**Supplementary Information**

**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 Sup. Fig 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 similarly implanted with a headplate and groundpin, as described in *Surgery*. Additionally, each mouse was bilaterally injected with 700 uL 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.

**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, volume and muscimol or saline application changed the responses during the pre- and post-application periods, finding that muscimol drastically reduced the firing rates between pre- and post-application periods, while saline moderately increased firing rates (Extended DataFigure 4c,d, Table 1). We speculate that the small increase in firing rate between pre- and post-saline application is 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) when compared to the effect size of muscimol (*η2* = 0.38). We then used a 3-way ANOVA to compare the effects of muscimol, contrast, and target volume 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 volume (*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 noise 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 stability 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 below 100 for further analysis (n = 129). For each neuron, we computed the 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 value for that pixel, and retained only pixels determined to be significant (three standard deviations of the shuffled value). Based on the de-noised STRFs, we computed average 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 a one-dimensional signal that evolves in discrete time steps:

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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):

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where stimulus filter is defined as a two-dimensional gaussian distribution as a function of history 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:

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| --- | --- | --- |
|  |  | (1) |

where at each time is a row vector of length (ie. a matrix of the stimulus spectrogram lagged by lags) and is a row vector of the filter 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

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

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. For ease of interpretation, we require to be adimensional, such that

|  |  |  |
| --- | --- | --- |
|  |  | (3) |

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

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|  |  | (4) |

which can be rewritten using equation 2 as

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|  | . | (5) |

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

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|  |  | (6) |

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

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| --- | --- | --- |
|  |  | (7) |

where is the harmonic mean of and :

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| --- | --- | --- |
|  |  | (8) |

Finally, to validate that our fitting methods are sensitive to real world neurons, which do not necessarily adjust their gain to perfectly account for changes in contrast, 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:

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| --- | --- | --- |
|  |  | (9) |

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

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|  |  | (9) |

*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:

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| --- | --- | --- |
|  |  | (11) |

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

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|  |  | (12) |

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 9,

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

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

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

we can rewrite equation 13 in a more compact form:

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

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

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|  |  | (16) |

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 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”).

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

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|  |  | (17) |

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’ll take a slightly longer and more formal route to get at 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 as 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 (assume for concreteness that , although this is not necessary for the derivation below). If , where is some scalar, then

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

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

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|  |  | (19) |

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

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|  |  | (20) |

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 (SupplementaryTable 3). 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 time course 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 noise scenes (Extended DataFigure 2i) compared to simulations where neurons were only exposed to 5 unique noise 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 noise scenes, even in the case of perfect gain control. As such, 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).

**Supplementary Table 1:** Statistical Comparisons.

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| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **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 corrected92 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 | 0.005 |
| 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 volume on firing rate in ACtx | S4c | n/a | n/a | 42 neurons | 3-way ANOVA | Fpre-post(1) = 812.54  Fcontrast(1) = 22.64  Fvolume(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 volume on firing rate in ACtx | S4d | n/a | n/a | 104 neurons | 3-way ANOVA | Fpre-post(1) = 15.40  Fcontrast(1) = 0.43  Fvolume(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 |
| 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 corrected92 for multiple comparisons)  Adjusted alpha level: 0.0088 | 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 + (1|mouse)  Fixed effects: target gain, contrast  Random effects: mouse ID  Outcome variable: threshold | 6g | **Model Coefficients**  Estimate ± standard error  [tstat(df), p-value] | | 168 sessions | Likelihood ratio test against model without gain:  threshold ~ contrast + (1|mouse) | (1) = 4.74 |  | 0.029 |
| Intercept: 10.81±1.25  t(120) = 8.62, p = 3.27e-14  Target gain: -25.64±11.80  t(120) = -2.20, p = 0.030  Contrast: 3.01±1.23  t(120)= 2.45, p = 0.016 | |
| Likelihood ratio test against model without contrast:  threshold ~ gain\_target + (1|mouse) | (1) = 5.84 |  | 0.016 |
| Mixed-effects model:  slope ~ gain\_target + contrast + (1|mouse)  Fixed effects: target gain, contrast  Random effects: mouse ID  Outcome variable: slope | 6h | Intercept: 0.042±0.0063  t(120) = 6.74, p = 5.72e-10  Target gain: 0.13±0.059  t(120) = 2.28, p = 0.024  Contrast: 0.0077±0.059  t(120)= 1.26, p = 0.21 | | 168 sessions | Likelihood ratio test against model without gain:  slope ~ contrast + (1|mouse) | (1) = 5.094 |  | 0.024 |
| Likelihood ratio test against model without contrast:  slope ~ gain\_target + (1|mouse) | (1) = 1.57 |  | 0.21 |
| Mixed-effects model:  thresh ~ gain\_adapt + contrast + (1|mouse)  Fixed effects: adaptation gain, contrast  Random effects: mouse ID  Outcome variable: threshold | S5m | Intercept: 6.53±1.51  t(120) = 4.34, p = 3.01e-5  Adaptation gain: 36.44±32.59  t(120) = 1.12, p = 0.27  Contrast: 3.11±1.66  t(120)= 1.88, p = 0.063 | | 168 sessions | Likelihood ratio test against model without gain:  thresh ~ contrast + (1|mouse) | (1) = 1.24 |  | 0.26 |
| Likelihood ratio test against model without contrast:  thresh ~ gain\_adapt + (1|mouse) | (1) = 3.47 |  | 0.062 |
| Mixed-effects model:  slope ~ gain\_adapt + contrast + (1|mouse)  Fixed effects: adaptation gain, contrast  Random effects: mouse ID  Outcome variable: threshold | S5n | Intercept: 0.063±0.0076  t(120) = 8.35, p = 1.40e-13  Adaptation gain: -0.16±0.16  t(120) = -0.96, p = 0.34  Contrast: 0.0058±0.0084  t(120)= 0.70, p = 0.49 | |  | Likelihood ratio test against model without gain:  slope ~ contrast + (1|mouse) | (1) = 0.91 |  | 0.34 |
| Likelihood ratio test against model without contrast:  slope ~ gain\_adapt + (1|mouse) | (1) = 0.49 |  | 0.49 |

**Supplementary Table 2:** Target SNRs used during psychometric testing.

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

**Supplementary Table 3:** 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 noise scenes |  |
| Contrast history |  |
| B-spline degree, knots |  |

Diagram, engineering drawing

Description automatically generated**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 grey lines) along with the average model estimate of the contrast (solid black line) over time. **c,** Discriminability as a function of time and contrast. Each trace indicates target from noise discriminability over time, 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 noise (blue or red) distributions as a function of time and contrast. The top row includes responses to targets and noise 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.

**Diagram, schematic

Description automatically generatedExtended 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 for the simulated neuron. This gain modulated output was then exponentiated and stochastic spikes were generated according to 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 left 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 grey 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.

Chart, scatter chart

Description automatically generated

**Extended Data Figure 3 (related to Figure 3). Behavioral slopes are affected by the target volume range.**

**a,** The effect of contrast on the false alarm rates in psychometric sessions (n = 25 mice). Each dot and line represent a mouse, the blue and red bars indicate the mean false alarm rate for low and high contrast ±SEM. Results of a paired t-test (*t*(23) = -6.02, *p* = 3.90e-6) across contrast revealed a significantly higher false alarm rate in high contrast (Mean(*M*) = 0.22, standard deviation(*std*) = 0.080) compared to low contrast (*M* = 0.13, *std =* 0.054). **b,** Comparison of psychometric slopes across all mice (n = 25). Formatting as in **a**. Results of a paired t-test (*t*(23) = -1.55, *p* = 0.135) across contrast revealed no significant difference between the slopes. **c,** Average psychometric curves and percent correct for mice presented with a narrow range of targets (range = 15 dB SNR; Table 2, row 4; dashed lines and open dots), and those presented with a wide range of targets (range = 25 dB SNR; Table 2, row 1; solid lines and filled dots) in low contrast. Errorbars indicate ±SEM. **d,** Psychometric slope for each mouse when low contrast targets came from narrow or wide target distributions. Different shaded bars indicate the mean for each condition ±SEM. Results of an unpaired t-test (*t*(9) = 2.33, *p =* 0.044) indicated significantly larger slopes in response to narrow target distributions (*M =* 0.061, *std*  = 0.0060) compared to wide target distributions (*M* = 0.051, *std* = 0.0073). **e**, Average psychometric curves and percent correct for mice presented with a narrow range of targets (average of range = 12 or 15 dB SNR; Table 2, rows 5 or 4; dashed lines and open dots) or wide range of targets (range = 25 dB SNR; Table 2, row 1; solid lines and filled dots) in high contrast. **f,** Psychometric slope for each mouse when high contrast targets came from narrow or wide distributions. Formatting as in **d**. Results of an unpaired t-test (*t*(28) = 5.49, *p* = 7.29e-6) indicated a significantly larger slopes in response to narrow target distributions (*M* = 0.11, *std* = 0.033) compared to wide target distributions (*M* = 0.049, *std* = 0.017) in high contrast. In all plots: ns*p*>0.1; †*p*<0.1, \**p*<0.05, \*\**p*<0.01, \*\*\**p*<0.001, \*\*\*\**p*<0.0001.

Diagram

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. A baseline recording of all stimuli was performed prior to muscimol application, then all stimuli were recorded again 30 minutes after application. Rasters are sorted by contrast and target volume, with color indicating low or high contrast backgrounds, color shade indicating target volume, and grey indicating noise only trials (-Inf). *Left panel:* raster of target and noise responses 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 volume 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 volume 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 noise 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.

Diagram

Description automatically generated

**Extended Data Figure 5 (related to Figures 5 and 6). STRFs are unaffected by contrast, and the relationship between gain during adaptation periods in the trial and behavior.**

**a,** Neural against behavioral psychometric slopes for n = 6 mice presented with the same target volumes in high and low contrast. Formatting as in Figure 5g. **b,** Example STRFs from one neuron estimated from each contrast period. *Left*: Low contrast STRF. The main plot depicts the thresholded STRF values as a function of time and frequency. Inset is the original STRF, which has the same axis. Above the main plot is the temporal average across columns of the STRF, and to the right is the frequency average across rows. *Right*: High contrast STRF. Colorbar indicates the color-mapping for both of the thresholded STRF plots. In both panels, blue traces indicate values estimated in low contrast, and red traces indicate values estimated in high contrast. **c,** Average centered frequency (*top*) and temporal (*bottom*) STRF components for low and high contrast (red and blue traces, respectively). Light shade indicates ±SEM across neurons. **d,** Histogram of correlations between low and high contrast STRFs for neurons with noise ratios (NR) below 100 (n = 129 neurons). Shaded bars indicate correlations that were not significantly different from chance, fwhile unshaded bars indicate significant correlations, as determined by a permutation test. *Inset*: Proportions of the correlations in the population found not-significant (grey) and significant (white). **e,** Maximum STRF value across all pixels for low and high contrast, plotted for each neuron. Solid line indicates unity. The size of each circle indicates the NR of each neuron, with larger dots for smaller NR (see legend). P-value indicates the results of a Wilcoxon sign-rank test. **f,** Best frequency for each neuron in low and high contrast. Formatting as in **e**. **g,** Lag of the maximum STRF response for each neuron in low and high contrast. Formatting as in **e** and **f**. **h,** Correlation coefficients between the prediction of a linear-nonlinear model using STRFs estimated from the a model without gain control (static-LN) versus a model with gain control (GC-LN). Each dot indicates a neuron. The red solid line indicates unity. The red “x” indicates the median correlation in each contrast. Asterisks indicate the significance of a Wilcoxon Sign-Rank test. **i,** Psychometric performance in low contrast, averaged based on a median split of average cortical gain during the adaptation period of the trial. Light dots and lines indicate the session average and psychometric fit to sessions in the bottom 50th percentile of gain, while dark dots and lines indicate the same values for sessions in the top 50th percentile of gain. Errorbars on the data are ±SEM across sessions. *Inset*: distribution of average gain in each session estimated from the adaptation period. The red dashed line indicates the median of the distribution, and the histogram bars are shaded according to whether they fall above (light blue) or below (dark blue) the median. **j,** Session-wise relationship between average gain in the adaptation period and psychometric threshold. Each dot indicates the gain and threshold for a single session, and its color indicates the contrast of the adaptation period. The grey line is the best linear fit to the data. The text in the lower right indicates the results of Likelihood Ratio Tests for models including gain as a predictor (in grey) or contrast as a predictor (in red). Full statistical results in Supplementary Table 1. **k,** Same as in **j**, but plotting psychometric slope as a function of gain. In all plots: ns*p*>0.1; †*p*<0.1, \**p*<0.05, \*\**p*<0.01, \*\*\**p*<0.001, \*\*\*\**p*<0.0001.