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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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
MGBm	medial division of the MGB
MGBv	ventral division of the MGB
NB	narrowband
PFC	prefrontal cortex
Q_{40}	inverse bandwidth
SPLs	sound pressure levels
VI	primary visual cortex
VII	second visual cortical area

Introduction

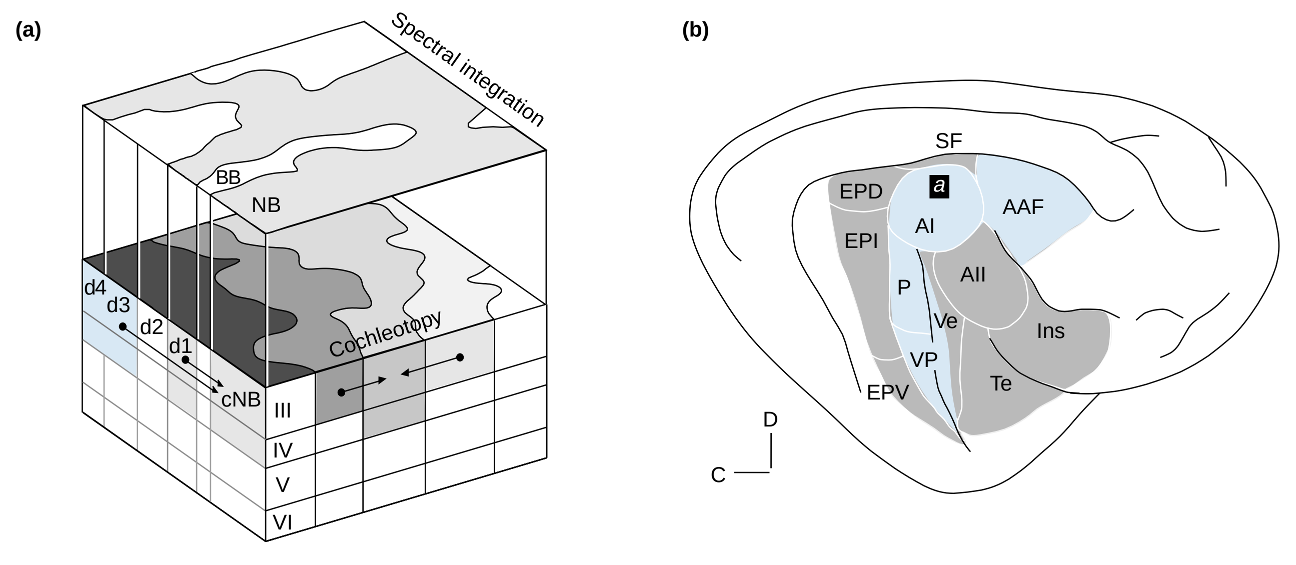
The essential uniformity in sensory neocortical structure might support the idea that the cortex is stereotyped in its layers and internal organization [1]. If so, then corresponding areas in different modalities could follow similar principles of physiology, connectivity and function, varying largely 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 corticocortical 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 (MGBv) 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

Figure 1



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Auditory cortex functional organization. (a) Modular arrangement of receptive field properties and intrinsic cortical connections in AI. CF and inverse bandwidth (Q_{40}) were mapped over a 3 × 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 MGBv 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. MGBv neurons project non-uniformly along the isofrequency 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 Q_{40} 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 (isofrequency neurons) and with similar bandwidth (e.g. d1 projects to the cNB subdomain). In dorsal AI, Q_{40} 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 MGBv. Non-cochleotopic regions (gray) are targets of other MGB subdivisions. All areas receive sparse parallel input from MGBm (not shown). AII, 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.

(NB) or extend to over five octaves. A continuum of bandwidth values [18,19•,20] forms alternating NB and broadband (BB) domains along the iso-CF axis of AI in cat and monkey [21•,22,23•]. Tracer injections in the NB compartment label clusters of neurons aligned to the iso-CF contour [23•,24]. The iso-CF horizontal connections are in register to bandwidth compartments, such that NB neurons receive convergent long-range (>1 mm) input primarily from neurons with similar bandwidths and CFs (Figure 1a). This overlapping pattern of response properties and connectivity creates modules aligned along the iso-CF axis in the cat. Thalamocortical axons also have a compartmental distribution, with alternating dense and sparse terminal fields [25,26] in the iso-CF dimension [27].

Like VI, AI contains several representations of the sensory domain. How are these properties interrelated? Binaural response type, intensity threshold, operating range, and frequency modulation rate are each embedded within the iso-CF axis [18,28,29,30•,31•,32•]. Broadband neurons often have a higher response threshold, so that bandwidth and threshold topographies are correlated [33]. Thus, bandwidth modules may covary with multiple gradients for SPL or operating range [34,35]. Binaural properties (coded as time and intensity differences) vary periodically along the iso-CF axis [36]; however, their relationship to bandwidth modules remains unclear. The relative size of binaural time and intensity pathways reflects acoustic experience and the species’ audibility range [37,38•]. Likewise, the expanded iso-CF dimension in cat and monkey extends concomitantly over binaural, bandwidth and intensity representations; how these might relate to auditory experience such as differences in binaural processing is unknown. A gradient representing a range of interaural intensities is aligned to the iso-CF axis in the pallid bat [37]. A second gradient for interaural time difference processing may exist along the iso-CF axis for species with an extended range of low frequencies [39•]. It is 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 ganglion cells are redirected onto the MGB [52]. Such manipulations can also affect cortical local circuitry even when the thalamus is unchanged [53].

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-amino butyric 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 associated with cochleotopic areas. Surrounding regions have other connectional patterns and may also differ in their functional or multisensory organization. Assignment of areas to belt and parabelt regions, as in the scheme adopted for monkeys [87•], is feasible but requires more data.

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.

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