**Diagram

Description automatically generatedFigure 2.**

**a,** Schematic for acute recordings from auditory cortex. **b,** Schematic of Poisson generalized linear model (GLM) design. *From left to right:* The external variables considered by the model are the stimulus spectrogram, the stimulus contrast, and observed spikes. First, a spectrotemporal receptive field (STRF) is estimated. Second, we fit the parameters of a GLM with gain control (GC-GLM) designed to isolate the contributions of: 1) Stimulus drive, ; 2) The multiplicative interaction between the contrast and the stimulus drive, ; 3) Pure contrast drive, . The history of the contrast predictors were smoothed with a B-spline basis set. The linear combination of the predictors and fitted weights was then passed through an exponential nonlinearity to produce spike rate predictions. **c,** Schematic of linear-nonlinear models. As in **b**, we first fit a STRF which is then passed through either a static exponential nonlinearity (static-LN) or independent nonlinearities fit separately to low and high contrast periods (GC-LN). **d,** Neuronal responses and model fits to a representative neuron. *Top*: a spike raster for the example neuron. Each period of contrast is indicated by the blue (low contrast) and red (high contrast) bars. *Middle*: PSTH of the example cell is plotted with a grey fill and black outline. The predictions of the static-LN model are plotted in grey, the GC-LN model in green, and the GC-GLM model in orange. All traces were smoothed with a 10ms wide Gaussian filter for visualization. *Bottom*: the gain modulation index, (red trace). Grey dashed line at 1 indicates the gain of a neuron with neutral gain. The dashed black line indicates the gain of a neuron with perfect, instantaneous gain control. **e,** The STRF fitted to this neuron. **f,** The nonlinearities fitted to low (blue) and high (red) contrast in the GC-LN model for the example neuron. Points indicate the mean observed firing rate (ordinate), binned according to observed filter prediction values (abscissa). Solid lines indicate exponential function fits to the underlying points. **g,** The estimate of the gain, , for the example neuron after each contrast switch (dashed red and blue lines). The solid red and blue lines are fits of an exponential function to the underlying traces. Dashed grey and black lines indicate neutral and perfect gain control values as in **d**. **h,** Cross-validated Pearson’s correlations between the trial-averaged firing rate trace and the model predictions. Grey, green, and orange dots indicate the correlations for each neuron (n=95) for the static-LN, GC-LN, and GC-GLM models, respectively. Open circles indicate the median correlation, and the error bars indicate 2.5-97.5 percentiles. Results of Wilcoxon Sign-Rank tests are indicated with asterisks. **i,** Distribution of gain control estimated by the GLM for the recorded population. Here, gain control is defined as after the estimate has stabilized to its final value (ie. after 1s). Dashed vertical line indicates no gain control, while the solid orange line indicates the median of the distribution. Asterisks indicate the results of a Wilcoxon Sign-Rank test. **j,** Correspondence between gain control estimates from the GC-GLM model (abscissa) and the previously reported GC-LN model (ordinate). Black dots indicate the data for each neuron, while linear model fit and error are indicated by the grey line. Asterisks indicate significance of the linear fit to the data. **k,** Average time course of the gain estimate w for neurons with true gain control (ie. their gain control value is less than 0, n = 45). Light red and blue lines indicate the average value of for transitions to high and low contrast, respectively (±SEM over neurons). Solid red and blue lines are exponential fits to the averages after the transition, which is marked by the dashed black line. **i,** Distributions of adaptation time constants of w after transitions to low, in blue, and high contrast, in red. Each dot indicates a neuron, with the black line linking within neuron measures. 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.

**Diagram

Description automatically generatedFigure 3.**

**a,** Schematic of GO/NO-GO paradigm. **b,** Behavioral performance for the contrast in which each mouse was first trained relative to the first session of task exposure (n=12 mice were first trained in low contrast, n=13 mice were first trained in high contrast). Dots indicate a session, while the traces indicate a running average using a 7 day window. Blue dots and traces indicate sessions in which mice detected targets in low contrast (ie. after high-to-low contrast transitions), while red dots and traces indicate sessions in which mice detected targets in high contrast (ie. after low-to-high contrast transitions). **c,** Psychometric functions in low and high contrast for one mouse (mouse ID indicated in the upper left). Each dot indicates percent correct for a single volume in a single session, while the solid lines indicate average psychometric fits. Colors as in **b**. **d,** Psychometric functions averaged for n=25 mice in low and high contrast. Error bars indicate ±SEM over mice at individual target SNRs, while the solid lines are logistic function fits to the average performance per contrast. **e,** Psychometric thresholds per contrast. Each dot represents a mouse, lines connect performance of individual mice on low and high contrast sessions. Bars indicate the average threshold over mice, while error bars in black indicate threshold ±SEM over mice. **f,** Behavioral psychometric functions for n=4 mice tested using the same target volumes in each contrast. Dots with error bars indicate average performance ±SEM over mice as a function of contrast and target volume. Overlaid, dark-colored curves indicate psychometric fits to the averages, with the black dot indicating the average threshold. Light-colored lines indicate the psychometric curves of individual mice. Black, dashed horizontal line indicates chance (0.5) performance. **g,** Psychometric thresholds per contrast. Each dot represents a mouse, lines indicate where mice participated in both low and high contrast sessions. Bars indicate the average threshold over mice, while error bars in black indicate threshold ±SEM over mice. **h,** Psychometric slopes per contrast. Presentation as in **g**. **i,** Behavioral performance as a function of contrast and target time relative to the switch in contrast for n=21 mice. Dots with error bars indicate average performance ±SEM over mice. Solid curves indicate exponential function fits to the average over mice. Black, dashed vertical line indicates the contrast switch. Horizontal lines at the top of the plot indicate significant changes in performance between the first target presentation time and subsequent target presentation times, as assessed by Wilcoxon Sign-rank tests with false discovery rate correction for multiple comparisons. **j,** Average time constant of exponential fits in low and high contrast. Presentation as in **h**. Unless otherwise noted, blue markers indicate data where targets were presented in low contrast and red indicates data where targets were presented in high contrast. In all plots: ns, not significant; †p<0.1; \*p<0.05; \*\*p<0.01; \*\*\*p<0.001; \*\*\*\*p<0.0001.

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**Figure 4.**

**a,** Setup schematic for muscimol application in behaving mice. *Bottom*: legend indicating colors used for each background condition. **b,** Behavioral psychometric functions during muscimol or saline application for n=4 mice. Dark solid lines and filled circles indicate average performance after saline injection. Dark dashed lines and open circles indicate average performance after muscimol injection. Light solid and dashed lines are psychometric curves from individual sessions. Error bars indicate ±SEM. across sessions. **c,** Behavioral performance metrics as a function of contrast and pharmacological intervention. Open circles indicate performance in individual sessions. Colored bars indicate average performance across sessions. Bars with low transparency and solid outlines are averages after saline application, while high transparency bars with dashed outlines are averages after muscimol application. Clockwise from the upper left, are plots of the max response rate, false alarm rate, psychometric threshold, and the maximum slope of the psychometric curve. **d,** *Left*: Example stimulus spectrogram for the target-in-noise detection task with the corresponding waveform below. The scale bar indicates 1 second, and the colorbar indicates the volume for each time-frequency bin (silence is black). *Right*: psychometric performance for n=2 mice in the target-in-noise task, with target volume on the abscissa and probability of responding on the ordinate. Filled circles and dark solid lines indicate average performance after saline injection and psychometric fits to the average. Red open circles and dark dashed lines indicate average performance after muscimol injection and psychometric fits to the average. Light red solid and dashed lines are psychometric curves from individual sessions. Errorbars indicate ±SEM across sessions. **e,** *Left*: Example stimulus spectrogram for the target-in-silence detection task with the corresponding waveform below. Time scale and volume scale as in **d**. *Right*: psychometric performance for n=2 mice (same mice as in **d**) in the target-in-silence task, with target attenuation relative to the highest volume target from the target-in-noise task on the abscissa and probability of responding on the ordinate. Black filled circles and dark solid lines indicate average performance after saline injection and psychometric fits to the average. Open circles and dark dashed lines indicate average performance after muscimol injection and psychometric fits to the average. Light grey solid and dashed lines are psychometric curves from individual sessions. Errorbars indicate ±SEM across sessions. **f,** Behavioral performance metrics as a function of task type (detection in noise or detection in silence) and pharmacological intervention. Formatting and metrics as in c (with the exception of response rate at threshold). Dark and light red bars indicate performance in the detection-in-noise task, with application of saline or muscimol. Dark and light grey bars indicate performance in the detection-in-silence task, with application of saline or muscimol. 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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**Figure 5.**

**a,** Experimental setup for chronic ACtx recordings from behaving mice. **b,** Example spiking responses to targets and noise in low contrast during behavior. The top portion of the plot is a spike raster ordered by target volume (colors indicate trial identity according to the legend). Below the raster is a trial-averaged PSTH, smoothed with a 2ms standard deviation Gaussian kernel. *Inset:* Area under the ROC curve (AUC) when discriminating noise from target responses across trials. The dashed horizontal line indicates chance performance (0.5). Error bars are the bootstrapped 95% confidence interval of the AUC value (see *Methods*). **c,** Neurograms of populations of simultaneously recorded neurons during a low contrast and high contrast session from the same mouse. Neurons are plotted along the ordinate, while target volume is plotted along the abscissa. Within each plot, the shade indicates the neural response to each target volume, with the average response to noise alone subtracted. Asterix indicates the responses of the neuron in panel **b**. **d,** Discriminating targets from noise using population responses. *Left:* schematic of coding direction analysis. In high dimensional neural space, noise trials are represented as a gray point-cloud, while target responses are represented as a blue point-cloud. The coding direction (CD) is the vector defining the average difference between these two point-clouds as indicated by the arrow. *Right:* trial distributions of projections along the coding direction for one session (session CA118-200707, as plotted in **c**). The blue distribution shows the projection values for 20 dB SNR targets while the gray distribution shows the projection values during noise only trials. The vertical red line is the criterion used to compute performance (percent correct for these distributions is indicated by the arrow in panel **e**). **e,** Example neurometric and psychometric curves. *Left:* Low contrast curves. Light blue circles and solid lines indicate psychometric performance and a logistic fit, respectively. Dark blue circles and solid lines indicate neurometric performance from the session plotted in the left panel of **c**. The horizontal dashed line indicates chance performance (0.5). The arrow indicates the neural performance computed from the distributions and criterion plotted in **d**. *Right:* High contrast curves from the same mouse for the session plotted in the right panel of **c**. **f,** Average psychometric and neurometric functions across mice. Light circles indicate average behavioral performance, dark red and blue circles indicate average neural performance. Light solid curves indicate logistic fits to average behavioral performance, while vertical lines indicate the fit thresholds. Dark solid lines indicate fits and thresholds for the neural data. The dashed vertical line indicates chance performance. Shades of blue and red indicate averages over low and high contrast respectively. **g,** Relationship between behavioral and neural thresholds. Each circle represents the average behavioral and neural threshold for each mouse for each contrast (as indicated by the circle fill color). Grey lines and shaded areas indicate the linear regression fit across contrasts, ±95% confidence interval. The solid black line indicates unity. Black asterisks indicate significant multiple regression fits to the data; within that model: grey asterisks indicate that neural thresholds are significant predictors of behavior, while red asterisks indicate that contrast is a significant predictor.  **H,** Relationship between behavioral and neural slopes. Appearance as in **g**. **i,** Population decoder performance in each contrast transition, as a function of target presentation relative to the transition (indicated by the dashed vertical black line at 0s). Ticks on the abscissa indicate average target time from the transition in milliseconds. Solid lines and circles indicate the percent correct performance of a target decoder after a switch to low contrast (blue) or high contrast (red). Errorbars indicate ±SEM over sessions. Horizontal lines indicate significant changes in performance between the first target presentation time and subsequent target presentation times, as assessed by Wilcoxon Sign-rank tests with false discovery rate correction for multiple comparisons. The span of the lines indicates the target times being compared, while the color of the lines indicates whether the test was performed within high contrast (red) or low contrast (blue). **j,** Adaptation time constants of exponentials fitted to the average neural decoder performance for each mouse in each contrast. Blue and red circles indicate the adaptation time constants from neural populations for each mouse in low and high contrast respectively. Solid black lines indicate time constants from the same mouse. 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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**Figure 6.**

**a,** Schematic of the linear nonlinear models fit to behavioral recordings. Spectrograms concatenated across trials were used to estimate a STRF using normalized reverse correlation. The relationship between the STRF prediction (grey trace) and observed spikes were used to estimate two models: a static model where the nonlinearity is estimated across all trial periods or a GC model where the nonlinearity is estimated separately for low and high contrast. **b,** Example background-locked responses from a well-tuned cortical unit across the trial duration. The top portion of the plot is a spike raster sorted by the frozen noise scenes (Scene 1-5) of the background. The contrast of the adaptation and target periods are indicated by the red and blue rectangles on the top of the plot. The bottom portion of the plot is a trial-averaged PSTH of the observed spiking, binned every 25ms (black trace). The colored traces are the predictions of the static model (grey) and GC model (orange). Correlations of the model predictions and trial-averaged PSTH are indicated in the legend. **c,** STRF for this example neuron. STRF values are indicated by the colorbar. **d,** Estimated nonlinearities for this example neuron. Points indicate the mean observed firing rate (ordinate), binned according to observed filter prediction values (abscissa). Solid lines indicate exponential function fits to the underlying points. Each line is a fit to the test set in 10 cross-validation runs (see *Methods*). Blue and red lines and dots are the nonlinearities in low and high contrast for the GC model, while the grey lines and dots are for the static model (here, they are obscured by the high contrast data). **e,** Gain control in auditory cortex during the task. In the main figure, each probability density is the distribution of gain values in high and low contrast across neurons with NR below 100. Lighter shaded histograms indicate gain during the adaptation period and darker shaded histograms indicate gain during the target period (labelled by “A” and “T”, respectively). Asterisks indicate post-hoc test results for adaptation vs. target gain in each contrast. *Inset*: gain distributions for each contrast, regardless of trial period. Dashed vertical lines indicate the median of each distribution, asterisks indicate the results of a Wilcoxon Sign-Rank test across contrast. **f,** Average psychometric curves in low contrast split by cortical gain estimated during the target period of the stimulus. Light blue data points indicate the average performance in sessions where average gain was below the across-session median gain. Dark blue data points indicate average performance in sessions where average gain was above the median. Solid lines are psychometric fits to the data, with the thresholds plotted vertically from 0.5. Errorbars indicate ±s.e.m. *Inset*: Histogram of average target gain over sessions. The dashed red vertical line indicates the median gain, light blue bars indicate sessions below the median, and dark blue bars indicate sessions above the median. **g,** Relationship between gain and behavioral threshold. Each circle represents the average gain and behavioral threshold for each session and contrast (blue and red dots indicate low and high contrast target periods, respectively). Grey lines indicate linear best fit. **h,** Relationship between gain and behavioral slope. Appearance as in **g**. In all plots: ns*p*>0.1; †*p*<0.1, \**p*<0.05, \*\**p*<0.01, \*\*\**p*<0.001, \*\*\*\**p*<0.0001.