The Inferior Colliculus

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Editors

The Inferior Colliculus

With 168 Illustrations

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Cover illustration: A transverse section through the center of the cat inferior colliculus showing its principal subdivisions. See page 20 of the text.

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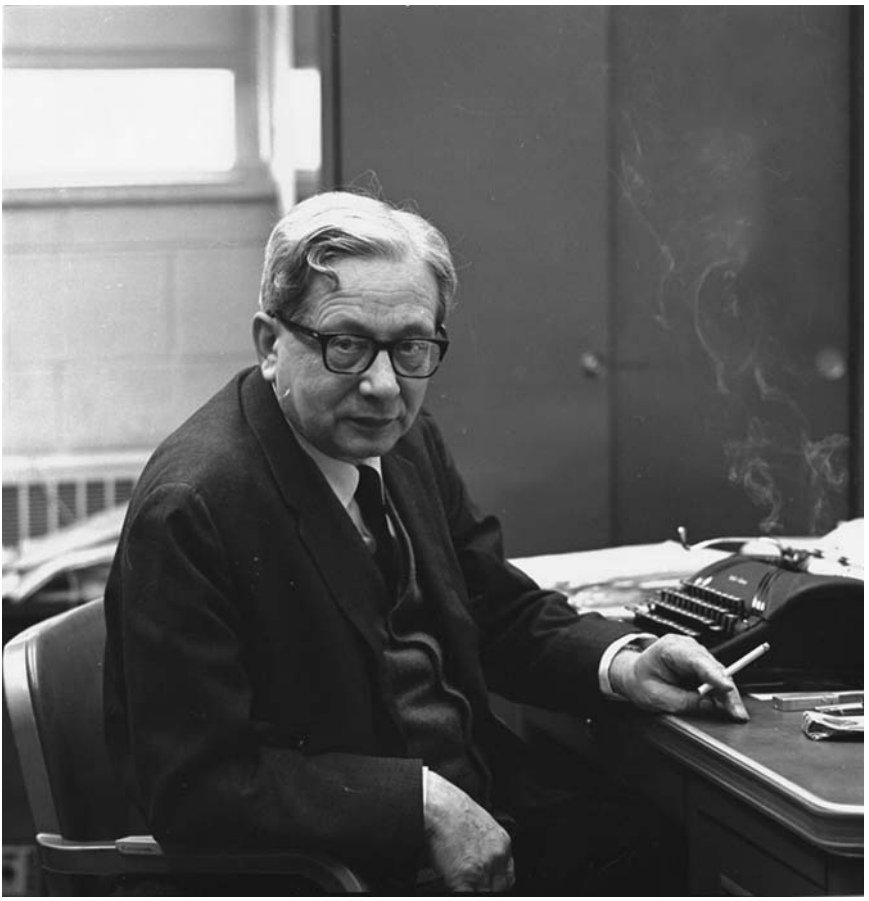

Photograph by courtesy of T. Stewart

Dedicated to the memory of
Jerzy E. Rose (1909–1992)
Scholar, scientist, colleague, mentor, friend

Preface

The purpose of this volume is twofold. First, it offers an in-depth analysis of current approaches and issues in the study of the auditory system. By concentrating on one structure, the inferior colliculus, a focused and coherent treatment of many aspects of auditory neural processing is possible. The position of the inferior colliculus is unique, as its study offers insights into the influence of the peripheral auditory system and at the same time reveals the initial stages of central processing principles. By providing, in the first chapter, an overview of auditory system function and structure, a framework is given that guides the interpretation of operational mechanisms and rules. Second, the book provides a state-of-the-art reference tool for researchers working on the inferior colliculus. The last such treatment appeared in the mid-1980s (Aitkin 1986) and was 246 pages long with 507 citations; since then, more than 1900 articles on the inferior colliculus have been published, and there has been no inclusive summary of facts and ideas about this critical junction in the auditory pathway. In this period, there has been substantial progress on the many facets of inferior colliculus function that constitute the subject matter for this volume. The mere accretion of publications alone would not in itself justify a new volume devoted to the auditory midbrain. The rationale, then, is to summarize recent advances in this discipline from the perspective of some of the many researchers who have engendered this progress. As a case in point, consider the growing body of data on the role of the inferior colliculus in seizure genesis and as a model system for the study of epilepsy (Chapter 21), an area that has grown considerably since 1986 and that has had a significant impact on diverse areas including sensory-to-motor transformations and the possible role of GABAergic neurons in kindling and seizure control. Any consideration of GABAergic neurons, of course, must include their role in local processing as putative interneurons (Oliver et al. 1991) as well as their ascending projection to the medial geniculate body (Winer et al. 1996), the differential, subdivision-specific concentration of GABAergic neurons and axon terminals (Oliver et al. 1994), and the maturation of GABAergic transmission (Yigit et al. 2003); each of these topics is of moment, each crosses interdisciplinary boundaries that can range from development to pathology, and none could have received the appropriate attention in prior synthe-

ses. Because we could not in conscience exclude a particular subject, we attempted to include all that seemed to us to capture best the sense of flux and excitement of current approaches. There remain, of course, many gaps: for example, the subject of synaptic organization has received less attention than might have been expected, and it remains an area that will require further scrutiny if we are to understand how signals arising from the many medullary auditory centers and converging onto the inferior colliculus are transformed locally before they ascend to the auditory thalamus or descend within the brain stem. Likewise, developmental studies are at their earliest stage other than the purely descriptive, and we have little knowledge of how closely the cellular ontogenetic molecules and migratory processes that shape the midbrain follow principles established in the cerebral cortex (Molnár and Blakemore 1995).

Other conceptual approaches that have not been included explicitly are those that can be subsumed under the umbrella of computational neuroscience. There are a few modeling approaches to aspects of temporal coding or binaural processing that were designed to reflect properties specific to the inferior colliculus (e.g., Hewitt and Meddis 1994; Cai et al. 1998; Shackleton et al. 2000; Borisyuk et al. 2002). But it is difficult, and perhaps premature, to assemble a coherent theoretically oriented treatment of inferior colliculus properties, mechanisms, and function.

Where it was possible, we asked that authors propose an agenda for the future in which the salient questions for their discipline are enumerated as an organic part of their exposition. To keep the reference list within manageable limits, we requested that authors cite only the most recent work when this was possible; this strategy acknowledges the historical and intellectual value of Aitkin's (1986) volume.

The conceptual framework for this volume is integrative and reflects a systems perspective. In this context, integrative implies that we sought authors who would collaborate with peers who often held a different perspective, thus producing what we hope are balanced accounts of a given area that are free of parochialism. Where there is only one author, it was our view that the consensus of opinion (or the limited knowledge) in that particular area could be captured by the author we chose. Likewise, chapter length was guided by the literature available and whether the issues at hand were perceived as volatile or matters of settled opinion. The systems viewpoint construes the brain in terms of interacting neural networks whose separate elements contribute to the abstraction of larger entities related to hearing, perception, and binding the disparate streams from independent neural channels into a coherent experience. Perhaps the next volume devoted to the auditory midbrain can realize that goal.

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Chapter 1
The Central Auditory System: A Functional Analysis

JEFFERY A. WINER AND CHRISTOPH E. SCHREINER

1. INTRODUCTION

Auditory neurons must encode and decipher the spectral, spatial, and temporal properties of sound. These processes are a prerequisite to the subsequent extraction of biologically meaningful signals from a noisy environment and to establish perceptual attributes. The goal of this survey is to provide a framework for thinking about how the auditory system performs these tasks. Such a framework seems essential when considering a network of neurons that extends from the external ear to the cochlea and through many synaptic relays before reaching the cerebral cortex (Figs. 1.1A and 1.2). The internal complexity of this system is apparent in each of the nuclei that comprise the auditory pathway: a given nucleus contains thousands of neurons, each connected to and sharing information with nearby neurons as well as many other, remote nuclei. These neurons thus interact with themselves and their neighbors through many neurotransmitters, a host of synaptic mechanisms, and a wide range of membrane channels. These neurochemical and physiologic features endow the various neuronal classes with an enormous range of response repertoires individually as well as the functional capacity to decipher the temporal, amplitopic, and spatial aspects of the auditory signal. In each nucleus, the several kinds of cells each have a particular constellation of response properties that defines them. Some discharge most strongly to sound onset, others respond to noise or frequency-modulated sound, and still others prefer changes in loudness, to name just a few of the many stimulus dimensions that the auditory system routinely extracts, encodes, and represents. Considering the diversity of response types, the possible multiplicity of their connections, and the many levels of interaction between nuclei from the medulla to the cortex, the auditory system presents a formidable challenge to, and an opportunity for, reductionistic thinking.

To confront such a challenge, this system is considered from the perspective of its operating elements, the neurons, and the circuits they form. This viewpoint is useful as the many cells and circuits and the operations they perform have now been characterized in sufficient detail that they can be described in a biological context. This level of discourse is among the first steps toward a mature

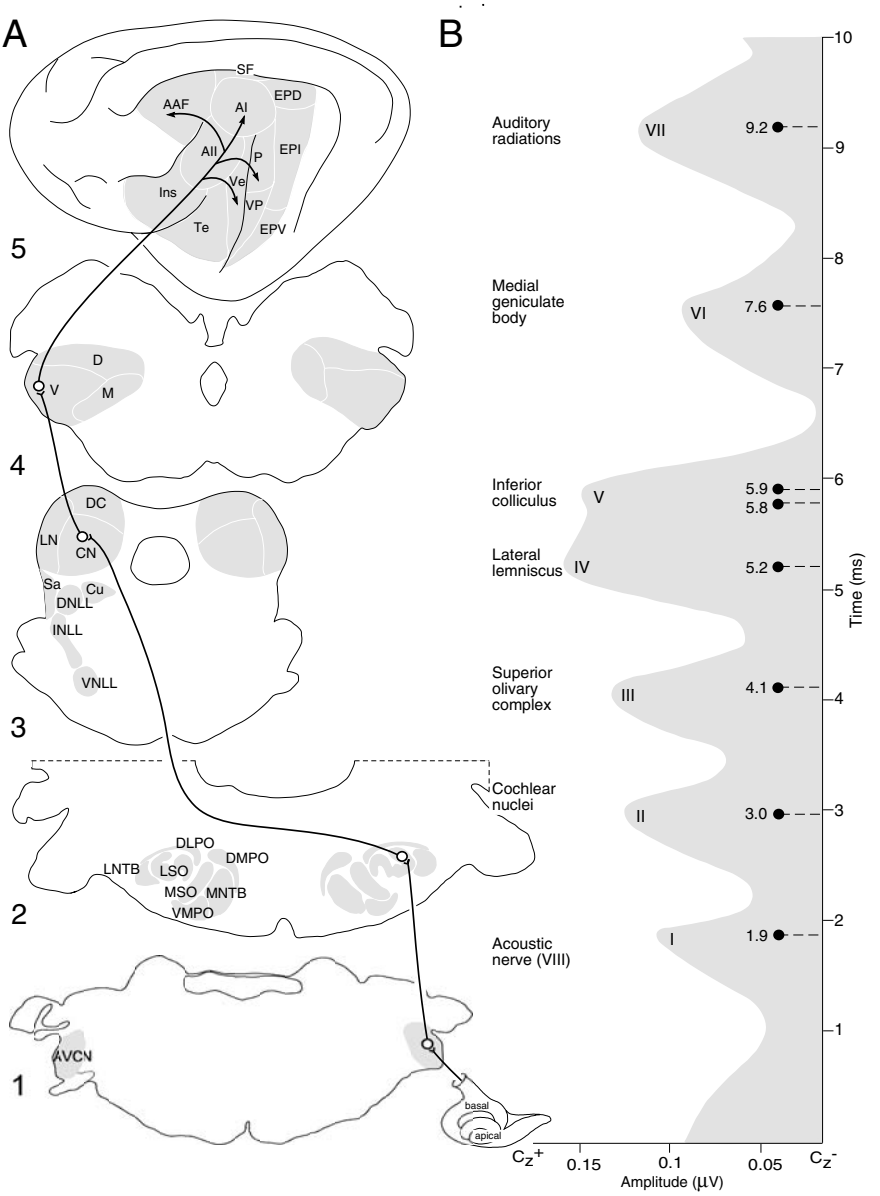

Figure 1.1. Primary components of the central acoustic system **(A)** and level-specific distribution of components of the auditory evoked potential **(B)**. **(A)** The major nuclei of the auditory pathway; for clarity, the cochlea has been omitted (see Fig. 1.2), as has the posteroventral cochlear nucleus (see Fig. 1.3A). *1:* The cochlear nucleus receives its ascending input via the cochlear nerve. Cochlear nucleus axons then decussate (present example) or terminate ipsilaterally (Fig. 1.2: cochlear nuclei). Intrinsic cochlear nucleus connections are not shown, and the totality of cochlear nucleus targets is extensive,

science of hearing, as these elements constrain the performance of the system by defining its permissible operations. This brief introduction concentrates on the central auditory system from the cochlear nucleus to the cerebral cortex; the cochlea is excluded because it merits a separate and extended treatment in its own right and because the issues it entails are beyond the scope of the themes addressed here.

The emphasis is explicitly functional and it treats the auditory pathway as a network of six interrelated parts whose organization will be explored in a neuroanatomical and a neurophysiological context. The parts are:

- Cochlear nucleus: genesis of basic response patterns and emergence of parallel pathways.
- Olivary complex: construction of binaural pathways and establishment of time lines.
- Lateral lemniscal nuclei: emergence of chemically specific nuclei.
- Inferior colliculus: site of brain stem convergence and multisensory integration.
- Medial geniculate body: modulation of auditory information by cortical and limbic systems.
- Auditory cortex: interface of hearing and higher order communication and cognitive networks.

Unless noted otherwise, the cat is the reference species because the literature available is so extensive. Surveys of basic auditory system organization should be consulted for other topics (Brodal 1981; Edelman et al. 1988; Popper and Fay 1992; Webster et al. 1992).

Figure 1.1. *Continued*
involving up to eight nuclei (Fig. 1.7). *2:* Input to the lateral superior olive *(LSO)* is topographic and ends in regular arrays (Feng and Vater 1985) that preserve the tonotopic arrangement in the cochlear nuclei (Fig. 1.3C, D). *3:* The LSO projects to the contralateral central nucleus of the IC; it conserves this topography (Servière et al. 1984) and may selectively target specific aural subregions in the IC (Ross et al. 1988; Brückner and Rübsamen 1995). *4:* The tectothalamic input is bilateral (not shown), with the ipsilateral component dominant (González-Hernández et al. 1991). *5:* The projection to auditory cortex is entirely ipsilateral, and highly divergent, involving several primary fields (Niimi and Matsuoka 1979) and has a specific laminar arrangement (Sousa-Pinto 1973); the latter feature could redirect thalamocortical influences to parts of the ipsilateral corticocortical system (Rouiller et al. 1991) or to the corticofugal network (Prieto and Winer 1999). Although the auditory system is depicted as hierarchical, its operations involve direct descending projections (Fig. 1.18) at almost every level (Aitkin 1986) as well as extensive connections with auditory-related areas of the neocortex (Seltzer and Pandya 1994). **(B)** The brain stem evoked response at seven levels (I to VII) in the auditory system. In humans, the superior olivary complex is in the pons and the cochlear nucleus at the junction of the pons and medulla. The arrival time of each waveform appears on the ordinate, while the abscissa shows their amplitude. For all figures, please refer to the list of abbreviations in the text. [Redrawn and modified from original sources (Chusid 1982; Webster and Garey 1990).]

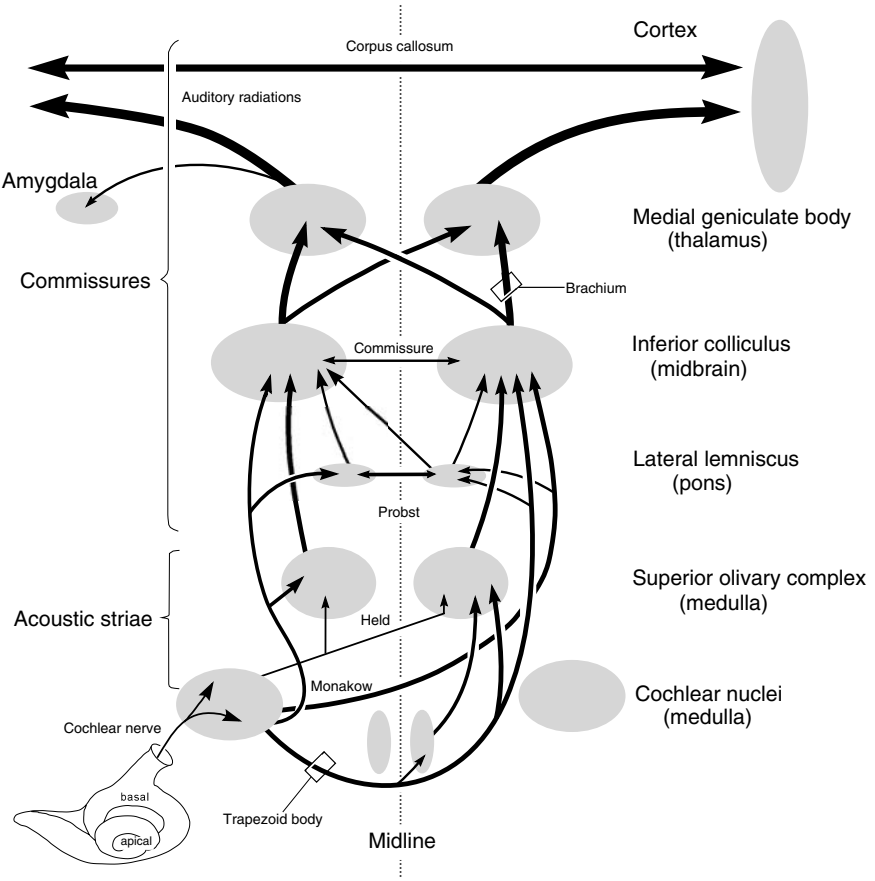

Figure 1.2. Schematic view of the principal ascending connections of the central auditory pathways. Local circuit arrangements and descending connections have been omitted for clarity, as have smaller nuclei such as the interstitial nucleus of the cochlear nerve root (Hutson and Morest 1996). Several important principles are embodied even in this highly schematic picture of connectivity. First, the output of almost every nucleus targets many centers and is highly divergent; this is accomplished either via branching axons from a single projection cell (Friauf and Ostwald 1988) or by different cochlear nucleus cell types targeting separate nuclei (Cant 1982; Thompson 1998). A second principle is connectional convergence: most nuclei receive multiple sources of input, of which the inferior colliculus is among the best examples, with more than 10 different projections to the central nucleus (Roth et al. 1978; Brunso-Bechtold et al. 1981). The acoustic striae are the main output tracts of the cochlear nuclei; their fibers converge ventral and medial to the superior olivary complex as the trapezoid body (Fig. 1.8A), in which many small nuclei are embedded (Brownell 1975). Third, commissural projections are present at most synaptic stations in the auditory system (Aitkin and Phillips 1984a). Not shown are commissural interconnections between the cochlear nuclei (Cant and Gaston 1982); an exception is the medial geniculate body, which has no commissural pathway. Fourth, there is an array of internal circuitry in every nucleus, and a nucleus- and sometimes a

2. The Cochlear Nuclei

In the cochlear nuclei the principles emerge that will dominate the auditory system at subsequent levels of processing (Osen 1988; Rhode and Greenberg 1992). The major themes are that there is (1) an orderly input that preserves the topography of frequency established in the cochlea (Osen 1970); (2) massive divergence of auditory nerve projections creates multiple new and nonequivalent maps from a single cochlear origin (Osen 1972); (3) great variety in structure and function among the specialized postsynaptic neurons that process the output of the auditory nerve (Osen 1969; Cant 1992); (4) an abundant number of inhibitory neurons to constrain, modulate, and refine the primary excitatory input (Adams and Mugnaini 1987); and (5) an array of descending projections from higher order auditory structures that provide feedback (Kane and Conlee 1979). The cochlear nucleus will be considered in slightly more detail because a large literature is available and because the functional principles that govern it are repeated and elaborated at many further levels.

The cochlear nuclei are among the first parts of the central auditory system to have evolved, and they are present in every vertebrate (Baird 1974). In amphibians and reptiles they form a semicircular mass of a few hundred neurons on the lateral edge of the medulla (Gregory 1974), and in carnivores and primates they represent a distinct lobe of highly differentiated cells beside the cochlea and the cerebellum. The auditory nerve is thus among the shortest cranial nerves in most species, and the thick coat of myelin on primary afferent axons and even covering ganglion cell perikarya ensures rapid transmission of acoustic impulses to the medulla. The auditory nerve axons spiral as they traverse the cochlea to reach the brain. They enter the cochlear nucleus rostroventrally, and then divide into descending and ascending branches (Ryugo 1992). This bifurcation redistributes the single sheet of the cochlear sensory epithelium across a volume; because each point (or, more properly, strip) represents a limited range of frequency (Fig. 1.3) and because each frequency is in topographic registration with its neighbors, the cochlear nucleus contains at least two independent maps of the frequency spectrum (Rose et al. 1959) (Fig. 1.4). The volume that corresponds to a frequency is termed isofrequency, and an isofrequency contour may contain several thousand neurons arrayed in flattened sheets and across which the cochlear axons are distributed more or less evenly (Fekete et al. 1984) (Fig. 1.3). This or analogous arrangements in which a distal map

Figure 1.2. *Continued*
species-specific distribution of interneurons and their synapses (Winer and Larue 1996). Fifth, many projections are reciprocal (not shown), especially those between the brain stem nuclei (Conlee and Kane 1982) and those of the thalamus and cortex (Colwell 1975). [Redrawn and modified from original sources: main diagram (Gulick et al. 1989); cochlea (Brödel 1946).]

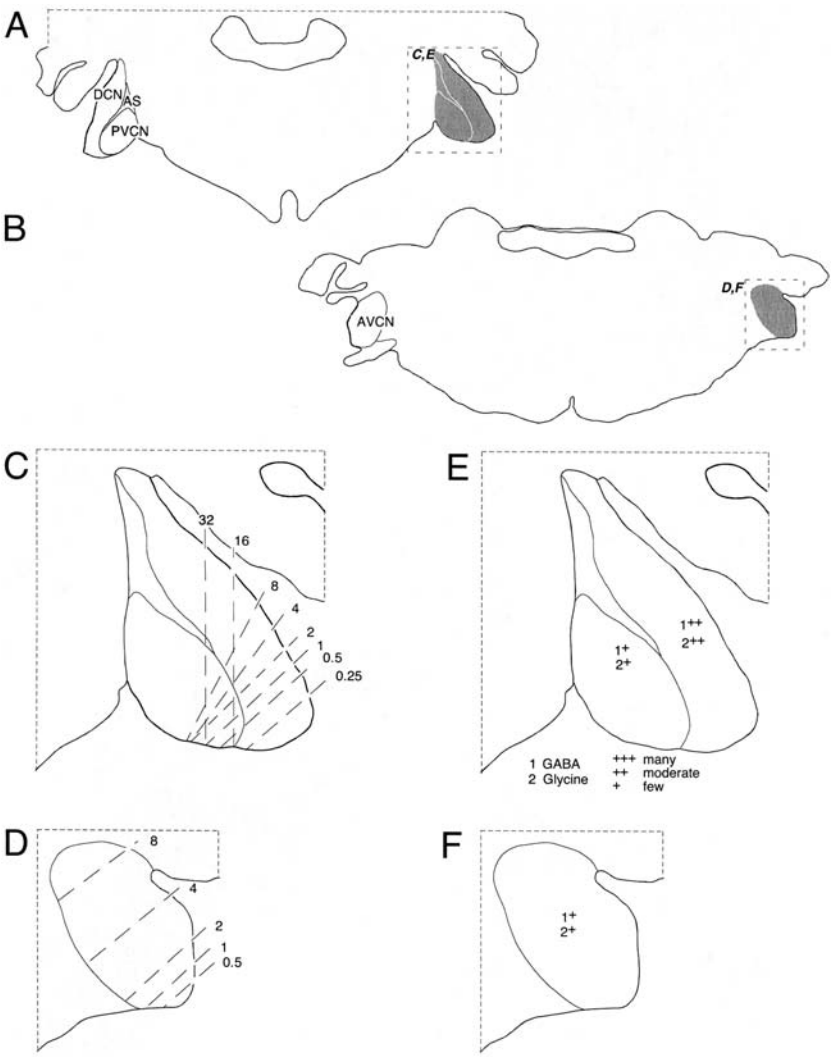

Figure 1.3. Some physiologic and neurochemical aspects of cochlear nucleus organization. **(A, B)** Cochlear nucleus subdivisions (Osen 1969; Brawer et al. 1974). In this and subsequent figures relating to other auditory nuclei, only the principal subdivisions are shown. **(C)** Spatial and nuclear arrangement of characteristic frequency as expressed in isofrequency lines *(dashed)* in the anteroventral and posteroventral cochlear nuclei (*AVCN* and *PVCN*). The systematic representation of frequency reflects the topography of cochlear nerve input (Leake-Jones and Snyder 1982) and it is conserved in both the AVCN and PVCN. Noteworthy features include the large spatial representation of frequencies $<$10 kHz, and the complexity of laminar overlap near nuclear borders and in regions where cochlear nerve axons bifurcate and their complex spatial geometry (Osen 1970) distorts a simple laminar organization; elsewhere in the central auditory system a spatial

of frequency is expanded, contracted, or distorted will be repeated many times between the cochlear nuclei and the cortex.

A constraint on a perfectly uniform distribution of the frequency spectrum is the biological significance of particular subregions: frequencies essential in communication are likely to have an enlarged representation (Suga and Jen 1976), and the degree of this expansion can match that in the cochlea itself (Feng and Vater 1985). This principle recalls the disproportionate sensory and motor neural representation of the primate hand relative to that of the foot (Kaas et al. 1984), or the central (foveal) part of the retina compared to its more peripheral regions (Tusa et al. 1981).

The divergence of the auditory nerve is not simply a bifurcation: it entails a structural reorganization of the postsynaptic neurons as well. The axons of the descending branch terminate in delicate boutons that will make synapses on the dendrites and cell bodies of neurons in the dorsal cochlear nucleus (DCN). These synapses—their number, location, and shape—will profoundly influence the physiologic behavior of the postsynaptic neurons. For example, synapses closest to the axon hillock, which is the electrogenic membrane controlling the discharge behavior of the cell, will have the maximum efficacy (Peters et al. 1991). The divergence of connectivity multiplies the channels of information exiting the cochlear nuclei and which, after reaching a variety of medullary auditory centers, converge on the inferior colliculus (IC). (See Fig. 1.5.)

The potential functional ramifications of the diverging projections from the auditory nerve are magnified by the great variety of morphologic cell classes that is targeted. As a consequence of morphology, convergence, and local circuitry, these cell classes differ functionally in distinct ways including their temporal response pattern, spectral selectivity, and discharge regularity. To highlight differences in their response properties, we next compare two types of cochlear nucleus neurons. Among the most conspicuous of the many types of DCN neu-

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Figure 1.3. *Continued*
compression of higher frequencies occurs (Morest 1965). This distortion is partly an artifact of collapsing a three-dimensional geometry onto two dimensions. [**(C, D)** Redrawn and modified from original sources (Bourk et al. 1981 with permission from Elsevier Science).] **(D)** In the AVCN the expanded volume devoted to low frequencies is even more pronounced than in the dorsal cochlear nucleus *(DCN).* **(E)** The distribution of GABAergic and glycinergic neurons follows specific patterns in the cochlear nucleus. In the DCN, both are concentrated in layers I to III; both neurons and axon terminals are plentiful here and much sparser elsewhere. GABAergic neurons may also colocalize glycine (Osen et al. 1990) and there is evidence for simultaneous corelease of both molecules (Jonas et al. 1998). In this and other nuclei, the vast majority of the other neurons are glutamatergic (Saint Marie 1996) or aspartatergic (Altschuler et al. 1981), as is the cochlear nerve (Wenthold 1985). [**(E, F)** Redrawn and modified from original GABA observations (Adams and Mugnaini 1987); redrawn and modified from original glycine observations (Wenthold et al. 1987).] **(F)** In the AVCN, there are few GABAergic or glycinergic neurons.

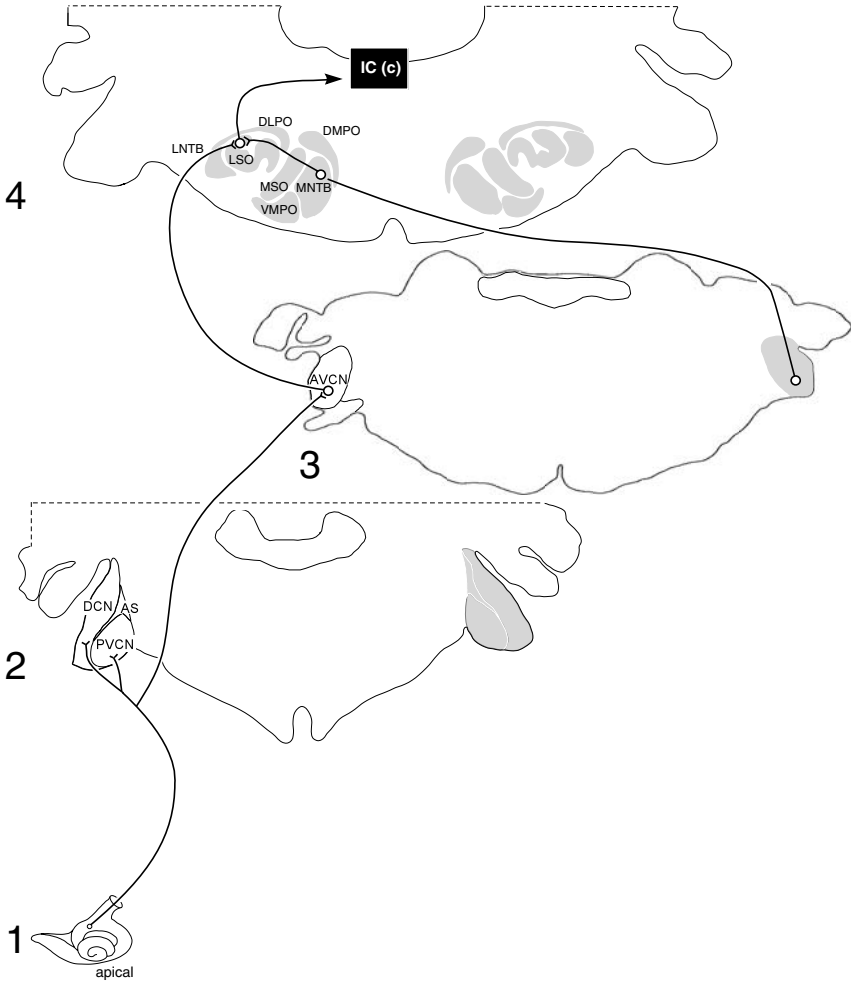

Figure 1.4. Representation of two basic principles of auditory brain stem connectivity—divergence and convergence—and their complementary functional roles. *1, 2:* Spiral ganglion cell axons divide and project to subdivisions of the cochlear nucleus (Lorente de Nó 1933, 1981). This creates independent maps of characteristic frequency (Rose et al. 1959). *3, 4:* Topographically matched projections from each anteroventral cochlear nucleus *(AVCN)* have different targets in the medulla: the ipsilateral projection ends in the lateral superior olive *(LSO)* (Cant and Casseday 1986), while the contralateral AVCN projects to the medial nucleus of the trapezoid body (*MNTB*) (Warr 1966), whose axons converge on the other primary dendritic trunk of the same postsynaptic neuron (Spangler et al. 1985; Vater et al. 1995). This creates binaural receptive fields among superior olivary complex neurons (Tsuchitani and Boudreau 1966; Tsuchitani and Johnson 1991).

rons is the fusiform cell; it has a pyramidal cell body and an extensive dendritic tree (Brawer et al. 1974). These processes act as postsynaptic sites: their thick trunks and slender spines are studded with presynaptic axon terminals, most from the auditory part of the eighth cranial nerve (Cant 1992). A consequence of this pattern of axodendritic organization is that it requires spatiotemporal summation to elicit a postsynaptic response that differs significantly from the rate of spontaneous discharge. A constraint is that the postsynaptic dendritic propagation of all-or-none signals is decremental because the dendritic membrane typically lacks the regenerative channels found in myelinated axons and that permit them to send spike codes over long distances while conserving amplitude or fidelity. Thus, inputs to the most distal dendrites usually have correspondingly less influence than terminals near the axon hillock (Jack et al. 1975), unless they are amplified at dendritic branch points (Stuart et al. 1997). Dendritic input may require a coordinated volley of presynaptic impulses arriving optimally to achieve the spatial and temporal summation necessary to cross the threshold of the postsynaptic neuron. The threshold and the electrotonic properties of the dendrites act as adaptive filters to reduce spontaneous discharges in an auditory environment filled with ambient noise. Many neurons respond best to changes in sound pressure level (dynamic response), while others prefer steady-state (tonic) conditions (Young 1984). These extremes effectively reduce noise yet preserve the ability to respond to static stimuli or to signals with a wide dynamic range.

The physiologic types of cochlear nucleus neurons have been determined using tonal or noise stimuli to generate peristimulus time histograms that provide insight into basic coding properties (Fig. 1.6). This strategy was applied originally in the auditory nerve to classify the responses of cochlear ganglion cell fibers (Kiang et al. 1965), and it has revealed the temporal profile of neuronal responses in many regions (Kiang et al. 1973). The discharge pattern of intracellularly identified fusiform cells in the DCN shows a pauser/buildup pattern (Fig. 1.6D, E). This consists of a delayed discharge after stimulus onset, a burst of spikes concentrated in the first few milliseconds, an abrupt decline to near-zero spikes, and, finally, a subsequent slow growth in spike rate punctuated by briefer reductions; the unit never reestablishes the spike density at onset, and the discharge can persist or even increase long after the poststimulus period (Rhode et al. 1983b).

As viewed in the electron microscope, many of these physiologic attributes have ultrastructural correlates that could support them. Thus, fusiform cells receive synapses indicative of independent excitatory and inhibitory input on their distal dendrites. The excitatory endings (Oliver et al. 1983) are axodendritic synapses of eighth nerve origin and terminals from granule cell parallel fibers, which project in long rows across these dendrites (Fig. 1.7B: pf). Prospective inhibitory input arises from four types of neuron—each with a specific synaptic arrangement on the postsynaptic cell. Stellate, vertical, Golgi, and cartwheel cells each project to fusiform cell dendrites (Berrebi and Mugnaini 1991). Some of these neurons may be glycinergic (Wenthold and Hunter 1990) and others

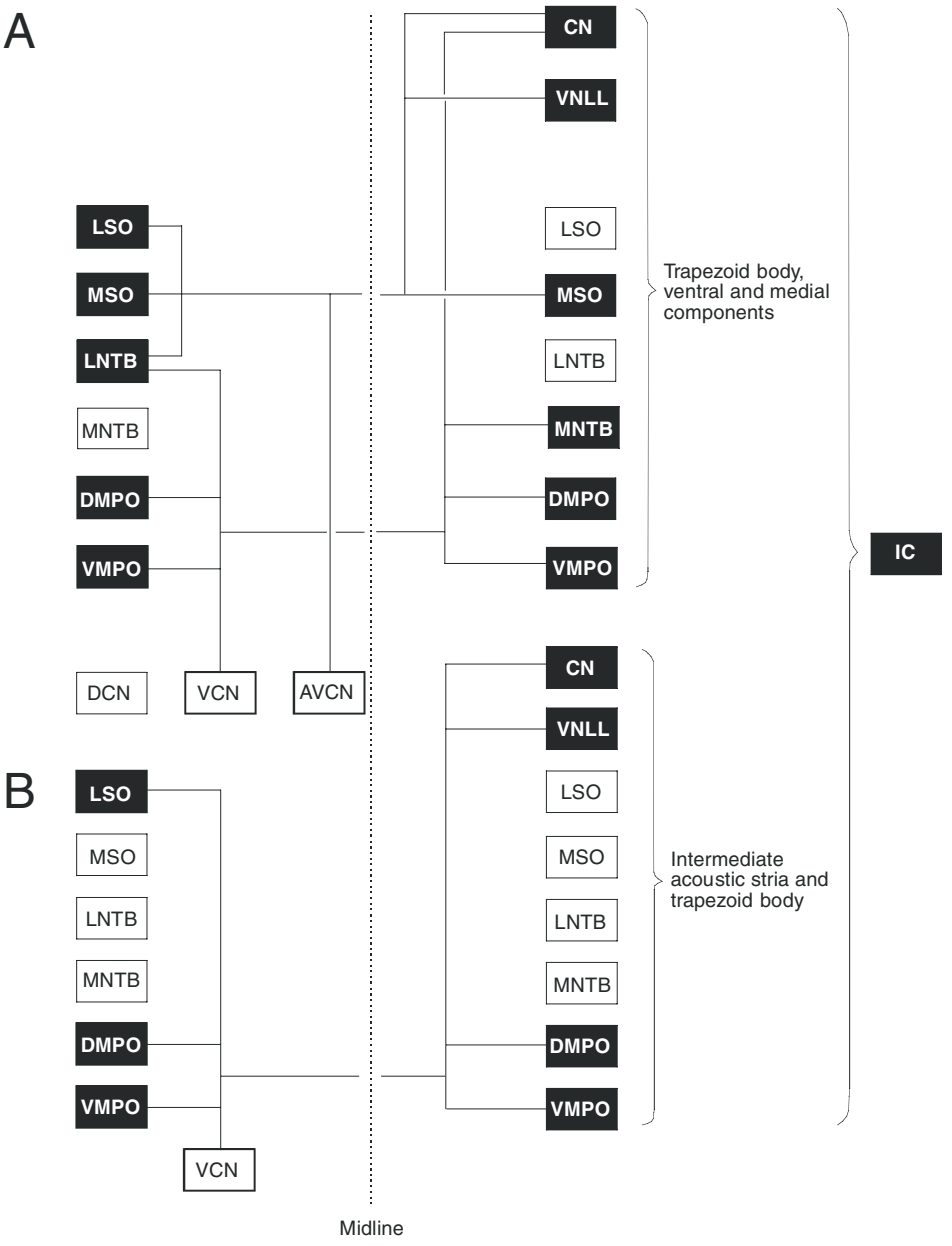

Figure 1.5. Components of the striae of Held and von Monakow and the trapezoid body (Fig. 1.2) shown schematically. Their medullary target nuclei each project to the inferior colliculus. **(A)** Trapezoid body, ventral and medial components. **(B)** Intermediate acoustic stria and trapezoid body. [Redrawn and modified from original sources (Warr 1982; Irvine 1986).] Key for this and subsequent schematics: *open boxes with heavy outlines,* origins of projections; *solid boxes with white lettering,* targets of projection; *lines,* axons; *dotted line,* midline; *brackets,* fiber tracts. Ascending pathways are shown in these diagrams unless indicated otherwise (Fig. 1.18).

γ-aminobutyric acid (GABA)-ergic (Adams and Mugnaini 1987); this suggests cell-specific interactions that mediate the discharge properties and influence the receptive field profile of postsynaptic neurons. Although the exact nature of the dynamic interactions among these convergent inputs on fusiform cells is not known, they could contribute to the periodic fluctuations and gradual decline in rate seen in pauser/buildup units. Overall, then, fusiform cells perform a profound and complex spectral and temporal transformation of the auditory nerve input whose ultimate functional purpose may contribute to several, still largely elusive, central auditory tasks.

In the anteroventral cochlear nucleus (AVCN), the response of a different type of neuron, the bushy cell, can be contrasted with, and complements that of, the DCN fusiform cell. Here, ascending auditory nerve fibers end on bushy cell somata. These neurons differ fundamentally from fusiform cells (Lorente de Nó 1981). Bushy cells have only one or two short dendrites, and their predominant synaptic ending is an auditory nerve axon, the endbulb of Held, which forms a massive cuplike terminal that encloses the perikaryon, with several such endings and with virtually identical tuning curves converging onto a cell (Cant and Morest 1979). Thus, the dendritic arbors of these cells are modest, while the most potent synaptic input from the endbulbs terminates near the axon hillock. The net probability of presynaptic signals evoking a postsynaptic discharge therefore is effectively unity (Rhode et al. 1983a). Moreover, these neurons discharge preferentially to the earliest, onset-related features of the stimulus. The tonotopic representation in the AVCN is unusual: frequencies <5 kHz are mapped selectively and expansively. The electrophysiologic profile of the response is also unique because of the size of the endbulb and the large-amplitude prepotential in the afferent fiber, neither of which is present in the DCN (Bourk et al. 1981). Frequency tuning, rate-intensity function, and discharge regularity of bushy cells closely resemble their auditory nerve inputs. Hence, they perform only a minimal transformation of the input and, rather, ensure a faithful information transmission beneficial for processes in the following stations, such as binaural comparators. The fusiform and bushy cells are just two examples of the wide range of structural/functional patterns represented in the cochlear nucleus, and they embody only some of the nuclear- and cell-specific response patterns (Rhode 1991). More than 20 kinds of neuron have been identified in the cochlear nucleus (Brawer et al. 1974).

The presence of local circuitry within the cochlear nucleus itself further refines signal processing. These circuits may function to reject unwanted signals, amplify weak inputs, provide inhibition that enhances the signal-to-noise ratio (Berrebi and Mugnaini 1991), or serve a disinhibitory role. Because the responses of auditory nerve axons are sharply tuned to specific frequencies with no inhibition, and because stimulation at unfavorable frequencies elicits a negative or no response (Kiang et al. 1965), such circuitry intuitively might not seem necessary. In the cochlear nucleus, however, the convergence of input from many different fibers onto a single neuron could blur the fine spatial and temporal patterns of activity, or help to retune or focus the cell's response area to a particular aspect of the stimulus, such as in monaural echo suppression

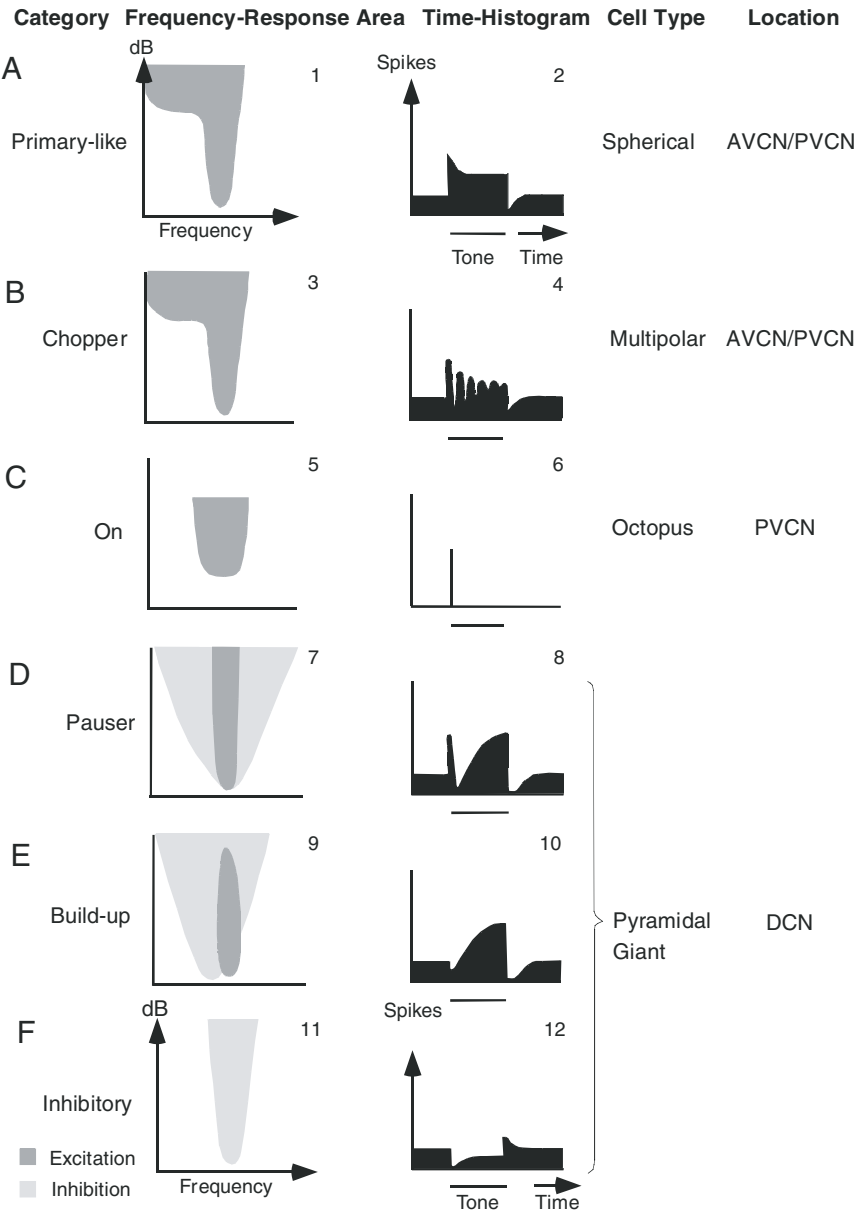

Figure 1.6. A categorical description of cochlear nucleus physiologic response profiles and their correlation with neuronal types. The frequency-response areas *(1, 3 . . . 11)* depict the tuning curve types, while the peristimulus time-histogram *(2, 4 . . . 12)* shows the interplay of intrinsic membrane properties and the excitatory–inhibitory interactions that shape the cell's dynamic response to tones. The inhibitory contribution to the receptive field is also visible in the frequency-response area (**D:** *7,* **E:** *9,* **F:** *11*). Although

(Wickesberg and Oertel 1990). Inhibition can impose unique filter properties on the tuning behavior and modify the neural response profiles. Thus, type II DCN interneurons are sharply tuned, with large excitatory response areas flanked by lateral zones of inhibition, and they have little spontaneous activity (Young and Voigt 1982). Type II cells are thought to have local feedforward projections onto type IV neurons, the fusiform or giant cells. Thus, type IV cells cease firing when the type II units increase their spike rate. The type II discharge creates powerful inhibitory subregions in the tuning curve of the type IV cell; the tight temporal cross correlation in spike discharge indicates that these neurons may be linked monosynaptically. Such circuits could underlie the type IV unit's robust response to broad-band noise and the inhibitory effects of pure tones (Young 1984). This circuit is analogous to one made in the cerebral neocortex by inhibitory interneurons (basket cells) on pyramidal cells (White and Keller 1989; Prieto et al. 1994a) and by similar kinds of IC cells (Oliver et al. 1994). Such circuits may be a common feature in many nuclei for regulating the output of projection neurons and for reorganizing their receptive fields in response to environmental demands (Bjordahl et al. 1998; Kilgard and Merzenich 1998a). It remains to elucidate in equal detail the functional connectivities among the many other cochlear nucleus neuronal populations.

Already in this first nucleus of the auditory pathway, several themes are established that have major consequences in subsequent processing and reflect equivalent mechanisms throughout the auditory system. Many of the different cell types distribute the transformed information to specific proximal targets. Although there is not necessarily a one-to-one relationship between type of projecting neuron and target nucleus or cell type, at least six parallel streams of diversely transformed or modulated auditory information emerge. Each stream embodies a different preprocessing principle that is likely best suited for further, specific central processing tasks. Accordingly, the auditory signal is decomposed not just in terms of its frequency content but also in terms of a variety of other stimulus features that are composed of complex aspects of spectral, temporal, and spatial signal attributes. The particular contributions of most of these concurrent streams originating in the cochlear nucleus to the process of feature extraction, object recognition, and, ultimately, perception remain to be established.

Figure 1.6. *Continued*
a detailed treatment of the individual categories is beyond the scope of this chapter, the range of responses in the primary auditory nuclei suggests that peripheral receptor diversity contributes little to coding, while in the somatic sensory system peripheral receptor diversity plays a major role in the establishment of separate processing streams (Sinclair 1981). A major basis for auditory coding is thus local circuitry, although diversity in hair cell responses (Ashmore 1991) and spiral ganglion cell behavior (Kim and Molnar 1979) and differential projections (Brown and Ledwith 1990) must contribute to this pattern. [Redrawn and modified from the original sources (Evans 1982 with the permission of Cambridge University Press; Webster and Garey 1990).]

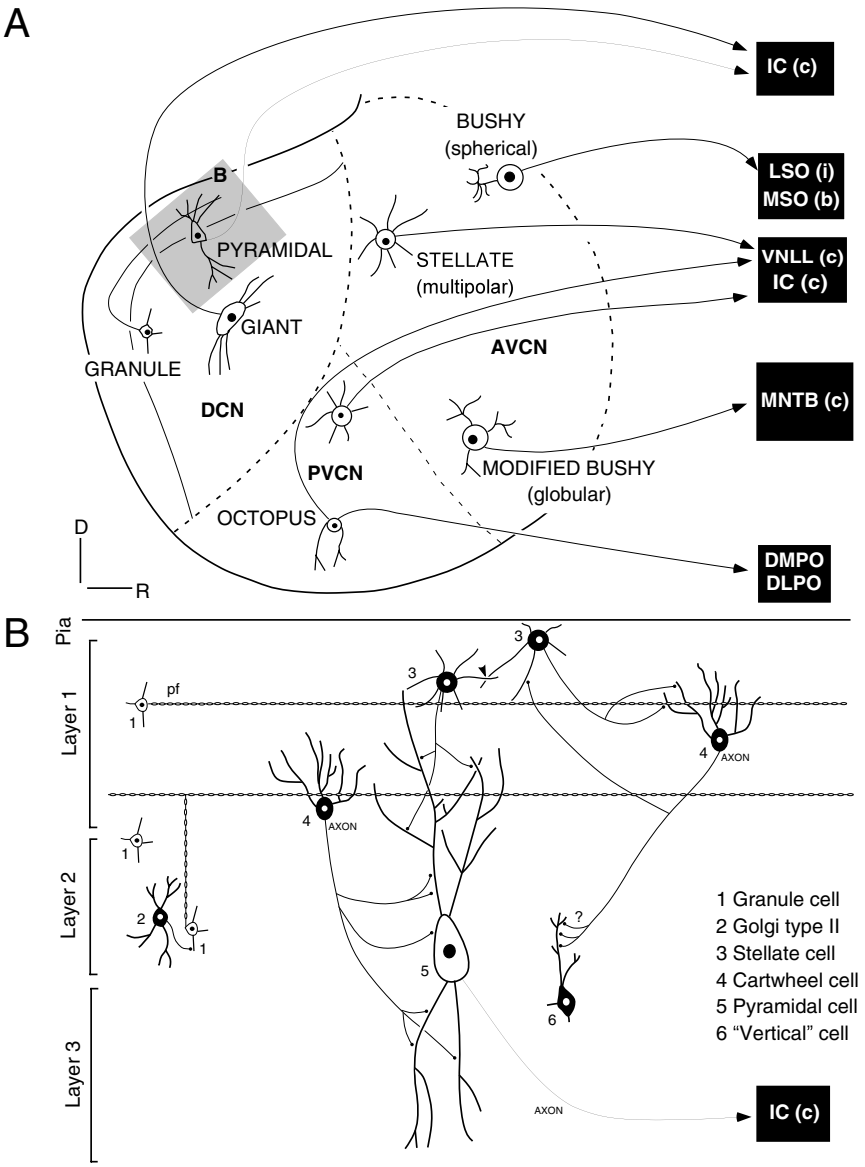

Figure 1.7. Some projections of cochlear nucleus neurons that may contribute to parallel processing in the superior olivary complex, lateral lemniscal nuclei, and inferior colliculus. **(A)** In a parasagittal schematic, cartoons of the principal cochlear nucleus neurons demonstrate that they have diverse ipsi- and contralateral targets. Differences in the temporal coding among these cell types (Fig. 1.6: *2, 4 . . . 12*) suggest that the streams leaving the cochlear nucleus are integrated in higher centers (when they converge) or contribute to parallel pathways (when they diverge) (Warr 1982). [Redrawn and modified from

3. The Olivary Complex

The olivary complex consists of four (humans) to nine (cats) nuclei (Moore and Moore 1971) that have several complementary physiologic roles. Neurons in the LSO integrate the monaural input of the cochlear nuclei to derive intensity-difference sensitive binaural signals, mainly for high frequencies, and to send this information to the lateral lemniscal nuclei (LLN) and the IC (Schwartz 1992). Neurons in the medial superior olive (MSO) encode phase relationships and delay sensitivity from the two ears (Fig. 1.8D), mainly from lower frequencies; these signals are essential for accurate spatial localization (Yin and Chan 1990). Neurons in the medial nucleus of the trapezoid body (MNTB) contribute to the creation of binaural subtypes via their inhibitory input to the LSO (Guinan and Li 1990). The construction and variety of binaural interactions represent a situation in which emergent function can be directly related to a particular neural circuit (Tsuchitani and Johnson 1991). The species-specific variability in the size, shape, and disposition of the olivary nuclei (Schofield and Cant 1991) suggests that ecologic factors (Masterton et al. 1975) might induce structural changes related to evolutionary adaptations in hearing (Papez 1929). All subdivisions have a tonotopic organization (Fig. 1.8B).

The striking precision of connectivity in the central auditory system is exemplified in the ascending projection onto principal cell lateral dendrites in the LSO. In this example, one primary dendrite is postsynaptic to input from the ipsilateral AVCN, whose output cells may be aspartatergic and are likely excitatory (Oliver et al. 1983). The other dendrite is the target of axons from cells in the MNTB (Cant and Casseday 1986), which are glycinergic and probably inhibitory (Bledsoe et al. 1990). The contralateral AVCN provides the excitatory drive to the MNTB. This convergence has important functional consequences, as olivary principal cells integrate ipsilateral (excitatory) and contralateral (inhibitory) input whose chemical signals can facilitate or suppress postsynaptic neurons. This convergence creates the first binaural neurons in the auditory system and their discharge pattern integrates excitation and inhibition.

Figure 1.7. *Continued*
Aitkin (1989).] **(B)** Schematic view of local circuits in layers 1 to 3 of the dorsal cochlear nucleus, showing the main types of neurons and their synaptic relationships. Some connections, for example, between stellate cells *(3),* have not yet been demonstrated. The major relationships shown here in the guinea pig depict cartwheel cells *(4)* projecting to the superficial and deep dendrites of pyramidal cells *(5);* the cartwheel cell input to the vertical cell *(6)* is likewise unconfirmed. Parallel fibers *(pf)* arising from granule cells *(1)* provide excitatory input to the layer 1 inhibitory neurons and to the apical dendrites of pyramidal cells. A '?' indicates a possible projection. Arrowhead, gap junction between stellate cell dendrites. [Redrawn and modified from original sources (Berrebi and Mugnaini 1991).] Neurons in *black* are considered inhibitory (Osen et al. 1990).