Functional architecture of auditory cortex
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Three complementary approaches demonstrate new types of organization in rodent, feline and primate auditory cortex, as well as differences in processing between auditory and visual cortex. First, connectional work reveals patterns of thalamocortical and corticocortical input unique to the auditory cortex. Second, physiological studies find multiple, interleaved auditory processing modules related to corticocortical connections and embedded in the isofrequency gradient. Third, functional analyses demonstrate independent processing streams for sound localization and identification analogous to the 'what' and 'where' streams in visual cortex, although the modular arrangements are modality-specific. Taken together, these data show that the auditory cortex has common and unique functional substrates.

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Published online 12 July 2002

Abbreviations
AAF anterior auditory field
AI primary auditory cortex
BB broadband
CF characteristic frequency
fMRI functional magnetic resonance imaging
IC inferior colliculus
MGB medial geniculate body
MGBl medial division of the MGB
MGBv ventral division of the MGB
NB narrowband
PFC prefrontal cortex
QB inverse bandwidth
SPLs sound pressure levels
VI primary visual cortex
VII second visual cortical area

Introduction
The essential uniformity in sensory neocortical structure might support the idea that the cortex is stereotyped in its layers and internal organization [1]. If so, then corresponding areas in different modalities could follow similar principles of physiology, connectivity and function, varying largely in the receptor populations that define them. Appealing as this proposition may be, several lines of evidence reviewed here suggest that the physiology and connectivity of the primary auditory cortex (AI) differs significantly from that of primary visual cortex (VI), which serves as a frame of reference for this account. For example, layer IV spiny stellate cells are a preferential target of thalamic input in VI [2], whereas in AI, pyramidal cells in deep layer III and layer IV cells receive medial geniculate body (MGB) input [3*]. These neuronal classes have specific, and perhaps unique, functions. Another difference is that layer III neurons in VI have almost exclusively ipsilateral corticothalamocortical projections [4], whereas many layer III cells in AI are commissural [5]. Here, we delineate some of the parallels and differences between auditory and visual cortex. A related issue concerns the status of auditory areas beyond AI and how these contribute to hearing and sensorimotor behavior. Our aim is to understand how auditory cortex participates in tasks ranging from local information processing to higher-order function, including how descending projections influence targets as peripheral as the cochlea [6].

Functional organization of AI
There is consensus that the one-dimensional gradient of characteristic frequency (CF) spanning the cochlear epithelium is represented topographically across AI. CF is the frequency at which a neuron responds most strongly at low sound pressure levels (SPLs). CF topography is highly conserved across species [7] and subregions representing biologically significant CFs are often enlarged, much like the foveal magnification in VI [8]. The relationship between CF and cortical area is logarithmic and its slope is species-specific (e.g. the 2–16 kHz region is nearly three-fold greater in cat AI [9] than in rat AI [10]). The frequency response areas of synaptically paired neurons in the ventral division of the MGB (MGV) and AI are overlapping, and spectral properties can be highly conserved (as in VI) or show convergence of CFs within one-third of an octave [11•]. This suggests considerable conservation of excitatory frequency information in the feedforward process, as information flows sequentially along serial synaptic stations from subcortical to cortical sites. An extended subregion of cortical space is dedicated to iso-CF contours oriented orthogonal to the CF-gradient. A large set of contiguous neurons are tuned to one CF, and these cells form elongated iso-CF contours (Figure 1a). The iso-CF axis is expanded in some species (e.g. the cat’s iso-CF dimension is three times as large as that of the rat [12]). Frequency representation at the level of single neurons is labile, contingent on experience, and susceptible to long-term reorganization [13,14•,15•]. The auditory representation is plastic in that it is input-dependent on subcortical [16] and cortical [17] sources.

The iso-CF axis has an internal functional organization resembling the modular organization in VI. AI neurons respond to a narrow range of frequencies at low SPLs. At higher SPLs, frequency responses can remain narrowband
Auditory cortex functional organization. (a) Modular arrangement of receptive field properties and intrinsic cortical connections in AI. CF and inverse bandwidth (Q40) were mapped over a 3 x 3 mm region in layers III and IV; the maps are stacked to show the spatial relationship of these two metrics. In the cochleotopic map, the CF gradient increases from caudal to rostral (as illustrated with one-third octave iso-frequency contours in progressively lighter shades of gray). Input from the MG Bv to AI (gray in layers III and IV) is arrayed along the caudal–rostral axis of AI. Their CFs match the synaptic targets in AI ± one-third of an octave. MG Bv neurons project non-uniformly along the iso-frequency axis, forming periodic clusters of axon terminals. Intrinsic corticocortical connections between layer III neurons (black circles and arrows) are uniform but limited in spread across the CF gradient, and periodic across the isofrequency axis. The spectral integration map is an interpolated map of Q40 for the same recording positions. Two subdomains with NB neurons (regions cNB and d1) and two interleaved subdomains with BB neurons fill the entire cochleotopic representation. In the spectral integration map, NB and BB domains are indicated as gray or white, respectively. The bandwidth receptive field dimension covaries with several other receptive field properties; for simplicity, only bandwidth is shown. The gray NB region appears to extend across all CFs, and therefore constitutes an iso-bandwidth representation. Horizontal cortical connections (arrows) link neurons centered about the same CF (iso-frequency neurons) and with similar bandwidth (e.g. d1 projects to the cNB subdomain). In dorsal AI, Q40 is also clustered (regions d3, d4, light blue panels) but its thalamic inputs and horizontal connectivity is less well understood. (b) Cat auditory cortical areas. The 'a' denotes the locus and approximate scale of the cortical cube shown in the first panel. Cochleotopic regions (light blue) receive input mainly from MG Bv. Non-cochleotopic regions (gray) are targets of other MG B subdivisions. All areas receive sparse parallel input from MG Bm (not shown). AI, second auditory cortical area; C, caudal; D, dorsal; EPD, posterior ectosylvian gyrus, dorsal part; EPI, posterior ectosylvian gyrus, intermediate part; EPV, posterior ectosylvian gyrus, ventral part; Ins, insular cortex; P, posterior field; SF, suprasylvian fringe; Te, temporal cortex; Ve, ventral auditory area; VP, ventral posterior auditory area.
unknown whether bandwidth and binaural modules are independent, like the visual representations of ocular dominance and orientation [40].

Do the bandwidth modules emerge from new peripheral sensory machinery or are they a consequence of novel, behaviorally driven or computational convergence? Other than changes in cochlear frequency range, there is little evidence for the evolution of new peripheral sensory machinery in the auditory system, although two contiguous cochlear representations in the cochlear nucleus arise from dorsal and ventral spiral ganglion cells [41]. Emergence of novel spectral integration properties in the cortex may embody transformations between correlated thalamic and cortical neurons [11•,42•]. No contiguous bandwidth modules have been described subcortically; however, spectral bandwidth diversity [43] and topographic gradients exist in the MGBv [44] and the central nucleus of the inferior colliculus (IC) [45]. Cortical BB response properties develop late in cats [46,47], perhaps because in this species thalamocortical or corticocortical convergence contribute to the emergence of modularity [19•].

Cortical connectivities
There is no consensus on how auditory cortex is defined. Because only four of the approximately 14 areas recognized in the cat have a cochleotopic map [48] (Figure 1b), this criterion is of limited value for such a definition. Accordingly, a combination of physiological properties, cytoarchitectonics, histochemistry, thalamocortical and corticocortical connection patterns, or neuroimaging methods collectively provide better points of reference for definition. Evidence exists that some of the areas regarded here as unitary contain further subdivisions [49,50]. Cochleotopic and non-cochleotopic cortices have distinct and robust thalamocortical input profiles [27] that are largely conserved even after peripheral insult [51]. This connectional stability contrasts with behavioral plasticity in the AI of ferrets when retinal peripheral insult [51]. This belies the notion that the thalamus is a simple relay, or that its input reaches only a few cortical layers.

The four cochleotopic cortical fields (Figure 1b, in blue) receive most of their thalamic input in layers IIIb and IV, much like the C-laminae to VI projection [54]. Non-cochleotopic cortices receive input from many more thalamic subdivisions, most of whose cells have broader tuning; their axons terminate more uniformly and in more layers [27]. AI and the anterior auditory field (AAF), like VI and the second visual cortical area (VII), appear to be closely allied as they respond with shorter latencies, have simpler response profiles [55,56], and are densely interconnected [57,58].

Neurons of the medial division of the MGB (MGBm) provide parallel thalamic input to all auditory cortices. The MGBm projection system differs from MGBv in several ways. First, it terminates in layers I, III, IV and VI. Second, it is multisensory and capable of long-term potentiation [59]. Third, it projects to all auditory cortical areas and beyond. Some large medial division axons innervate layer Ia, where they evoke early responses [60•] among a population whose cells are nearly all γ-aminobutyric acid (GABA)-positive [61]. Other input to rabbit layer I arises from the same thalamocortical axons terminating in layers II–V, implying concomitant activation across 1500 µm-wide tangential zones [62] and perhaps more than one mode of lemniscal thalamocortical activation. Even layer V, regarded widely as independent of thalamic input, receives more than 10% of the total boutons [27]. This belies the notion that the thalamus is a simple relay, or that its input reaches only a few cortical layers.

Massive auditory corticofugal feedback [63–66] may constitute several parallel pathways [64]. This influence reaches the MGB [67], the IC [68], and rat olivocochlear neurons [6] monosynaptically. The corticothalamic projection arises from heterogeneous pyramidal cells in layers Va, Vc and VI, and is as divergent as the thalamocortical projection [69]. All areas send giant boutons chiefly to non-cochleotopic thalamic regions [70,71]. Corticothalamic input affects many facets of physiology [72•] and signal selection [73]. Cortical output to the basal ganglia [74•] may influence motor planning or cognition.

The corticocollicular system arises from homogeneous layer V cells situated between the sublayers that project to the MGB [75]; few neurons project to both the MGB and the IC [76]. Cortical projections chiefly target IC nuclei outside the cochleotopic pathway [68]. In contrast to corticothalamic axons, these projections are more segregated, convergent and homogeneous. Auditory cortex neurons also project to the dorsal cochlear nucleus [63,77], although these projections are neither large nor dense. The corticofugal system modulates the frequency tuning of thalamic and collicular neurons; such effects appear greater in subregions with highly magnified CF domains [78].

Functional organization beyond AI
The present view of AI functional and structural organization suggests several parallel and serial input/output systems. These can be identified by their laminar arrangement [27], nuclear targets [67], synaptic effects [79•], cellular specificity [3•], histochemical profiles [80], and receptive field characteristics [81•]. The impact of these streams on other auditory areas is unclear.

Optical recording in the guinea pig [82•] and chinchilla [83•] found several cortical fields that differ in their cochleotopy, response latencies and spectral integration properties. The spatial spread of activation from the cochleotopic fields suggests the presence of several pathways. Electrophysiological and neuroanatomical studies in the gerbil [84] and guinea pig [85,86] revealed that fields AI and AAF (Figure 1b) share cytoarchitectonic, myelo-architectonic, and histochemical patterns usually
Physiological studies in cat and monkey find many differences between cortical areas that may clarify their role in the several functional streams. A reevaluation of cat posterior field physiology [88*] (Figure 1b) found more complex inhibitory bands than in AI, a range of tuning shapes, and spectral and temporal properties suggesting more information convergence and more complex integration than in AI. In the monkey, the rostral and the caudal–medial fields also differ from AI [89] in their sensitivity to the spatial location of a sound source. This supports the idea of a separate spatial processing pathway [20,89]. Evidence for increased spatial processing in the caudal belt area contrasts with enhanced selectivity for call types to a set of natural monkey vocalizations in the anterior belt areas [31*].

Whether spatial and spectral receptive field properties in non-primary cortices are inherited from AI or undergo extensive remodeling remains to be seen. No systematic representation besides cochleotopy, as described in cat [18], squirrel monkey [21*] and owl monkey AI [90], has been seen in non-primary areas. It remains vital to determine whether specialized cortical regions (e.g. the frequency-modulated FM-FM area) in echolocating bats are functionally or anatomically analogous to fields in cat and monkey [91*]. Area-specific suppression of activity can affect both spatial and spectral discrimination abilities [92,93*] indicating the behavioral relevance of these representations. The differential contribution of input, output, or representational alterations on these properties is unknown.

Evidence for different auditory fields in subhuman species was augmented by work in human auditory cortex, where multiple regions were identified in functional magnetic resonance imaging (fMRI) and magnetoencephalographic studies [94*,95]. Click-evoked potentials recorded from pial-surface electrodes on the lateral superior temporal gyrus of awake humans reveal an acoustically responsive region distinct from the auditory fields on Heschl’s gyrus [96]. Differences in location, anesthetic effects, and the time course of response recovery imply that it may belong to the non-cochleotopic region. Cochleotopic and non-cochleotopic (core-belt) distinctions [97*] reflect differences in processing NB and BB stimuli [98]. A dorsal cortical region, potentially involved in spectral motion [99], suggests that the search for functionally homologous regions in monkey and human is incomplete [100]. Further parallels between feline, human, and subhuman primate auditory cortex are emerging from imaging [97*], cytoarchitectonic [87*], and tract-tracing [101] approaches. The evidence confirms that multiple areas exist [102]. Moreover, histochemical and metabolic staining delineate related areas in macaques and chimpanzees [87*] and humans [87*,103]. Deposits of diffusible tracers label anisotropic corticocortical projections [101] like those in cat [104], and a hierarchical plan has been proposed for primates and other species [97*]. Further parallels include clustered thalamocortical connections whose laminar distribution in macaque AI [26] resembles the pattern in the cat.

**Multiple processing streams in auditory cortex**

In the visual system, a global distinction between a dorsal cortical pathway associated with the analysis of motion (where) and a ventral form and color (what) stream has been proposed [105,106]. This hypothesis is strengthened by findings that link the origins of each pathway to anatomically, histochemically and functionally distinct compartments in VI and VII [106], to thalamic targets in the parallel magnocellular and parvocellular systems [107], as well as to other corticofugal projections upon premotor structures [108]. By analogy, corticocortical acoustic outflow forms independent streams that target rostral and caudal domains in prefrontal cortex (PFC) that serve different functions [109,110]. Rostral and orbital PFC areas are connected to rostral belt and parabelt areas, whereas the caudal and inferior convexities are connected with the caudal belt and parabelt. Functional divergence between these two streams is supported by differences in local connections, physiology, and differences in PFC targets. A physiological evaluation of PFC finds a circumscribed region with many neurons that are predominantly or exclusively auditory [111*].

The distinction between a dorsal, localization pathway and a ventral, identification pathway in primates rests upon the role of the caudal belt region for spatial information processing [31*,90,110] and the rostral belt’s preference for complex vocalizations [31*,109]. Other distinctions between them come from imaging studies in humans showing that phonetic and object recognition, speaker identification [112], pitch tasks [113*] and spectrotemporal feature processing [114*] localize to the ventral pathway, whereas spectral motion in phonemic [112] and sound location tasks [113*] resides in the dorsal pathway. Confirmation of the independence of these pathways, the role of the modular organization of bandwidth in AI, and the influence of the cochleotopic and non-cochleotopic MGB projections requires further work on functional properties and their prospective cortical segregation. Species without an expanded iso-CF axis in AI have other auditory cortical fields; perhaps AI modularity represents a recent evolutionary adaptation [115].

**Conclusions**

A more refined picture of the function and organization of auditory cortex is emerging from different lines of enquiry. Anatomical distinctions between several types of input/output relationships and connectivities are paralleled by physiologically defined differences. Direct relationships between anatomical and physiological substrates for parallel and serial processing streams remain to be firmly established;
however, both approaches confirm local modularity and suggest a global multiplicity of processing streams. Common themes in visual and auditory cortical organization, including several processing streams and the functional plasticity of cochleotopic auditory cortex, support general, modality-independent principles. Other evidence for modality-specific anatomical and physiological properties constrains these parallels.

Acknowledgements
We thank JJ Frietoe, DT Larse and CC Lee for helpful comments. Supported by United States Public Health Service grants 2 R01 DC2600-06 to GE Schreiner and 2 R01 DC02319-22 to JA Winer.

References and recommended reading
Papers of particular interest, published within the annual period of review, have been highlighted as:

• of special interest
• of outstanding interest


These authors show that layer III–IV neurons in AI and VI, which receive input from the thalamus, differ. The finding that in AI, layer III–IV pyramidal cells are the main thalamic target, whereas in visual cortex spiny stellate cells are chiefly postsynaptic, implies modality specific differences in cortical processing of thalamic input.


This study compares the degree of receptive field overlap in auditory thalamic and cortical neurons, whose spike correlation profiles indicate mono-synaptic connectivity. The receptive field overlap in thalamocortical neuron pairs ranges from perfect (as in the visual system) to as much as one-third of an octave of non-overlap. The strength of the output correlation does not predict the degree of receptive field similarity in the auditory system. This reflects the large variations in the inhibitory patterns of thalamic versus cortical receptive fields. Thus, the thalamocortical auditory receptive field transformation appears to be more divergent than the corresponding visual information.


This study finds that auditory cortical spectral and temporal receptive field features are differentially affected by sensory experience and concomitant nucleus basalis activation. Spectral and temporal domains are thus independently modifiable at the level of single cells and at the level of population profiles.


These authors demonstrate that local auditory field potentials in guinea pig show flexible associative tuning, retention and consolidation extending up to the 10-day duration of the study. Thus, the auditory cortex of the guinea pig can represent and retain learned changes.


Rajan finds that chronic damage to peripheral receptors can increase the size of the excitatory receptive field subregions in cortical layers III–IV and can elicit new receptive field subareas. This result complements earlier findings that show changes in inhibitory receptive field organization.


In this paper, the authors map the receptive fields of AI neurons in squirrel monkeys. They find systematic spatial gradients of best frequency, response threshold and latency, as well as a modular organization of spectral receptive field width.


Here, we show that intrinsic long-range cortical connections in AI occur predominantly among compartments with similar iso-frequency and level-dependent spectral bandwidths.


These authors employ white noise analysis techniques to describe the separability of linear components in cortical neuronal responses, an accomplishment that has been virtually impossible with conventional techniques.
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This study compares neuronal activation in two non-cochlearie cortical fields in response to complex vocalizations delivered from various spatial directions. It reveals differences in neuronal responsiveness to spatial and spectrotemporal domains. The findings are interpreted in the context of a framework of specialized processing streams.


The authors provide a new and powerful demonstration that the representation of spatial cues is distributed within AI. They also describe an as yet unexplored cortical binaural response property in AI neurons.


This study shows that cortical feedback induces a predictable shift in subcortical receptive field properties across species and that the precise nature of the change can be related to species-specific features of the cortical representation. Thus, some bat subtypes with expanded cortical representation have a wider dynamic range for corticofugal feedback modulation.


A thorough description of a binaural property that is vital for integration of low frequencies across many frequencies is given here. The authors find that interaural time differences (ITDs) are coded by two types of cell: those with constant ITD responses and those whose ITD narrows by an inverse frequency function. The constant ITD cells are common above the superior olivary complex, suggesting that they participate in the detection of just noticeable differences in ITD change.


Here, white noise analysis and simultaneous thalamocortical recording reveal significant receptive field differences between thalamus and cortex. These findings suggest parallels and differences in spatiotemporal receptive field organization in these stations. Thus, spectral integration, as determined by mapping excitatory bandwidth and spectral modulation properties, was conserved. On the other hand, cortical temporal modulation was twice as slow as in the thalamus, the spectral and temporal integration properties of cortex and thalamus were independent, and there were more cortical cells driven by the contralateral ear alone. This is an important approach to understanding thalamocortical transformations.


83. Harel N, Mori N, Sawada S, Mount RJ, Hanson RV: Three distinct auditory areas of cortex (AI, All, and AAF) defined by optical imaging of intrinsic signals. Neuroimage 2000, 11:302-312. Similarly to a2+, optical recording of intrinsic signals in chinchilla reveals three auditory cortical fields that differ in their cochleotopic gradient.


A detailed study of spectrotwagional response properties in cat posterior auditory field reveals receptive fields with greater complexity than in AI. This is indicative of hierarchical, field-specific processing principles between different areas of the auditory cortex.


111. Romanski LM, Goldman-Rakic PS: An auditory domain in primate prefrontal cortex. Nat Neurosci 2002, 5:15-16. Here, auditory, modality-specific neurons are observed in a circumscribed ventral area of the prefrontal cortex of awake monkeys. This region appears to be more responsive to complex sounds than to pure tones and has been shown to receive separate projections from dorsal and ventral regions of auditory cortex[109,110].


