

# Active listening: Task-dependent plasticity of spectrotemporal receptive fields in primary auditory cortex

Jonathan Fritz \*, Mounya Elhilali, Shihab Shamma

*Centre for Auditory and Acoustic Research, University of Maryland College Park, MD 20742, USA*

Received 20 November 2004; accepted 23 January 2005

Available online 16 April 2005

## Abstract

Listening is an active process in which attentive focus on salient acoustic features in auditory tasks can influence receptive field properties of cortical neurons. Recent studies showing rapid task-related changes in neuronal spectrotemporal receptive fields (STRFs) in primary auditory cortex of the behaving ferret are reviewed in the context of current research on cortical plasticity. Ferrets were trained on spectral tasks, including tone detection and two-tone discrimination, and on temporal tasks, including gap detection and click-rate discrimination. STRF changes could be measured on-line during task performance and occurred within minutes of task onset. During spectral tasks, there were specific spectral changes (enhanced response to tonal target frequency in tone detection and discrimination, suppressed response to tonal reference frequency in tone discrimination). However, only in the temporal tasks, the STRF was changed along the temporal dimension by sharpening temporal dynamics. In ferrets trained on multiple tasks, distinctive and task-specific STRF changes could be observed in the same cortical neurons in successive behavioral sessions. These results suggest that rapid task-related plasticity is an ongoing process that occurs at a network and single unit level as the animal switches between different tasks and dynamically adapts cortical STRFs in response to changing acoustic demands.

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*Keywords:* Auditory; Cortex; Plasticity; Attention; Adaptive; Behavior

## 1. Introduction

The cortical effects of learning have probably been more extensively studied in the auditory system than in any other sensory modality. Over the past 20 years, studies of behaviorally driven plasticity in the auditory cortex have revealed profound effects on the global level, notably by the reshaping of cortical maps, and on the local level, by the transformation of neuronal receptive field properties (A1 plasticity was originally described by Gonzalez-Lima and Scheich, 1986; Weinberger et al., 1984; Diamond and Weinberger, 1984, 1986 and reviewed by Edeline, 1999, 2003; Suga et al., 2002; Suga and Ma, 2003; Weinberger, 2001, 2003a,b, 2004). A myr-

riad of changes emerges in cortical plasticity (and at least nine varieties of plasticity have been defined by Calford, 2002). The form of cortical plasticity in primary auditory cortex (A1) which appears in a given experiment appears to be partly determined by (a) the experimental design and nature of the behavioral task, (b) the time course of behavioral training, (c) the behavioral salience of the spectral and temporal characteristics of the acoustic stimuli, and perhaps (d) by the species being studied (Recanzone et al., 1993; Irvine et al., 2004). In important non-behavioral models of salience-shaped plasticity, frequency-specific modification of receptive fields and maps in A1 are induced by pairing a tone with non-motivational stimulation of the cholinergic nucleus basalis (Bakin and Weinberger, 1996; Bjordahl et al., 1998; Dimyan and Weinberger, 1999; Kilgard et al., 2001a,b; Kilgard and Merzenich, 2002a; Kilgard et al., 2002b).

\* Corresponding author. Tel.: +1 301 405 6596; fax: +1 301 314 9920.  
E-mail address: [ripple@isr.umd.edu](mailto:ripple@isr.umd.edu) (J. Fritz).

In this review, we focus on a particular form of plasticity in primary auditory cortex. Rapid task-related receptive field plasticity (Fritz et al., 2003a,b, 2004a,b, 2005) that may play a role in active listening (Handel, 1989), is characterized as modulation of auditory cortical receptive fields that is (1) behaviorally driven by attentive focus on a salient acoustic feature necessary for task performance, (2) rapid – occurring within minutes of a change in task requirements or acoustics, (3) measured in the awake, behaving animal. There is some evidence that plasticity in the auditory system may also occur subcortically, perhaps due to corticofugal projections, but we will not discuss this work since it has been reviewed recently (Suga and Ma, 2003) except to note that plastic changes throughout the auditory system are very likely to be highly interdependent. It is also important to explain our emphasis on the rapid time course of short-term cortical plasticity – which is meaningful since rapid changes are most likely the result of unmasking, disinhibition or potentiation of previously existing connections, whereas slower changes may involve the development of new connectivity arising from collateral sprouting or dendritic remodeling, or to changes in synaptic efficacy brought about long-lasting changes in transmitter or receptor levels and distribution, all of which may act together to consolidate the initial, rapid changes. Since only a handful of previous studies of auditory task-related plasticity have measured receptive field changes in the auditory cortex within this narrow time window, we will briefly and selectively summarize important previous studies, but concentrate primarily on recent results from our laboratory.

### 1.1. Earlier studies of rapid task-related plasticity in A1

One of the classic studies demonstrating task-related plasticity in A1 measured cortical changes occurring after weeks of training on a frequency discrimination task during which the experimental monkeys reached a high level of performance (Recanzone et al., 1993). In similar studies, receptive field properties were generally measured before training and then measured again for comparison, after a behavioral endpoint in task performance had been attained, some days, weeks or months later. Such comparisons are based upon the responses of different neurons, sometimes from different animals, sampled from a similar A1 population. Although very valuable, these studies cannot succeed in pinpointing the time course of plastic changes in receptive field properties of individual neurons during learning. However, another complementary set of studies has shown that frequency receptive fields of cortical neurons can be rapidly modified, on a time scale of minutes, by a variety of learning paradigms, including classical conditioning (Bakin and Weinberger, 1990; Diamond and Weinberger, 1986) two tone classical discrimination training

(Edeline and Weinberger, 1993), aversive differential conditioning (Ohl and Scheich, 1996, 1997; Ohl et al., 2001), one-tone and two-tone instrumental avoidance conditioning (Bakin et al., 1996) or by expressing “latent” plasticity acquired in a specific behavioral context (Diamond and Weinberger, 1989) for example, when switching states from a passive state to a behavioral state in which the animal performs a previously learned positively reinforced two-alternative forced choice task (Yin et al., 2001, 2005). As Weinberger has observed (1998) the fact that receptive field plasticity occurs in very different tasks, and learning situations, suggests that “it is a general process of information storage and representation”.

Each of these earlier studies measured changes in receptive field properties of A1 neurons that arose from behavior – we highlight two specific results from the earlier experiments in this field: (1) cortical receptive field plasticity can be induced fairly rapidly, often within a few trials (Edeline et al., 1993), (2) such plasticity has a short-term component which is dependent for expression on the behavioral context (Diamond and Weinberger, 1989; Yin et al., 2001, 2004).

One of the most striking and important demonstrations of rapid task-related receptive field plasticity in the literature showed that receptive field changes in multi-unit clusters could occur in as few as five (CS-US) training trials in an associative fear conditioning task. Moreover, these receptive field changes paralleled the appearance of the first behavioral signs (bradycardia) of learning (Edeline et al., 1993). The CS was a tone, 6 s in duration. The US was a hindpaw shock delivered at the offset of the CS. The intertrial interval was 2 min. Hence the five trials took place over a time-course of 8.5 min. The receptive field measurements took 20–30 min in this study, so the total time elapsed between the onset of behavioral training and the measured receptive field change was ~30–40 min. The difficulty of measuring ongoing plasticity during auditory learning lead Diamond and Weinberger (1989) to describe the problem as “a neurobiological parallel to the Heisenberg uncertainty principle of quantum physics – the process of obtaining a measurement actually influences the state of the system.” Of course, one can never make any measurements without perturbing the measured system to a certain extent. But, based on our control studies in the naïve animal, we do not think that this particular type of problem encountered in the study of the neurophysiology of learning, has major perturbing effects in our investigation of attentional modulation of receptive fields during detection or discrimination tasks. Moreover, as described below, the advantage of our technique of rapid on-line single-unit measurements of receptive field tuning is to provide a set of snapshot moment-to-moment images of the time course of receptive field change in relation to behavior. This degree of time

resolution may also prove helpful in future studies to clarify the mechanisms involved in receptive field change in task-related plasticity.

In the same paper, the authors (Diamond and Weinberger, 1989) made an interesting observation about the importance of behavioral context in expressing learning-induced plasticity of cortical and proposed a “functional mosaic” model which distinguished between behavioral context-dependent and context-independent plasticity. They found that changes in neuronal receptive field properties could be expressed in some behavioral circumstances and not in others. In more recent studies by Yin et al. (2001, 2005) monkeys were over-trained to respond selectively for water reward to a short melodic target sequence of pure tones that was presented occasionally against a background of other acoustic stimuli. Individual A1 cortical neurons with faint responses to individual tonal components in the melody when these stimuli were presented in isolation, displayed a selective, strong, potentiated response to these tones when presented as part of the target sequence, an effect that was not observed in naïve animals. These results suggested that the receptive fields and frequency response profiles of A1 neurons might be behaviorally gated to adaptively assume different states or filter properties depending upon behavioral demands. In order to more carefully quantify these on-line adaptive changes, we developed a new procedure to study task related plasticity.

## 2. Task-related plasticity in A1 – changes in spectrotemporal receptive fields (STRFs)

Our approach was to record from single neurons in A1 while the animal performed under different auditory task conditions, with the goal of quantitatively analyzing the nature and time-course of state-dependent adaptive plasticity in the auditory cortex on a cellular level. Once we obtained a stable recording of an isolated A1 neuron in the awake ferret, the design of our experiments was simple: (1) rapidly and comprehensively characterize the cortical STRF in the “pre-behavioral” quiescent condition, (2) characterize the behavioral STRF while the animal was actively engaged in one type of auditory task and compare this “behavioral-STRF-1” to the initial “pre-behavioral” and subsequent “post-behavioral” quiescent STRFs, (3) if possible, characterize and compare STRF plasticity in the *same* cell while the animal performed *different* auditory task (leading to additional behavioral STRFs always flanked by pre- and post-behavioral quiescent STRFs).

All experiments followed the same basic behavioral paradigm of conditioned avoidance (Heffner and Heffner, 1995), which we have slightly modified. In our

experiments, animals were trained to continuously lick water from a spout during a series of similar reference sounds, and to stop licking after a distinctive warning target in order to avoid mild shock. In all experiments, reference sounds were drawn from a class of ripple stimuli called TORCs (temporally orthogonal ripple combinations) which are temporally and spectrally rich, broadband stimuli that also serve during physiological experiments to characterize the STRF of the cell under study. By contrast, the target sound varied from one experiment to another, providing distinctive acoustic cues with salient spectral or temporal, or combined spectrotemporal features. We grouped the tasks by the type of target that the animal learned to attend (tones, silent gaps, tone duration, click rate, FM sweep direction, etc.). The major goal of the research we will describe here was to investigate auditory cortical plasticity induced by tonal targets in spectral tasks, and to contrast their effects in two distinct behavioral contexts: tone detection and two-tone discrimination. We shall also describe preliminary results of our studies of plasticity arising from temporal tasks in which the animal performs either gap detection, tone duration discrimination or click rate discrimination.

### 2.1. Basic paradigm and training procedure

The basic behavioral paradigm is illustrated in Fig. 1. Ferrets were trained to lick water from a spout during the presentation of a variable number of reference sounds (1–7) and learned by aversive conditioning to refrain from licking following the presentation of single target sounds, which came at the end of a sequence of reference sounds. As mentioned above, during their training, the ferrets learned a general or “cognitive” version of the tone detection and two-tone discrimination tasks, and reached a stable behavioral performance level in which they could perform equally well on *any* target frequencies chosen during the experiment (target frequencies were randomly chosen from a range of 125–8000 Hz). Ferrets were trained twice a day (50–100 trials/session), five days/week. Initial training on the tone detection task took 2–3 weeks for the ferrets to reach criterion (discrimination ratio >0.65). Subsequent task variations took an additional 1–2 weeks for the ferrets to learn. Some additional training was required to train the animals to switch easily between tasks. Thus, initial training to criterion in the spectral tone detection and discrimination task took about 6 weeks for each ferret. This initial training was conducted in a testing box in which the animals could move freely. After initial training, the animal received a surgical headpost implant that allowed the head to be stably positioned. After recovery from surgery, the ferrets were retrained on the task while restrained in a

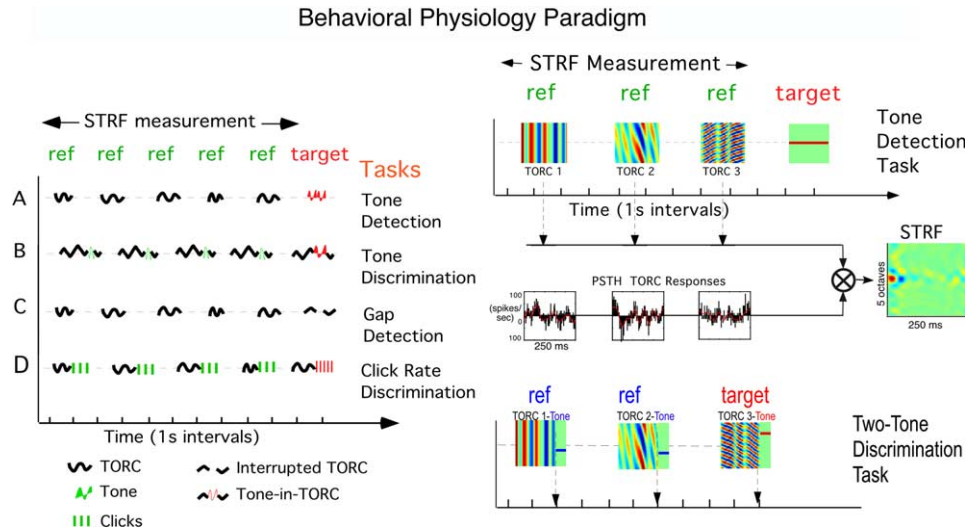


Fig. 1. Design of experimental stimulus presentations in conditioned avoidance tasks. (Upper right) On a given trial during a behavioral session, a random number of TORCs (1–6 reference signals) is followed by a target tone. The panels illustrate spectrograms of three such TORCs and of the following target. Responses to each TORC are collected in PSTH histograms that are cross-correlated with the TORC spectrograms to estimate the STRF. Although the animal behaves in anticipation of the target, all spike measurements to derive the STRF are made during the presentation of the reference TORCs. (Lower right) Similar design for a two-tone discrimination task in which the ferret is presented with a random number of TORC-tone combinations (1–6 reference signals in which the reference tone is fixed in frequency) followed by a target TORC-tone combination (in which the tone component changes to a different frequency than that of the reference tone). (Left) Schematic of various possible experimental paradigms, including (A) tone detection, (B) two-tone discrimination, (C) gap detection, and (D) click rate discrimination. All follow the same basic design. The reference signals are (or include) TORCs used to measure the STRF. The target varies from one experiment to another.

cylindrical, horizontal holder, with the head fixed in place.

## 2.2. Stimuli and STRF measurements

In all tasks, reference stimuli were chosen from a set of 30 different TORCs (for a detailed discussion of TORCs, and the use of TORC responses to characterize neuronal STRFs using reverse correlation techniques see Klein et al., 2000; Depireux et al., 2001; Miller et al., 2002a; Escabi and Read, 2003). The amplitude of tone stimuli, and TORC stimuli for all subsequent STRF measurements at a given recording site was set at 5 dB below best amplitude at best frequency – measured during initial characterization of multiunit response properties during physiological recording. For subsequent behavioral and control studies conducted while recording from this site, stimuli were 1.25 s in duration and consisted of TORCs or TORC-tone combinations, with intensity typically fixed at a value within the range 65–75 dB SPL. All passive STRF measurements used TORC stimuli that were 3 s in duration. The STRF of an isolated unit was first measured while the animal was in a pre-behavioral, quiescent state, in which there was *no* waterflow through the waterspout and *no* target was presented. This was followed by an STRF measurement made while the animal performed the detection or discrimination task, ending with an STRF measurement in a post-behavioral quiescent state.

An essential feature of our method for quantifying changes in the STRF is that we have focused on changes in normalized STRF shape rather than on changes in overall gain. An illustration of the changes in shape between quiescent and active STRFs of a single unit is given in Fig. 2, which also indicates how they were quantified. In this unit, when the tonal target was placed near an excitatory region of the STRF (marked by the arrow in the middle panel) it created a new excitatory extension of the original region. To quantify this change, we independently normalized the passive and behavior STRFs by the Euclidean norm. We computed the difference between the normalized behavioral and quiescent STRFs ( $\text{STRF}_{\text{diff}}$  in Fig. 2). We then extracted two measures from the  $\text{STRF}_{\text{diff}}$ : a *local* maximum difference within  $\pm 0.25$  octaves around the frequency of the target ( $\Delta A_{\text{local}}$  denoted by a black asterisk), and a *global* maximum difference ( $\Delta A_{\text{global}}$ ). In subsequent figures the  $\text{STRF}_{\text{diff}}$  panels will be replaced by a quiescent post-behavior STRF.

## 2.3. Physiological recording

Experiments were conducted in a double-walled sound attenuation chamber. Small, sterile craniotomies (<1 mm in diameter) were made over primary auditory cortex prior to recording sessions, each of which lasted 6–8 h. Responses were recorded with tungsten microelectrodes (3–8 M $\Omega$ ) and then stored, filtered and spike-sorted offline using custom software. A typical recording yielded



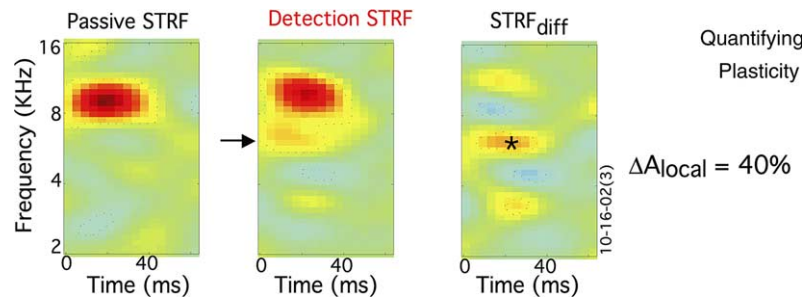


Fig. 2. Comparison of a pre-behavior, quiescent STRF (left panel) and a behavioral STRF (middle panel). Each panel depicts an STRF with a color scale, representing increased (red) to suppressed (blue) firing about the (green) mean. The STRF in each panel is normalized. The dashed contours depict the regions with statistically significant fluctuations (level =  $\sigma$  from the mean). All excitatory (red) and inhibitory (blue) features of the STRF discussed in subsequent figures are statistically significant by this measure. The black arrow indicates the frequency of the target tone during the detection task. The difference between the normalized quiescent and detection STRF is shown in the right panel (STRF<sub>diff</sub>). The asterisk marks the location of maximal change.

1–4 simultaneously active single units. Physiological verification of recording sites in A1 was based on the presence of distinctive A1 physiological characteristics (e.g., latency, tuning) and on the position of the neural recording relative to the cortical tonotopic map in A1 and to surface landmarks (Kowalski et al., 1995, 1996a,b). During physiological recording, computer-generated stimuli were delivered through inserted earphones that were calibrated in situ at the beginning of each experiment.

#### 2.4. STRF lability and stability in naïve and non-behaving animals

In order to assess the stability of our STRFs in the absence of any behavioral tasks, we measured STRF pairs in completely naïve animals that were untrained except for an initial habituation to the head-restraint holder. For the control “behavior” STRF, the naïve animals were simply exposed to the regular TORC references and target tone, but without the presence of training, water reward or the aversive shock. This control “behavior” STRF from the naïve animal was then compared to the pre-control quiescent STRF measured earlier from the same neuron. About 50% of the cortical STRFs remained unchanged, and the distribution of the cells with STRF changes was approximately symmetrical (see Fig. 5(a) in Fritz et al. (2003a)) with the “random” scatter off-the-midline presumably reflecting STRF changes due to uncontrolled sources of error arising from animal movement or other task-independent state changes between the two tests. A similar symmetrical distribution of  $\Delta A_{\text{local}}$  was also found in data pooled from trained animals when they were tested with the paradigm as in Fig. 1, but were simply quietly listening to the sounds without performing one of the trained behavioral tasks (see Fig. 5(b) in Fritz et al. (2003a)). These negative results in the naïve and the non-behaving trained animals, argue against the possibility that STRF

changes in the detection task are the result of an automatic auditory “oddball effect” (Ulanovsky et al., 2003), where the tone plays the role of low probability narrow-band “oddball” ( $\sim 25\%$  likelihood in our behavioral procedure) in relation to the broadband background of TORCs. However, these results also indicate that there is a subpopulation of A1 neurons that appear to show intrinsic STRF response variability, and spontaneous changes in STRF shape which cannot be simply explained as behavioral in origin (Elhilali et al., 2005). Such intrinsic STRF population variability is symmetrical in its  $\Delta A_{\text{local}}$  distribution, whereas in contrast, the  $\Delta A_{\text{local}}$  distribution is clearly asymmetrical for the behavioral conditions (see Fig. 5(c) in Fritz et al. (2003a)).

Although there have been recent valuable studies of receptive field stability in the awake animal (Galvan et al., 2001, 2002), two recent studies have also demonstrated instability in receptive field tuning during conditions of sleep (Edeline et al., 2001) and over a seven-day period under conditions of ketamine anesthesia (Kisley and Gerstein, 2001). In the latter case, specific, associatively induced receptive field plasticity could nevertheless still be observed. These studies, though not conducted in the awake animal, suggest the possible presence of significant “spontaneous” changes in the FRCs (frequency response curves) in recordings from some labile A1 multineurons in passive, behaviorally quiescent conditions. In contrast, tuning of local field potentials (LFPs) in A1 has been reported to be highly stable (random daily variation in frequency tuning of  $\sim 0.2$  octave) in the waking state over a period of 2–4 weeks (Galvan et al., 2001) in chronic recording in the awake guinea pig. However, it is not clear from this LFP study, how much variability might be occurring at the single neuron level (which might be masked by smoothing associated with the broad multineuronal pooling which occurs in LFP measurements). In our recordings from single units in ferret A1, we find that the degree of

spontaneous STRF variation differs considerably from cell to cell – some show variability while other STRFs (at the stable end of the spectrum) under quiescent (non-behavior) conditions, appear very stable and reproducible in multiple measurements from the same neuron over many hours (Elhilali et al., 2005). Following the induction of specific receptive field plasticity by classical conditioning, LFPs went into a new “quasi-stable” state, in which they retained and consolidated the plastic changes in their receptive field tuning (Galvan et al., 2002). In agreement with the latter studies, we will see below that significant task-related plastic changes in STRFs are clearly visible above the “noise” of these spontaneous receptive field variations.

### 3. STRF changes in tone detection task

In the tone detection task, the ferret identifies the presence of a tone against a background of TORCs. This may be thought of as a tone detection task, or alternatively as a discrimination task in which the ferret discriminates between tones (narrow-band) and broadband rippled noise (the TORCs). In either case, the ferret must attend to the appearance of a narrow-band tonal stimulus (which is fixed in frequency during each behavioral session) in order to avoid shock. Examples of the measured STRF changes found in tone detection are illustrated and quantified in Fig. 3, indicating that the target can enhance or even induce an excitatory field, or reduce an inhibitory field in the STRF.

The most common change in an STRF observed during this task was “facilitation” at the target frequency as a result of either an enhancement of its excitatory field, or a weakening of the inhibitory sidebands. Fig. 3 illustrates examples of each of these kinds of changes in single-unit recordings from A1. Placing the target at the excitatory region of an STRF resulted in its enhancement (Fig. 3(a)). The opposite usually occurred when the target frequency coincided with STRF inhibitory sidebands, i.e., it caused a reduction of the strength of the inhibition as illustrated in Fig. 3(b). In about half of all cases, STRF changes were local, restricted to the region of the target frequency. By contrast, in other cases, the changes were global, for example, sometimes all inhibitory regions of the broad STRF were significantly reduced during the task, and the maximum change occurred away from the target tone frequency (see Fig. 2(d) in Fritz et al. (2003a)). Nevertheless, global STRF change was usually also accompanied by a local facilitation. In many units (such as in Fig. 3(a)), post-behavioral quiescent STRFs were also measured, and in a majority of these cells the STRFs rapidly returned to their original pre-behavioral shape.

Overall, about 72% of cortical cells showed a significant STRF change while the animal was engaged in per-

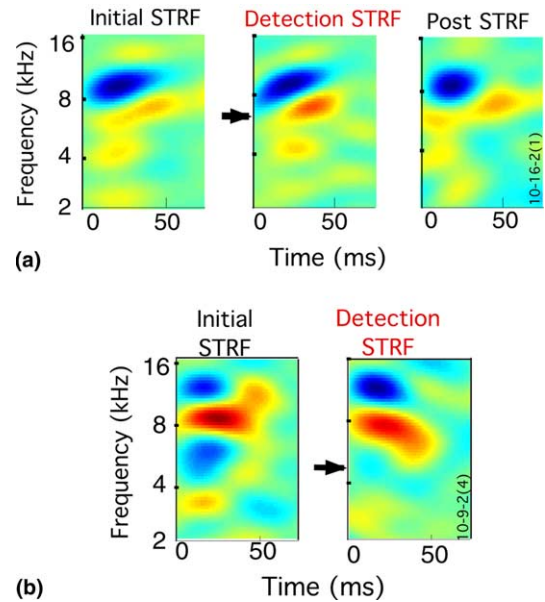


Fig. 3. Facilitative STRF plasticity in A1. STRFs from two single-units in A1 illustrate typical changes observed during performance of the detection task. (a) Pre-behavior STRF (left panel). Localized enhancement of an excitatory region in the STRF at the target frequency during behavior (middle panel). The post-behavior quiescent STRF (right panel) reverted immediately to a receptive field very close to its original shape.  $\Delta A_{\text{local}} = 37\%$ ,  $\Delta A_{\text{global}} = 42\%$ . The maximum change was nearly coincident with the target frequency. (b) Pre-behavior STRF (left panel). Local decrease (near elimination) of lower inhibitory sideband at the target frequency in the detection STRF.  $\Delta A_{\text{local}} = 40\%$ ,  $\Delta A_{\text{global}} = 40\%$  (coincident maxima at target frequency).

formance of a detection task (see Fritz et al., 2003a for details). In 80% of these cells, a *facilitative* or positive STRF change occurred, i.e., an enhancement of the excitatory fields or a reduction of the inhibitory sidebands during tone detection task, averaging about +46% (median = +45%) of the maximum amplitude in the STRF. Furthermore, in about half of these units, the maximum change in the STRF occurred near the frequency of the target (i.e., locations where  $\Delta A_{\text{local}}$ , and  $\Delta A_{\text{global}}$  coincided). Additional evidence for a correlation of neuronal plasticity and behavior was provided by comparing the relationship between behavioral performance and the pattern of STRF changes (see Figs. 2 and 5 in Fritz et al. (2003a)). These overall effects of tone detection on the STRF are illustrated in cartoon form in Fig. 4.

#### 3.1. Long-lasting, cumulative STRF plasticity

In some experiments, STRFs were measured in a series of tone-detection tasks with different target frequencies, which were chosen in order to probe different excitatory and inhibitory regions of the same STRF. Remarkably, in a number of cases, the effects of performing successive tone-detection tasks were imprinted on the STRF for long durations of time, well after the

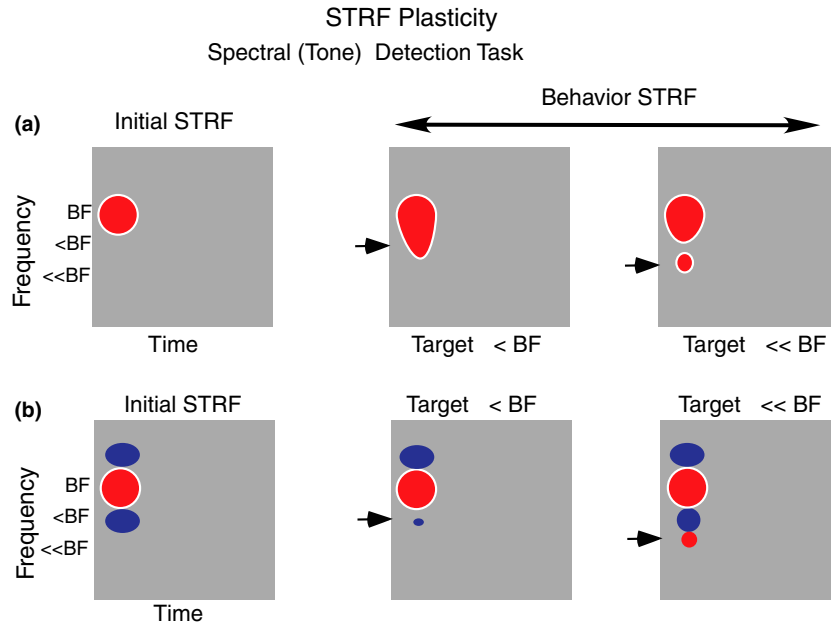


Fig. 4. Idealized cartoon illustrating typical changes in the shape of the cortical STRF during performance of a detection task. In the upper panel, the initial STRF has one excitatory field and no inhibitory side-fields. During detect behavior, the excitatory field may be elongated if the target frequency is placed nearby. If the target frequency is placed even further away from the excitatory field (BF of the neuron), then a second excitatory field may form. In the lower panel, the initial STRF has one excitatory field and flanking inhibitory fields. During detect behavior, if the target frequency is chosen to coincide with the center of one of the inhibitory fields, then it will reduce the size of this field. If the target frequency is placed to the far side of an inhibitory field, then a second excitatory field may form.

tasks were completed. About half of all cells encountered in our experiments exhibited a change that persisted after one or more tasks. Fig. 5 illustrates a remarkable example of a recording series, in which there was a cumulative, persistent, build-up of sensory memory following several behavioral tasks (detection tasks with different targets) many hours earlier.

Persistence of receptive field changes following cessation of a behavioral task or conditioning, represents a form of sensory memory (Fuster, 1995; Weinberger, 2004). Different forms of persistent neuronal activity following rapid plasticity have been demonstrated before in the primary motor cortex (Li et al., 2001) in the context of motor adaptation and also may be present in the somato-

sensory cortex (Harris et al., 2002; Romo and Salinas, 2003). Although the design of our experiment did not allow us to follow these persistent effects for more than 5–6 h, we conjecture that the persistent changes we have observed may represent the first of a series of receptive field modulations that underlie long-term changes in neuronal frequency tuning and may also lead to the observed changes in the whole tonotopic map.

#### 4. STRF changes with two-tone discrimination tasks

When an animal is *discriminating* between the frequencies of two tones (as opposed to simply detecting

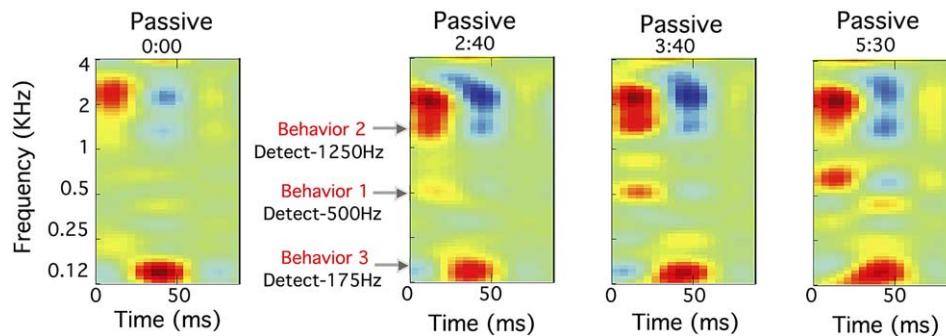


Fig. 5. Quiescent pre-behavioral STRF measured before (left panel), and post-behavioral STRFs (remaining panels) derived after a series of three detection tasks with different targets as indicated by the gray arrows. The STRF changes induced by the behavioral tasks persist, to varying extents, for several hours afterwards (elapsed post-behavior time indicated above the STRF panels).

the presence of one tone as above), the STRFs could change adaptively so as to improve performance by enhancing “foreground” over “background” by facilitating the STRF at the target (foreground) frequency while suppressing it at the reference (background) frequency. This hypothesis is consistent with earlier results obtained by Edeline and Weinberger (1993). In theory, another equally viable strategy to achieve discrimination might be to enhance “background” while suppressing “foreground” stimuli, since the key point for the nervous system is to enhance the contrast between the stimuli. In order to investigate this question, ferrets were trained on a tone discrimination task, which was a modified version of the earlier detection task except that now, each reference TORC was immediately followed by a *reference tone* (distinct from the target tone) (see Fig. 1). The animal learned to attend to the reference tone frequency and respond only when the frequency changed, which occurred when the target tone was presented. Fig. 6 illustrates the changes observed in one case. The cell was tuned to 250 and 500 Hz. When the reference and target tones were placed at these two frequencies, respectively, the reference tone suppressed the excitatory field at 250 Hz, leaving 500 Hz as the only excitatory frequency. The cell recovered somewhat after the behavioral test, but the same suppression of the 250 Hz excitatory field occurred when the test was repeated with a 1000 Hz target. Subsequent studies have shown that this pattern of specific suppression of STRFs at the reference frequency is prevalent during discrimination (Fritz et al., 2003b, 2004b). Interestingly, in overall amplitude and in spectral selectivity, the average STRF change (at the reference frequency) during discrimination appears to be exactly the opposite of the average STRF change (at

the target frequency) during detection and may be operating by a common mechanism (with a sign reversal). At the population level, we have also observed an overall enhancement of the STRF at the target frequency in the discrimination task. We note that these results from the discrimination task are consistent with receptive field changes which would be predicted as a result of an auditory “oddball effect” (Ulanovsky et al., 2003), where the reference tone plays the role of high probability standard and the target tone plays the role of low probability “oddball” (~25% likelihood in our procedure). Hence we performed a set of control studies in a naïve, untrained ferret, in which we compared an initial “quiescent” STRF, computed from neural responses to TORCs, to a subsequent “discrimination control” STRF, computed from responses in the same neuron to our “discrimination-task” (TORC-tone) stimuli (also in a non-behavioral, quiescent condition). The results of these control experiments indicate that the STRF plasticity observed in the behavioral condition in the discrimination task cannot be explained by a purely stimulus driven “oddball effect” or by habituation to the repeated reference tone. These overall effects of two tone discrimination on the STRF are illustrated in cartoon form in Fig. 7.

#### 4.1. Task nomenclature – “detection” vs. “discrimination”

Although we think that the terminology we have chosen to describe the acoustic tasks used in this study is appropriate, it is also important to acknowledge other perspectives. For instance, it may be argued that both the two behavioral paradigms described in this study are, in a sense, discrimination tasks. After all, in the “detection” task ( $T_1, T_2, T_3, \dots, A$ ), the ferret must

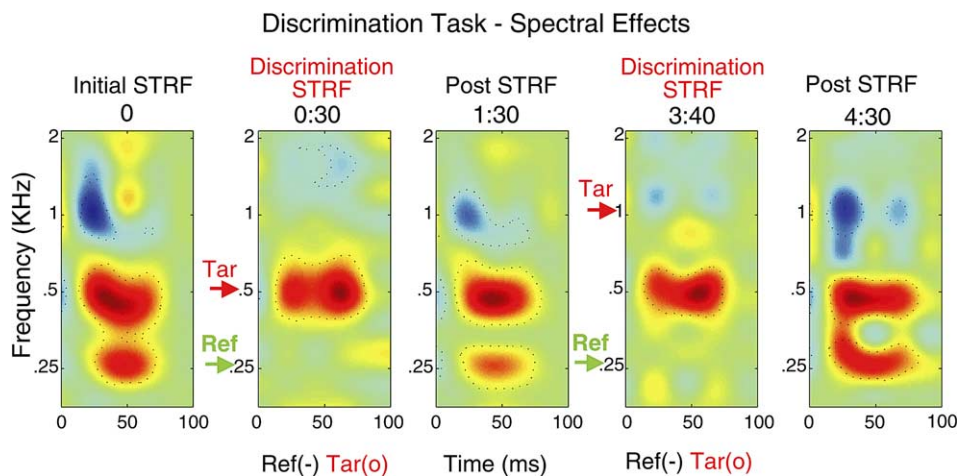


Fig. 6. Three quiescent STRFs interleaved with two sequential two-tone discrimination tasks, all measured during recordings from the same neuron. The times at which STRFs were measured relative to the beginning of recording are shown on top of each panel. The arrows mark the reference (green) and target (red) frequencies used. Note the disappearance of the excitatory area in the near 250 Hz in the STRFs measured during the discrimination tasks.



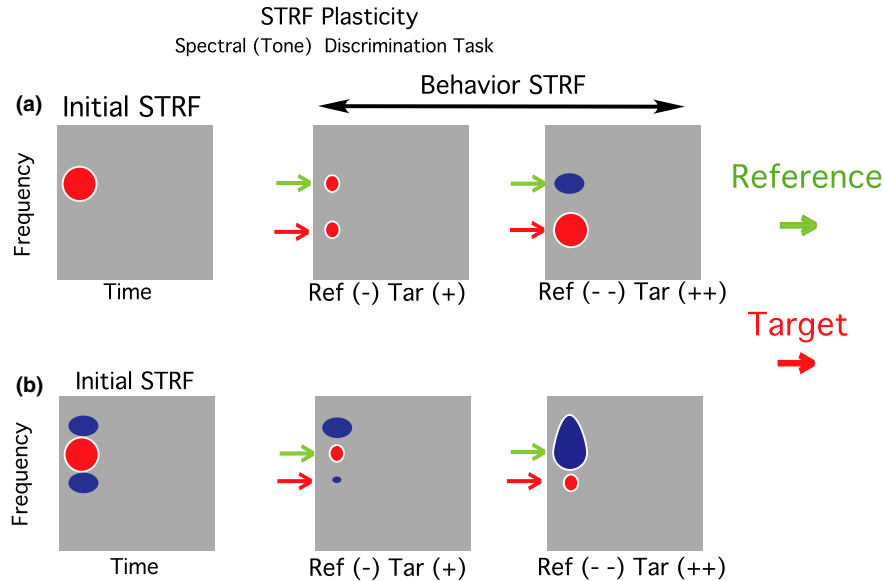


Fig. 7. Idealized cartoon illustrating typical changes in the shape of the cortical STRF during performance of a two-tone discrimination task. Overall, there are enhanced responses to the target frequency, similar to what is seen in the tone detection task. In contrast, there are reduced responses at the reference frequency. In the upper panel, the initial STRF has one excitatory field and no inhibitory side-fields. During tone discrimination behavior, a new excitatory field may be created if the target frequency is placed far away from the BF. If the reference frequency is placed near the center of the excitatory field (BF of the neuron), then the initial excitatory field is reduced or in some cases, an inhibitory field may appear. In the lower panel, the initial STRF has one excitatory field and flanking inhibitory fields. During discrimination behavior, if the target frequency is chosen to coincide with the center of one of the inhibitory fields, then it will reduce the inhibition, or even, in some cases, an excitatory field may appear. If the reference frequency is placed at the center of an excitatory field, then the excitatory field will be suppressed or an inhibitory field may form.

discriminate a pure tone stimulus (A) from a sequence of broadband noise stimuli ( $T_1$ – $T_n$ ). Detection, in this view, is a special case of discrimination. Conversely, one might argue that the “frequency discrimination” task ( $T_1A$ ,  $T_2A$ ,  $T_3A$ , ...,  $T_nB$ ) is in fact is a detection task, inasmuch as the ferret can perform the task by detecting a change in the tonal frequency (from A to B) in a sequence of TORC-tone stimuli. However, in order to detect the change in tone frequency, clearly the ferret must discriminate between the two tones. Each perspective is valuable, but we emphasize that whatever terminology is chosen, it is clear that the two tasks can be distinguished from one another, not only by the complexity of the stimuli, but also by the differing salient cues to which the animal must attend in order to perform the tasks correctly. We propose that in the first “detect” task, the ferret is vigilant for the appearance of any narrow-band sound at any frequency against a background of modulated broadband sounds, whereas in the second two-tone “frequency discrimination” task, the ferret attends to the change in the frequency of the target tone relative to the frequency of the reference tone, and thus must monitor the frequencies of both reference and target tones. In the “frequency discrimination” task, unlike the “detection” task, the ferret need not attend to the class of TORCs since they carry no direct task-relevant information.

## 5. STRF changes with temporal tasks

Several recent papers have shown that temporal plasticity can be induced in A1 by pairing electrical stimulation of cholinergic basal forebrain with tone pips at a high temporal rate (Kilgard and Merzenich, 1998), or by auditory perceptual learning (Beitel et al., 2003; Bao et al., 2004). We have only recently begun to study the STRF changes in A1 that may result from performance on temporal tasks using our behavioral paradigm (Fritz et al., 2005). Ferrets were trained on a gap detection task, in which they learned to detect the presence of a short gap in TORCs, and also on a click-rate discrimination task in which they learned to discriminate between the rate of clicks in TORC-click combinations (see Fig. 1). Unlike the spectral tasks (tone detection and two-tone frequency discrimination described above) in which the ferret attended to one or more spectral frequencies, in both the temporal tasks, the ferret needed to attend to the temporal dynamics of the sounds irrespective of frequency. We conjectured that both temporal tasks should yield faster STRF dynamics, as evidenced, for example, by shortening latencies or by a concomitant sharpening of the outlines of its excitatory and inhibitory fields along the temporal axis. The measured STRF changes in one unit is illustrated in Fig. 8 showing the changes in the sharpness of the STRF fields that implies faster temporal transitions and hence faster dynamics. We have

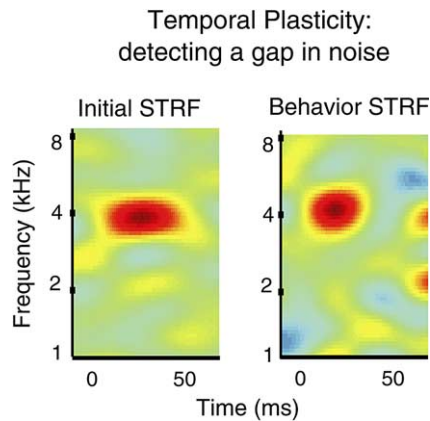


Fig. 8. Example of STRF changes during a temporal gap detection task showing increasing contrast (sharper delineation) in the excitatory field of the STRF during behavior.

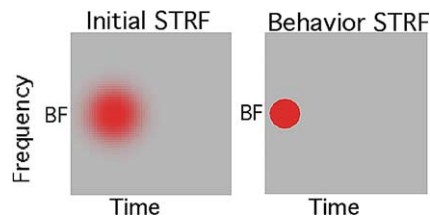


Fig. 9. Idealized cartoon illustrating typical changes in the shape of the cortical STRF during performance of a temporal task (gap detection or click-rate discrimination). Overall, the excitatory field becomes more compact and shifts to shorter latencies.

recorded from over 40 neurons performing temporal tasks and find consistent changes summarized in Fig. 9. These data suggest that it may be possible to influence both the temporal, as well as the spectral dimensions of the STRF, depending upon the behavioral task, and the task-salient stimuli. We are currently engaged in further research to explore this question.

## 6. Responses in prefrontal cortex during performance of auditory tasks

We have recently initiated a new set of studies to examine the possible role of top-down influences in mediating task-related changes in A1 (Fritz et al., 2004c). The PFC is known to be involved in working memory, encoding of task-relevant features, task monitoring, task switching, executive control and goal-directed behavior (Miller and Cohen, 2001; Miller et al., 2002b). It may also play a role in top-down attentional modulation of salient sensory inputs, and their linkage to a repertoire of actions. We asked whether top-down inputs from prefrontal cortex (PFC) to A1 might contribute to task-related plasticity in the primary auditory cortex of the ferret as the animal focused attention on salient acoustic

cues, and switched attention between targets in different auditory tasks.

In preliminary physiology experiments, we have begun recording from premotor and PFC neurons during auditory task performance. These neurophysiological studies on PFC have been guided by neuroanatomical studies on the ferret conducted by our colleague Dr. A. Duque (Yale University Medical School) who has defined the ferret PFC as the recipient of projections from the medial-dorsal nucleus of the thalamus (Duque and Goldman-Rakic, 2003). We have recorded a number of cells in the premotor and prefrontal cortices of the ferret. Examples of two types of neurons are shown in Figs. 10 and 11.

These results suggest that some neurons in premotor-PFC encode task-related motor output and/or differentially fire to salient, task-relevant target stimuli. Such multiplexing of behaviorally relevant inputs and motor outputs may be a characteristic feature of PFC.

A number of polysynaptic pathways connect the PFC and the auditory cortex in the ferret. Dr. Duque and Dr. J. Bizley (Oxford University) have also recently found intriguing evidence for direct (though sparse) projections between PFC and auditory cortex (Fritz et al., 2004a). Either direct or indirect pathways could potentially mediate attentional influences from PFC on filter properties of A1 neurons (a recent study by Barbas et al., 2005 indicates direct projections from PFC to inhibitory auditory cortical neurons in the primate). Further studies are needed to discover whether the PFC is necessary for the induction of task-related plasticity. To elucidate the role of PFC in task-related plasticity in A1, we are planning lesion studies to ascertain whether (a) the ferrets can still perform these tasks in the absence of PFC, and if so, (b) whether A1 task-related plasticity is dependent upon the PFC.

## 7. Discussion

The experiments described here suggest that *rapid auditory task-related plasticity* is an ongoing process that occurs as the animal switches between different tasks and dynamically adapts auditory cortical STRFs in response to changing acoustic demands. Rapid plasticity modifies STRF shapes in a manner consistent with enhancing the behavioral performance of the animal, monitored through externally supplied feedback signals. The specific form of the STRF change is dictated by the salient acoustic cues of the signals in the behavioral task, and is modulated by general influences reflecting the animal's state of arousal, attention, motor preparation and reward expectation. Such plasticity occurs in the majority of cells in A1 in trained animals engaged in our behavioral paradigms – this is similar to the percentage of labile cells expressing rapid receptive field plasticity

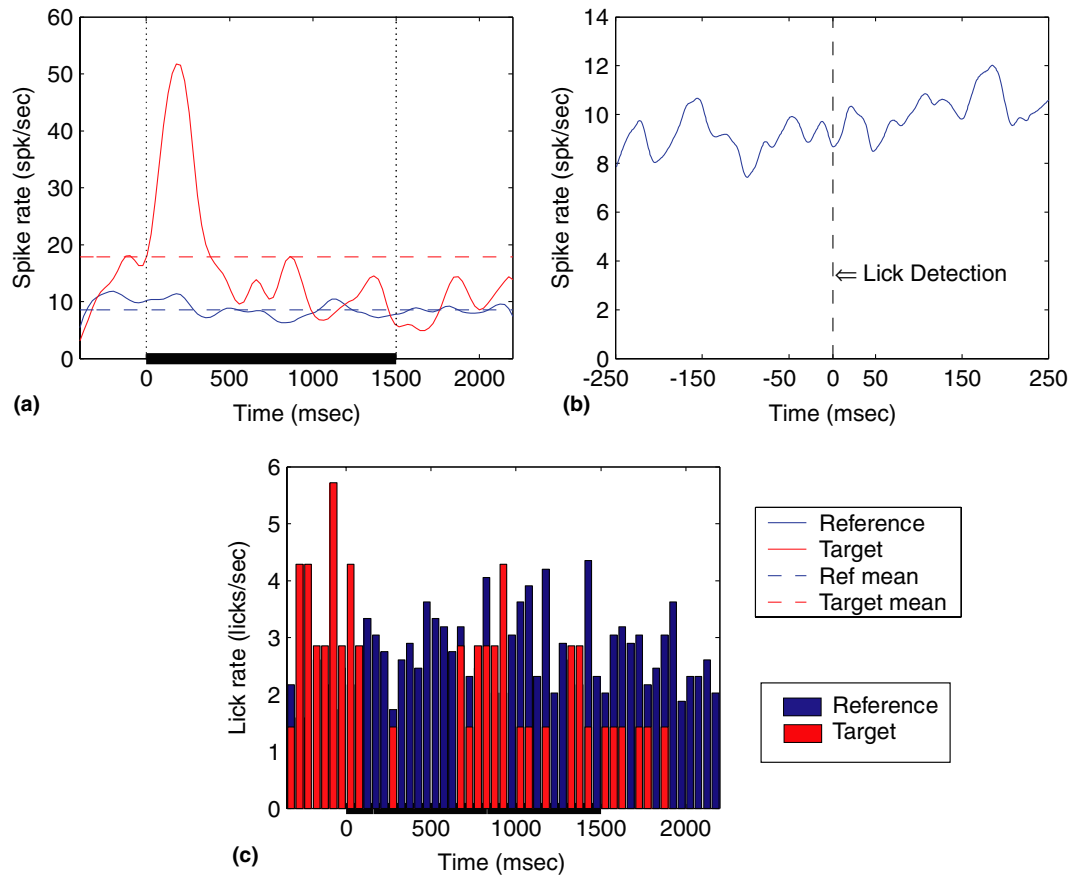


Fig. 10. Recording from prefrontal cortex while the ferret performed a tone-detection task. (a) Firing rate during 1500 ms stimulus period for TORC reference stimuli (blue line) and average (dashed blue line) compared to enhanced response to the target tone (beginning at onset of the tone stimulus) (red line) and average (dashed red line). When the same tone was presented to the animal in a passive condition, there was absolutely no neural response or change in firing rate (data not shown in this figure). (b) Lick-related neural activity – every time the ferret licked the water from the spout, its tongue interrupted an infrared photobeam. Neural activity was plotted relative to lick onset. In this neuron, there was no apparent correlation of firing rate with licking. (c) The ferret licked continuously before, during and after the “safe”reference TORC stimuli (lick rate = blue bars) but stopped licking when the “warning”target tone stimulus was presented (lick rate = red bars).

found in other A1 studies (although the proportion of behaviorally labile cells may be much greater in higher auditory areas (Diamond and Weinberger, 1984)). Recent studies have also demonstrated the presence of neuronal responses in A1 which encode not only the acoustic features of the stimulus, but also may reflect the behavioral state of the animal in relation to the dimensions of expectation, attention, relevant non-auditory sensory cues, motor response and reward (Yin et al., 2001, 2004; Fu et al., 2003; Durif et al., 2003; Brosch et al., 2004).

Achieving goals in changing environments requires adaptive behavior. Since changes to organisms occur continuously in a dynamic environment, it would obviously be useful adaptively, if animals continuously modulated their nervous systems on-line (Mountcastle, 1995; Ulanovsky et al., 2004). As indicated in the introduction, our results are consistent with previous studies of A1 cortical receptive field plasticity that have shown similar rapidity of onset (Weinberger and Diamond,

1987; Edeline et al., 1993; Edeline, 1999; Ma and Suga, 2003).

Our findings on attentionally modulated task-related plasticity suggest that some forms of cortical receptive field plasticity may occur on a rapid time-scale. How may these results be integrated with studies demonstrating cortical plasticity over much longer time-scales? There may be multiple forms of plasticity, each with its own timecourse, which could explain these multiple time-scales. An alternative conceptual view that harmoniously relates the fast and slow time-scales of plasticity is that of an ongoing series of rapid-onset adaptive processes (seconds to a few minutes), with persistent but relatively short-lived changes that closely reflect new, changing behavioral contexts. However, if reinforced by repeated or consistent stimulation (e.g., exposure to the same target over a period of days and months), these rapid changes may accumulate and become more permanent, giving rise eventually to the widely observed long-term plastic effects. In this one-process view, *rapid-*

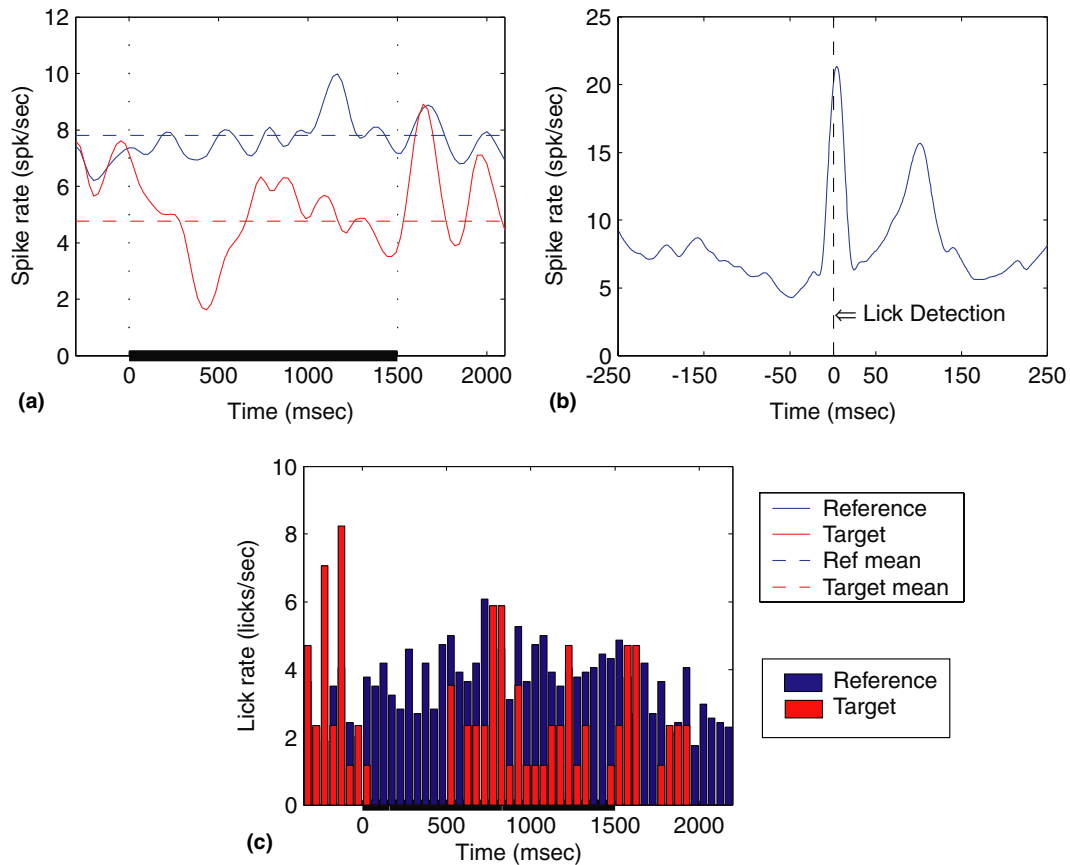


Fig. 11. Recording from prefrontal cortex while the ferret performed a tone-detection task. (a) Firing rate during 1500 ms stimulus period for TORC reference stimuli (blue line) and average (dashed blue line) compared to inhibited response to the target tone (beginning at onset of the tone stimulus) (red line) and average (dashed red line). When the same tone was presented to the animal in a passive condition, there was absolutely no neural response or change in firing rate (data not shown in this figure). (b) Lick-related neural activity—every time the ferret licked the water from the spout, its tongue interrupted an infrared photobeam. Neural activity was plotted relative to lick onset. In this neuron, there was a clear correlation of firing rate with licking. (c) The ferret licked continuously before, during and after the “safe” reference TORC stimuli (lick rate = blue bars) but stopped licking when the “warning” target tone stimulus was presented (lick rate = red bars).

onset plasticity is a precursor process that contributes to long-term changes. We emphasize that such a one-process view, or single-trace view of memory, is simply one hypothesis among many. An important alternate hypothesis, for which there is substantial supporting evidence, is that there are at least two types of cortical plasticity with different time-courses that may reflect different processes (Weinberger, 2003).

However, it is still important to emphasize that many of the cortical changes we observe have short life-times, and that STRFs often return to their original shapes soon after the behavior is over. Since most cortical sensory neurons participate in multiple behavioral contexts, it is likely that their receptive field properties are continuously being modified, against the basic scaffolding of the synaptic inputs, as the animal enters new acoustic environments and initiates new tasks. In a sense, the STRF gives “linear” snapshots of a non-linear set of adaptive transformations of the receptive field. We suggest that plasticity is part of an ongoing process that is

constantly adapting and re-organizing cortical receptive fields to meet the challenges of an ever-changing environment and new behavioral demands (Edeline, 2003).

### 7.1. Conceptual framework

In light of previous studies, and the results of our current research, we propose three linked hypotheses that place rapid task-related plasticity in the interplay of the sensory and motor systems in behavior. The first hypothesis is strongly supported by our data:

- (1) Some A1 cortical cells undergo rapid, short-term, context-dependent, adaptive changes of their receptive field properties, when an animal performs an auditory task that has specific behavioral demands and stimulus feature salience (Diamond and Weinberger, 1989; Fritz et al., 2003a). Not all cortical neurons display plasticity, which may represent a cortical compromise in the trade-off



between stability and adaptability of sensory information processing (Elhilali et al., 2005).

In this review, we have presented research designed to test the first hypothesis (our current experiments do not address the other hypotheses, which are offered as a guide to future studies). Questions arising from the following two hypotheses are the topic of ongoing research in our laboratory.

(2) Such rapid task-related plasticity is adaptive and is a part of an ongoing, dynamic process that underlies normal, active listening.

In this view, plasticity plays a functional role by causing a selective re-setting of the cortical circuitry. This tweaking of synaptic input strengths leads to changes in the receptive field properties of cortical neurons, which may enable the animal to achieve enhanced performance of the auditory task. The spectrotemporal receptive field (or STRF) in A1 sits at the focal juncture of this process, depicted by the highly schematic diagram in Fig. 12. In a trained and well-behaving animal which engages in a previously learned task, the STRF swiftly adapts so as to enhance behavioral performance, monitored through externally supplied (reward or aversive) feedback signals.

(3) Rapid task-related plasticity operates on the framework of a pre-existing bidirectional sensory-to-motor map.

In our behavioral paradigm, the STRF receives *target/reference* input cues, and generates corresponding *sensory representations* that are ultimately associated with, or mapped to motor behavior. This mapping, which defines a specific learnt task or behavioral context, connects a set of stimuli and their associated sensory representations with a set of motor acts that enhance the future probability of reward or decrease the likelihood

of punishment (Romo and Salinas, 2001; Blake et al., 2002). Such a learned sensorimotor mapping can be a highly specific (1–1), or in the case of the tasks we have used in our studies, can be a many–one mapping, in which any member of a broad class of stimuli can elicit the same motor response. These tasks are “cognitive” in the sense that the animal is trained on the task with a broad range of different stimulus values, generalizes, and eventually learns the “rule” or the basic structure of the same-different task, independent of stimulus value. Although the ferret can respond appropriately to all stimuli, the specific form of task related plasticity depends upon the currently relevant stimuli or salient features as well as the structure of the learned task.

On a highly speculative note, we conjecture that a top–down link between motor and sensory systems may constitute a very special type of behavior – a form of “invisible”, or perhaps more correctly, of “internal” behavior, in which the motor system does *not* direct motor output resulting in an externally visible act, but rather influences a change in “perceptual filters”, thus selectively modulating or tagging the most salient incoming sensory information for future action (Leopold and Logothetis, 1999; Maravita and Iriki, 2004).

In the case of the tone detection task, ferrets were trained to detect the presence of *any* pure tone in the context of broadband noise, and hence learned a general sensorimotor schema or mapping (which could be summarized as a rule: if you hear *any* pure tone, stop licking the waterspout for 2s). In a particular behavioral session, where only one tonal frequency was used, the ferret performed the task and focused its attention on the salient frequency, leading to a reshaping of A1 receptive fields to enhance response at this frequency. It is important to emphasize that as many as 2/3 of cortical neurons

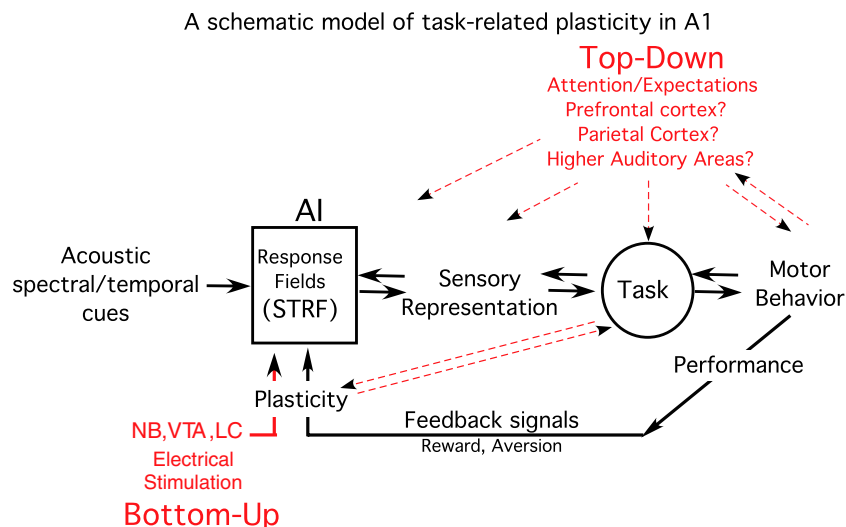


Fig. 12. Schematic diagram of context for rapid STRF plasticity in A1.

in A1 showed such frequency-selective enhancement during tone detection task performance (Fritz et al., 2003a).

The provocative idea has been advanced that perceptual decisions arise from a subtraction between the activities of neurons with opposite sensory preferences (Lafuente and Romo, 2003). This model of decision by neuronal democracy offers a perspective on the ferret's decision to respond at the detection target frequency. Since most neurons in A1 show an enhanced response and/or suppressed inhibition at this frequency, the target frequency may "win" the popular vote in A1. Of course, A1 is not likely to be the only place where such a behavioral decision is made, but the observed STRF changes may play an important role in the evaluation of incoming sensory information and assist in behavioral performance.

What role does attention play in modulating the STRFs in A1? Is attention gating the STRF changes we have described, perhaps by increasing the adaptability of neurons rather than their selectivity? (Boynton, 2004). There has been considerable recent research on attentional effects on response properties of V1 neurons (Crist et al., 2001; Ito and Gilbert, 1999; Li et al., 2004; McAdams and Maunsell, 1999a; Motter, 1993; Reynolds et al., 2000; Roelfsema et al., 1998; Treue, 2001). Although there is evidence that attention may play an important role in modulating responses of A1 STRFs in our behavioral paradigm, we note that our findings cannot be explained by a multiplicative neural model of attention (McAdams and Maunsell, 1999b), nor by models which suggest that attention acts by enhancing effective stimulus strength (Reynolds et al., 2000; Reynolds and Chelazzi, 2004). Both models have received support from research on attentional effects on neural processing in visual cortex but have drawbacks in explaining our data. For instance, in the tone detection task we observe additive effects of acoustic salience (i.e., enhanced response if the target frequency is placed near an excitatory field in the neural STRF, and a suppressed response if the target frequency is placed near an inhibitory field in the STRF). Neither of the two attention models above can explain these results nor explain the neural responses we have observed in the two-tone frequency discrimination task (assuming that the ferret must attend to both reference and target frequencies). As an aside on modulatory mechanisms, recent findings (Wehr and Zador, 2003; Tan et al., 2004) that excitatory and inhibitory tuning curves are quite similar in A1, raise the question of whether the rapid receptive field changes we have observed are the consequence of modulation of the synaptic efficacy of the inhibitory input, the excitatory input, or both.

Recent human imaging studies (Ozaki et al., 2004; Petkov et al., 2004) have shown attentional modula-

tory effects in A1 and also in higher associative areas in auditory cortex. Such techniques have also provided a window into short-term plasticity in the human auditory cortex (Menning et al., 2000; Jancke et al., 2001).

## 7.2. Other forms of adaptive cortical plasticity

Intriguing results from motor and other sensory systems indicate that rapid adaptive task-related plasticity is a general principle of neural processing throughout the brain and may also share some common neural mechanisms with perceptual learning (Ghose, 2004). The STRF plasticity found in our experiments is remarkably similar to the neuronal plasticity resulting from use-related experience observed in saccade-related neurons in the monkey superior colliculus (Dorris et al., 2000), to task-related attentional responses in the primary visual cortex (Crist et al., 2001) and in V4 (Mazer and Gallant, 2003; Yang and Maunsell, 2004) and to the dynamic motor adaptation to an external force field recently described in the monkey primary motor cortex (Gandolfo et al., 2000; Li et al., 2001; for further discussion see Fritz et al., 2003a).

Another interesting comparison is with the adaptive rapid plasticity of body schema observed in higher order parietal cortex in monkeys that had been trained to use a tool (a rake) to retrieve distant objects (Iriki et al., 1996; Iwamura et al., 2000; Maravita and Iriki, 2004) (see Fig. 13). In recordings from bimodal (visual and somatosensory) neurons in the IPS (intraparietal sulcus) of the monkey parietal association cortex, they demonstrated that the visual receptive fields, which were usually closely linked to their associated somatosensory receptive fields, and normally extended as far as the normal reach of the monkey's hand in space, quickly changed in size when the monkey was given a rake to use to gather food. After a few minutes of tool use, the visual receptive fields of neurons in this area extended further to include the entire reach of the rake, and expanded to cover the new accessible space. Thus the tool rapidly became an extension of the hand in both a physical and a perceptual sense. After the monkey retrieved food *without* using the rake for about 3 min, the expanded visual receptive field shrunk back to its original size, even if the monkey kept grasping the tool. In short, these bimodal cells rapidly shifted the spatial boundaries of their receptive fields in accord with the new spatial range of interest to the animals during ongoing behavior. We propose that the changing map of visual salience described in parietal cortex in these monkey experiments, is comparable to the dynamic map of acoustic salience that we have described in our experiments in ferret A1. A recent study has also demonstrated short-term plasticity in S1 during tool use in humans (Schaefer et al., 2004).

### Task-related changes in visual receptive field in monkey parietal cortex during tool use (Iriki et al)

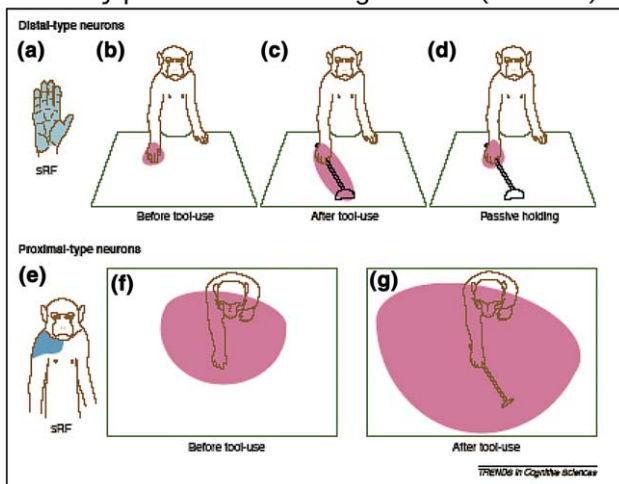


Fig. 13. Changes in bimodal receptive field properties following tool use. The somatosensory receptive fields (sRF) were identified by light touch, passive joint manipulation or active hand use. The visual RF (vRF) was defined as the area in which cellular responses were evoked by visual probes moving towards the sRF. (Top panel) (a) sRF (palmar hand surface) of the distal type bimodal neurons shown on the left, and vRF shown (b) before tool use, (c) immediately after tool use, (d) when passively holding the rake. (Bottom panel) (e) sRF (shoulder) of proximal-type bimodal neurons and their vRF (f) before and (g) immediately after tool use. Adapted from Maravita and Iriki (2004) and used with permission.

### 7.3. Search for the mechanisms of cortical plasticity

What are the candidate neural mechanisms that might underlie such selective, rapid-onset plasticity? Such dynamic changes may be mediated by top-down and/or bottom-up control (Suga and Ma, 2003) over local cortical circuitry, operating by mechanisms such as LTP or LTD to rapidly modulate synaptic efficacy or dynamics (Cruikshank and Weinberger, 1996; Finnerty et al., 1999; Dinse et al., 2003), to unmask silent synapses (Ahissar et al., 1998), by rapid synaptogenesis, alteration of neuronal gain or change in the overall level of excitability (Xiao and Suga, 2002; Butefisch et al., 2000). Neuromodulators such as acetylcholine, dopamine, noradrenaline and serotonin are all influential in mediating plasticity and stimulus coding (Gu, 2002; Manunta and Edeline, 2004; Hurley et al., 2004) through direct as well as indirect projections (Bouret and Sara, 2004). The projection from the basal forebrain cholinergic system may be particularly important in mediating cortical plasticity during learning (Conner et al., 2003). An important arena for such rapid synaptic modulation may be the set of widespread subthreshold horizontal synaptic connections found in sensory and motor neocortex (Das and Gilbert, 1995; Huntley, 1997; Rioult-Pedotti et al., 1998; Laubach et al., 2000) which exhibit plasticity and whose synaptic efficacy has been shown to strengthen in proce-

dural motor learning (Rioult-Pedotti et al., 2000). Once temporarily formed, these rapid changes can be stabilized by slower concurrent mechanisms of long-term synaptic plasticity such as the formation of new functional connections through axonal sprouting, dendritic remodeling, or by long-term induction of changes in transmitter or receptor levels (Sun et al., 2005) and distribution, that take place over longer periods of time (hours and days). Additional studies will be needed to clarify the cellular mechanisms of rapid-onset cortical task-related plasticity, and its role in mediating adaptive changes in brain and behavior.

### Acknowledgments

We thank Alvaro Duque and Jenny Bizley for help with the neuroanatomy of prefrontal cortex, David Klein for computational analysis, Shantanu Ray for assistance with task development and software programming, Henry Heffner for advice and guidance on behavioral training, and Tamar Vardi and Christine Haisfield for help with ferret care and training. We are also grateful for the grant support of NIDCD, NIH.

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