Auditory Cortex - 1

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(with thanks to Xiaoqin Wang)
Road Map for Auditory Cortex Lectures

Lectures 1-2: Introduction

Overview
Historical background >130 years of research
Basic anatomical structure and connectivity of auditory cortex
Tonotopic and odotopic organization - evidence and debates
Stimulus selectivity and firing patterns
State dependent responses

Lecture 3: Frequency, Pitch, Temporal, Intensity Processing

Lecture 4: Cognitive Properties of the Adaptive Auditory Cortex
Task dependence of receptive field properties and auditory responses
Long-term changes in attention, learning and memory

1-2
Outline: Lecture 1

• Broad Overview
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• Basic neuroanatomical structure and connectivity of auditory cortex
• Functional organization – Tonotopy and Odotopy – evidence and debates
• Stimulus selectivity and firing patterns
• State dependent responses
Multiple functional pathways in auditory cortex (Winer)
What is unique about the auditory systems?

1) Longer subcortical pathway
2) Spectrally overlapping, time-varying input signal
3) Sounds entering the ear from anywhere at anytime
4) Hearing-speaking: sensory-motor processing
Additional Unique Aspects of the Auditory System and Auditory Cortex:

(5) Extremely precise temporal precision (50 μsec in NLL, 1 ms in A1) – Kv3

(6) Short-latency responses in A1 (~10-20 ms vs. 80-100 ms in V1)

(7) Computational mapping of space – i.e. not reflecting direct map of receptor surface (as in vision or touch) since cochlear receptive surface is a map of frequency, not space

(8) Broad receptive fields in A1 - comparable to V4 or SII

(9) Extensive topdown projections connecting all levels (10x > bottom-up)

(10) Extraordinarily adaptive and plastic properties of cells in auditory system
Organizational and Functional Themes

• Cortical Maps and map-making
• Tonotopy – Frequency analysis and tuning
• Odotopy – Maps of echo-delay (time) and distance
• Binaural bands – Spatial analysis and tuning
• Temporal tuning – Cortical gradient? Sequence and serial processing
• Feature extraction – cortical representations of pitch, auditory objects, acoustic scenes, computational maps
• Forms of behaviorally mediated plasticity
• Context-dependent responses
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Historical Introduction

Initial studies of Ferrier and Schafer in 19th century
Fig. 1.1 Figures from Ferrier (1876) illustrating his stimulation and ablation experiments in monkeys; from these, he located the auditory cortex in the superior temporal gyrus. Left: the locations of regions which when stimulated electrically gave rise to movements of different parts of the body. From regions labeled 14 he reported “pricking of the opposite ear, head and eyes turn to the opposite side, pupils dilate widely.” Right: the locations of bilateral lesions that led to “loss of hearing in both ears, and loss of sight in the right eye.” The dotted lines indicate the extent of brain surface exposed by removal of part of the skull.
Fig. 1.2 Left: the extent of bilateral superior temporal lesions in one of Ferrier’s monkeys, demonstrated at the International Medical Congress in 1881 and found to be profoundly deaf. From Ferrier (1886). Right:
Fig. 1.6 Results of Ferrier's electrical stimulation experiments in a jackal (top left), cat (top right), rat (lower left) and guinea pig (lower right). In each case, stimulation of the area labeled 14 resulted in pricking of the ears and turning of the head to the opposite side. This area was therefore identified as the auditory cortex. From Ferrier (1876)
Fig. 1.4 Sir David Ferrier (1843–1928) and Sir Edward A. Schäfer (later Sharpey-Schäfer) (1850–1935), who fought bitterly over the location of the auditory cortex in the superior temporal gyrus. From Biographical Memoirs of the Fellows of the Royal Society (left) and from the Quarterly Journal of Experimental Physiology (right)
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Layers of Cortex

White matter

= 3 - 4 mm
Varieties of Spiny (Excitatory) and Non-Spiny (Inhibitory) Neurons

Figure 12: Basic cell types in the monkey cerebral cortex. Left: spiny neurons that include pyramidal cells and stellate cells (A). Spiny neurons utilize the neurotransmitter glutamate (Glu). Right: smooth cells that use the neurotransmitter GABA. B, cell with local axon arcades; C, double bouquet cell; D, H, basket cells; E, chandelier cells; F, bitufted, usually peptide-containing cell; G, neurogliaform cell.
Laminar Organization of Cortical Neurons
Neuroanatomical Characterization of Cortical Areas based on Cytoarchitecture

Fig. 1.22 Photomicrographs of Nissl-stained sections through the human somatic sensory (a), visual (b) and auditory (c) areas. The auditory area is distinctly less granular and more radially disposed than the other two. Bar 500 μm
Fig. 1.14 Campbell’s drawings of cells and cell laminations in the auditory-sensory area (left) and the auditory-precerebral area (right) of the human brain. From Campbell (1905)

Fig. 1.10 The structure of the human anterior sphenoidal (superior temporal) gyrus as seen in Nissl (left) and Weigert (right) stains by Santiago Ramón y Cajal. From Cajal (1904, left, 1900b, right)
Organization of auditory cortex is largely preserved across primate species.
Brodmann’s and von Economo’s Cortical Mapping in Human Brain

Fig. 1.16 Brodmann’s drawings of the insular region and upper surface of the superior temporal gyrus (left) and of the lateral aspect of the human cerebral hemisphere (right) showing areas 41 and 42, which are called the internal or anterior and the external or posterior transverse temporal areas, respectively. Area 52 is the parietal area and area 22 the cortex on the exposed surface of the superior temporal gyrus. From Brodmann (1909)

Fig. 1.17 Map of the cytoarchitectonic areas of the human cerebral cortex by Economo and Koskinas (1925). Te and Ts are the two transverse temporal areas of Brodmann and Campbell. From Economo and Koskinas (1925)
Campbell (1905)

Brodmann (1909)

Von Economo and Koskinas (1925)
Fig. 3.1 (a) Wilder Penfield, pioneer neurosurgeon and founder of the Montreal Neurological Institute. (b) Sites on human temporal lobe from which electrical stimulation elicited experiential responses. Top: Lateral surface. Middle: Supratemporal plane; HG labeled AUD. SENSORY. Bottom: Inferior surface. (Adapted from Penfield & Perot, 1963.)
Recording, Cooling (Inactivating) and Stimulating AC (Howard)

Fig. 3.4  Acute experiments. Photographs taken in the operating room showing a recording grid (R), hand-held bipolar electrical stimulator (S), and cooling probe (C) in direct contact with brain surface.
Characterizing Auditory Cortical Areas based on MGN input
Different MGN subnuclei have different input-output profiles
Neuroanatomical Characterization of Cortical Areas based on Thalamic Connectivity

Fig. 1.24  Stephan Polya (1889–1955) a and his depiction of the auditory radiation (ar), as stained by the Marchi method after a lesion interrupting the outflow from the medial geniculate nucleus (b, c), b and c from Polya (1932)

Fig. 1.40  Left: predicted typical responses to auditory stimuli of neuron located in the dorsal (D), ventral (V) and magnocellular (mc) nuclei of the monkey medial geniculate complex. Based on work by Calford (1983) in the cat. Right: differential expression of the calcium binding proteins, parvalbumin and calbindin, in the nuclei of the medial geniculate complex, their innervation by brain stem pathways expressing the same proteins, and their projections to the auditory cortex. Based on Molinari et al. (1995) and Jones (2007)
Fig. 1.9 *Left:* Constantine von Monakow (1853–1930). *Right:* summary of Monakow's experiments in cats in which he identified the thalamic nuclei projecting to different areas of the cerebral cortex on the basis of the retrograde atrophy that ensued from localized lesions of the cortex. The colored region labeled c gen int was identified as the projection field of the medial geniculate body and was thus equated with the auditory cortex. From Monakow (1895)
Table of projections (many-to-many) from thalamic nuclei to different auditory cortical areas in the cat (Winer)
Cortico-cortical connectivity of some cat auditory cortical areas (Winer)
Rough Wiring Diagram (Not a Connectome!) of some Cat Auditory Cortical Areas (Winer)
A1 Chemoarchitecture (Morosan)
Fig. 6. Series of adjacent coronal sections through caudal areas of auditory cortex stained for several chemoarchitectonic markers: Parvalbumin (PV), vesicular glutamate transporter 2 (VGlut2); cytochrome oxidase (CO); acetylcholinesterase (AChE); myelinated fibers (MF); Nissl (N). Note that the dense band of staining in layer IIIb/IV is highest in the core area, A1, and weaker in the belt and parabelt areas. Arrowheads denote borders between areas. Scale bars, 2 mm. From Hackett and de la Mothe (2009).
Asymmetries

Temporal Lobe
“What”, “where” and “who” pathways?
Another view of streams in human auditory cortex
Overall organization of AC
Some cortico-cortical connections in AC (Hackett)
Some cortico-cortical connections from AC (Hackett)
Outline: Lecture 2

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Discoveries and Debates on Tonotopic Organization
Basic Idea of Tonotopy (Cochleotopy)
Functional Characterization of Auditory Areas based on Responses to Clicks

Fig. 1.26 Drawings from Bremer and Dow (1939) showing the extent of the area of cortex activated by click stimuli in the cat (upper) and the smaller extent of granular cortex in the same animal.
Earliest evidence for tonotopic organization in AC

Fig. 1.8 Results obtained by Larionow (1899) showing the distribution of tone centers in the brain of the dog. Lesions located at different points along the S-shaped trajectory result in a failure to respond to tones of different frequencies. Lower tones are represented posteriorly and higher tones anteriorly. From Bechterew (1911)
Tonotopic organization of auditory cortex:
First demonstration in anesthetized cat (at Hopkins!)

Fig. 4. Exp. 2/14. Right cortex; left cochlea; stimulation of nerve fibers 6 mm. (basal turn) and 14 mm. (middle turn) from basal end. Note that there are two response areas for the 14 mm. point. See text p. 320 and p. 327. Labs identify sulci. 24 X.

Woolsey and Walzl (1942)
Auditory cortex is tonotopically organized

Suprasylvian sulcus

iso-frequency axis

Merzenich et al. (1975)
Systematic changes of CF across auditory cortex

Slope = 1 oct/mm

Merzenich et al. (1975)
Tonotopic organization in marmoset auditory cortex

- High frequency regions
- Low frequency regions
- Al
- R
- RT

Left Hemisphere M2P
- Recording site (519 total units)
- Pitch neuron site (19 pitch units)

Bendor and Wang (2005)
Tonotopic organization across mammals

Morel and Kaas (1992)
But .... Not everyone agreed on the tonotopic organization of A1

Is auditory cortex tonotopically organized?
Lack of an orderly organization in unanesthetized cat

"Standard cortex"

Suprasylvian sulcus

Goldstein et al. (1970), Neural Encoding Lab, BME, JHU
“Why are Evans et al. and our single track penetrations so out of agreement with the orderly representation of the cochlea within AI reported by Merzenich et al.? First and foremost in our view is the different anesthetic state. There is no question that the sorts of anesthetics Merzenich et al. used render many cortical units unresponsive to sound. Further the effect is probably selective so that units with more indirect input pathways are more likely to be affected.” (p.190)

Goldstein and Abeles, Brain Res., 100:188-191 (1975)
What have we learnt from the old debate?

- Anesthetized
- MGB input layer IV
- Multi-unit
- Near threshold
- Single hemisphere
- Unanesthetized
- Cortical response
- Other layers
- Single-unit
- Supra-threshold stimulus
- Averaging across hemispheres
“In this chapter and elsewhere, we have stressed the diversity of the neural coding properties of the units in the auditory cortex. This diversity makes the cortex a difficult region to study and makes it especially unattractive to those who like their science in neat packages. Let us hope that new studies, new techniques, and new findings will move us out of what will someday be called the early phases (or even the dark ages) of neuroscientific study of the cortex.”

New Debate: Is there Tonotopic Organization in Mouse A1?
Evidence for Tonotopic Organization in Mouse (Polley)
Evidence Against Tonotopic Organization in Mouse from Nelken and Kanold labs using 2-photon imaging of layer II-III neurons (2010)
Variability in Spine Tuning in A1 - Substrate for Plasticity??

(Chen et al., 2011, Nature)
Variability in Spine Tuning in A1 - Substrate for Plasticity??

(Chen et al., 2011, Nature)
Nuanced View of Tonotopic Organization in Mouse (Polley)

Tonotopic organization is present in all cortical layers of the mouse auditory cortex based upon electrical activity ranging from theta waves to single units, and in states of consciousness ranging from areflexic to fully alert.

However there were three circumstances in which the robustness of tonotopy was significantly reduced or absent:

(1) tonotopic organization was not observed when recordings were made from the middle layers of the three belt fields that surround A1 and AAF

(2) tonotopy within the core fields was substantially reduced, though not eliminated altogether, when frequency tuning was characterized with a single, suprathreshold sound level. The loss of tonotopic mapping precision at higher sound intensities is well known (Phillips, 1994)

(3) a substantial minority of recording sites in the superficial (29.5%) and deep (20.5%) layers were driven by pure tones, yet exhibited irregular frequency tuning and no discernible tonotopic organization
Are there auditory space maps in A1?
Echolocation in Bats - Auditory Specialists
Three types of Biosonar Calls in Bats

(A) FM call of *Eptesicus* and CF-FM call of *Rhinolophus*. (B) Frequency profile over time showing search phase, approach, and attack.
Echo-Delay Tuning in the Panamanian Mustached Bat

Diagram A:
- FM1–FM2,4
- Frequency and Time Axes
- Graphs labeled a-g
  - a: DSCF
  - b: FM-FM
  - c: CF/CF
  - d: DF
  - e: DM
  - f: VF
  - g: PFM1 + EFM2 + EFM4

Diagram B:
- Frequency in kHz
- Time in ms
- Scale: 2.0 mm

Experiment: PFM: 29.38 → 23.38
- 61 dB SPL
- BD: 3.1 ms

Experiment: EFM2: 60.61 → 48.61
- 35 dB SPL
- BD: 3.6 ms

Experiment: EFM4: 122.36 → 98.36
- 31 dB SPL
- BD: 3.6 ms

Experiment: PFM1 + EFM2
- BD: 3.1 ms

Experiment: PFM1 + EFM4
- BD: 3.6 ms

Experiment: EFM2 + EFM4
- Delay: 0 ms

Experiment: PFM1 + EFM2 + EFM4
- BD: 3.3 ms
"Combination sensitive" neurons in auditory cortex of echo-locating bats

A

Time (ms)

Frequency (kHz)

H4 CF4 FM4
H3 CF3 FM3
H2 CF2 FM2
H1 CF1 Delay FM1

D

Frequency (kHz)

1: P
2: E
3: P-E
4: PH1-EH3
5: PH1-EH3(SFM)

1: P
2: E
3: P-E
4: PFM1-EMF2
5: PFM1-EMF2
6: PFM1-EMF2

3-13

Suga (1997)
Auditory Cortex of the Mustached Bat (Suga and colleagues)

Evidence for Odotopy – i.e. Delay or Distance Map (Z-axis) in FM-FM area
Specialized auditory cortical area for processing sonar signals in echo-locating bats

Suga (1994)
Echo-Delay Neurons in Eptesicus (Big Brown Bat)
Dynamic Representation of Multiple Echo Delays – Simultaneous View of Objects at Multiple Distances
Scene Analysis of Acoustic Images
Multiresolution Decomposition

- Delay-tuning curves 10 ms after vocalization
  \[ Q_{50\%BC} = 0.41 \]

- 20 ms
  \[ Q_{50\%BC} = 1.05 \]

- 30 ms
  \[ Q_{50\%BC} = 1.69 \]

- 40 ms
  \[ Q_{50\%BC} = 2.33 \]
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• State dependent responses
Auditory cortical neurons respond to many acoustic features of sounds

- Frequency (pitch)
- Timbre
- Intensity (amplitude)
- AM modulation (waveform envelope)
- FM modulation
- Location and distance (computed)
- Rate of presentation
- Stimulus statistics
- Acoustic objects and scenes – gestalt perception
Mysteries of Auditory Cortex

Why it’s so silent?
Because of anesthesia & non-optimal stimuli!

Onset responses to brief sounds (anesthetized rats)

Onset responses to continuous sounds (anesthetized marmosets)

DeWeese and Zador (2003)
deCharms and Merzenich (1996)
Auditory cortex is capable of sustained firing in awake animals

Primary Auditory Cortex
(Stimulus: Tone)

Non-Primary Auditory Cortex
(Stimulus: Noise)
Auditory cortex neurons respond to preferred stimuli with sustained firing and adapt quickly to non-preferred stimuli.
From a stimulus’ point of view:

Responses to one particular sound by all neurons

“When a sound is heard, a particular population of auditory cortex neurons fire continuously throughout the duration of the sound. Responses of other, less optimally driven neurons fade away quickly after the onset of the sound.” (Wang et al. *Nature* 2005)
From a neuron’s point of view:

Responses of one neuron to entire acoustical parameter space

Acoustic parameter space

- Preferred stimulus (sustained firing)
- Non-preferred stimuli (onset firing)
- Outside RF (no response)
Increased stimulus selectivity along ascending auditory pathway

- Auditory cortex
  - Preferred stimulus (sustained firing)
  - Non-preferred stimuli (onset firing)
- Thalamus
- Inferior colliculus
- Auditory nerve
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Activity of the cerebral cortex depends on brain state. So, what are the different “states” of awareness?

- Anesthetized (Isoflurane, Ketamine, Nembutal, urethane, etc.)
- Anesthetized (Up States – global activity, Down States – network silence)
- Conscious, unconscious - arousal, comatose
- MCS (Minimally conscious state)
- Sleep (SWS, REM)
- Synchronization, desynchronization
- Awake - quiescent
- Awake - attentive (selective)
- Awake - attentive (global)
- Emotional state (relaxed, stressed)
- Different drug-induced states

What are the behavioral & neural correlates of these different states? Responsiveness, activation of reticular activating system, TRN, midline thalamic nuclei?
What are the effects of these states on auditory processing?

Issa & Wang, 2013

Marguet and Harris, 2011

Wilson, 2008
Auditory Attention, Context and Associative Meaning

• Auditory cortex as a “semantic processor” (Scheich et al., 2011) deducing the task-specific meaning of sounds by learning and also an “attentional processor” that predicts, updates and selects the most salient sound in the landscape.

• Multisensory context also plays a very important role in defining auditory meaning – for example, the crackling of a twig in the jungle means quite a different thing if you just smelled the fresh scent of jaguar. Mice exposed to predator odor changed evoked responses to sound (Halene et al., 2009) and lactating mouse mothers reshape their responses to sound when they are exposed to their pup odors (Cohen et al., 2011).

• Acoustic context (adapting to environmental acoustic landscape)
Effect of Pup Odor on Auditory Responses in A1 (Cohen, Mizrahi, Nelken, 2011)
Summary : Lecture 1

- There are multiple areas in auditory cortex with different characteristic inputs from MGB and distinctive cytoarchitecture, chemoarchitecture and gene expression
- There are also multiple neuroanatomical and functional pathways (networks) in auditory cortex, and descending topdown projections
- Neurophysiological mapping reveals presence of frequency (tonotopic) maps as well as odotopic and binaural maps
- Neurons respond to frequency, bandwidth, timbre, intensity, location of sounds with multiple spectral/temporal windows
- Auditory cortical neurons can be highly selective – and show onset, offset and sustained responses
- Auditory neurons are highly state dependent in their responses – to context, to behavioral state and to learned sound meaning