

SOME BASIC FEATURES OF ORGANIZATION OF THE
CENTRAL AUDITORY NERVOUS SYSTEM

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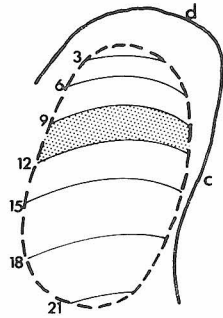
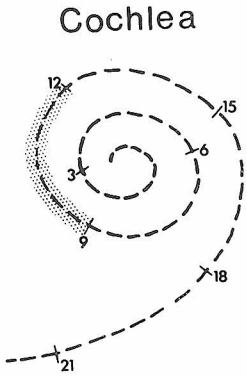
1. INTRODUCTION

An understanding of the spatial framework of the information processing machinery within (and interconnections between) component nuclei and cortical fields of the auditory nervous system is prerequisite for analysis of how different aspects of sound sensation are encoded within this system. Microelectrode unit mapping techniques and anterograde and retrograde anatomical tracing methods have been employed to define some of the principles of the spatial organization of the system. Although studies have been conducted in several species, described results shall be limited to those obtained in experiments in cats.

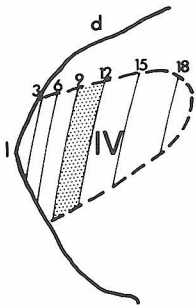
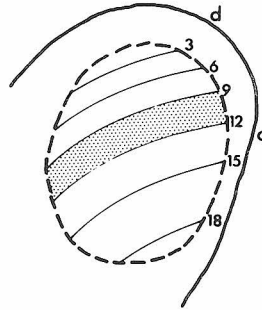
2. RECENT FINDINGS

(a) Auditory nuclei and cortical fields are strictly cochleotopically organized.

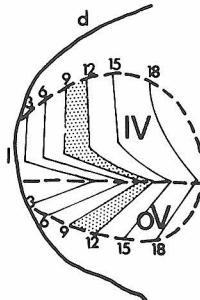
Recent microelectrode mapping studies and horseradish peroxidase and radioactive amino acid anatomical tracer studies have led to an understanding of how the cochlea is represented within the three dimensions of many auditory nuclei and cortical fields. There is a highly ordered representation of the cochlear sensory epithelium within the three dimensions of major subdivisions of the auditory nervous system in the cat, including divisions of the cochlear nuclear complex, medial and lateral superior olives, central nucleus of the inferior colliculus, lateral and ovoidal parts of the ventral nucleus of the medial geniculate body, and at least two large auditory cortical fields. In all of these auditory nuclei and cortical fields, *any given restricted sector of the cochlear sensory epithelium is represented within a slab (or strip) of neurons of nearly constant thickness (or width) that crosses those nuclei or cortical fields from edge to edge (see Fig. 1).*



Central Nucleus of Inferior Colliculus



Ventral Nucleus of Medial Geniculate



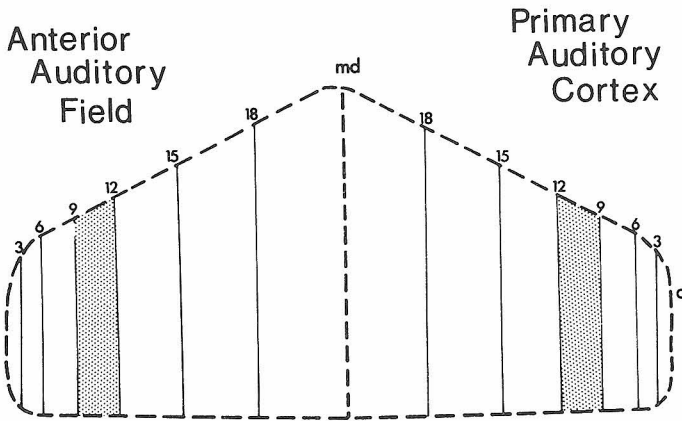


Fig. 1. Representation of the cochlea within auditory nuclei and cortical fields in the cat. All drawings are to the same scale. The representation of 3 mm sections (9-12 mm sector shaded) of the cochlear sensory epithelium is shown in each nucleus or cortical field. In this and in following drawings, r=rostral, c=caudal, d=dorsal, v=ventral, l=lateral, m=medial. Drawings of the lateral and medial superior olives (LSO, MSO) were based on data of Guinan & colleagues (1972), and on retrograde tracing studies of arrays of neurons projecting to physiologically-defined ICC loci (Aitkin et al, 1977). The folded and curved LSO and MSO have been drawn as flattened, symmetrical plates. The drawings of the representation of the cochlea within sagittal planes in the central nucleus of the inferior colliculus (ICC) near its medial margin (upper), and two thirds of the way across the nucleus from its medial edge, were based on microelectrode mapping data (Merzenich & Reid, 1974). Drawings of two frontal sections through the rostral (upper) and middle thirds of the medial geniculate body (MGB) were based on physiological-anatomical studies of the organization of the projections to and from MGB subdivisions (Merzenich & Colwell, 1975). The representation within both the lateral (LV) and ovoidal (oV) parts of the ventral nucleus of MGB are shown. Drawings depicting the representation of the cochlea within AI and AAF were based on data derived in microelectrode mapping experiments (Merzenich et al, 1975; Knight, 1977). AI and AAF have been flattened in this schematic drawing.

The shapes of all nuclei and cortical fields are drawn schematically. They can not be generalized to individual cats.

(b) *Basic subdivisions of auditory cortex in the cat have been redefined.*

Application of unit mapping and neuroanatomical tracing techniques has led to a redefinition of auditory cortical fields in the cat (Merzenick *et al.*, 1974, 1975; Knight, 1977). Differences between boundaries defined by those studies, and those drawn in the important classical evoked potential studies of Woolsey and colleagues (Woolsey and Walzl, 1942; Woolsey 1960, 1961, 1964) are illustrated schematically in *Fig. 2*. The "primary auditory cortex" (AI) is smaller than depicted by Woolsey. A large "anterior auditory field" (AAF) lies rostral to AI. This second complete and highly ordered cortical representation of the cochlea has approximately the same area as AI (Knight, 1977). There is a reversal in cochlear place representation across its border with AI, with the most basal portion of the cochlea represented along their mutual boundary. In both fields, any sector of the cochlea is represented across a relatively straight belt of cortex of nearly constant width that crosses the field from border to border; and, in both fields, there is a proportionately larger representation of successively more basal sectors of the cochlear sensory epithelium (see *Fig. 1*). The first spike latencies in AI and AAF are virtually identical; these two large mirror-image representations are apparently processing information in parallel.

There is also a reversal in the representation of the sensory epithelium across the caudal boundary of AI and an adjacent posterior auditory field ("a" in *Fig. 2-B*), with the most *apical* aspect of the cochlea represented across their mutual border. Woolsey (1960, 1961) located the representation of the *basal* cochlea within the "posterior ectosylvian field" (field "EP" in *Fig. 2-A*) high on the posterior ectosylvian gyrus nearby. The recording of a reversal in the sequence of represented cochlear place, with the extreme apex represented within the part of this posterior field adjacent to AI indicates that there must be at least two auditory cortical fields within Woolsey's "posterior ectosylvian field."

Microelectrode mapping studies have also led to appreciation of the fact that auditory cortical fields vary significantly in location, when referenced to brain surface landmarks (*Fig. 3*). The variation in location of auditory fields is, unfortunately, not predictable from examination of the sulcal configurations in a given cat. Therefore, physiological controls are required for definition of the actual boundaries of AI, AAF or other cortical subdivisions in the conduct of experiments within these fields.

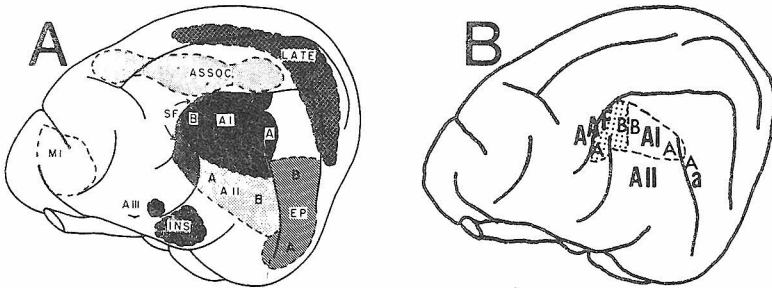


Fig. 2. Diagrammatic representation of subdivisions of auditory cortex in the cat, defined in surface evoked potential mapping studies of Woolsey & colleagues (see text) (A), and in microelectrode mapping studies (B). Regions of representation of the cochlear apex (A) and base (B) are indicated in each field. Drawings modified from Knight, 1977, and Woolsey, 1960, with permission.

(c) The topological representation of the cochlear sensory epithelium within auditory nuclei and cortical fields differs fundamentally from the patterns of representation of other sensory epithelia.

Visual or somatic sensory epithelia are two-dimensional surfaces (retinal and body surfaces). The cochlear sensory epithelium is, by contrast, a *line* of cells of insignificant width (4 cells wide and, in the cat, over 3000 cells long). The two-dimensional surfaces of the retina or skin project *via* a point-to-point projection system to reconstruct those two-dimensional receptive surfaces (with some distortions) within visual and somatosensory cortical fields. If there were a similar continuous point-to-point representation of the auditory sensory epithelium in auditory cortex, the cochlea would be represented within a very thin slab of cortex of insignificant width. Of course, AI and AAF have a *second* dimension. In this dimension, there is an expansion of the cortical representation in a direction orthogonal to the point-to-point representation of the receptor surface. Thus, any *sector* along the basilar partition is "re-represented" within a *belt* of cortex that crosses AI or AAF (and possibly other auditory cortical fields).

In the three-dimensional nuclei representing the two-dimensional surfaces of the retina or skin (e.g., the dorso-

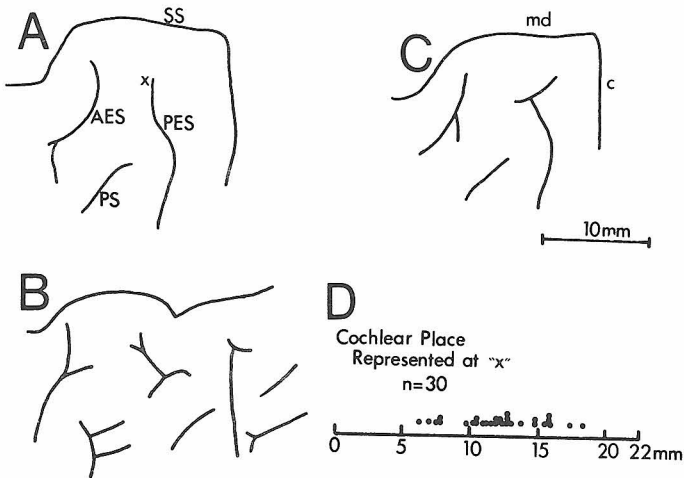


Fig. 3. A-C: Sulci in the auditory cortical region of 3 cats, illustrating variations of brain surface landmarks. Compare with "standard" cat sulci in Fig. 2. AES=anterior ectosylvian sulcus; PES=posterior ectosylvian sulcus; PS=pseudosylvian sulcus; SS=suprasylvian sulcus. D: Represented cochlear place defined in microelectrode penetrations near the top of the posterior ectosylvian sulcus ("x" in A), in 30 studied cats in which the landmark was prominent.

lateral geniculate, or the ventroposterior nucleus), there is a re-representation of any given locus on the visual or somatic sensory epithelia along a *line*. In studied three-dimensional auditory nuclei, by contrast, any given locus on the cochlear sensory epithelium is represented across a *sheet*.

While imaginary "isofrequency lines" or isofrequency sheets" can invariably be defined within auditory nuclei, the representation of the cochlea is probably more complicated in at least several (probably all) auditory structures. In the inferior colliculus, for example, sequential step changes in represented cochlear location are observed in detailed mapping penetrations introduced perpendicular to the "isofrequency sheets" of the central nucleus. As step changes of approximately constant distance in represented cochlear place are encountered in penetrations introduced all across the dorsal surface of the central nucleus, sectors of the cochlear sensory epithelium might be individually represented across functional subunits, probably the anatomically defined cell laminae of the central nucleus (see Morest, 1964; Rockel and Jones, 1973a).

(d) *There are complex, convergent highly-ordered projections from level to level in the auditory nervous system.*

Interconnections in the auditory nervous system are spatially more complex than those described in other sensory systems. For example, studies of the arrays of neurons in brainstem nuclei projecting to functionally defined loci in the central nucleus of the inferior colliculus (ICC) have revealed that there is a *convergence* of input from slabs (or strips) of neurons of relatively constant thickness (or width) to restricted ICC loci. Thus, when projections from the ventral cochlear nucleus (VCN) were observed, arrays of neurons projecting to the restricted injection locus were invariably slabs of cells of nearly constant thickness, crossing both the posteroventral and anteroventral cochlear nuclei from edge to edge. If a projection from the dorsal cochlear nucleus (DCN) was observed, the restricted ICC locus invariably received input from a strip of cells crossing the two-dimensional fusiform cell layer from margin to margin (some neurons in the deep layer of DCN also projected to ICC). If the projection originated from the medial or lateral superior olives, the projection array was invariably a narrow slab of relatively constant thickness, again crossing these nuclei from edge to edge. In every case, these converging slabs or strips of projecting neurons defined the "isofrequency lines" or isofrequency sheets" of their respective nuclei.

A second example is drawn from studies of the arrays of neurons projecting to restricted, functionally defined loci in auditory cortical fields (*Fig. 4*). There, spatially restricted columns or sheets of neurons project to restricted loci within these fields. A site 1-2 mm in diameter in AI, for example, receives input from a "sheet" of neurons in the lateral part of the ventral nucleus of the medial geniculate body; from a second sheet in the ovoidal part of the ventral nucleus (continuous with the lateral sheets; see *Fig. 4*); and from restricted "columns" of neurons in the dorsal and medial divisions of the nucleus. The arrays of neurons projecting to restricted field loci in AAF and AII were also marked by convergence of input (*Fig. 4*). This repeatedly observed spatial convergence of input in the projection from level to level in the auditory system is apparently unique to this system.

(e) *There is, at least to some degree, segregated, parallel processing of information fed forward from different brainstem auditory nuclei into the central nucleus of the inferior colliculus.*

ARRAYS OF NEURONS PROJECTING TO
RESTRICTED AUDITORY FIELD LOCI

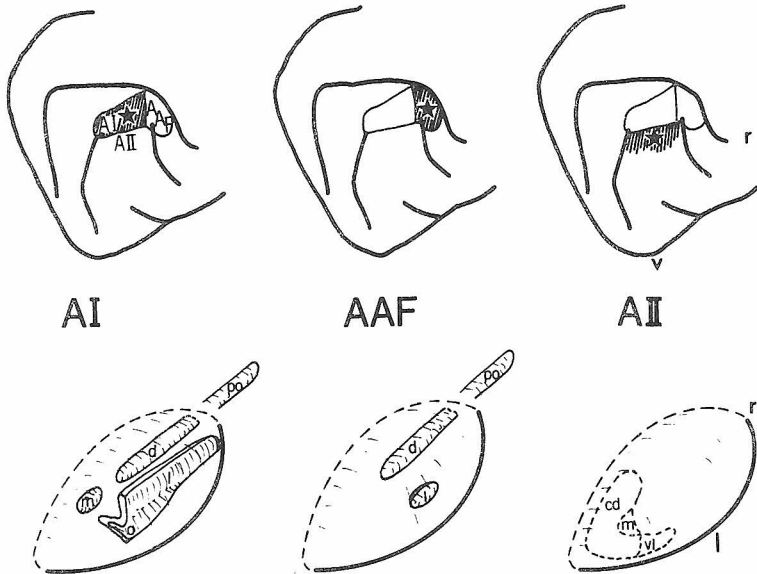


Fig. 4. Diagrammatic representation of arrays of MGB neurons projecting to restricted loci within AI, AAF and AII. Drawings are representative of results of horseradish peroxidase (HRP) projection-tracing studies in which the injections were centered in these fields, and in which there was an effective spread of the tracer at injection loci (★) about 1-1.5 mm in diameter. MGB is viewed from its caudodorsolateral aspect. Projection arrays from lateral (l), ovoidal (ov) and ventrolateral (vl) parts of the ventral division of MGB, medial (m) division of MGB, deep (d) and caudal (cd) parts of the dorsal division of MGB, and from the posterior group (po) are drawn. Solid lines within MGB enclose densely packed HRP-labelled cells; dashes (AII case) enclose a disperse distribution of HRP-labelled neurons.

The principal midbrain auditory nucleus, the central nucleus of the inferior colliculus, receives input from many brainstem auditory nuclei. Although these projections to the ICC have been relatively well documented, the patterns of distribution of these inputs to the anatomically defined laminae of the central nucleus has never been determined. Recently, microelectrode mapping and anatomical tracing

studies have revealed that input arising from different brain-stem nuclei is, at least to a large extent, *segregated* within the ICC. Every projecting nucleus feeds information into only a restricted part of the nucleus. While evidence for some overlap of inputs has been repeatedly observed and some sections of the ICC may be processing input from 2 or 3 brain-stem nuclei, it is clear that input from different projecting nuclei is, to at least a very significant extent, processed in parallel within the nucleus.

Despite the large number of sources of input to ICC (including the contralateral DCN and VCN, the contralateral LSO, the ipsilateral LSO and MSO, the ipsilateral ventral nucleus of the lateral lemniscus, and both the ipsilateral and contralateral dorsal nuclei of the lateral lemnisci), all input falls in register within the overall cochleotopic organization of the nucleus --- a formidable developmental accomplishment. It is also interesting to note that this multivariate input is distributed across continuous ICC laminae (see Morest, 1964; Rockel and Jones, 1973a,b), which appear (at least grossly) to have a relatively constant structure across the nucleus.

(f) The contralateral side of the free sound field appears to be represented within the ICC.

The distribution of delay-sensitive neurons within the three dimensions of the ICC of the cat has been studied in an attempt to determine whether or not there is a systematic spatial neural representation of the free sound field in that nucleus. These studies have revealed: 1) Delay-sensitive neurons are found within only a part of the low frequency ICC. In other ICC regions, neurons are predominantly monaural, or are predominantly binaural but not delay-sensitive; 2) All delay-sensitive neurons respond strongly with interaural time delays within the behavioral range; 3) Neurons recorded at any given location tend to have similar delay-sensitive properties, but very significant exceptions are common; 4) The "characteristic delays" (Rose *et al*, 1966) of the great majority of delay-sensitive neurons in ICC fall within the behavioral range. All but a few respond maximally with stimuli arriving first at the contralateral ear, or with no greater than a 50-100 μ sec lead to the ipsilateral ear, i.e., with interaural time differences that would occur with sound in the middle and contralateral parts of the free sound field. Neurons are usually driven poorly, if at all, with stimulation on the far ipsilateral sector of the sound field.

These and other experiments provide strong evidence that the contralateral side of the free sound field is represented within a restricted region of the ICC.

3. CONCLUSIONS AND IMPLICATIONS

a) The demonstration of an orderly representation of the cochlear sensory epithelium within the auditory thalamus and cortex reopens the possibility (originally suggested in the classical evoked potential mapping studies of Woolsey and Walzl, 1942) of a spatial coding of pitch within the auditory forebrain.

b) Data derived in physiological, ablation-behavioral, and anatomical studies in the cat should be interpreted in light of this redefinition of auditory cortical field boundaries and the individual variations in cortical field locations. Physiological controls that define field boundaries in individual cats are a necessary part of such experiments.

c) Information from different brainstem auditory nuclei projects differentially into the ICC. Thus, information abstracted in a variety of ways by different brainstem nuclei is processed in parallel within ICC. Experiments in ICC (and at higher levels) should be conducted with the understanding that given aspects of sound sensation are probably encoded or represented within restricted parts of the nucleus.

d) The contralateral side of the free sound field appears to be represented within the central nucleus of the inferior colliculus. Studies of patients with temporal lobe lesions suggest that this organization is preserved at the cortical level (e.g., Sanchez-Longo and Forester, 1958).

e) The additional dimension of the topological representation of the cochlear sensory epithelium (its "re-representation") in auditory nuclei and cortical fields might be utilized to encode aspects of sound sensation. However, there is as yet no direct evidence that any specific parameter of sound (excepting sound frequency) is systematically represented across this additional dimension.

f) The functional significance of the apparent discontinuous, layered representation of short sectors of the cochlear sensory epithelium within at least the laminated auditory nuclei (e.g., the ICC and the ventral MGB), and of the repeatedly observed convergence in the projections from level to level in the auditory nervous system are still unknown. These unique organizational features are undoubtedly fundamental to the understanding of the processing of auditory information,

and are currently under investigation.

These limited data have established some basic features of the spatial organization of the auditory nervous system. Some of these features are apparently unique to this system. Although the spatial processing of information is more complex in the auditory system than in other sensory systems, spatial order is the rule. With an increasing understanding of this spatial order, experiments can be more appropriately designed to define how aspects of sound sensation are encoded or represented within this information processing system.

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DISCUSSION

Evans:

It should be pointed out that not all single unit studies in the unanaesthetized or lightly anaesthetized cortex find a cochleotopic organization more than a trend (E.F. Evans, H.F. Ross & I.C. Whitfield, 1965, *J. Physiol.* 179, 238-247; M.H. Goldstein, Jr. & M. Abeles, 1975, *Brain Res.* 100: 188-191). A weakness of some of these data is that they involved pooling across cortices. Jolley and I have therefore examined units in tangential penetrations in individual primary cortices. Most animals did not show a cochleotopic organization, but undoubtedly two did. Whether this was related to anaesthetic depth or level in cortex is not clear.

What is clear however is that in no case could the behaviour of the units be considered to be frequency specific, i.e: the organization to be tonotopic. Most were widely tuned, had unassignable CFs, or would not respond consistently to pure tones.

Merzenich:

Differences between these results and those derived in our studies are inexplicable, as:

- (1) We have now derived mapping data from AI in more than 100 cats. The field has been found to be cochleotopically organized in all studied animals. Moreover, the representation (once it is located) has been found to be dimensionally very constant.
- (2) Differences between Jolley and Evans' and our results (and their finding of a cochleotopic organization in AI in two but not in other cats) cannot be due to hemispheric differences; we have derived mapping data from AI in both hemispheres in many of these studied cats.
- (3) Differences are not very likely due to the use of tangential penetrations; we have defined best frequency as a function of location within very many such penetrations, and find best frequency sequences to be consistent with other surface mapping data.
- (4) Differences in results are apparently not due to depth of anaesthesia, as, again, we have derived similar mapping data in awake cats and in preparations in which other anaesthetics have been employed.
- (5) Studies of the afferent connections of AI in which the retrograde tracer HRP was introduced into each of a series of locations distributed widely across this cortical field invariably revealed strictly delimited and highly ordered projections from auditory thalamic subdivisions.
- (6) We have completely mapped the orderly representation of the cochlea within AI within three other species (M.M. Merzenich, J.H. Kaas & G.L. Roth, 1976, *J. Comp. Neurol.* 166, 387-401; Oliver, *et al.*, 1976).
- (7) Finally, T.

Imig and colleagues (1977, *J. Comp. Neurol.* 166, 387-401; (personal communications) have conducted extensive mapping studies in AI in the cat, and their mapping data are basically consistent with ours.

We believe that these results, taken collectively, demonstrate unequivocally that the primary auditory cortex in the cat (as well as in all other species that have been completely mapped) is strictly cochleotopically organized.

We have emphasized (M.M. Merzenich, P.L. Knight & G.L. Roth, 1975, *J. Neurophysiol.* 38, 231-249) that these descriptions of AI organization apply only to its middle layers. As has long been appreciated, most neurons in superficial cortical layers are relatively unresponsive to tonal stimuli in anaesthetized cats. Perhaps the data of Jolley and Evans derived in those of their cats in which a cochleotopic organization was not observed were largely from superficial cortical layers and/or from extra-primary cortex.

Evans:

The last suggestion was not the case.