Physics of Hearing: From Neurobiology to Information Theory and Back
Summer 2017
Tutorial: Cortical pathway organization for encoding frequency, timing and location of sound

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1. **Sound Frequency** audibility in human other mammals

2. **Cochleotopy** in ascending primary auditory pathway

3. **Cochleotopic** sound processing streams in Inferior Colliculus

4. **Cochleotopic** auditory cortices

5. **Parallel** ascending thalamocortical pathways to primary and non-primary cortex
Audible sound frequency range in humans

Adapted from,
Gleich Otto and Strutz Jürgen (2012).
Heffner et al., Hearing Res. 1985, 1994
Koay, Heffner, Heffner, Hearing Res. 2002
Heffner, Anatomical Records, 2004
Audible sound frequency range varies in mammals

Adapted from,
Gleich Otto and Strutz Jürgen, 2012)
Heffner et al., Hearing Res. 1985, 1994
Koay, Heffner, Heffner, Hearing Res. 2002
Background: Organization of ascending pathways

Human Ascending Auditory Pathway

Cochlear Nuclei

Olivary Nuclei

Cochlea

High

Low
Inferior colliculus (IC) is a minimum of 3 synapses away from the cochlea.

Human Ascending Auditory Pathway

Penetrating electrode mapping
~30 deg angle from midline

Inferior colliculus

Cochlear Nuclei

Cochlea

1 high

low
“Dynamic moving ripple” sounds probe large range of spectral temporal neuronal responses
Probe neuronal spectral temporal response fields (STRF) with “dynamic moving ripple” sounds

Neural spike train

Spectrogram
Probe neuronal spectral temporal response fields (STRF) with "dynamic moving ripple" sounds.
Natural sounds differ in short-term correlation statistics

**Running Water**

**Speech**

Water and backgrounds sounds are typically stationary

Speech and vocalizations are nonstationary
Spike rate responses to brief tone sounds to probe intensity-frequency response fields

Storace, Higgins and Read, J Comp. Neurol. 2011

![Graph showing spike rate responses to brief tone sounds.](image)
Tone Receptive Field (RF) mapping confirms low-to-high frequency gradient in dorsal-to-ventral dimension of Inferior Colliculus.

Schreiner and Langner, Nature 1997
Physiologic shifts in BF align to IC neuron dendrites and input from the cochlear nucleus.

Rodriguez, Read and Escabi, J Neurophys, 2010
**Dynamic moving ripple** and **tone** receptive fields same low-to-high best frequency gradient direction

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**Significance:**
Best frequency responses and the gradient direction are stable properties observed with many sounds in IC.

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_Modified from_  
Rodriguez, Read and Escabi, J Neurophys, 2010
Same low-to-high frequency gradient direction for all dorso-ventral electrode penetrations in Inferior Colliculus

Modified from
Rodriguez, Read and Escabi, J Neurophys, 2010
STRF properties vary across penetrations and within frequency layers

Penetration D:
STRF’s don’t change outside Central IC

Penetrations A and C:
Same low-to-high best frequency (BF) gradient
....but STRF shape is changing.

Modified from
Rodriguez, Read and Escabi, J Neurophys, 2010
Laminar organization when STRF best frequency (BF) is rendered in 3-dimensions.

Correlated responses?

Best Frequency (octaves)

Rodriguez, Read, Escabi, in prep.
Variation in STRF spectral and temporal properties for neurons with same best frequency (BF)

Long sound integration time responds to Slow sound modulation frequencies

Rodriguez, Read and Escabi J Neurophys, 2010
IC neurons with matched Best Frequency (BF) can vary in other spectral and temporal properties evident in the STRF.

1. STRFs recorded from same frequency layer but different electrode positions
2. Best Frequency (BF) similar yet STRF very different!!!
The population of STRFs demonstrates “trade-offs”, possibly reflects optimal processing of different acoustic features in IC

Rodriguez, Read, Escabi., J Neurophys, 2010
Significant correlations between neuron pairs with < 1/3 octave separation for Best Frequency

*Red dot* significant correlations $p < 0.0001$

STRF correlations higher than spike train
STRF and spike train correlations are both ~1/3 octave
Higher correlations between STRF excitatory peak for pairs of neurons in IC

Antencio, Shen, Schreiner, Neuroscience, 2016
Examine response correlations as a function of proximity within Inferior Colliculus

Adjacent Tetrodes
(> 150 μm)

Same Tetrode
(≤ 25 μm)
Spike train and Receptive field (STRF) correlations highest for neighboring neuron pairs with same Best Frequency (BF)

Adjacent Tetrodes
(> 150 μm)

Same Tetrode
(≤ 25 μm)

Spike Train correlation index

0 0.5 1

STRF correlation index

0 0.5 1

Chen, Rodriguez, Read and Escabi
Frontiers Neural Circuits, 2012
Minimal Correlations
Far apart and >1/3 octave
Maximal Correlations nearby <1/3 octave
1) Consistent with *sparse* correlated neuronal spike output.

2) Potential neural mechanism for *grouping sound features* within perceptual limits such as critical bandwidth (cat frequency perception: Pickles, 1975).

3) Neurons must be *nearby* [25-150 μm] to have highly correlated spike time output.

4) Inferior Colliculus output pathways are *highly parallel*!!
General Conclusions

1. **Cochlea** - one frequency gradient

2. **Inferior Colliculus** – one frequency gradient but many “sparse” parallel correlated neural output pathways.

3. **Cortex** - one frequency gradient or more?
Flattening magnetic resonance image (MRI) reveals human auditory cortex in deep sulci

\[
\text{green} = \text{gyri} \\
\text{Red} = \text{sulci}
\]
Four “low frequency” areas sensitive to 1 kHz tones

Primary (A1) and Rostral (R) fields share border responding to high (arrow) tone frequency

Forminsano et al., Nature 2003
Optical imaging of intrinsic metabolic tone responses in *rat* brain

1. Surgically expose surface of temporal cortex
2. Play continuous sound sequence
3. Measure light reflectance change ($\Delta R$) known to be associated with oxygenation of hemoglobin
4. Compute phase delay between sound and response

Phase $\phi$ time when response reaches maximum relative to a reference point ($Q_s$, stim; $Q_d$, hemodynamic delay)

*Dalsa CCD camera, 30 frames/sec*

*Kalatsky Stryker, Neuron 2003*
*Kalatsky et al., PNAS 2005*
Optical image of intrinsic metabolic tone responses in rat brain

Read lab,
Higgins et al., J Neurosci 2010
Optical image of intrinsic metabolic tone responses in rat brain

Three “low frequency” areas sensitive to 2 kHz tones Multiple Areas:

Primary (A1) and Anterior (AAF) fields share border responding to high (arrow) tone frequency

Read lab, Higgins et al., J Neurosci 2010
Tone frequency response gradients define multiple fields

Read lab,
Higgins et al., J Neurosci 2010
Cochleotopy evident electrocorticography (ECoG) surface local field potentials if using high density surface electrode arrays

14 x 14 array
196 electrodes
150 μm spacing

Multi-investigator team
Escabi, Read, Viventi et al., 2014
Wide-field micro-ECoG brain mapping of *tone* responses with single trial taking 60 seconds total

One trial = 60 seconds

Six trial BF

$1 = 60 \text{ seconds}$

$r = 0.95$

Multi-investigator team

Escabi, Read et al., 2014
Wide-field micro-ECoG brain mapping of dynamic moving ripple STRF

Multi-investigator team
Escabi, Read et al., 2014
Micro-ECoG and Optical wide-field brain maps are correlated

Multi-investigator team
Escabi, Read et al., 2014
Cortical (ECoG) STRF bandwidths increase with the cortical site Best Frequency.
Significance regarding cortical cochleotopies

1) There are multiple cortical fields with cochleotopic organization.

2) Cross-validation with fMRI, Optical, Multi-unit, ECoG and anatomy indicates a robust response topographically akin to retinotopy in visual cortices (aka, V1, V2, V3..).

3) 150 μm ECoG array spacing sufficient for mapping cochleotopy.

4) Multiple cochleotopies in mammals indicates a highly parallel cortical processing.
Do different cochleotopic cortical fields process sound differently?
Ventral auditory field (VAF) resolves sound frequency better than more dorsal Primary (A1) auditory field.
Similar phenomenon observed in cat which has alternating domains with neurons having broad and narrow bandwidths.
Retrograde tracers label high density of cortico-cortical connections between narrowband regions.

**Significance:** spectral resolution differs across regions and determines cortical network connectivity.
Virtual sound position fMRI: Each acoustic hemifield activates contralateral cortex in **humans**

Heschl’s Gyrus

Human
Formisano lab
Derey et al., Cerebral Cortex, 2016

Cat
Stecker et al., PLoS Biol, 2005
Virtual sound position responses: Each acoustic hemifield activates contralateral cortex in rats

Receptive fields in “B” similar to Formisano and Stecker receptive fields

Higgins et al., 2010
Azimuth response fields form an “acoustic fovea” with tuning to midline observed in non-primary cortex of rat.

Receptive fields in “C” similar to Semple and Kitzes in cat.

Spatially “tuned” VAF and SRAF responses only with low sound levels.

Read lab
Higgins et al., 2010
Ventral non-primary cortex better at resolving sound frequency and azimuth and responds

**A1**

- **Coarse frequency response**
  - Spike rate
  - **Frequency**
  - **Intensity**

- **cSRAF/VAF**
  - **Resolved frequency, intensity response**

**Coarse, contralateral (45° azimuth)**

**No binaural interaction**

**Resolved, midline (0° azimuth)**

**High binaural interaction**

- **Binaural Interaction Index**
  - \( BII = \frac{R(SPL_c, SPL_i)}{R(SPL_c) + R(SPL_i)} \times 100 \)

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**Figure A**

- **midline**
- **contra**
- **ipsi**

**Legend:**
- **Azimuth:**
  - **Cue:**
  - **(ILD, dB):**
  - **Level (dB):**

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**References**

- Storace et al., J Comp. Neurol. 2011
- Higgins et al., J Comp. Neurol. 2010
Stimulus-specific adaptation prominent in non-primary auditory cortex (PAF and SRAF)

Smoothed Spike Rate
Best Frequency (BF) Map

Stimulus Specific Adaptation (SSA)

Nieto-Diego Malmierca PLOS 2016
"Single inherited cochleotopy concept" ventral (V) division thalamus common source of cochleotopy

Kaas, Hackett, Weinberger Schreiner, Winer

Medial Geniculate Thalamus

V

A1

VAF

cSRAF

D

L
New Conceptual Framework: Multiple parallel pathways afford simultaneous distinct sound processing ability

...distinct spectral processing bandwidths
...distinct stimulus-specific adaptation
...distinct azimuth tuning, acoustic fovea
...distinct thalamic pathways

Thalamus
rostral
middle
caudal

A1
Acoustic periphery

VAF
Acoustic periphery

cSRAF
Acoustic fovea

Time processing differences on Friday

Read lab,
Storace et al., J Neurosci., 2012
The End
Thanks!

to laboratory members, collaborators, funders

**Current graduate Students on project**
Ahmad Osman (Biomed. Engineering, PhD)
Fatemeh Firoozzabad (Biomed. Engineering, PhD)
Erica Eddy (Behavioral Neuroscience, PhD)
Mike Jacobs (Biomedical Engineering, PhD)

Integrative organismal systems

**Former Grad Students**
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Francisco Rodriguez (Biomedical Engineering, PhD)

**Collaborators**
Monty Escabi, University of Connecticut
Ian Stevenson, University of Connecticut
Jon Vivente, Duke University
Parallel Paths Discriminate: Sound Timing, Spectral, Spatial Cues

A1
VAF
cSRAF

Tone Frequency (kHz)
2k 2k 2k
PAF A1 AAF
VAF SRAF

Level (dB)
Azimuth Cue (ILD, dB)

Higgins et al., J Comp. Neurol. 2010
Storace et al., J Comp. Neurol. 2011

Parallel Paths Discriminate:
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