**Cortical efficient coding shapes behavioral performance.**

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**Abstract**

The efficient coding hypothesis postulates that neurons shape their response properties to match their dynamic response range to the statistics of the incoming signals. However, whether and how efficient neuronal code inform behavior has not been previously shown directly. Neurons in auditory cortex (AC) adapt the gain of their response function to effectively match their dynamic range to that of the sound in contrast gain adaptation. Here, we trained mice to detect a target presented in noise shortly after a change in the noise contrast. Mice followed the predictions of a normative model of cortical sound processing for magnitude and the time course of detection performance. Target detection and sensitivity improved in low contrast as compared to high-contrast noise. The time course of target detectability varied depending on contrast, decreasing rapidly after a transition to high contrast, and increasing at a slower rate after a transition to low contrast. We found that AC was necessary for detection of targets in noise and cortical neuronal responses exhibited the predicted patterns of target detectability. Furthermore, the magnitude of gain modulation in cortical neurons predicted behavioral performance from session to session. Combined, our results demonstrate that efficient neural code in auditory cortex directly influences behavioral performance.

**Introduction**

As we navigate the world around us, the statistics of the environment can change dramatically. The efficient coding hypothesis postulates that neurons match their limited dynamic range to the statistics of the incoming sensory signals through the process of adaptation, in order to preserve the ability to encode information about environment. Such neuronal adaptation to the statistics of the environment has been found throughout different sensory modalities, and throughout brain regions. In the auditory system, neurons exhibit contrast gain control, adapting the gain of their response function to match the contrast (variance) of the incoming sounds. Yet it remains unknown whether and how contrast gain control in the auditory system informs behavior, as a direct link between neuronal adaptation and behavior not been previously established.

The efficient coding hypothesis has been formally implemented through normative models of brain function. These models allow for making predictions for neuronal function or psychophysical performance to optimize encoding or belief about the environment. Whereas a predictive framework for directly linking efficient neural codes to auditory percepts has not yet been proposed (Wei & Stocker, 2015), normative models can be used to predict task performance given a distribution of the stimuli, and even a change in that distribution, such as a transition in sound contrast.

At the psychophysical level, the auditory system exhibits adaptation to the sound contrast. In humans, the just-noticeable-difference between targets of different volume decreased in low contrast (REF). This improvement in volume acuity is consistent with higher neural gain in low contrast found in the primary auditory cortex (REF). Similar effects have also been shown in ferrets performing an acoustic localization task, where it was also demonstrated that neural responses in the inferior colliculus of anesthetized ferrets changed in a manner consistent with observed perceptual shifts (Dahmen et al., 2010). However, it remains unclear whether the observed behavioral effects are indeed due to changes in gain in auditory neurons, as previous behavioral studies were not performed with simultaneous neural recordings, so a direct relationship between neural gain and perceptual performance has yet to be assessed.

Our goal for the study was to first build a formal framework for prediction of behavioral performance for detection of targets upon the shift in background sound contrast.Next, to directly test the role of efficient coding in auditory behavior, we trained mice to detect targets in variable contrast backgrounds. Mouse behavior followed the model predictions. Simultaneous chronic neural recordings found that the neural code in auditory cortex is not only predictive of individual differences in behavior, but also that variability in neural contrast adaptation is predictive of task performance in a contrast-dependent manner and on a trial-by-trial basis. Combined, our results identify a novel relationship between efficient neuronal coding and acoustic behavior, and provide a normative framework that can be used to predict behavioral performance across other behaviors and sensory modalities.

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1. Experimental setup. Mice were head-fixed are presented with sounds from an ultrasonic speaker. During behavior, mice receive water rewards through a lick spout. In a subset of mice, tetrodes were implanted in ACtx to record spiking activity.
2. GO/NO-GO task design. *Left:* example NO-GO trials. From top to bottom: spectrogram of an example low-to-high contrast trial (colorbar indicates volume in dB SPL); waveform for sample spectrogram; example spectrogram for a high-to-low contrast trial; waveform for example spectrogram; temporally jittered response window to estimate false alarms over time; schematic lick responses during in the window; timeout delivered after the first lick for 7 seconds. Vertical red dashed line indicates the contrast switch after 3 seconds. Black horizontal scale bar indicates 1s. *Right:* example GO trials. From top to bottom: same as in left panel, except the response window immediately follows target presentation and licks within the target window trigger a ~5uL water reward.
3. Target manipulation example waveforms. *Top:* overlaid trials where target volume differed. Volume is indicated by the amplitude and colorbar, with low volume targets shaded in cyan, and high volume targets shaded in magenta. *Bottom:* overlaid trials where target timing differed. Target timing is indicated in the colorbar, with light magenta targets occurring shortly after the contrast switch, and darker targets occurring at increasing delays. The red vertical dashed line indicates the contrast switch.
4. Percent correct performance relative to the first session of task exposure. 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).
5. Psychometric functions averaged for n=21 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. Colors as in d).
6. Psychometric thresholds per contrast. Each dot represents a mouse, lines connect individual mouse performance on low and high contrast sessions. Bars indicate the average threshold over mice, while error bars in black indicate threshold SEM over mice. Bar colors as in d).
7. Psychometric thresholds as a function of task exposure. Dots indicate thresholds on individual sessions. Lines indicate linear regression fits, while the dotted lines and shaded background indicate the 95% confidence interval of the linear fit. Dot and fit colors as in d).

**Results**

*Mouse behavioral detection is modulated by background contrast.*

To assess how perceptual performance is impacted by stimulus contrast, we devised a GO/NO-GO task in which head-fixed mice were trained to detect targets embedded in different contrast backgrounds. During each trial, the mouse was first presented with 3s of dynamic random chords (DRCs) of one contrast, after which a switch occurred, either to a higher or lower contrast background. At variable delays after the 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. Target trials were interleaved with noise-only trials, during which the mouse was trained to withhold licking, but would receive a 7s timeout if licking after the contrast switch (Figure 1a,b). To assess behavioral sensitivity to targets, we parametrically varied target volume in each contrast (Figure 1c, top panel) and to assess behavioral adaptation, we parametrically varied target timing (Figure 1c, bottom panel).

Mice learned this task reliably, typically reaching criterion performance of 80% correct within 2-3 weeks in either contrast and stably performed this task for many weeks (Figure 1d). In all of the mice we tested, we found that targets were easier to detect in low contrast, observing significantly lower detection thresholds in low contrast (p = 8.14e-14, paired t-test, n = 21, Figure 1e,f). Additionally, detection thresholds decreased significantly with task exposure in high contrast (p = 0.02, linear regression, STATS), and showed a decreasing trend in low contrast (p = 0.10, linear regression, STATS), suggesting that mice improved became more sensitive to targets with exposure (Figure 1g).

*A normative model for target detection during contrast gain control predicts behavioral performance.*

To build an intuition for the effects of contrast gain control on target detectability, we simulated a neuron designed to estimate the variance (aka. contrast) of the recent stimulus by adjusting the gain of its nonlinearity. A detailed description of the model is provided in the methods, but briefly: 1) at each timestep, a stimulus which varied in contrast over time generated stochastic spikes in the model neuron, 2) based on this spiking activity, the variance of the stimulus in a brief window before the current timestep is estimated, 3) the variance estimate error is then fed back to the model neuron and the neuron updates its gain to improve the estimate (Figure 2a, panels 1-3). We find that the timescale of gain control in this model has a few key features: 1) gain decreases after a switch from low-to-high contrast and vice-versa from high-to-low contrast, and, 2) gain adaptation times are asymmetric, adapting faster for high contrast than low contrast, as indicated by the time taken to reach half of the range of each curve (Figure 2a, panel 4).

Using this framework for efficient coding of stimulus contrast, we simulated how well the model can detect targets added to this fluctuating background. By varying the target mean in each contrast, we observed that in low contrast, the model is more sensitive to changes in volume, as indicated by the steeper slope, and has lower detection thresholds compared to high contrast (Figure 2b). Additionally, when holding target volume fixed and varying target time relative to the switch, we see target detection adaptation in line with model gain adaptation (as mentioned in Figure 2a, panel 4). Specifically, after a low-to-high contrast switch, targets are readily discriminable from noise, and this discriminability decreases as gain decreases, while after a high-to-low contrast switch, we see the opposite trend (Figure 2c). We next tested these two predictions, 1) increased performance in low contrast, and, 2), stereotyped adaptation of target detection performance in each contrast in behaving mice.

Using psychometric testing, we found that behaving mice were more sensitive to target volume in low contrast, demonstrating significantly lower target thresholds in low contrast (Figure 2d, middle panel; p<0.01, paired t-test, n=4), and significantly steeper slopes in low contrast (Figure 2d, right panel; p<.05, paired t-test, n=4). We also observed behavioral time-courses consistent with our model: in high contrast, mice initially were able to detect targets with high accuracy which fell off over time, while in low contrast we observed increasing detection rates over time (Figure 2e, left panel). By fitting each mouse’s adaptation time-course with an exponential function and comparing time constants for each contrast, we also found that behavioral adaptation is significantly faster in high contrast (Figure 2e, right panel; p < 0.05, paired t-test, n = 13).

*Auditory cortex is necessary for detection in noise.*

We predicted that contrast adaptation in auditory cortex shapes performance in this behavioral task. To test this prediction, we inactivated auditory cortex using the GABA agonist muscimol to assess whether it is necessary for task performance. We first validated that muscimol disrupts cortical coding of target sounds by applying muscimol topically to the cortical surface of awake, untrained mice while recording neuronal responses during passive playback of the behavioral stimuli (Figure 3a). We first recorded baseline responses to all stimuli,

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**Figure 2.**

1. Model schematic. (1) Spike generation process: a 1-dimensional sensory stimulus that transitions between low and high contrast feeds into a model neuron. The response of the model neuron is governed by a sigmoidal function which then generates stochastic spikes through a Poisson process. (2) Based on the observed spiking, a variance estimator integrates spike counts to estimate the current variance of the stimulus. (3) This estimate is then used to adjust the gain of the model neuron to optimize the estimate of stimulus variance at each time step. (4) The average change in gain of the model after each contrast transition. Dashed lines and dots indicate the time taken to reach half of the range of gain values in each contrast. Right panels show the average model nonlinearities for the first 25 time steps, with the arrows indicating the direction of change in gain over time.
2. Model psychometric functions. Discriminability between model spike rates in response to the background and targets as a function of contrast and target volume. Arrow indicates target mean of 1.50 which is the volume used to assess time courses in c).
3. Model target discrimination as a function of time and contrast. Dashed vertical line indicates the time where the background contrast switched.
4. *Left:* Behavioral psychometric functions. Dots with error bars indicate average performance +- SEM over mice as a function of contrast and target volume. Overlaid dark colored lines 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 horizontal line indicates chance (0.5) performance. *Middle:* Psychometric thresholds per contrast. Each dot represents a mouse, lines indicate where a 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. *Right:* Psychometric slopes per contrast. Presentation as in middle panel.
5. *Left*: Behavioral performance as a function of contrast and target time relative to the switch in contrast. Dots with error bars indicate average performance +- SEM over mice. Solid colored lines indicate exponential function fits to the average over mice. Black, dashed vertical line indicates the contrast switch. *Right:* average time constant of exponential fits in low and high contrast. Presented as in d). In all plots, blue indicates when targets were presented in low contrast and red indicates high contrast.

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 (Figure 3b). Notably, in our saline control, we observed little to no change in neural responses after saline application (Figure 3c). Comparison of target responses after saline vs muscimol application revealed nearly complete suppression of responses to both targets and noise in high and low contrast (Figure 3d). These results confirmed that muscimol effectively disrupts the cortical coding of our behavioral stimuli.

To test whether this cortical disruption perturbs behavioral performance, we repeated the same experiments in behaving mice, administering muscimol or saline through chronically implanted cannulae (Figure 3e). As observed in cortical activity, there was a profound decrease in the rate of responding to both targets (hits) and noise (false alarms) in both contrasts (Figure 3f). We quantified these effects on the psychometric curve, and observed significant decrease in the response rate at the highest volume, false alarm rate, and slope of the psychometric functions (Figure 3g). The only parameter that was unaffected by muscimol was the behavioral threshold (Figure 3g, bottom left panel).

A potential alternative effect of muscimol is a general loss of function that is not specific to hearing target sounds, which would manifest in an overall inability to lick. 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 (Figure 3h, top and bottom right panels). Mice also tended to lick immediately after the trial onset (Figure 3h, adaptation period), but we found that the lick rates under muscimol and saline conditions were identical during this period. 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.

*Population responses to targets track 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 while mice performed the behavioral task (Figure 4a). In the psychometric task where we varied target volume, many cortical neurons monotonically increased their firing rate with increased target volume (example neuron, Figure 4b; simultaneously recorded populations from two example sessions, Figure 4c).

To leverage our ability to simultaneously record from multiple neurons, we adapted a population vector approach from (CITE DRUCKMANN PAPER) to generate metrics of target from noise discriminability from population activity. To do this, we estimated the coding direction in the high dimensional space of simultaneously recorded neurons by subtracting population vector responses to noise alone from population vector responses to targets. The resulting coding direction vector is the direction in high dimensional space between the average response to noise and targets (Figure 4d, left panel). This vector was trained on all but one trial, and the remaining trial’s population response timecourse was projected along this coding direction to generate a single projection value over time along this coding direction. This was repeated for all trials, and the projection values were averaged for every trial within a 30ms window after target onset. We then grouped these values into trial distributions for each target volume, and compared them to noise trial distributions by estimating a criterion projection value that best predicted whether each was a target or noise trial (example projection value distributions from the recording in Figure 4C, left panel is shown in Figure 4d, right panel).

Using this criterion, we then computed the accuracy of the neural population in discriminating targets from noise at each volume and at each contrast. This allowed us to estimate neurometric functions for direct comparison to the corresponding psychometric functions of each mouse (Figure 4e). On average, neurometric and psychometric functions were qualitatively similar, with neurometric functions exhibiting slightly lower thresholds, and shallower slopes (Figure 4f). We found that behavioral thresholds were highly predictive of the observed neural thresholds across both contrasts (n=21, p = 9.57e-6, linear regression, Figure 4g). We also observed a significant relationship between behavioral and neural thresholds in low contrast alone, suggesting that the observed correlation across contrasts is not just due to contrast, but that cortical neurons track behavioral thresholds independently of contrast (n=12, p=.02, linear regression, Figure 4g). Additionally, we find that across both contrasts there is a significant relationship between neurometric and psychometric slopes (n=21, p=0.03, linear regression), although this relationship doesn’t hold within low contrast alone (n=12, p=0.23, linear regression, Figure 4h).

*Cortical gain tracks individual behavioral performance.*

Our behavioral results and model provide strong evidence that gain control in the auditory system shapes patterns of behavioral performance. To more directly assess the role of gain control in auditory cortex in shaping

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**Figure 3.**

1. Setup schematic for acute muscimol recordings in ACtx.
2. Example spike rasters pre- and post-muscimol 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 (FA). *Left panel:* raster of target and noise responses of a representative neuron recorded prior to muscimol application. *Right panel:* raster of the same neuron 30 minutes after muscimol application. *Insets:* Mean firing rate for each condition. Shade indicates target volume and the scale bar indicates a firing rate of 50Hz. Error bars indicate S.E.M. across trials.
3. Example spike rasters pre- and post-saline application. Plots as in b).
4. Average firing responses after drug application in muscimol and saline recording sessions. Filled circles and solid lines are responses after saline was applied while open circles and dashed lines are responses after muscimol was applied. Light shaded open and closed circles that are unconnected by lines are the responses to noise alone. Error bars indicate S.E.M. across neurons.
5. Setup schematic for chronic muscimol application in behaving mice.
6. Behavioral psychometric functions during muscimol or saline application. 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 S.E.M. across sessions.
7. 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 rat, the false alarm rate, psychometric threshold, and the maximum slope of the psychometric curve.
8. Effects of muscimol on licking throughout the trial. *Top:* 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 S.E.M. across sessions. *Bottom left:* comparison of lick probability during the adaptation period. Each circle indicates a session and color is as in the top panel. *Bottom right:* comparison of lick probability during the target period.

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**Figure 4.**

1. Experimental setup for chronic ACtx recordings from behaving mice.
2. 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 identity. Colored bars indicate the target volume, grey bars indicate noise only trials. The bottom portion of the plot contains spike rates for each target condition, averaged over trials and smoothed with a 5ms standard deviation Gaussian kernel. *Inset:* Grey solid line indicates the behavioral percent correct for this session. Closed circles and the solid blue line indicate the performance of an ideal observer in discriminating between noise responses and target responses at each volume. Circle colors indicate the presented volume. The dashed horizontal line indicates change performance (0.5). Error bars are the 95% confidence interval of ideal observer performance as assessed through a bootstrap procedure.
3. 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, shade indicates the neural response to each target, with the average response to noise alone subtracted. White indicates no change in firing rate, blue/red indicate increases in firing rate relative to the noise response, and cyan indicates suppression below the noise response. Asterix indicates the responses of the neurons in panel b).
4. 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 by 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 CA118-200529, as plotted in c). The blue distribution is the average projection value in a 40ms window after presentation of 20 dB SPL targets. The gray distribution is the average projection value in the same window during noise only trials. The vertical black line is the criterion which yielded the highest performance in predicting target presence across all trials.
5. Example neurometric and psychometric curves. *Left:* Low contrast curves. Open circles and solid lines indicate psychometric performance and a logistic fit, respectively. X markers and dashed lines indicate neurometric performance from the session plotted in c). The horizontal dashed line indicates chance performance (0.5). The arrow indicates the neural performance computed from the distributions and criterion plotted in the right panel of d). *Right:* High contrast curves for the session plotted in c) (plot appearance as in left).
6. Average psychometric and neurometric functions across mice. Light open circles indicate average behavioral performance, light x markers indicate average neural performance. Solid curves indicate logistic fits to average behavioral performance, while solid vertical lines indicate the fit thresholds. Dashed lines indicate fits and thresholds for the neural data. The dashed vertical line indicates chance performance.
7. 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, +- the 95% confidence interval. The solid black line indicates unity.
8. Relationship between behavioral and neural slopes. Appearance as in g).

behavior, we leveraged the design of our background sounds to estimate the gain of cortical neurons using a generalized-linear-nonlinear model (gLN). Briefly, we estimated the spectrotemporal receptive fields (STRFs) of individual cortical neurons using generalized linear regression and convolved them with the stimulus spectrogram to generate linear predictions of cortical activity (Figure 5a, panels 1-3). We could then compare the linear prediction to the observed firing rate elicited by the background to estimate the nonlinearity of each neuron in high and low contrast (Figure 5a, panel 4). This modeling strategy allowed us to estimate cortical gain during different periods in the task, and assess how gain is related to behavioral performance.

During the task, we used DRC backgrounds with fixed patterns, allowing us to quantify reliability of the responses to the background by taking the ratio of noise power of the responses to the signal power (Sahani and Linden CITE, see Methods) (Figure 5b, spike raster). The estimated STRF for this example unit is shown in Figure 5c, along with the nonlinearities estimated for low and high contrast in Figure 5d. By fitting nonlinearities separately to high and low contrast portions of each trial, we were able to estimate neural gain for all of the recorded units during the task. After pooling all of the neurons recorded across all mice and sessions, and including only neurons with high reliability in both contrasts (noise ratio < 100 in low and high contrast), we observed substantial gain control during the task (n=XXX, p = 7.40e-168, Wilcoxon sign-rank test) confirming previous findings in mouse auditory cortex (CITE).

We then assessed whether gain in auditory cortex reliably predicts how well a mouse is able to hear targets in these different backgrounds. To do so, we averaged the gain of target-selective neurons during the target period of the task for each mouse and then compared the target period gain for each mouse to the behavioral thresholds and slopes collected in the psychometric task. We found a significant negative relationship between cortical gain and behavioral threshold across contrasts (n = 14, p = 3.51e-4, linear regression), suggesting that increased gain yielded greater sensitivity to lower target volumes. However, we didn’t observe this relationship when only looking in low contrast (n = 9, p = 0,27, linear regression), so we cannot definitely conclude that contrast-independent fluctuations in gain predict behavioral thresholds (Figure 5f). We conducted the same analysis between gain and psychometric slopes, and found significant positive relationships across contrasts (n = 14, p = 0.005, linear regression) and within low contrast (n = 9, p = 0.03, linear regression), suggesting that individual differences in cortical gain influence behavioral sensitivity to changes in volume, independently of contrast gain control.

**Discussion**

On daily basis, we navigate through sensory environments with vastly different statistics. As we exit a coffee shop onto a crowded street, the acoustic environment changes contrast from low to high. The efficient coding hypothesis predicts that as acoustic contrast shifts, neurons throughout the auditory pathway adjust their sensitivity, so as to match the dynamic range of their response to that of the stimulus statistical distribution. This process would allow us to keep hearing our conversation partner. Multiple studies have demonstrated that indeed, neurons throughout the auditory pathway exhibit contrast adaptation. However, whether contrast adaptation plays a role in auditory behavior has not been previously examined directly. In this study, we directly linked the neuronal contrast gain control to auditory behavior.

To tackle this complex question, we first developed a normative framework that allowed us to make specific predictions for behavioral performance as expected by contrast gain control. The model predicted that (1) The detection threshold of a target in noise under low contrast should be lower than under high contrast;(2) Upon shift of background noise contrast, detection improves upon transition from high to low contrast, but is impaired upon transition from low to high contrast; and (3) The time contrast for this change in detection performance is slower for transition from high to low contrast than from low to high contrast. To test these predictions, we trained mice to detect a target in noise background, as noise contrast shifted from low to high or from high to low. As predicted by the normative model, mice exhibited a lower threshold for detecting targets in low as compared to high background. They also exhibited a decrease in detection of tones in high contrast background, and in increase in detection of tones in low contrast background over time. This shift occurred faster in high contrast, as compared to low contrast backgrounds. We furthermore found that AC is necessary for the detection task, and that AC activity reflected the behavioral shifts. Combined, our results provide evidence for the relevance of efficient coding in auditory behavior.

Neurons throughout the auditory system adapt to the statistics of the acoustic environment, including distribution of stimuli over time (Ulanovsky, etc.), sound level, sound timing, and more complex sound patterns. In the auditory system adaptation to mean sound pressure level is present already at the level of the auditory nerve. Furthermore, context-dependent adaptation is manifested across temporal and spectral regularities, as for example with two tone suppression. In this study, we focused on contrast gain control as a fundamental statistical adaptation that relates to efficient coding: The responses are adjusted to the distribution of the stimulus intensities, not just the meads. Drawing on a normative model for making predictions for behavioral performance is a powerful approach for testing the key expectations of efficient coding. Because a normative model does not make any assumptions about the neuronal responses, but rather serves to maximize the information between the response and the stimulus, it can be generalized to different levels of stimulus complexity. The behavioral effects of auditory adaptation likely extend to more complex forms of statistical regularities, and likely underlies many behavioral effects measured in humans.

Contrast adaptation has been found at multiple stages in the auditory system, including the inferior colliculus, the medial geniculate nucleus and the auditory cortex. We focused on the auditory cortex, as we found that its inactivation selectively impaired the detection of target in noise background. Importantly, cortical inactivation did not impair performance in detection of target without background (Figure XX), therefore confirming that cortical inactivation is not generally required for detection behavior. Our findings are consistent with multiple previous studies, which found that the auditory cortex is not requires for performance in simple tasks but is required for more complex behavioral tasks. In fact, whether AC is required for a specific auditory behavior depends not simply on the stimulus selection, but how differentiable stimuli are from each other at the level of population cortical activity (Wood, 2021). AC neurons exhibit slower time scales of contrast adaptation than the auditory thalamus or the inferior colliculus. For behaviors that use more simple tasks or stimuli, we therefore expect the relevant time scales for those effects to be more consistent with the faster adaptation at earlier stages of the auditory system.

Whereas previous studies largely studied the behavioral or psychophysical performance separately from the neuronal activity, which was recorded in anesthetized or passive subjects, we were able to record neuronal responses during the behavioral task. Not only is this important to control for the level of arousal and attention, that can dramatically alter responses in AC (REF), but also we were able to test for a statistical relationship between the effects of contrast on neuronal encoding and behavioral performance within subjects and within sessions. As the behavioral performance differed across subjects and sessions, we were able to identify a correlation between the gain control at the neuronal and at behavioral level (Figure XX). The high variability in performance between subjects can be used to disentangle the role of neuronal activity in a task (Aizenberg, 2013, Wood, 2015). We therefore consider within subject tests to be critical to linking neuronal circuits to behavior.

Methodologically, another important decision in task design was the selection of background sounds to be dynamic random chords – a stimulus that has traditionally been used to map the complex spectro-temporal receptive fields of neurons. These stimuli have the advantage of presenting a distribution of intensity values drawn from a Gaussian distribution within each of the frequency bands. As such, it is possible to reconstruct the modulation filter that predicts the neuronal responses. We used this stimulus to fit a full model of neuronal responses. To incorporate the contrast change to the model of neuronal activity, we included a set of predictors for temporally delayed contrast changes (REF), similar to previous work (David, 2018). Particularly attention was paid to build a non-linearity over the potentially asymmetric effects of shifts to low or to high contrast (Figure XX). The selection of background sound should therefore be carefully considered in experimental design in order to build predictive models of neuronal responses.

One limitation of the present study is the limited number of neurons that were recorded simultaneously. We used chronically implanted custom-built microdrives along with the Openephys system, which allowed us to record from up to XX neurons for over XX sessions/days. The primary auditory cortex in the mouse comprises several hundreds of thousands of neurons. Therefore, whereas our results exhibit strong correlation at a small population level, recordings with recently developed probes such as Neuropixels will likely yield more comprehensive sets of data.

An important question left unanswered is the potential differences between different types of neurons in the auditory cortex. We have likely recorded from a population of excitatory and inhibitory neurons. Different inhibitory neuronal subtypes exhibit specific roles in adaptation. For example, somatostatin-positive inhibitory neurons have been implicated in temporal and stimulus-specific adaptation, and along with parvalbumin-positive neurons facilitate two-tone suppression. It is plausible that specific inhibitory neuronal subtypes facilitate contrast adaptation in the auditory cortex, whereas other contribute to target detection and behavioral choice. These questions can be explored in future studies that use optical identification of specific neuronal cell types in similar behavior.

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**Figure 5.**

1. Schematic of the generalized-linear-nonlinear model. 1) Schematic of a spectrotemporal response function. 2) Example stimulus spectrogram of low and high contrast. 3) The gray trace is the filter response when convolving the STRF with the spectrogram. The black trace is the observed spike rate during the same stimulus period. 4) Schematized nonlinearities fit separately to low and high contrast periods.
2. 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 pattern (FN1-5) of the background. The bottom portion of the plot is a PSTH of the observed spiking, binned every 25ms (black trace). The colored traces are the model predictions in each contrast (red trace uses the red nonlinearity in d), blue trace uses the blue nonlinearity in d)).
3. STRF for this example neuron. STRF values are indicated by the colorbar.
4. 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 a cross-validation run (see Methods).
5. Gain control in auditory cortex during the task. Each histogram is the distribution of gain values in high and low contrast across all cells recorded during behavior. Dashed vertical lines indicate the median of each distributions.
6. Relationship between gain and behavioral threshold. Each circle represents the gain and behavioral 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, +- the 95% confidence interval.
7. Relationship between gain and behavioral slope. Appearance as in f).

**Methods**

*Animals*. All experiments were performed in adult male (n = xxx) and female (n = xxx) mice (The Jackson Laboratory; age 12-15 weeks; weight 20-30g; STRAINS, etc.), 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.

*Surgery*. Mice were anesthetized under isoflurane (1-3%, vol/vol). Prior to implantation, all mice were administered subcutaneous doses of buprenorphine (Buprenex, DOSE) for analgesia, dexamethasone (DOSE) to reduce brain swelling, and bupivicane (DOSE) for local anesthesia. In mice undergoing electrophysiological experiments, 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 base of the tetrodes were covered with GelFoam (CITE) or sterile silicone lubricant (CITE) and sealed with QuikCast (CITE). The plastic body of the microdrive and a custom titanium 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 custom titanium headplate was mounted on the skull as previously described. An antibiotic (Baytril, DOSE) and analgesic (Meloxicam, DOSE) were administered daily (for 3 days) during recovery.

*Water Restriction*. Following surgical recovery (3 d postop), each mouse’s weight was monitored for three 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 methods (CITE) and approved by the Institutional Animal Care and Use Committee at the University of Pennsylvania.

*Behavioral Apparatus*. During the Go/NoGo 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) to calibrated to deliver approximately 4-5uL of water per reward (CITE Brian Isett). 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 serial port. Digital waveforms were 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 previously (CITE). 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 the 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 simultaneously habituated to head-fixation in the behavioral chambers and receiving water through the lick spout, by providing a water reward for any 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 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 (~2-3 weeks). 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 studies (CITE). This stimulus was used 1) to measure the spectrotemporal receptive fields of neurons by fitting a linear-nonlinear model, and 2) to modulate the gain of auditory neurons by manipulating stimulus contrast. 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.

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 was initialized with 3 seconds of DRC noise of 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 by the animal 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 noise would have an SNR of 0 dB). We note that because the targets only contained power in half of the frequency bands used to construct the noise background, target SNRs were typically above 0 dB. \*\*\*\* INSERT TABLE DESCRIBING ALL DIFFERENT EXPERIMENTAL CONDITIONS \*\*\*\* In all trials, targets were embedded after a change in the background contrast, with a delay and volume dependent on the current training or testing stage (see Behavioral Task).

*Behavioral Task*. We employed a Go/NoGo task to measure mouses’ perceptual ability to detect targets in noise. 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 detect a target (hit), or to withhold licking in the absence of a target (correct reject). This behavior was reinforced by providing a 4-5uL water reward when the mouse performed a hit, and by initiating a 7-10s timeout when the mouse licked in the absence of a target (false alarm). Any licks detected during the timeout period resulted in the timeout timer 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 reset after a 7-10s 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 would be reset.

Several of our behavioral tasks varied the timing of the target relative to the contrast shift, which 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 as responses only during a 1 s response window after a target presentation in the trial (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 noise-only trials, in which no targets were presented, we considered noise trials as target trials containing infinitely small target amplitudes. For each noise 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 noise trials during the same temporal windows as those licks considered during target trials. Using this scheme, we treated target and noise 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, noise 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 1000ms after the contrast change in each trial. During the psychometric testing task, there 7 trial types consisting of noise trials and target trials spanning six different SNRs (\*\*\* TABLE\*\*\*). Based on behavioral piloting, we presented high SNR trials with a greater probability, to prevent mice from giving up during the task. In low and high contrast psychometric sessions, the probability of a noise 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 (\*\*\*but, make Supplemental Figure for tasks with equal presentation probability\*\*\*). As in training, target timing was varied randomly between 250, 500, 750 and 1000ms 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 volumes (noise 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 estimating target detection thresholds in each contrast condition during psychometric testing sessions, and varied between ~2-12 in low contrast and ~8-16 dB SNR in high contrast. Based on behavioral piloting, noise 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 noise trials in a row.

*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 microdrives 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. Prior to spike analysis, broadband signals were filtered between 0.5 and 6000 Hz, offset corrected, and re-referenced to the median across all active channels. The preprocessed data was then sorted using KiloSort (CITE) or KiloSort2 and the resulting clustering was manually corrected in phy (CITE) 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 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.