are saline sessions. The shading around each trace indicates ±SEM across sessions. **h,** *Left:* comparison of lick probability during the adaptation period. *Right:* comparison of lick probability during the target period. Each circle indicates a session and color is as in **g**. **i,** Cumulative probability of licking throughout the trial, normalized within muscimol or saline conditions to sum to 1. Colors as in **g**, **h**. Shading indicates ±SEM across sessions. In all plots: ns*p*>0.1; †*p*<0.1, \**p*<0.05, \*\**p*<0.01, \*\*\**p*<0.001, \*\*\*\**p*<0.0001.

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| Graphical user interface, application, Teams  Description automatically generated |
| ranges,h. Black and magenta symbols represent whether neural slope and contrast, respectively, significantly improved the fits of a mixed effects model (Extended Data Table 1). |