**Diagram

Description automatically generatedFigure 2.**

**a,** Schematic for acute recordings from auditory cortex. **b,** Schematic of generalized linear model (GLM) design. *From left to right:* The external variables considered by the model are the stimulus spectrogram, the stimulus contrast, and the observed spikes of cortical neurons. In the first step we estimate the spectrotemporal receptive field (STRF) of the cell. In the second step, we designed a GLM with gain control (GC-GLM) to isolate to contributions of: 1) Pure stimulus drive; 2) The multiplicative interaction between the stimulus contrast and the stimulus drive, which we define as the gain of the neuron; 3) Pure contrast drive. To estimate smooth temporal trajectories of the gain predictor and contrast contributions, these predictors were convolved with a b-spline basis set at lags between 0 and 1s. The summed output of all the predictors 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) lines. *Middle*: PSTH 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 blue, and the GC-GLM model in red. All traces were smoothed with a 10ms wide Gaussian filter for visualization. *Bottom*: the gain estimate, w, inferred from the GLM parameters (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, w, for the example neuron for 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,** Pearson’s correlations between the trial averaged firing rate trace and the model predictions. Grey, blue, and red 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 errors 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 wlow - whigh after the estimate has stabilized to its final value (ie. after 1s). Dashed vertical line indicates no gain control, while the solid red 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 w 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.