

Functional architecture of auditory cortex

Heather L Read*, Jeffery A Winer† and Christoph E Schreiner*‡

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, connective 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.

Addresses

*WM Keck Center for Integrative Neuroscience, University of California at San Francisco, San Francisco, California 94143-0732, USA; e-mail: heather.read@phy.ucsf.edu

†Department of Molecular and Cell Biology, University of California at Berkeley, Berkeley, California 94720-3200, USA; e-mail: jawiner@socrates.berkeley.edu

‡e-mail: chris@phy.ucsf.edu

Correspondence: Christoph E Schreiner

Current Opinion in Neurobiology 2002, 12:433–440

0959-4388/02/\$ – see front matter

© 2002 Elsevier Science Ltd. All rights reserved.

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
MGBm	medial division of the MGB
MGBv	ventral division of the MGB
NB	narrowband
PFC	prefrontal cortex
Q₄₀	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

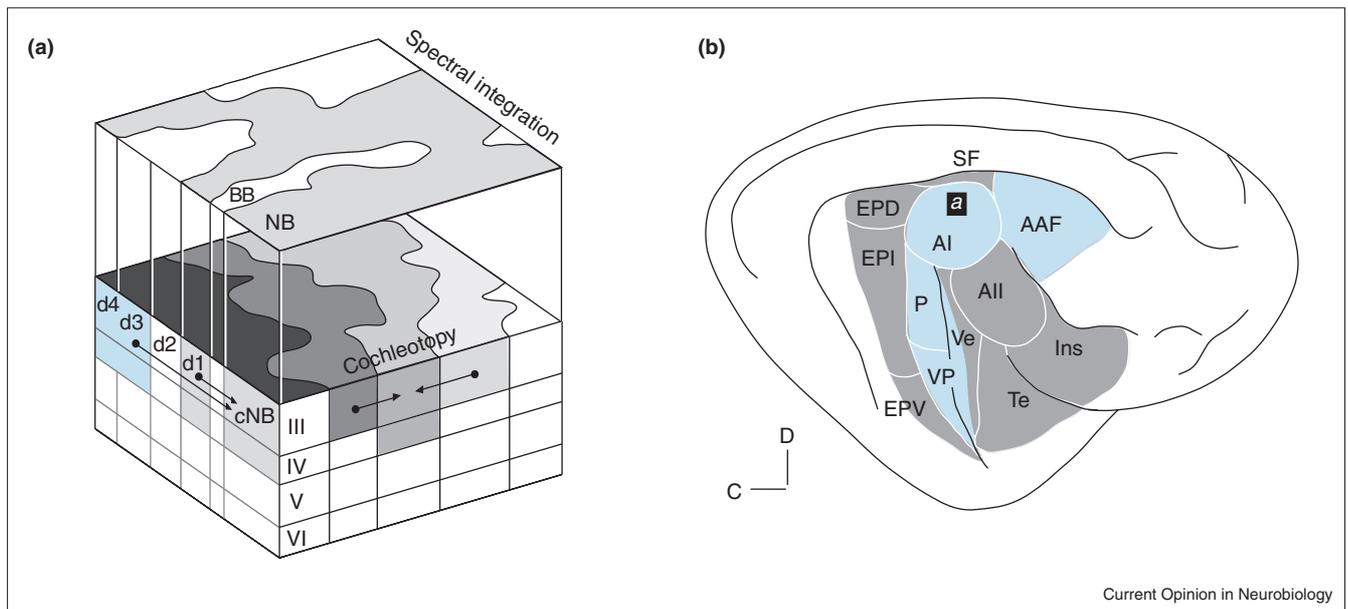
reference for this account. For example, layer IV spiny stellate cells are a preferential target of thalamic input in VI [2], whereas in AI, pyramidal cells in deep layer III and layer IV cells receive medial geniculate body (MGB) input [3]. These neuronal classes have specific, and perhaps unique, functions. 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



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 \pm 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). All, 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 connective 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 μ m-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.

Acknowledgements

We thank JJ Prieto, DT Larue and CC Lee for helpful comments. Supported by United States Public Health Service grants 2 R01 DC2260-06 to CE 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

1. Rockel AJ, Hiorns RW, Powell TPS: **The basic uniformity in structure of the neocortex.** *Brain* 1980, **103**:221-244.
2. McGuire BA, Hornung J-P, Gilbert CD, Wiesel TN: **Patterns of synaptic input to layer 4 of cat striate cortex.** *J Neurosci* 1984, **4**:3021-3033.
3. Smith PH, Populin LC: **Fundamental differences between the thalamocortical recipient layers of the cat auditory and visual cortices.** *J Comp Neurol* 2001, **436**:508-519.
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.
4. Fisker RA, Garey LJ, Powell TPS: **The intrinsic, association and commissural connections of area 17 of the visual cortex.** *Phil Trans R Soc B* 1975, **272**:487-536.
5. Code RA, Winer JA: **Commissural neurons in layer III of cat primary auditory cortex (AI): pyramidal and non-pyramidal cell input.** *J Comp Neurol* 1985, **242**:485-510.
6. Mulders WHAM, Robertson D: **Evidence for direct cortical innervation of medial olivocochlear neurons in rats.** *Hear Res* 2000, **144**:65-72.
7. Luethke LE, Krubitzer LA, Kaas JH: **Cortical connections of electrophysiologically and architectonically defined subdivisions of auditory cortex in squirrels.** *J Comp Neurol* 1988, **268**:181-203.
8. Hubel DH, Wiesel TN: **Uniformity of monkey striate cortex: a parallel relationship between field size, scatter, and magnification factor.** *J Comp Neurol* 1974, **158**:295-306.
9. Merzenich MM, Knight PL, Roth GL: **Representation of cochlea within primary auditory cortex in the cat.** *J Neurophysiol* 1975, **38**:231-249.
10. Sally SL, Kelly JB: **Organization of auditory cortex in the albino rat: sound frequency.** *J Neurophysiol* 1988, **59**:1627-1638.
11. Miller LM, Escabi MA, Read HL, Schreiner CE: **Functional convergence of response properties in the auditory thalamocortical system.** *Neuron* 2001, **32**:151-160.
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.
12. Kilgard MP, Merzenich MM: **Cortical map reorganization enabled by nucleus basalis activity.** *Science* 1998, **279**:1714-1718.
13. Weinberger NM: **Physiological memory in primary auditory cortex: characteristics and mechanisms.** *Neurobiol Learn Mem* 1998, **70**:226-251.
14. Kilgard MP, Pandya PK, Vasquez J, Gehi A, Schreiner CE, Merzenich MM: **Sensory input directs spatial and temporal plasticity in primary auditory cortex.** *J Neurophysiol* 2001, **86**:326-338.
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.
15. Galvan VV, Weinberger NM: **Long-term consolidation and retention of learning-induced plasticity in the auditory cortex of the guinea pig.** *Neurobiol Learn Mem* 2002, **77**:78-108.
The 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.
16. Roe AW, Garraghty PE, Esguerra M, Sur M: **Experimentally induced visual projections to the auditory thalamus in ferrets: evidence for a W cell pathway.** *J Comp Neurol* 1993, **334**:263-280.
17. Pallas SL, Littman T, Moore DR: **Cross-modal reorganization of callosal connectivity without altering thalamocortical projections.** *Proc Natl Acad Sci USA* 1999, **96**:8751-8756.
18. Schreiner CE, Read HL, Sutter ML: **Modular organization of frequency integration in primary auditory cortex.** *Annu Rev Neurosci* 2000, **23**:501-529.
19. Rajan R: **Plasticity of excitation and inhibition in the receptive field of primary auditory cortical neurons after limited receptor organ damage.** *Cereb Cortex* 2001, **11**:171-182.
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.
20. Recanzone GH: **Response profiles of auditory cortical neurons to tones and noise in behaving macaque monkeys.** *Hear Res* 2000, **150**:104-118.
21. Cheung SW, Bedenbaugh PH, Nagarajan SS, Schreiner CE: **Functional organization of squirrel monkey primary auditory cortex.** *J Neurophysiol* 2001, **85**:1732-1749.
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.
22. Schreiner CE, Mendelson JR: **Functional topography of cat primary auditory cortex: distribution of integrated excitation.** *J Neurophysiol* 1990, **64**:1442-1459.
23. Read HL, Winer JA, Schreiner CE: **Modular organization of intrinsic connections associated with spectral tuning in cat auditory cortex.** *Proc Natl Acad Sci USA* 2001, **98**:8042-8047.
Here, we show that intrinsic long-range cortical connections in AI occur predominantly between compartments with similar iso-frequency and level-dependent spectral bandwidths.
24. Wallace MN, Kitzes LM, Jones EG: **Intrinsic inter- and intralaminar connections and their relationship to the tonotopic map in cat primary auditory cortex.** *Exp Brain Res* 1991, **86**:527-544.
25. McMullen NT, de Venecia RK: **Thalamocortical patches in auditory neocortex.** *Brain Res* 1993, **620**:317-322.
26. Hashikawa T, Molinari M, Rausell E, Jones EG: **Patchy and laminar terminations of medial geniculate axons in monkey auditory cortex.** *J Comp Neurol* 1995, **362**:195-208.
27. Huang CL, Winer JA: **Auditory thalamocortical projections in the cat: laminar and areal patterns of input.** *J Comp Neurol* 2000, **427**:302-331.
28. Mendelson JR, Schreiner CE, Sutter ML, Grasse KL: **Functional topography of cat primary auditory cortex: responses to frequency-modulated sweeps.** *Exp Brain Res* 1993, **94**:65-87.
29. Mendelson JR, Schreiner CE, Sutter ML: **Functional topography of cat primary auditory cortex: response latencies.** *J Comp Physiol A* 1997, **181**:615-633.
30. Depireux DA, Simon JZ, Klein DJ, Shamma SA: **Spectro-temporal response field characterization with dynamic ripples in ferret primary auditory cortex.** *J Neurophysiol* 2001, **85**:1220-1234.
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.

31. Tian B, Reser D, Durham A, Kustov A, Rauschecker JP: **Functional specialization in rhesus monkey auditory cortex.** *Science* 2001, **292**:290-293.
- This study compares neuronal activation in two non-cochleotopic 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.
32. Schnupp JW, Mrsic-Flogel, TD, King AJ: **Linear processing of spatial cues in primary auditory cortex.** *Nat Neurosci* 2001, **4**:14:200-204.
- 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.
33. Brosch M, Schreiner CE: **Correlations between neural discharges are related to receptive field properties in cat primary auditory cortex.** *Eur J Neurosci* 1999, **11**:3517-3530.
34. Sutter ML, Schreiner CE: **Topography of intensity tuning in cat primary auditory cortex: single-neuron versus multiple-neuron recordings.** *J Neurophysiol* 1995, **73**:190-204.
35. Ehret G: **The auditory cortex.** *J Comp Physiol A* 1997, **181**:547-557.
36. Imig TJ, Adrián HO: **Binaural columns in the primary auditory field (A1) of cat auditory cortex.** *Brain Res* 1977, **138**:241-257.
37. Razak KA, Fuzessery ZM: **A systematic representation of interaural intensity differences in the auditory cortex of the pallid bat.** *Neuroreport* 2000, **11**:2919-2924.
38. Sakai M, Suga N: **Plasticity of the cochleotopic (frequency) map in specialized and nonspecialized auditory cortices.** *Proc Natl Acad Sci USA* 2001, **98**:3507-3512.
- This study shows that cortical feedback induces a predictable shift in sub-cortical 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 subspecies with expanded cortical representation have a wider dynamic range for corticofugal feedback modulation.
39. Fitzpatrick DC, Kuwada S: **Tuning to interaural time differences across frequency.** *J Neurosci* 2001, **21**:4844-4851.
- 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.
40. Crair MC, Ruthazer ES, Gillespie DC, Stryker MP: **Ocular dominance peaks at pinwheel center singularities of the orientation map in cat visual cortex.** *J Neurophysiol* 1997, **77**:3381-3385.
41. Snyder RL, Leake PA, Hradek GT: **Quantitative analysis of spiral ganglion cell projections to the cat cochlear nucleus.** *J Comp Neurol* 1997, **379**:133-149.
42. Miller L, Escabi MA, Read HL, Schreiner CE: **Spectrotemporal receptive fields in the lemniscal auditory thalamus and cortex.** *J Neurophysiol* 2002, **87**:516-527.
- 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.
43. Ramachandran R, Davis KA, May BJ: **Single-unit responses in the inferior colliculus of decerebrate cats. I. Classification based on frequency response maps.** *J Neurophysiol* 1999, **82**:152-163.
44. Rodrigues-Dagaeff C, Simm G, de Ribaupierre Y, Villa A, de Ribaupierre F, Rouiller EM: **Functional organization of the ventral division of the medial geniculate body of the cat: evidence for a rostro-caudal gradient of response properties and cortical projections.** *Hear Res* 1989, **39**:103-125.
45. Schreiner CE, Langner G: **Periodicity coding in the inferior colliculus of the cat. II. Topographical organization.** *J Neurophysiol* 1988, **60**:1823-1840.
46. Eggermont JJ: **Differential effects of age on click-rate and amplitude modulation-frequency coding in primary auditory cortex of the cat.** *Hear Res* 1993, **65**:175-192.
47. Bonham B, Cheung S, Godey B, Schreiner C: **Frequency tuning in segregated areas of primary auditory cortex develops differently.** *Assn Res Otolaryngol Abs* 2001, **24**: 21706.
48. Imig TJ, Morel A: **Organization of the thalamocortical auditory system in the cat.** *Annu Rev Neurosci* 1983, **6**:95-120.
49. Clascá F, Llamas A, Reinoso-Suárez F: **Insular cortex and neighboring fields in the cat: a redefinition based on cortical microarchitecture and connections with the thalamus.** *J Comp Neurol* 1997, **384**:456-482.
50. Clascá F, Llamas A, Reinoso-Suárez F: **Cortical connections of the insular and adjacent parieto-temporal fields in the cat.** *Cereb Cortex* 2000, **10**:371-399.
51. Stanton SG, Harrison RV: **Projections from the medial geniculate body to primary auditory cortex in neonatally deafened cats.** *J Comp Neurol* 2000, **426**:117-129.
52. von Melchner L, Pallas SL, Sur M: **Visual behaviour mediated by retinal projections directed to the auditory pathway.** *Nature* 2000, **404**:871-876.
53. Gao W-J, Pallas SL: **Cross-modal reorganization of horizontal connectivity in auditory cortex without thalamocortical projections.** *J Neurosci* 1999, **19**:7940-7950.
54. Kawano J: **Cortical projections of the parvocellular laminae C of the dorsal lateral geniculate nucleus in the cat: an anterograde wheat germ agglutinin conjugated to horseradish peroxidase study.** *J Comp Neurol* 1998, **392**:439-457.
55. Schreiner CE, Urbas JV: **Representation of amplitude modulation in the auditory cortex of the cat. II. Comparison between cortical fields.** *Hear Res* 1988, **32**:49-64.
56. Eggermont JJ: **Representation of spectral and temporal sound features in three cortical fields of the cat. Similarities outweigh differences.** *J Neurophysiol* 1998, **80**:2743-2764.
57. Rouiller EM, Simm GM, Villa AEP, de Ribaupierre Y, de Ribaupierre F: **Auditory corticocortical interconnections in the cat: evidence for parallel and hierarchical arrangement of the auditory cortical areas.** *Exp Brain Res* 1991, **86**:483-505.
58. Budinger E, Heil P, Scheich H: **Functional organization of auditory cortex in the Mongolian gerbil (*Meriones unguiculatus*). III. Anatomical subdivisions and corticocortical connections.** *Eur J Neurosci* 1999, **12**:2425-2451.
59. Gerren RA, Weinberger NM: **Long term potentiation in the magnocellular medial geniculate nucleus of the anesthetized cat.** *Brain Res* 1983, **265**:138-142.
60. Cruikshank SJ, Rose HJ, Metherate R: **Auditory thalamocortical synaptic transmission in vitro.** *J Neurophysiol* 2001, **87**:361-384.
- Cruikshank *et al.* demonstrate that a novel fast activation of the auditory cortex by non-lemniscal thalamic input may be unique to the auditory system.
61. Prieto JJ, Peterson BA, Winer JA: **Morphology and spatial distribution of GABAergic neurons in cat primary auditory cortex (AI).** *J Comp Neurol* 1994, **344**:349-382.
62. Cetas JS, de Venecia RK, McMullen NT: **Thalamocortical afferents of Lorente de Nó: medial geniculate axons that project to primary auditory cortex have collateral branches to layer I.** *Brain Res* 1999, **830**:203-208.
63. Weedman DL, Ryugo DK: **Projections from auditory cortex to the cochlear nucleus in rats: synapses on granule cell dendrites.** *J Comp Neurol* 1996, **371**:311-324.
64. Ojima H, He J-F: **Cortical convergence originating from domains representing different frequencies in the cat AI.** *Acta Otolaryngol* 1997, **532**:126-128.
65. Villa AEP, Rouiller EM, Simm GM, Zurita P, de Ribaupierre Y, de Ribaupierre F: **Corticofugal modulation of the information processing in the auditory thalamus of the cat.** *Exp Brain Res* 1991, **86**:506-517.
66. Rouiller EM, Welker E: **A comparative analysis of the morphology of corticothalamic projections in mammals.** *Brain Res Bull* 2000, **53**:727-741.

67. Winer JA, Diehl JJ, Larue DT: **Projections of auditory cortex to the medial geniculate body of the cat.** *J Comp Neurol* 2001, **430**:27-55.
68. Winer JA, Larue DT, Diehl JJ, Hefti BJ: **Auditory cortical projections to the cat inferior colliculus.** *J Comp Neurol* 1998, **400**:147-174.
69. Winer JA, Prieto JJ: **Layer V in cat primary auditory cortex (AI): cellular architecture and identification of projection neurons.** *J Comp Neurol* 2001, **434**:379-412.
70. Rouiller EM, Welker E: **Morphology of corticothalamic terminals arising from the auditory cortex of the rat: a *Phaseolus vulgaris*-leucoagglutinin (PHA-L) tracing study.** *Hear Res* 1991, **56**:179-190.
71. Winer JA, Larue DT, Huang CL: **Two systems of giant axon terminals in the cat medial geniculate body: convergence of cortical and GABAergic inputs.** *J Comp Neurol* 1999, **413**:181-197.
72. Villa AEP, Tetko IV, Dutoit P, de Ribaupierre Y, de Ribaupierre F: **Corticofugal modulation of functional connectivity within the auditory thalamus of rat, guinea pig and cat revealed by cooling deactivation.** *J Neurosci Meth* 1999, **86**:161-178.
73. King AJ: **Signal selection by cortical feedback.** *Curr Biol* 1997, **7**:R85-R88.
74. Beneyto M, Prieto JJ: **Connections of the auditory cortex with the claustrum and endopiriform nucleus in the cat.** *Brain Res Bull* 2001, **54**:485-498.
- Here, the authors find extensive, often reciprocal, connections between 11 auditory cortex areas and the claustrum. The projection pattern was topographic and involved the subcortical limbic forebrain endopiriform nucleus. This suggests that the auditory cortex has widespread input to structures implicated in motor planning and cognition.
75. Winer JA: **The functional architecture of the medial geniculate body and the primary auditory cortex.** In *Springer Handbook of Auditory Research, Volume 1. The Mammalian Auditory Pathway: Neuroanatomy*. Edited by Webster DB, Popper AN, Fay RR. Berlin: Springer-Verlag; 1992:222-409.
76. Wong D, Kelly JP: **Differentially projecting cells in individual layers of the auditory cortex: a double-labeling study.** *Brain Res* 1981, **230**:362-366.
77. Weedman DL, Ryugo DK: **Pyramidal cells in primary auditory cortex project to cochlear nucleus in rat.** *Brain Res* 1996, **706**:97-102.
78. Suga N, Gao E, Zhang Y, Ma X, Olsen JF: **The corticofugal system for hearing: recent progress.** *Proc Natl Acad Sci USA* 2000, **97**:11807-11814.
79. Atzori M, Lei S, Evans DI, Kanold PO, Phillips-Tansey E, McIntyre O, McBain CJ: **Differential synaptic processing separates stationary from transient inputs to the auditory cortex.** *Nat Neurosci* 2001, **4**:1230-1237.
- In a cortical slice study, simultaneous recordings from connected neurons in AI layers II/III reveal two classes of functional synaptic properties. The authors interpret the results in terms of the differential or parallel processing of transient and stationary features.
80. Wallace MN, Kitzes LM, Jones EG: **Chemoarchitectonic organization of the cat primary auditory cortex.** *Exp Brain Res* 1991, **86**:518-526.
81. Lu T, Liang L, Wang X: **Temporal and rate representations of time-varying signals in the auditory cortex of awake primates.** *Nat Neurosci* 2001, **4**:1131-1138.
- This single-unit study in the awake marmoset monkey confirms two coding schemes for temporal information in auditory cortex: a timing-based code for infrequent events and a rate-based code for rapidly occurring events.
82. Horikawa J, Hess A, Nasu M, Scheich H, Taniguchi I: **Optical imaging of neural activity in multiple auditory cortical fields of guinea pigs.** *Neuroreport* 2001, **12**:3335-3339.
- Optical recording with voltage-sensitive dye in guinea pigs reveals 10 auditory fields distinguished by their functional properties, including cochleotopy, response latency, and pathways of activation spread.
83. Harel N, Mori N, Sawada S, Mount RJ, Harrison RV: **Three distinct auditory areas of cortex (AI, AII, and AAF) defined by optical imaging of intrinsic signals.** *Neuroimage* 2000, **11**:302-312.
- Similarly to [82], optical recording of intrinsic signals in chinchilla reveals three auditory cortical fields that differ in their cochleotopic gradient.
84. Budinger E, Heil P, Scheich H: **Functional organization of auditory cortex in the Mongolian gerbil (*Meriones unguiculatus*). IV. Connections with anatomically characterized subcortical structures.** *Eur J Neurosci* 2000, **12**:2452-2474.
85. Wallace MN, Rutkowski RG, Palmer AR: **Identification and localisation of auditory areas in guinea pig cortex.** *Exp Brain Res* 2000, **132**:445-456.
86. Rutkowski RG, Wallace MN, Shackleton TM, Palmer AR: **Organisation of binaural interactions in the primary and dorsocaudal fields of the guinea pig auditory cortex.** *Hear Res* 2000, **145**:177-189.
87. Hackett TA, Preuss TM, Kaas JH: **Architectonic identification of the core region in auditory cortex of macaques, chimpanzees, and humans.** *J Comp Neurol* 2001, **441**:197-222.
- Hackett *et al.* identify a core region in the auditory cortex of primates and humans, consisting of two or three parts, including AI, a belt with seven areas, and a parabelt with two areas. They conclude that homologous core regions occur in these species.
88. Loftus WC, Sutter ML: **Spectrotemporal organization of excitatory and inhibitory receptive fields of cat posterior auditory field neurons.** *J Neurophysiol* 2001, **86**:475-491.
- A detailed study of spectrotemporal 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.
89. Recanzone GH: **Spatial processing in the auditory cortex of the macaque monkey.** *Proc Natl Acad Sci USA* 2000, **97**:11829-11835.
90. Recanzone GH, Schreiner CE, Sutter ML, Beitel RE, Merzenich MM: **Functional organization of spectral receptive fields in the primary auditory cortex of the owl monkey.** *J Comp Neurol* 1999, **415**:460-481.
91. Fitzpatrick DC, Suga N, Olsen JF: **Distribution of response types across entire hemispheres of the mustached bat's auditory cortex.** *J Comp Neurol* 1998, **391**:353-365.
- Here, an analysis of 11 cortical areas for local representations and modes of processing finds six response types, including three kinds of frequency-modulated processing. The authors describe areas with preferential neural responses outside the biosonar representation.
92. Jenkins WM, Merzenich MM: **Role of cat primary auditory cortex for sound-localization behavior.** *J Neurophysiol* 1984, **52**:819-847.
93. Talwar SK, Gerstein GL: **Reorganization in awake rat auditory cortex by local microstimulation and its effect on frequency discrimination behavior.** *J Neurophysiol* 2001, **86**:1555-1572.
- This paper shows that cortical microstimulation changes receptive field properties but can leave auditory frequency perception unaffected. The experiments demonstrate the importance of exploring the behavioral and perceptual significance of changes in auditory receptive field dynamics and plasticity.
94. Di Salle F, Formisano E, Seifritz E, Linden DE, Scheffler K, Saulino C, Tedeschi G, Zanella FE, Pepino A, Goebel R *et al.*: **Functional fields in human auditory cortex revealed by time-resolved fMRI without interference of EPI noise.** *Neuroimage* 2001, **13**:328-338.
- DiSalle *et al.* present evidence for several auditory fields in Heschl's gyri and planum temporale of human cortex using fMRI imaging under low noise conditions.
95. Talavage TM, Ledden PJ, Benson RR, Rosen BR, Melcher JR: **Frequency-dependent responses exhibited by multiple regions in human auditory cortex.** *Hear Res* 2000, **150**:225-244.
96. Howard MA, Volkov IO, Mirsky R, Garell PC, Noh MD, Granner M, Damasio H, Steinschneider M, Reale RA, Hind JE *et al.*: **Auditory cortex on the human posterior superior temporal gyrus.** *J Comp Neurol* 2000, **416**:79-92.
97. Wessinger CM, VanMeter J, Tian B, Van Lare J, Pekar J, Rauschecker JP: **Hierarchical organization of the human auditory cortex revealed by functional magnetic resonance imaging.** *J Cog Neurosci* 2001, **13**:1-7.
- This fMRI study shows that core regions in human auditory cortex respond more strongly to simple sounds, such as pure tones, whereas surrounding regions are activated preferentially by stimuli with greater spectral complexity.
98. Rauschecker JP: **Cortical processing of complex sounds.** *Curr Opin Neurobiol* 1998, **8**:516-521.
99. Thivard L, Belin P, Zilbovicius M, Poline JB, Samson Y: **A cortical region sensitive to auditory spectral motion.** *Neuroreport* 2000, **11**:2969-2972.

100. Kaas J, Hackett TA: **Subdivisions of auditory cortex and processing streams in primates.** *Proc Natl Acad Sci USA* 2000, **97**:11793-11799.
101. Rivier F, Clarke S: **Cytochrome oxidase, acetylcholinesterase and NADPH-diaphorase staining in human supratemporal and insular cortex: evidence for multiple auditory areas.** *Neuroimage* 1997, **6**:288-304.
102. Schleicher A, Amunts K, Geyer S, Kowalski T, Schormann T, Palomero-Gallagher N, Zilles K: **A stereological approach to human cortical architecture: identification and delineation of cortical areas.** *J Chem Neuroanat* 2000, **20**:31-47.
103. Tardif E, Clarke S: **Intrinsic connectivity of human auditory areas: a tracing study with Dil.** *Eur J Neurosci* 2001, **13**:1045-1050.
104. Winguth SD, Winer JA: **Corticocortical connections of cat primary auditory cortex (AI): laminar organization and identification of supragranular neurons projecting to area AII.** *J Comp Neurol* 1986, **248**:36-56.
105. Rauschecker JP, Tian B: **Mechanisms and streams for processing of 'what' and 'where' in auditory cortex.** *Proc Natl Acad Sci USA* 2000, **97**:11800-11806.
106. Van Essen DC, Anderson CH, Felleman DJ: **Information processing in the primate visual system: an integrated systems perspective.** *Science* 1992, **255**:419-423.
107. Murphy PC, Duckett SG, Sillito AM: **Feedback connections to the lateral geniculate nucleus and cortical response properties.** *Science* 1999, **286**:1552-1554.
108. Abel PW, O'Brien BJ, Lia B, Olavarria JF: **Distribution of neurons projecting to the superior colliculus correlates with thick cytochrome oxidase bands in macaque visual area V2.** *J Comp Neurol* 1997, **377**:313-323.
109. Romanski LM, Tian B, Fritz J, Mishkin M, Goldman-Rakic PS, Rauschecker JP: **Dual streams of auditory afferents target multiple domains in the primate prefrontal cortex.** *Nat Neurosci* 1999, **2**:1131-1136.
110. Kaas JH, Hackett TA, Tramo MJ: **Auditory processing in primate cerebral cortex.** *Curr Opin Neurobiol* 1999, **9**:164-170.
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].
112. Belin P, Zatorre RJ, Lafaille P, Pierre A, Pike B: **Voice-selective areas in human auditory cortex.** *Nature* 2000, **403**:309-312.
113. Alain C, Arnott SR, Hevenor S, Graham S, Grady CL: **'What' and • 'where' in the human auditory system.** *Proc Natl Acad Sci USA* 2001, **98**:12301-12306.
Alain *et al.* present evidence for two specialized higher auditory pathways with fMRI and evoked potentials that use stimuli with combined pitch and sound localization information. A ventral, pitch-related pathway could be distinguished from a more dorsal, sound-location related pathway.
114. Hall DA, Johnsrude IS, Haggard MP, Palmer AR, Akeroyd MA, • Summerfield AQ: **Spectral and temporal processing in human auditory cortex.** *Cereb Cortex* 2002, **12**:140-149.
Further evidence for segregated auditory fields in human auditory cortex is established here, using differences in fMRI responses to simple, but spectrotemporally distinguishable, signals.
115. Krubitzer L: **The organization of neocortex in mammals: are species differences really so different?** *Trends Neurosci* 1995, **18**:408-417.