Dynamic, adaptive task-related processing of sound in the auditory and prefrontal cortex

Jonathan Fritz¹, Stephen David¹,³, Bernhard Englitz¹,⁴, Serin Atiani¹,⁵, Diego Elgueda¹, Michael Locastro¹, Pingbo Yin¹, Susanne Radtke-Schuller⁶, Dan Winkowski¹,², Mounya Elhilali⁷, Patrick Kanold¹,², Shihab Shamma¹,⁴

¹ Institute for Systems Research, University of Maryland, USA
² Department of Biology, University of Maryland, USA
³ Oregon Health and Sciences University, Portland, USA
⁴ Ecole Normale Superieure, University of Paris, France
⁵ BRAMS, Montreal Neurological Institute, McGill University, Canada
⁶ Department of Neurobiology, LMU, Munich, Germany
⁷ Department Electrical and Computer Engineering, Johns Hopkins University, Baltimore, USA
Task-related changes in visual receptive field in monkey parietal cortex during tool use (Iriki et al.)
Auditory Attention
Interface of perception and action

- Allows us to rapidly and precisely direct our acoustic search-light towards sounds of interest in our acoustic environment - these shifts of attention can be nearly instantaneous.

- Auditory attention leads to enhanced information processing, behavioral sensitivity and shortened response latency

- Can be top-down (voluntary or task-dependent) or bottom-up (sound-based “pop out” salience)

- Top-down attention is a selection process that focuses cortical processing resources on the most relevant sensory information, in order to maintain goal-directed behavior in the presence of multiple distractions
AUDITORY ATTENTION

- Earliest studies of the neurobiology of auditory attention in the Galambos lab at Walter Reed in the 1950s - enhanced responses of single units in cat AC (Hubel et al. 1959), increased ERPs (Hillyard et al. 1973). Many studies since then - single unit, EEG, MEG and neuroimaging with PET and fMRI

- Auditory attentional effects occur at multiple levels and stages of auditory processing from the cochlea (Delano et al. 2007) to prefrontal cortex. Effects become stronger as you ascend auditory processing hierarchy.

- Auditory spatial attention - shared frontoparietal network with visual spatial attention - enhanced activity when expecting a sound to come from one location - Shomstein and Yantis (2004), Ahveninen et al. (2006), Voisin et al. (2006)

- Auditory feature and object attention - Brechmann and Scheich (2005), Polley et al. (2006), Paloglou et al. (2009)

- Auditory attention in time - Jaramillo and Zador (2009)
Attention-driven plasticity in adult auditory cortex

Plasticity during development has greater magnitude and ease, at a synaptic and cellular level. It may be easier to change wiring because there is no strong pre-existing pattern of connectivity. While in the sensitive period, circuits can be changed just by exposure, in the adult, plasticity requires behavioral relevance (cognitive association between sensation and reward), and thus active attention to the stimulus.

Behaviorally-induced plasticity in adult owl IC

- Hunting increases adaptive adjustments in the auditory SC space map in owls whose visual field has been displaced by prisms (Bergan and Knudsen, 2005).
Overview: Attention-Driven Receptive Field Plasticity in A1

- Auditory attention leads to rapid, selective, task-specific plasticity of A1 receptive fields (STRFs) during behavior.

- Although these modulatory effects in A1 take only seconds or minutes to occur, they can persist for hours after task completion, and may lead to long-term changes.

- Thus, attention plays two roles: it modulates the response properties of cortical receptive fields during task performance, and also triggers long-lasting changes.
What is Cortical Plasticity?

Calford (2002) offers over a dozen different meanings of plastic change, overlapping forms or flavors of plasticity, conferred by the addition of various modifiers:

1. **Functional plasticity** in cortical sensory and motor representations of adult animals, attributed to existing connections which were not normally expressed.

2. **Topographic plasticity** refers to induced topographic map changes.

3. **Receptive field plasticity** refers to induced changes in receptive field properties.

4. **Anatomical plasticity** is used where the change in neural properties is dependent upon an alteration in neuronal projections (axonal growth).

5. **Ultrastructural plasticity** refers to cases where the anatomical changes are minor or local (growth of new spines or change in spine shape for instance) and where synapse number, density, type, or location is altered.

6. **Synaptic plasticity** is the term used when there is a change of synaptic efficacy as in LTP, LTD, but when there is little or no ultrastructural change (see #12).
2 What is Cortical Plasticity?

(7) Developmental plasticity includes all cases restricted to early developmental stages - e.g. the critical period

(8) Restorative plasticity includes compensatory neural regeneration and recovery following cortical damage (e.g. Sur experiments on misrouting)

(9) Dynamic representational plasticity refers to cases with rapid induced changes in neural response properties and to the subsequent changes in representations formed by neurons with these properties. The term is used specifically by Calford to refer to the rapid cortical changes arising from peripheral denervation.

(10) Behavioral plasticity refers to long-lasting plasticity which is behavioral in origin

(11) Rapid, task-related plasticity is short-term plasticity which occurs nearly instantaneously when the animal engages in task performance of a previously learned behavioral task (Note: this form of plasticity is context and task-specific)

(12) Unmasking plasticity has been used to refer to cases of functional plasticity where new neuronal properties are revealed without apparent involvement of anatomical or ultrastructural plasticity (usually refers to activation of silent synapses)
Ancient History (1950-1980)

David Hubel

Fig. 1. Response of an auditory cortical unit in cat No. 17. Lower line shows response of a microphone located near the cat's ear; the deflections seen there were produced by squeaks emitted when a toy mouse was squeezed. The upper line shows the unit responding to the squeaks to which the animal was paying attention; this unit almost never responded to clicks, tones, or noise from a nearby loud-speaker.

8 MAY 1959

Unfortunately attention is an elusive variable that no one has as yet been able to quantify. It may be that studies in which cortical unit activity is examined during the course of conditioning and learning will illuminate these matters.
Learning that a tone is important shifts tuning “re-tunes” individual auditory cortex cells to the important frequency.

Weinberger (1985) - Classical conditioning

After Learning Best Response
Before Learning Best Response

Before Learning
After Learning

Pre
Post
States of attention

• States of passive hearing vs active listening

• Different states of selective attention – focusing on different features of sound
The Adaptive Auditory Brain

Rapid Receptive Field Plasticity in A1
Talk Outline
Four Levels of Plasticity in the Auditory Attention Network
A1, dPEG, vPEG, dlFC

• Spectral, temporal and spectrotemporal task-related receptive field changes in A1 during behavior in the adult ferret – activating adaptive cortical contrast filters (enhancing foreground and suppressing background)

• During behavior, attention acts to gate behaviorally relevant inputs to frontal cortex. Responses in ferret frontal cortex reveal an extraordinarily flexible, selective representation of the functional equivalence class of target stimuli

• How do topdown projections from frontal cortex shape responses in auditory cortex? Two intermediate steps in higher order auditory cortex between A1 and dlPFC
Attention & Cortical Plasticity

During task performance, A1 and secondary AC receptive fields rapidly adapt to change their spectral tuning or dynamics. These changes are in accord with ongoing task predictions and expectations (top-down) and salient sensory cues (bottom-up).
Behavioral Paradigm

Parallel Auditory and Visual Tasks - Conditioned Avoidance

<table>
<thead>
<tr>
<th>A</th>
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Tasks:
- Tone Detection
- Two-Tone Discrimination
- Click Rate Discrimination
- Click Rate Detection
- Light Discrimination

Time (1s intervals)

Symbols:
- TORC (Ref)
- Interrupted TORC
- Tone (Ref)
- Tone-in-TORC
- Clicks (Ref)
- Clicks (Target)
- Steady Light
- Flashing Light
Cortical Receptive Fields

Time (ms)

Temporal Frequency (Hz)

Ripple Frequency is 0.4 cycles/oct

|TF(ω,Ω)|

|F{|}

|STRF(t,x)|

35dB
Cortical *Multiscale* Representation

![Cortical Multiscale Representation Diagram](image)

- Auditory Spectrogram
  - Frequency (Hz)
  - Time (ms)
- STRFs
  - Frequency (Hz)
  - Rate (Hz)
- Cortical Output
  - Scale (Ω) (Cyc/Oct)
  - Rate (ω) (Hz)
  - Time (t)

4 Hz, 2 Cycle/Octave
Ferret in Experimental Set-up

Quantifying Spectral Plasticity* (i.e. Change in STRF shape)
Tone Detection Task

Aversive

Behavior is essential for plasticity

Population Analysis of Plasticity in the Detection Task

Discrimination Task - Spectral Effects
Evidence for top-down modulation: context-dependent STRF changes in task sequences e.g. Tone Discrimination, then Tone Detection
Comparison of STRF Changes in Discrimination and Detection Tasks

Fritz et al., (2005) Journal of Neuroscience
Detection followed by Discrimination

[Graph showing frequency vs time with labels for initial, discriminate 1kHz vs 2.7kHz, detect 1kHz, and post stages]
“Signature” Profiles for Different Auditory Tasks Representing Contrast Matched Filters

- **Tone Detection**
  (Fritz et al., 2003, Nature Neuroscience)

- **Two Tone Discrimination**
  (Fritz et al., 2005, Journal of Neuroscience)

- **Multiple-Tone Detection**
  (Fritz et al., 2007, Journal of Neurophysiology)
Additional Neuroimaging Evidence for Attention-Driven Rapid Plasticity in Core Auditory Cortical Fields

Two behavioral paradigms

Paradigm #1: Conditioned avoidance

Tone detection task:

Reference 1
Reference 2
Reference N
Target

OR

Tone discrimination task:

Conditioned avoidance:

Positive reinforcement:

Paradigm #2: Positive reinforcement

Task valence also profoundly influences cortical plasticity
a) The diagram illustrates the sequence of events in positive reinforcement. There are multiple references (Reference 1, Reference 2, etc.) followed by a target event. Positive reinforcement occurs during the period when licks are punished (time-out) and rewarded.

b) The graphs show lick probability over time. The blue line represents the reference, and the red line represents the target. The graphs are labeled as follows:

- Reference: Lick probability is low before the stimulus onset and increases sharply after the stimulus onset. The peak probability occurs around 0.4 seconds after the stimulus onset, and the probability returns to baseline by 0.8 seconds.

- Target: Lick probability is low before the stimulus onset and increases sharply after the stimulus onset. The peak probability occurs around 0.4 seconds after the stimulus onset, and the probability returns to baseline by 0.8 seconds.

The graphs indicate that the lick probability is significantly higher for the target compared to the reference. The sample size (n) for the reference is 157, and for the target, it is 130.

c) The rightmost graph shows lick probability over a longer time frame, similar to the previous graphs but with a broader time scale. The lick probabilities are shown in blue and red, with shaded areas indicating the standard error of the mean. The graphs again show a peak around 0.4 seconds after the stimulus onset, with a return to baseline by 1.5 seconds.
A1 Plasticity in Appetitive Tasks

Similar stimuli, but opposite actions, induce opposite plasticity!

- Suppression of instinctive behavior
- Optimizing reward or aversive feedback

David et al., (2012) PNAS
Comparison of STRF Changes in Discrimination and Detection Tasks

Fritz et al., (2005) Journal of Neuroscience
Do receptive fields of A1 neurons adapt to salient temporal as well as spectral cues in auditory tasks?
STRF changes in a series of *click* discrimination tasks
Nucleus basalis and Plasticity

- Neocortex receives diffuse extrathalamic projections from at least four different neuromodulator systems: noradrenaline (from LC), dopamine (VTA), serotonin, and acetylcholine. The most extensively studied is the cholinergic system from basal forebrain (NB).
- Pairing a tone with direct application of cholinergic agents (McKenna et al., 1989; Metherate and Weinberger, 1990) enhances response to tones at or near the paired frequency, suggesting that endogenous ACh has a role in modulating frequency selectivity of A1 neurons.
- Tones paired with direct NB stimulation leads to frequency-selective changes in frequency tuning in A1 neurons and an enlarged representation of paired frequency region in A1 of rat (Bakin & Weinberger, 1996; Kilgard & Merzenich, 1998).
Cholinergic Projections in Brain
“Learning” that a tone is important shifts tuning globally to the important frequency at the level of the cortical map

Kilgard and Merzenich (1998)
Nucleus basalis and plasticity - 2

Patch clamp whole-cell recordings from A1 neurons during NB-tone pairing has shown sequence of changes in excitatory and inhibitory currents (significant long-lasting changes after only 6 seconds of pairing) (Froemke et al., 2006)

Paired stimulation leads to specific autonomic changes (Miasnikov et al., 2006) and improvements in behavioral learning at the paired frequency (Kilgard et al. 2009; Froemke et al., 2013; Weinberger et al., 2013)

Note: GABAergic, Peptide-Y released from NB - ACh may act on DA receptors
Nucleus basalis and plasticity - 3

Diagram A: Schematic representation of nerve and receptor connections with labels for Tone, Stim, Rec, AI, and NB.

Diagram B: Graph showing normalized response over frequency (kHz) for Cell A with markers indicating Exc and Inh.

Diagram C: Graph showing normalized response over frequency (kHz) for Cell A after 30 minutes.

Diagram D: Graph showing normalized response over frequency (kHz) for Cell B after 180 minutes.
Two roles for NB: decorrelation and reliability

Goard and Dan (2009)
Conclusions-1: Receptive Field Plasticity in A1

- A1 cortical filters change rapidly and precisely, reflecting task demands and salient target cues in the behaving animal.
- STRF changes occur for both spectral and temporal tasks and can be explained as the result of contrast filter transformations.
- The magnitude of filter changes is influenced by motivation, task difficulty and overall behavioral performance.
- These changes can persist long after task completion, and may constitute a form of sensory memory.
- Adaptive plasticity in A1 may optimize signal processing for a given task and context. The plasticity is driven by attention.
- Recent findings suggest plasticity may also be modulated by behavioral valence (positive vs negative reinforcement).
The Adaptive Auditory Brain
Selective attention in Prefrontal Cortex
Lateral view of the ferret brain. Recordings from PRG (proreal gyrus), ASG (anterior sigmoid gyrus), and A1 (primary auditory cortex).

Location of frontal cortex recording (dashed ellipse) and injection sites.

Coronal Nissl-stained sections through 3 rostrocaudal levels of ferret frontal cortex showing recording sites and injection sites of fluorescent green beads.
Adaptive Task-Dependent Responses

(a) Reference = TORC, Target = tone (550 or 2200 Hz)

(b) Reference = TORC + tone (550 Hz), Target = TORC + tone (2200 Hz)

(c) Discrimination tone A (target) response vs. Detection tone A (target) response
   \[ r = 0.51, \quad p < 0.001, \quad n = 66 \]

(d) Discrimination tone B (reference) response vs. Detection tone B (target) response
   \[ r = 0.16, \quad p < 0.112 \]
Nourski … Steinschneider, Howard (ARO, 2014)

Responses from prefrontal cortex

- High gamma activity from prefrontal cortex (site X) may reflect task difficulty.
Persistent “Memory” Effects
Auditory Long-Term Memory
Pitch Discrimination Task

Ferrets

Blue: 15-tone training set
Red: 54-tone testing set

Note: tone frequency range are the same as used in the Weisman’s studies on birds, rats and humans.

Yin et al., (submitted 2014)
FC “Memory” Responses
(positive reinforcement training)

Yin et al., (submitted 2014)
Plasticity Induced by PFC Stimulation Paired with Tones
Winkowski et al. (2013) Journal of Neuroscience

2-photon imaging
The Adaptive Auditory Brain

Selective attention in Higher Order Auditory Cortex
What does secondary AC do?

- Extracts “auditory gestalt perception” or “behavioral meaning” - Ehret on mouse isolation calls, Caretta et al, 1999
- Extracts “functional classes of complex acoustic signals” – Cousillas et al, 2008
- Extracts “IBPs – information bearing parameters” for biosonar – Suga and colleagues 1990
- Extracts pitch information – Bendor and Wang 2005-2011
- Enhanced responses to broadband vs narrow band stimuli – Rauschecker 2005
- Extracts “what” and “where” and “who” – Rauschecker 2008
- Enhanced or different forms of cortical plasticity – Weinberger and Diamond, 1989; Puckett et al, 2007; Dong et al., 2013
- Auditory memory in fear conditioning – Sacco and Sachetti 2010
• But …

• Pitch (and timbre and spatial location) information widely distributed (e.g. no “pitch” areas) – Bizley et al., 2009
• Conspecific vocalizations represented in both core and belt areas – no evidence for enhanced firing rate for vocalizations in rostral areas – Recanzone, 2008
• Similarities outweigh differences in representation of spectral and temporal sound features in Al, AAF, AII – Eggermont, 1998
Ferret Auditory Cortex
Do similarities outweigh differences?

Best Frequency

Latency

STRF Duration

STRF Phaselocking

STRF Sparseness
Injection Sites in dIPFC

Anterograde and Retrograde Label in Auditory Cortex
Examples of “PFC-like” changed responsiveness to target stimuli in Pro-PPF during tone detection behavior

Cell-1

Cell-2
Response Changes in Pro-PPF – change in click response
Selectivity and Timing
avo055a CLK  8 vs 28 Hz

Passive  Behavior  Passive  Passive
vaPEG

A

Tone detection

Pre- Passive

Behavior

Normalized Firing Rate

Time from onset (s)

$n_i = 64/109$

Click Rate discrimination

Normalized Firing Rate

TORC

Clicks

Time from onset (s)

$\tau = 65/95$

reference
target
Elgueda et al. (2014) ARO Meeting
Conclusions – 2 – Beginning of stimulus selectivity in PEG

• Many cells in PEG exhibit rapid plasticity during behavior, showing strong modulations of target and/or reference responses. We have not yet studied receptive field transformations in PEG, but have focused on changes in response to classes of target and reference sounds.

• Overall, PEG plasticity may enhance the discriminability of sound classes by increasing the neural “distance” (differential spike response) between the presentation of target and reference sounds. The average (population) PSTH response in both A1 and PEG shows suppression of noisy stimuli. However, compared to A1, PEG cells show a substantially enhanced response to target tones during the tone detect task.

* This is even more marked in Pro-PPF.

• There appear to be changes in magnitude of attention-driven plasticity at different auditory cortical levels. This may be similar to what has been described in the visual system in the magnitude of attentional effects as you ascend from LGN to V1, V2, V4, MT, MST, IT – ranging from 5% to over 60%.

• There is even greater stimulus selectivity in frontal cortex.
Summary

• **Auditory A1 cortical** receptive fields *adapt rapidly* in a task-specific fashion to enhance processing of attended stimuli.

• **Behavior (and attention)** is critical to induce this rapid plasticity and changes can persist for hours after task completion, and may lead to long-term changes.

• **Secondary auditory cortical** responses show increased selectivity for the attended stimulus and decreased response to the reference stimulus.

• An open question is how these transformations in A1 and secondary auditory areas are made, and the role of top-down inputs from PFC.

• **Frontal cortex** responses show dramatic selectivity for salient target stimuli, are similarly contingent on behavioral state and may act as the source of the top-down attentional signals that reshape receptive fields during task performance.
Multiple functional pathways (Winer)
Thank-you for your attention!
Neuroanatomy of Nucleus Basalis – in Basal Forebrain

**Nucleus Basalis of Meynert** (NBM) is a group of nerve cells in the SI (substantia innominata) of the basal forebrain which has wide projections to the neocortex and is rich in ACh and CAT (choline acetyltransferase).

NB is part of a node (Ch4) of a larger cholinergic network (BFCS) that projects to neocortex (and that includes NB and also SI, Ansa peduncularis).

Most of the sensory, motor and association cortical areas that receive inputs from Ch4 do NOT send reciprocal projections back.

The Ch4 neurons receive their cortical inputs from prepyriform cortex, orbitofrontal cortex, anterior insula, temporal pole, entorhinal cortex, MT cortex and subcortical inputs from septal nucleus, NA, hypothalamus
The **Inverse** Model for Reconstruction

Forward model: $H(t, f)$

- $S(t, f) \rightarrow r(t)$

Stimulus: $S(t, f)$

Inverse model: $G(t, f)$

- $r(t) \rightarrow S(t, f)$

**Predicted responses**

- $r_1(t)$
- $r_2(t)$
- $r_3(t)$

**Neural responses**

- $r_1(t)$
- $r_2(t)$
- $r_3(t)$

**Reconstructed speech**

**Original**

**Reconstructed**

(<100 neurons)