

hair cells respond to the *displacement* of the membrane. Inner hair cells therefore seem suited to detecting the a.c. component in the response of the basilar membrane, which they signal to the central nervous system. Outer hair cells respond to the d.c. as well as the a.c. component. It is possible that the outer hair cell afferents signal the d.c. component in the response of the basilar membrane.

H. Further Reading

Cochlear function has been reviewed by several authors in *Hearing Research* 1986, volume 22, and by Pickles (1985a). *Auditory Biochemistry* (ed. D.G. Drescher, C.C. Thomas, Springfield, 1985), *Neurobiology of Hearing: The Cochlea* (eds R.A. Altschuler *et al.*, Raven Press, New York, 1986), and *Peripheral Auditory Mechanisms* (eds J.B. Allen *et al.*, Springer, Berlin, 1986) have many useful chapters.

6. The Brainstem Nuclei

The responses of the brainstem auditory nuclei will be described in terms of the neural temporal firing patterns, neural frequency resolution, excitatory-inhibitory interactions, response to complex stimuli and, where appropriate, binocular interactions. Auditory brainstem reflexes and what little information we have on the involvement of brainstem auditory nuclei in learning will be described.

A. Considerations in Studying the Central Nervous System

Many experiments have shown that single auditory nerve fibres have qualitatively uniform properties, although the fibres may vary quantitatively in factors such as bandwidth, spontaneous firing rate, and threshold. It is therefore comparatively easy (but still difficult!) to describe the properties of the whole population from a small number of experiments. In the cochlear nucleus, however, there are many different cell types and regions. Therefore, giving a complete description is already very difficult, and it is much easier to undertake experiments and analyse the results, if we have some theories as to the function of the system.

Three themes can be discerned in the analysis of sensory systems. One concerns "feature detection". In such an analysis, we suppose that certain features of the sensory environment are selectively extracted. In the visual system, the scheme of Hubel and Wiesel (1962) has had great appeal. Here, cortical cells were described as responding selectively to lines and edges in various orientations. Unfortunately, in the auditory system, it has been difficult to describe any critical features beyond the rather elementary ones, either from psychological experiments aimed at finding important features to look for, or from electrophysiological experiments in which neuronal responses to complex stimuli were analysed. For instance, at a simple

level, lateral inhibition seems to emphasize the contrast in the neuronal representation of a spectral pattern. This could be said to be one example of feature detection. At a slightly more advanced level, cells in the dorsal cochlear nucleus have been found that give particularly strong responses to stimuli that are amplitude- or frequency-modulated. But even here, there seems to be a continuum in the complexity of neuronal responses, and it is very difficult to decide the extent to which such features are preferentially extracted. It is therefore difficult to decide whether we are entitled to think of such modulated stimuli as forming specific "features" of particular significance for the nervous system. These problems are compounded further, when the analysis of complex sounds such as those of speech is considered in a high-level structure such as the auditory cortex.

A second theme is the localization of functions to the activity of individual cells. In the context of feature detection, it involves finding cells that respond to specific features, so that the detection of a feature can be defined by the activity of single cells studied in isolation. At the other end of a continuum, detection might only be defined by the pattern of activity over many cells. In a common analogy, the first case might be compared to a photograph, in which each point on the photograph represents one point in space, whereas the opposite end of the continuum might be compared to a hologram, in which each point on the hologram represents many points in space, and in which individual points in space can be reconstructed only by the integration of information from many points on the hologram. Undoubtedly, many of the more complex features will only be represented in the second form, and at any level of the auditory system we might expect to find many coexisting stages in between the two extremes. In the context of feature detection, features that are not represented by the activity of individual cells can only be represented by the pattern of activity over many cells. A simple example is seen in the auditory nerve. The fibres of the auditory nerve, by their sharp tuning, appear to be specialized for the detection of specific frequencies. Sharp tuning in such a quasilinear system is necessarily correlated with poor temporal resolution. Yet sound localization experiments show the auditory system is able to detect temporal disparities of the order of 10 μ s, and it is hypothesized that such accuracy is achieved by the integration of activity over many fibres.

A third theme is that of hierarchical processing, in which successively more complex analyses are performed at ascending levels of the nervous system. If the only points of interest in an acoustic environment are, say, vowel formants, then it is obviously economical to extract the formants at an early stage in the system, reject all other information, and perform further processing on the information given by the formants.

Schemes for sensory analysis based on the logical extremes of each of the

three themes – that is, on the extraction of specific features, on the representation of the features in the activity of single cells, and on hierarchical analysis – naturally spring to mind. But it is likely that the auditory system operates far from these logical extremes on all three points. Such a mode of operation has contributed greatly to the difficulty of the electrophysiological analysis of the central auditory nervous system.

A successful scheme for describing the organization of the auditory central nervous system is based on quite different criteria, being anatomical. The neurones are tonotopically organized in all specific central auditory nuclei. That is, they are arranged in a regular order of best frequency along one dimension across the nucleus. Searches have been made for complementary schemes of organization, with a gradation orthogonal to the frequency axis, based on other criteria. Possible complementary schemes are based on properties such as sharpness of tuning, or binaural dominance.

B. The Cochlear Nuclei

1. Anatomy

In view of the diversity of the properties of cochlear nucleus neurones, anatomical studies are vital in aiding the physiologist in his analysis of the functions of the nuclei.

Each fibre of the auditory nerve branches on entering the nucleus, sending one branch rostrally and the other caudally. The rostral branch innervates the division known as the anteroventral cochlear nucleus, whereas the caudal branch innervates both the posteroventral division of the nucleus and the dorsal cochlear nucleus (Fig. 6.1A). We might expect the orderly arrangement of the incoming fibres to be reflected in an orderly arrangement of characteristic frequencies of the neurones they innervate, leading to a "tonotopic" frequency map. Such maps are indeed found (Rose *et al.*, 1960). But instead of two maps, one for each branch of the auditory nerve, there are in fact three, one corresponding to each of the above-named divisions of the nucleus. One map is supplied by the rostral branch of the auditory nerve, and the other two by the caudal branch. Figure 6.1C shows two of the tonotopic maps, encountered as an electrode was moved from the dorsal to the anteroventral cochlear nuclei.

These three divisions of the cochlear nucleus show broadly different response properties, and it is very likely that they have correspondingly different functions. In general, neurones of the anteroventral cochlear nucleus have properties rather similar to those of auditory nerve fibres, and may well function much as a simple relay for afferent information. Cells of

the dorsal cochlear nucleus, on the other hand, have very much more complex response properties, and may therefore contribute to complex signal analysis. Their output axons bypass the next nucleus in the auditory pathway, the superior olivary complex, and end in the nuclei of the lateral lemniscus and the inferior colliculus. The properties of many neurones of the posteroventral nucleus are intermediate to those of the other two. Interestingly, the dorsal cochlear nucleus is comparatively small in primates.

The detailed study of the cells of the cochlear nucleus has led to the hope that different functional characteristics can be associated with the different cell types. The mapping of cell types is due to Osen (1969) and Brawer *et al.* (1974), both in the cat. The schemes are generally similar; the terminology used here is that of Osen. Cant and Morest (1984) discuss the relation between the different schemes of neuronal organization.

Certain areas can be defined as most obviously being occupied by certain cells. In the anterior pole of the anteroventral cochlear nucleus there is an area of large spherical cells (Fig. 6.2), although there are other cells among them. Auditory nerve fibres contact the large spherical cells by means of particularly large synaptic endings known as end-bulbs of Held, as well as by smaller endings. Caudal to this area there is an area of smaller spherical cells, and then one of globular cells (Fig. 6.2). All these types were classed as bushy cells by Brawer *et al.* (1974). Octopus cells, known as such from the pattern of their dendrites, although Morest *et al.* (1973) remark that they look more like ostrich cells (Fig. 6.3), occupy a region of the posteroventral cochlear nucleus called the octopus cell area. The area consists almost entirely of octopus cells. The other areas of the posteroventral cochlear nucleus contain a variety of cells. The dorsal cochlear nucleus caps the posteroventral nucleus both dorsally and caudally. It contains a striking layer of cells with double processes, one oriented towards the surface of the nucleus and one towards the centre. The cells have been called fusiform cells or pyramidal cells in different terminologies. There are also "giant" cells deep in the dorsal nucleus. Many other smaller cells are distributed throughout the whole cochlear nucleus, some of which are likely to be interneurons. Young (1984) has suggested that the cells of these different types form separate, parallel, systems for relaying the auditory information.

In man, many of the cell groups associated with interneurons are reduced in size, while the number of relay neurones is increased (Moore, 1987). Thus, it appears as though the amount of signal processing at the lower levels of the auditory system is reduced in man, compared with the cat.

2. Neurotransmitters

The neurotransmitter, or neurotransmitters, released by the primary auditory neurones are not certain: excitatory amino acids such as glutamate and

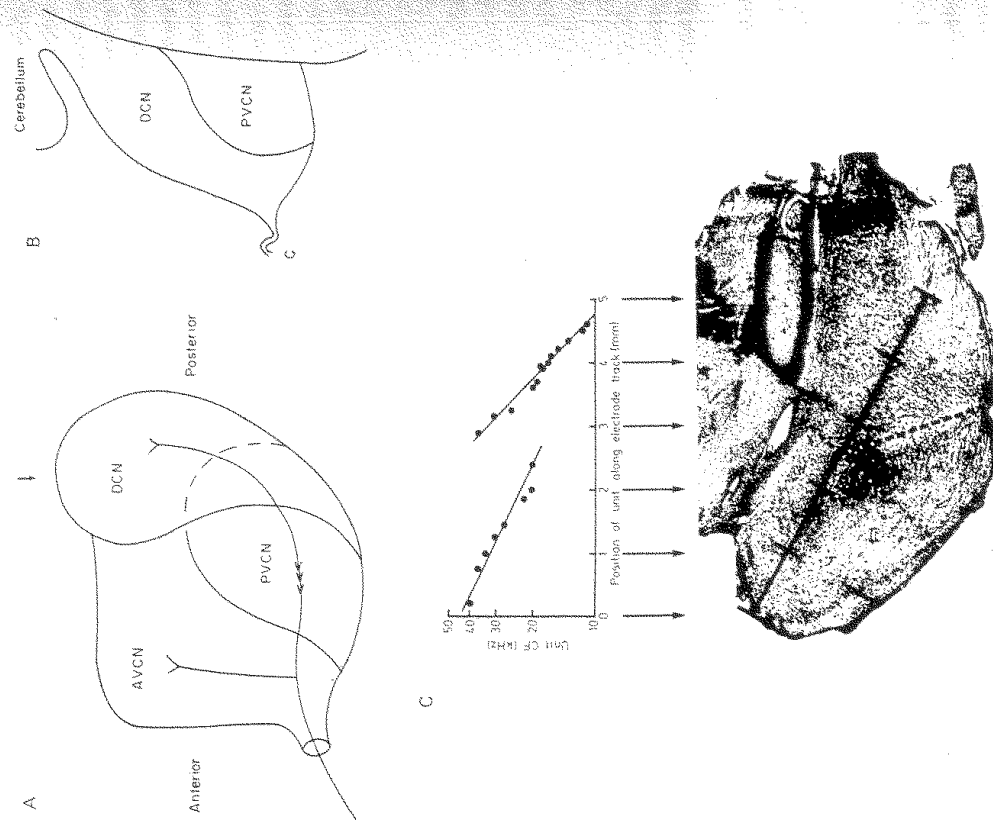


Fig. 6.1(A) A sagittal section of the cat cochlear nucleus shows the three divisions of the nucleus, innervated by a branching auditory nerve fibre. AVCN, anteroventral cochlear nucleus; PVCN, posteroventral cochlear nucleus; DCN, dorsal cochlear nucleus. (B) Transverse section of the cochlear nucleus, at the point marked by the arrow in A. C, choroid plexus. (C) The tonotopic organization of the cochlear nucleus. Two separate high-low sequences were seen as a recording electrode was moved from the dorsal to the anteroventral cochlear nucleus. Sagittal section. From Evans (1975a, Fig. 28).

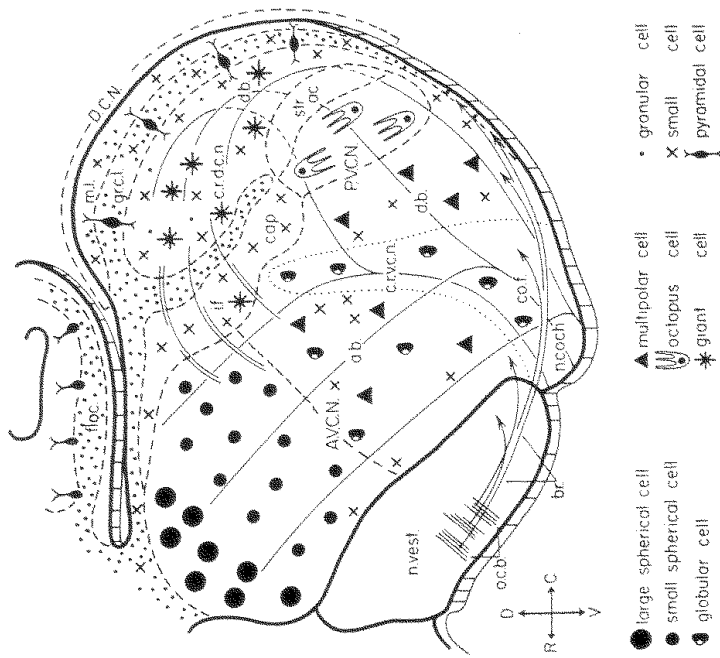


Fig. 6.2 A cytoarchitectural map of the cochlear nucleus is shown in sagittal section. The predominant cell types in each region are represented. AVCN, anteroventral nucleus; cap, peripheral cap of small cells; crdcn, central region of DCN; crvcn, central region of ventral nucleus; DCN, dorsal nucleus; floc, flocculus (cerebellum); gcl, granular cell layer; if, intrinsic fibres; ml, molecular layer; PVCN, posterioventral nucleus; strac, dorsal and intermediate acoustic striae. From Osen and Roth (1969, Fig. 1).

aspartate are often suggested (e.g. Godfrey *et al.*, 1984; Martin, 1985). The evidence is derived from high levels of the amino acids and their associated enzymes in the auditory nerve root, and the effects of the acids and their agonists and antagonists on cells of the cochlear nucleus. The evidence has been reviewed by Wenthold and Martin (1984).

GABA (γ -amino butyric acid) and glycine may be inhibitory transmitters, particularly in the DCN, and associated with interneurons (Godfrey *et al.*, 1978; Peyret *et al.*, 1987). Glycine has also been suggested as the transmitter of fibres which run directly between the cochlear nuclei of the two sides

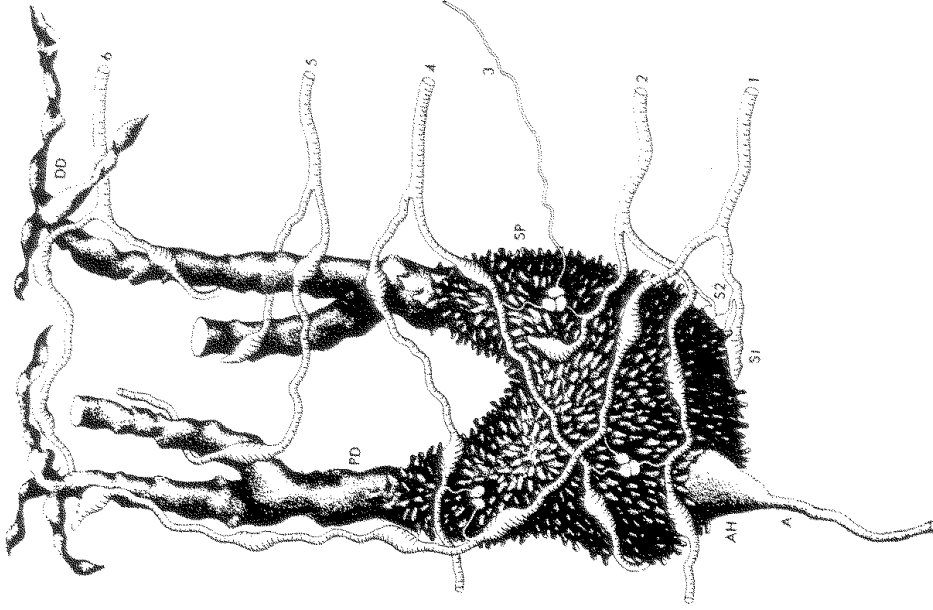


Fig. 6.3 An octopus cell. The thick auditory nerve fibres (1,2,4,5,6) give rise to large endings (S1) on the cell. They may also branch to give thin fibres, which, together with thin afferent axons (3) give rise to small secondary endings (S2). The cell is covered with stubby appendages (SP). AH, axon hillock; A, axon. From Morest *et al.* (1973, Fig. 2).

(Wenthold, 1987). Acetylcholine and noradrenaline in the cochlear nuclei are thought to be mainly transmitters of the centrifugal, or "descending", innervation arising from the central nervous system. These will be discussed further in Chapter 8.

3. Physiology

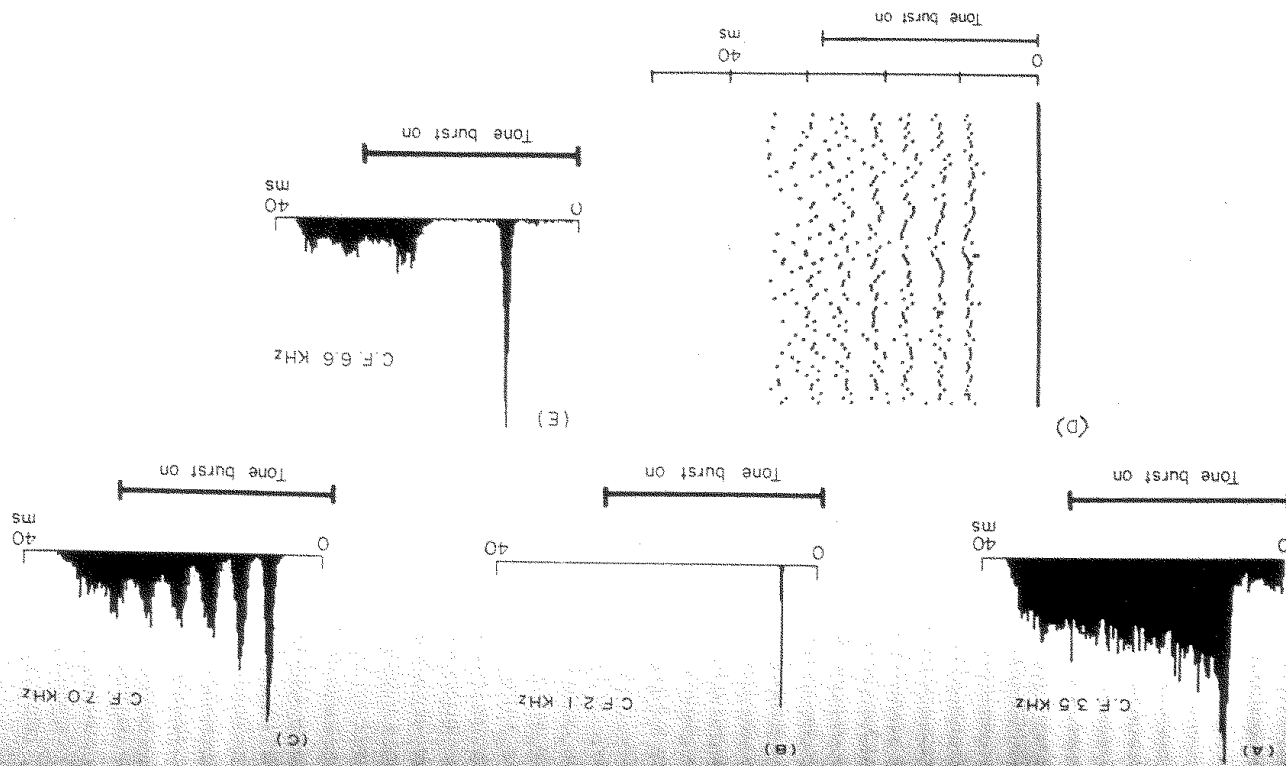
(a) Classification on the basis of response in time

In an electrophysiological experiment, Pfeiffer (1966a) classified cells of the cochlear nucleus by the apparently arbitrary, but in fact useful, criterion of the time pattern of the response to short tone bursts, delivered just above threshold at the neurone's characteristic frequency.

(i) *Primary-like cells.* These have post-stimulus time histograms (PSTHs) to tones similar to those of auditory nerve fibres, with an initial peak at the onset, declining gradually to lower levels (Fig. 6.4A). Such units are found throughout the ventral cochlear nucleus. In particular, those in the antero-ventral cochlear nucleus resemble auditory nerve fibres in other ways, for instance in the shape of the tuning curve, the degree of phase-locking to low-frequency stimuli, monotonic rate-intensity functions, lack of inhibitory sidebands, and relative independence of response classification on intensity. There is evidence that some of the spherical (bushy) cells of the anteroventral nucleus form at least some of the primary-like neurones. For instance, primary-like responses are obtained from the spherical cell area. Further indirect evidence comes from the waveform of the extracellular action potential. Many such recordings show a positive deflection just before the usual monophasic or biphasic waveform recorded from a cell body, and Pfeiffer (1966b) suggested that this corresponded to the depolarization of the large end-bulbs of Held, the presynaptic endings on the auditory nerve fibres on the cells. The correspondence was supported by the intracellular labelling of primary-like cells by Rhode *et al.* (1983b) and Rouiller and Ryugo (1984). The primary-like responses, together with the short synaptic delay on these cells, as well as the time pattern of the spontaneous activity, suggests the existence of what have been called "secure" synaptic connections, in which each afferent action potential produces an action potential in the output. This suggests that the cells act to relay the activity of auditory nerve fibres to the higher centres in a straightforward manner.

(ii) *Onset responses.* Cells showing onset responses produce a sharp peak in the PSTH at the beginning of a tone burst, and then either no activity, or a low level of sustained activity (Fig. 6.4B). Such cells are found throughout the cochlear nucleus. However, one region has proved of particular interest. The octopus cell area produces only onset responses, and the area consists almost entirely of octopus cells. Intracellular labelling confirms that octopus cells in this region generate onset responses (Rhode *et al.*, 1983b, Rouiller and Ryugo, 1984). We might suppose that there is an excitatory input, and

Fig. 6.4 Post-stimulus-time patterns of cells in the cochlear nucleus. (A) Primary: (B) Primary: (C) onset: (D) chopper: (E) raster pattern of firing for chopper cell. The trace was swept horizontally after each tone pip, and successive traces are shown one above the other. The occurrence of each spike is shown by a dot. (E) Pauser. From Pfeiffer (1966a, Figs. 1 and 2).



then a delayed inhibitory input. The origin of the inhibitory input is not known. Kane (1973) showed that there were two types of synapse on octopus cells. There are large, primary endings covering much of the cell surface arising from the auditory nerve. There are also finer axons ending in smaller boutons (Fig. 6.3), and Kane suggested that the inhibitory phase might be produced by a delayed inhibition produced by the smaller endings. However, the position is uncertain, because intracellular recordings show that many types of onset cell maintain a sustained *depolarization* during the stimulus, and this is inconsistent with synaptic inhibition (Britt and Starr, 1976a). Ritz and Brownell (1982) have tentatively suggested that the reduction in firing may arise from a depolarization block following intense synaptic activation.

Presumably the inhibition following the onset response will inhibit a response to the next stimulus if the stimuli are presented rapidly enough. Such units will follow every click in a rapid train of clicks up to a certain click rate, beyond which the response drops precipitously (Godfrey *et al.*, 1975a; Rhode and Smith, 1986a). They may therefore respond to the period of complex stimuli. The cells have wide tuning curves, likely to be a correlate of the great degree of synaptic convergence in their inputs (e.g. Rhode and Smith, 1986a).

(iii) *Chopper responses.* Chopper units tend to fire repetitively during a sustained tone burst at a rate that is unrelated to the period of the stimulus waveform. The PSTH therefore shows a series of peaks, which, because the timing of the spikes becomes rather ragged during the latter part of the tone burst, declines towards the end (Fig. 6.4C). The increasing raggedness is better seen in the raster diagram showing the timing of the spikes during each tone burst (Fig. 6.4D). Presumably, such cells receive a large number of synaptic inputs, which summate to produce a smooth depolarizing membrane potential, with firing and resetting whenever it reaches threshold. Identification of chopper responses with any particular cell type is not possible, since the responses are found throughout the cochlear nucleus. However, they are strongly represented in some regions of the posteroventral nucleus and the deep layers of the dorsal nucleus (Godfrey *et al.*, 1975a,b; Rhode and Smith, 1986b).

(iv) *Pauser and buildup responses.* Pauser cells show an initial onset response, a silent period, and then a gradual resumption of activity (Fig. 6.4E). Buildup units were identified by Rose *et al.* (1959) as those that did not show the initial onset component, but whose activity increased slowly with time. Cells with these two patterns of response are found particularly in the fusiform layer of the dorsal cochlear nucleus, and intracellular labelling with

horseradish peroxidase shows that at least some of the pauser and buildup cells are fusiform cells (Godfrey *et al.*, 1975b; Rhode *et al.*, 1983a). The response properties change markedly with changes in stimulus parameters, and it is likely that the temporal pattern is an indication of the complex excitatory and inhibitory inputs playing on the cells (Rhode and Smith, 1986b). It is therefore possible that such cells may be extracting certain complex features from the auditory stimulus.

(b) Patterns of excitation and inhibition

No neural inhibitory responses are seen in single fibres of the auditory nerve. All suppressive phenomena arise from the nonlinearity of the excitatory transduction process, or from rebounds following a period of excitation. However, cells of the cochlear nucleus show strong inhibition arising from inhibitory synapses. In contrast to the auditory nerve, spontaneous as well as stimulus-evoked activity can be reduced. In general, least inhibition is found in the anteroventral division of the cochlear nucleus, where the cells seem to be closest to auditory nerve fibres in their response characteristics, and increasing degrees of inhibition are found as the posteroventral, and then the dorsal cochlear nuclei, are approached.

Extensive investigations of the excitatory-inhibitory properties of cells in the cat cochlear nucleus have been carried out by Evans and Nelson (1973a) and Young (e.g. Young, 1983; Shofner and Young, 1985). At one extreme, cells are found with properties very similar to those of auditory nerve fibres, with similar response areas and no inhibitory responses beyond those arising from suppression in the auditory nerve (Fig. 6.5A). Young classed these cells as Type I cells. It is reasonable to suppose that they correspond most closely to the primary-like cells of Pfeiffer (1966a). Intermediate types of cell, called Type II and Type III cells, show excitatory tuning curves surrounded by inhibitory sidebands (Fig. 6.5B and C). Type II cells do not have spontaneous activity, and therefore their inhibitory sidebands cannot be detected directly. There is, however, evidence that the strength of inhibition is greater in Types II cells (Young, 1984). In some cells, the inhibitory sidebands can overlap the excitatory response area at high intensities, and serve to narrow down the region of excitation. Thus lateral inhibition can at high intensities increase the frequency resolving power of the cochlear nucleus, at least for tones. This only applies to the response well above threshold. It seems that the *tips* of the tuning curves are only a little narrower than in the auditory nerve (Young and Voigt, 1982). The increasing degrees of inhibition seen at high intensities are often associated with nonmonotonic rate-intensity functions (Fig. 6.6). Types II

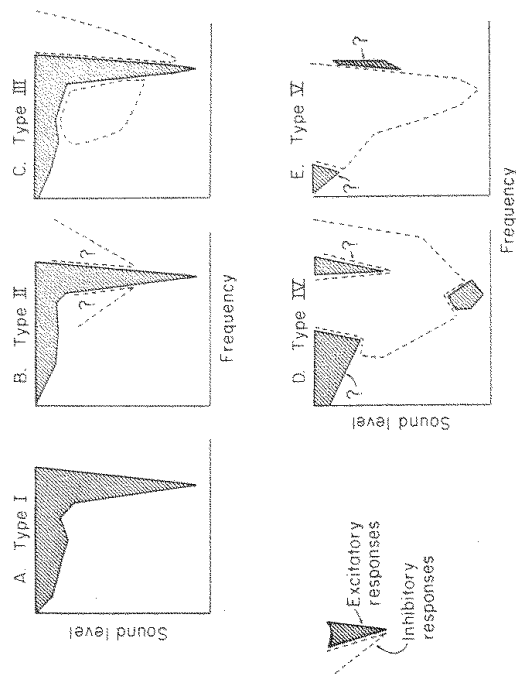


Fig. 6.5 Tuning curves of excitation and inhibition in the cat cochlear nucleus are shown in order of increasing amounts of inhibition (A-E). Purely excitatory responses as in A are predominant in the AVCN. Greater amounts of inhibition are found towards the DCN (D and E). Question marks show variable or uncertain features. From Young (1984, Fig. 12.3).

and III cells are found in all areas of the cochlear nucleus (Young, 1984; Shofner and Young, 1985).

Still stronger inhibitory phenomena are found as the sampling electrode moves towards the dorsal cochlear nucleus. In the dorsal nucleus of chloralose-anaesthetized or decerebrate animals, Evans and Nelson found neurones whose response areas were entirely or almost entirely inhibitory, perhaps possessing narrow islands of excitation (Figs. 6.5D and E). The particularly strong inhibition was blocked by barbiturate anaesthesia and therefore was not seen in earlier experiments. Pfeiffer's classification, performed in experiments under barbiturate anaesthesia, did not include any wholly inhibitory classes, but it is likely that some of his onset, buildup and pauser types resulted from delayed inhibitory inputs. These cells have been classified as Type IV and Type V cells by Young, Type IV cells being distinguished by having an island of excitation at threshold near the CF. Such cells predominate in the fusiform cell layer of the DCN, and fusiform cells make up at least some of the Type IV and Type V cells (Rhode *et al.*, 1983a).

Two different sources have been suggested for the inhibitory input to the cells of the DCN. Evans and Nelson (1973b) suggested that it arose from

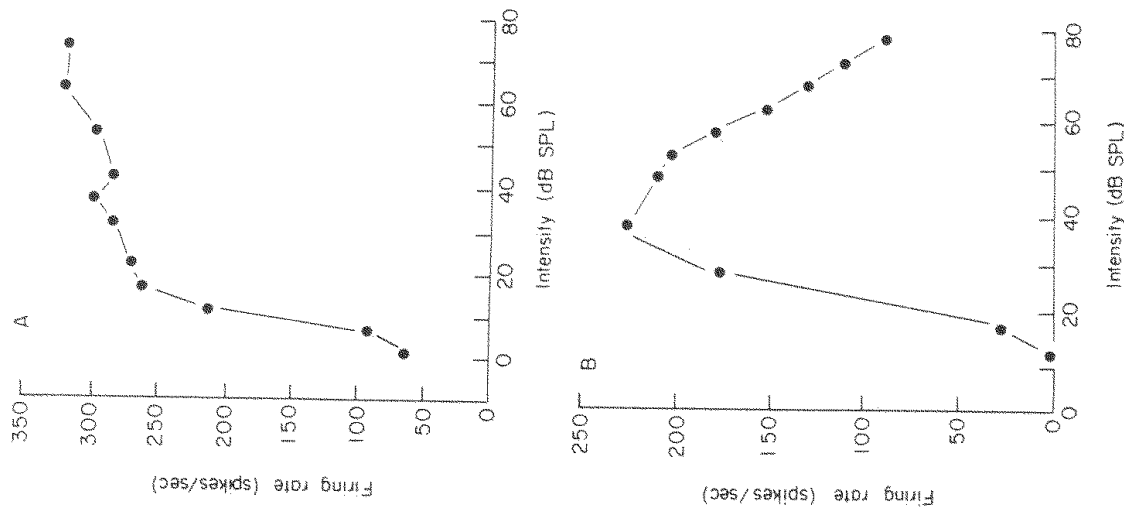


Fig. 6.6 Monotonic (A) and nonmonotonic (B) rate-intensity functions in the cochlear nucleus. A is typical of neurones showing only weak inhibitory sidebands, and B of those with strong ones. Adapted from Greenwood and Goldberg (1970, Figs 1 and 4).

the AVCN, since inhibition in DCN cells could be produced by shocks applied to the AVCN. This has been more recently supported by Shofner and Young (1987), who showed that injections of the local anaesthetic lidocaine into the AVCN, could reduce the inhibitory responses shown by cells in the DCN. Voigt and Young (1980), by an ingenious experiment involving multi-unit recording, have suggested that some of the inhibition could also arise from interneurons in the DCN. They extracted the responses of the different cells from their records, and then cross-correlated the times of firings of the cells. They were able to show that cells with excitatory centres and inhibitory surrounds, which in this experiment they called Type II/III cells, inhibited the Type IV cells in their record. Each action potential in the Type II/III cell tended to be followed by a reduction in firing in the Type IV cell.

Figures 6.7A and B show the response areas of a Type II/III cell and a Type IV cell for which just such an inhibitory relation had been shown by cross-correlation. Fig. 6.7C also shows the response area of the Type IV cell after the activity of the Type II/III cell had ceased following an injury discharge. An injury discharge is a transient high rate of firing, produced just before a cell becomes inactive after it has been damaged by an electrode. After the end of the injury discharge, the inhibitory region of the Type IV cell's response area became smaller, with excitation replacing inhibition in the frequency region of the Type II/III cell's excitatory response area. This is in agreement with the idea that the Type II/III cell had been providing an inhibitory input in this frequency region.

The analysis of excitation and inhibition suggests that a functional division between two components of the auditory pathway has already occurred at the cochlear nucleus. One pathway, arising from the ventral cochlear nucleus, preserves in many ways the response characteristics of primary auditory nerve fibres. That pathway feeds directly by secure, short-latency synapses to the superior olivary complex, where, among other things, spatial information is extracted. The other, arising from the dorsal nucleus, introduces extensive complexity early in the auditory pathway, and by bypassing the superior olivary complex feeds directly to higher centres, such as the nuclei of the lateral lemniscus and the inferior colliculus. There the results of the complex frequency analyses are combined with the results of the spatial analyses performed at the superior olive.

(c) The analysis of complex stimuli

We might expect the complex response areas of the dorsal cochlear nucleus to be appropriate for the analysis of complex stimuli. It is unfortunate that

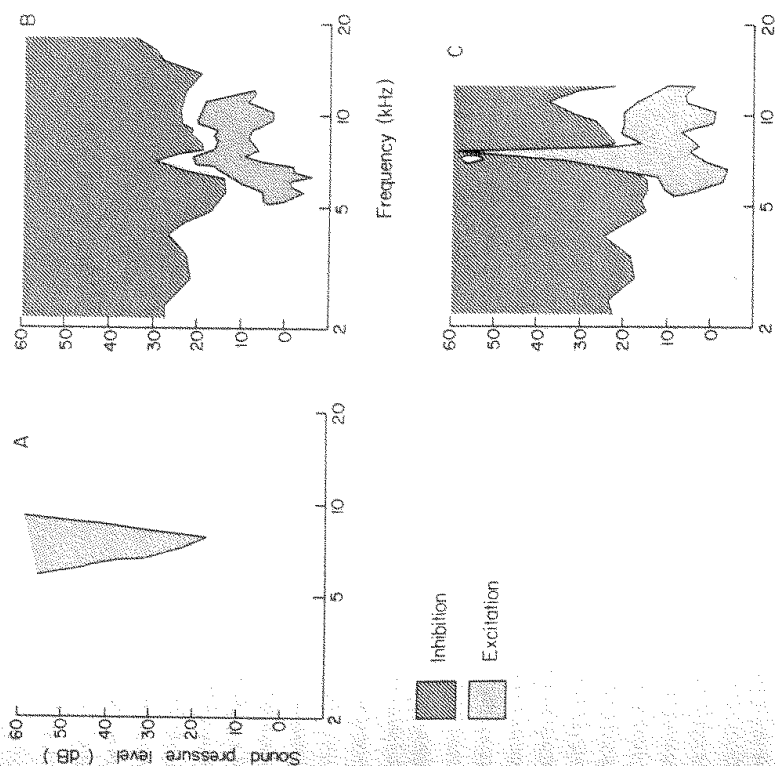


Fig. 6.7 An inhibitory relation was shown between the type II/III cell (excitatory response area in A) and the type IV cell (B). After the response of the type II/III cell had been lost following an injury discharge, the response area of the type IV cell changed (C). The original published response areas have been slightly simplified for clarity. From Pickles (1985b, Fig. 13.10), adapted from Voigt and Young (1980, Figs 4 and 6).

most of the experiments with complex stimuli have been performed under barbiturate anaesthesia, which reduced the amount of inhibition.

Stimuli which spread onto the inhibitory sidebands of neurones possessing them will, of course, reduce the firing rate. Therefore, if a band of noise is centred on the characteristic frequency of such a neurone, and increased in width, the firing rate will at first increase, as more noise falls into the excitatory response area, and then decrease, as some of the noise falls in the inhibitory sidebands. Such effects, which are analogous to those occurring in the auditory nerve as a result of suppression, were described by Greenwood

and Goldberg (1970) in the cochlear nucleus. They are stronger in the nucleus than the nerve, because in the nucleus the effect of inhibition is superimposed on the effect of suppression.

When a tone is presented in wideband noise, we might expect the inhibitory sidebands to suppress the weaker parts of the stimulus pattern, so emphasizing the stronger parts. We would therefore expect them to enhance the response, relative to the background, of a tone in wideband masking noise. Gibson *et al.* (1985) showed that this was indeed the case in cells with inhibitory sidebands. We would also expect that under such circumstances the firing would depend on the net *contrast* in the stimulus pattern rather than on the overall intensity; such a point was confirmed in cells of the dorsal cochlear nucleus by Palmer and Evans (1982).

More detailed investigation shows that, although this picture may be representative for those cells with an excitatory centre and inhibitory sidebands, it may not be so for cells with more complicated response areas, similar for instance to those shown in Fig. 6.5D. Young and Brownell (1976) in unanaesthetized cats showed that broadband noise was able to drive such cells more strongly than any tone. In some cases, both tones and noise were excitatory near threshold, but at higher intensities tones became inhibitory and noise was excitatory. Such a finding may seem rather paradoxical, since we would expect the interplay of excitation and inhibition in a complex response area to *reduce* the response to broadband stimuli in comparison with that to tones. However, the responses can be understood simply in terms of the circuitry worked out by Voigt and Young (1980). As described above, they showed that the Type IV cells were themselves inhibited by those cells with the simpler organization of an excitatory centre and an inhibitory surround. If the inhibitory surround was strong, as it is in Type II cells, broadband backgrounds would completely inhibit the responses of the Type II cells. Broadband stimuli therefore inhibited an otherwise inhibitory input to the Type IV cells, leading to excitation. Such cells may, therefore, be specialized for the detection of broadband stimuli. However, it is clear that we do not have the evidence to assess the role of cells with complex response areas in the detection of complex features.

In view of the interplay of excitation and inhibition in the responses of single cells, and the likelihood of different latencies for the different inputs, it is not surprising that interesting responses can be obtained with stimuli which vary in time, such as for instance tones swept in either frequency or intensity across the response area. Dynamic factors have been shown to be important in determining the responses of such cells, because the responses to time-varying stimuli cannot be predicted from the responses to static tones. In this, they are in contrast to cells with simpler response areas, or primary nerve fibres (Britt and Starr, 1976b). Moreover, neurones with

either complex and asymmetrical response areas, or many with buildup or pauser time patterns, show marked asymmetries as a tone is swept in frequency across the response area (Britt and Starr, 1976b). In some extreme cases, neurones are found which respond to a frequency sweep in one direction and not to one in the other. Britt and Starr (1976b), by intracellular recording, showed that two different types of inhibition were involved, one arising from stimulation of the inhibitory surround, and the other arising from the off-inhibition following a period of excitation.

Møller (1978) has shown that in certain cells of the cochlear nucleus frequency-modulated tones could produce stronger responses than steady tones. Sometimes the cells were responsive to very small changes in the stimulus parameters. Similar, though less dramatic, selectivities were shown for amplitude-modulated tones. Many of these cells responded to the stimulating waveform in a relatively unchanged way over a wide range of stimulus intensities. It has been hypothesized that a regulating mechanism, perhaps negative feedback from inhibitory interneurones, tends to keep the mean firing rate constant while allowing rapid changes to be transmitted (Møller, 1976b).

What is uncertain is the extent to which we are able to think in terms of feature detection in the cochlear nucleus. There seems to be a continuum of response characteristics along every category of response that has been analysed. It is not therefore certain that we are justified in asserting that the degree to which any one complex feature is extracted results from anything other than a random arrangement of excitation and inhibition on the constituent neurones. However, as a provisional hypothesis, we can assume that the cell types that have been demonstrated form the functional basis for a sensory analysis, that lies in between the logical extremes of the completely holistic and the completely nonholistic.

In the alert animal, the situation is even more complicated. Centrifugal connections from the higher centres innervate the nucleus, and the activity of the nucleus is likely to reflect later sensory processing, and the central state of the animal.

C. The Superior Olivary Complex

1. Innervation and Anatomy

There are three main outflows from the cochlear nucleus, as shown in Fig. 6.8. The fibres in the dorsal acoustic stria arise in the dorsal cochlear nucleus, and those in the intermediate acoustic stria in the posteroventral cochlear nucleus. However, the greatest outflow runs in the ventral acoustic stria or trapezoid body, and arises in both the anteroventral and posteroventral

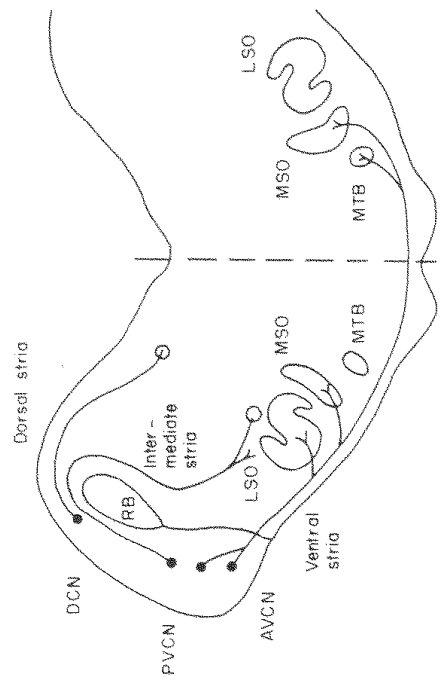


Fig. 6.8 The three main outflows of the cochlear nucleus are shown on a transverse section of the cat brainstem. The dorsal and intermediate acoustic striae pass dorsally around the reticuliform body (RB), or inferior cerebellar peduncle. The largest outflow is in the ventral acoustic stria or trapezoid body. AVCN, anteroventral cochlear nucleus; DCN, dorsal cochlear nucleus; MSO, medial nucleus of the superior olive; LSO, lateral nucleus of the superior olive; MTB, medial nucleus of the trapezoid body; PVCN, posteroventral cochlear nucleus. The small circles indicate fibres passing to higher levels. The fibres are represented diagrammatically, and do not necessarily branch or join as indicated. Some fibres (not shown) also run directly to the cochlear nucleus of the opposite side (Cant and Gaston, 1982).

tral nuclei. The pathways of the dorsal acoustic stria bypass the superior olivary complex and end in the next highest nuclei, the nuclei of the lateral lemniscus and the inferior colliculus, predominantly on the opposite side (Fig. 6.9). The outflows in the ventral and intermediate striae end in the superior olivary complex of both sides, as well as to a lesser extent in the nuclei of the lateral lemniscus. Within the superior olivary complex itself, several subnuclei can be distinguished (Fig. 6.10), all receiving different distributions of fibres from the different regions of the cochlear nuclei. The main nuclei associated with the ascending auditory system are the lateral and medial nuclei of the superior olive (LSO and MSO), and the medial nucleus of the trapezoid body (MTB). The nuclei are surrounded by other nuclei, known as the pre-olivary and peri-olivary nuclei, which are mainly associated with the centrifugal auditory system, although they receive an ascending input as well. They will be discussed in Chapter 8. As far as the ascending system goes, the MTB is a relay carrying information from the opposite cochlear nucleus to the ipsilateral LSO. The MSO is a disc-shaped

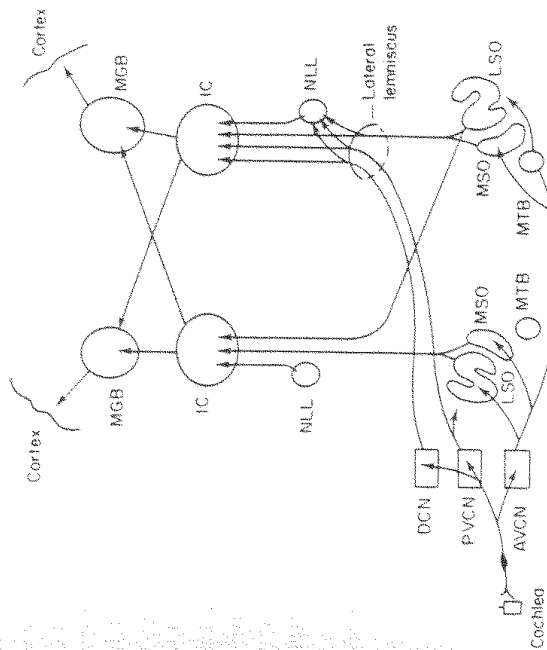


Fig. 6.9 The main ascending auditory pathways of the brainstem. Many minor pathways are not shown. IC, inferior colliculus; MGB, medial geniculate body; NLL, nucleus of the lateral lemniscus. For other abbreviations see Fig. 6.8. The branching and joining of arrows does not mean that the fibres branch or join.

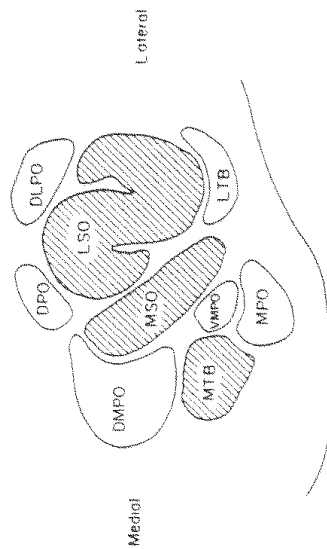


Fig. 6.10 The nuclei of the superior olivary complex are shown in a transverse section in the cat. The main nuclei associated with the ascending system are shaded. DLPO, dorsolateral peri-olivary nucleus; DMPO, dorsomedial peri-olivary nucleus; DPO, dorsal peri-olivary nucleus; LSO, lateral superior olive nucleus; LTB, lateral nucleus of the trapezoid body; MPO, medial pre-olivary nucleus; MSO, medial superior olivary nucleus; MTB, medial nucleus of the trapezoid body; VPMO, ventromedial pre-olivary nucleus. From Harrison and Howe (1974b, Fig. 8).

structure, and receives direct fibres from the cochlear nuclei of both sides. It predominantly represents low-frequency stimuli, and is involved in detecting the direction of a sound source by means of the main cue available in low-frequency stimuli, namely temporal disparities in the waveforms at the two ears. The LSO is the largest of the component nuclei, and has a characteristic structure of a folded sheet, which in the cat is S-shaped in transverse sections, but which in other species appears more like a boxing glove. It receives direct connections from the ipsilateral cochlear nucleus, and indirect ones from the contralateral nucleus via the MTB. The LSO predominantly represents high-frequency stimuli, and in so far as it plays a role in sound localization, detects the main cues available in high frequency stimuli, namely disparities in interaural intensity, and to a lesser extent disparities in the onset time of the stimulus envelopes. The MSO in man is relatively large, and the LSO relatively small (Moore, 1987).

2. Physiology and Function

(a) Introduction

Analysis of the dorsal cochlear nucleus has demonstrated that it may be difficult to assess the functional significance of a nucleus from the response characteristics of its neurones. However, the superior olive shows an advance in sensory processing, that of receiving information from the two ears, which surely must be of functional significance. It is reasonable to suppose that the nucleus plays a part in sound localization.

(b) The lateral superior olive (S-segment)

The principal cells of the LSO have dendritic trees joining the two surfaces of the folded sheet of the nucleus, with afferents from the ipsilateral cochlear nucleus and the ipsilateral MTB contacting the two branches (Fig. 6.11A). The cell characteristic frequencies are arranged tonotopically (Fig. 6.11B), although for a long time this was difficult to detect because of the complex folding of the structure (Tsuchitani and Boudreau, 1966; Glendenning *et al.* 1985). In the anaesthetized preparation, the responses to ipsilateral stimuli are entirely excitatory with tuning curves similar to those of primary fibres, best thresholds in the range 10–20 dB SPL, and chopper time patterns (Tsuchitani, 1977). Brownell *et al.* (1979) have shown that when unanaesthetized cats are used, inhibitory sidebands can be seen to ipsilateral stimuli, and the chopper pattern disappears. Figure 6.12 shows an example of the response to a stimulus at the excitatory centre, and in the inhibitory sidebands. The organization of the excitatory response is more complex

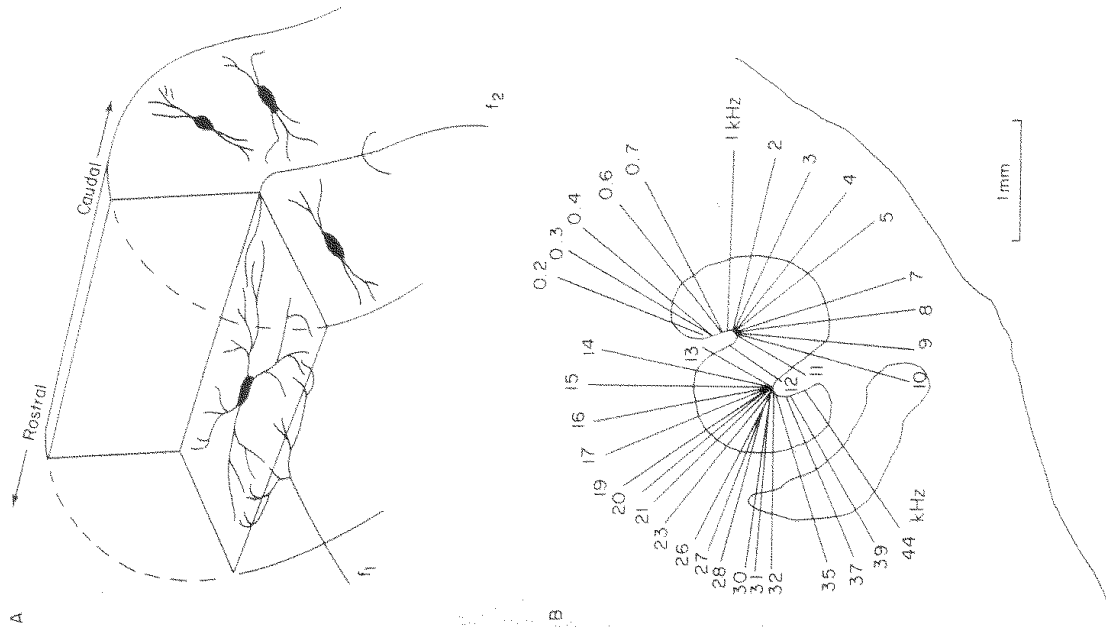


Fig. 6.11 (A) The neural organization of the LSO. f_1 , f_2 , afferent fibres. Adapted from Scheibel and Scheibel (1974). (B) The tonotopic organization of the LSO. A high proportion of the nucleus is devoted to high frequencies. The numbers denote the characteristic frequencies of the sectors. From Tsuchitani and Boudreau (1966, Fig. 6).

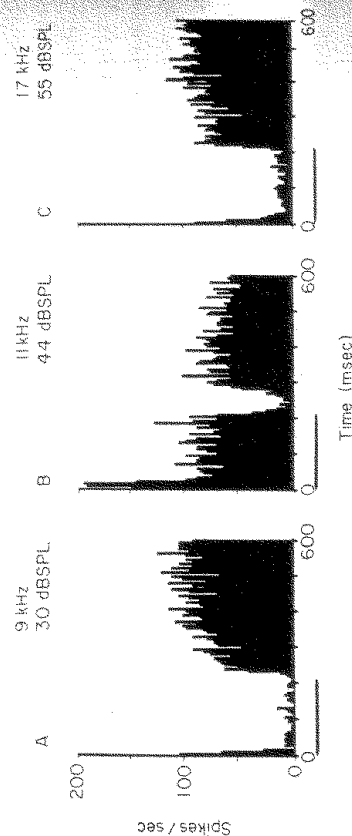


Fig. 6.12 Post-stimulus-time histograms of a cell in the LSO. From Brownell *et al.* (1979, Fig. 1).

than that of the inhibitory one, since it is followed by a complementary rebound. Unlike the responses to ipsilateral stimuli, the responses to contralateral stimuli are predominantly inhibitory in both anaesthetized and unanaesthetized animals. Therefore, the majority of binaural neurones in anaesthetized animals are excited by ipsilateral stimuli and inhibited by contralateral ones, forming the so-called "EI" neurones. The threshold and tuning of the ipsilateral excitatory and contralateral inhibitory effects are often comparable (Caird and Klinke, 1983). We might, therefore, imagine that the LSO responds to differences in intensity at the two ears, defined on a spectral basis. Sounds from a source on, say, the left side, will be more intense in the left ear, and the LSO might use this difference as a cue in sound localization. Sounds from a source on the left side will also be delayed in the right ear, and Caird and Klinke (1983) showed that delaying the onset of the stimulus to the inhibitory ear increased the response in EI cells. The LSO therefore appears to perform sound localization on the basis of intensity and timing differences, coding sounds on the ipsilateral side. The intensity differences will be largest at high frequencies, where the degree of diffraction around the head will be small. In accordance with this, most of the LSO is devoted to high frequencies (Fig. 6.11B).

(c) The medial superior olive (accessory olive)

The MSO receives a direct innervation from the anteroventral cochlear nucleus of both sides. The axons innervate opposite sides of the sheet of cells constituting the MSO. It will be remembered that most cells of the anteroventral cochlear nucleus have short-latency, secure, synaptic connections by means of the large end-bulbs of Held, and so the cells of the

MSO are able to receive temporally matched and temporally accurate signals from the two ears.

Single unit studies of the MSO face severe difficulties, because the sheet of cells is thin, and because gross potentials from neighbouring cell groups tend to swamp the single unit action potentials. Such studies as have been successful in identifying cells in the nucleus, found that most were excited by stimuli at both ears, with relatively simple tuning curves and simple temporal patterns of discharge (Guinan *et al.*, 1972; Goldberg and Brown, 1968, 1969). In the dog, which has a particularly large MSO, Goldberg and Brown found that almost all the cells were binaural. Three-quarters of the cells were excited by both ears (EE cells), and the remainder were excited by one and inhibited by the other (EI cells). Many of the low-frequency units with CFs less than 1 kHz were responsive to the relative phases of the stimulating sinusoids at the two ears. Figure 6.13A shows the discharge rate of an MSO neurone as a function of interaural time delay. The firing rate showed a cyclic dependence. The period of the cycle was equal to the period of the sound stimulus. The neurone was therefore responsive to the interaural time difference. This interpretation was supported by experiments in which the stimulus frequency was varied. The time disparity for the optimal response was independent of stimulus frequency, showing that the cells were responsive to time disparity, rather than phase disparity (Fig. 6.13B). We might suppose that this arose from a difference in the speed of transmission of signals from the two ears. Such a position was supported by the timing of the discharges in response to stimuli at the two ears separately (Fig. 6.14). The two delays calculated for ipsilateral and contralateral stimuli separately could be used to predict the optimal interaural phase disparity. In this way, when the relative phases of the two stimuli were adjusted so that their excitatory effects coincided, there was a large binaural response (Goldberg and Brown, 1969; Moushegian *et al.*, 1975). This was true for neurones where both stimuli had a net excitatory effect (EE neurones), as it was for many EI neurones. Such experiments lead to the notion of a *characteristic delay*, different for each cell, and resulting from differences in the speed of transmission of signals from the two ears. The notion of a characteristic delay, and its relation to the mapping of sound source direction, will be discussed further in Chapter 9.

It appears that the stimuli in the two ears cause cyclic phases of inhibition as well as excitation for both EE and EI neurones, because the response to binaural stimuli in the most effective phase relation could be larger than, and in the least effective smaller than, the response to either monaural stimuli alone (Fig. 6.13A). In the excitatory phase relation, the interaction between stimuli was one of facilitation, because binaural stimuli could drive

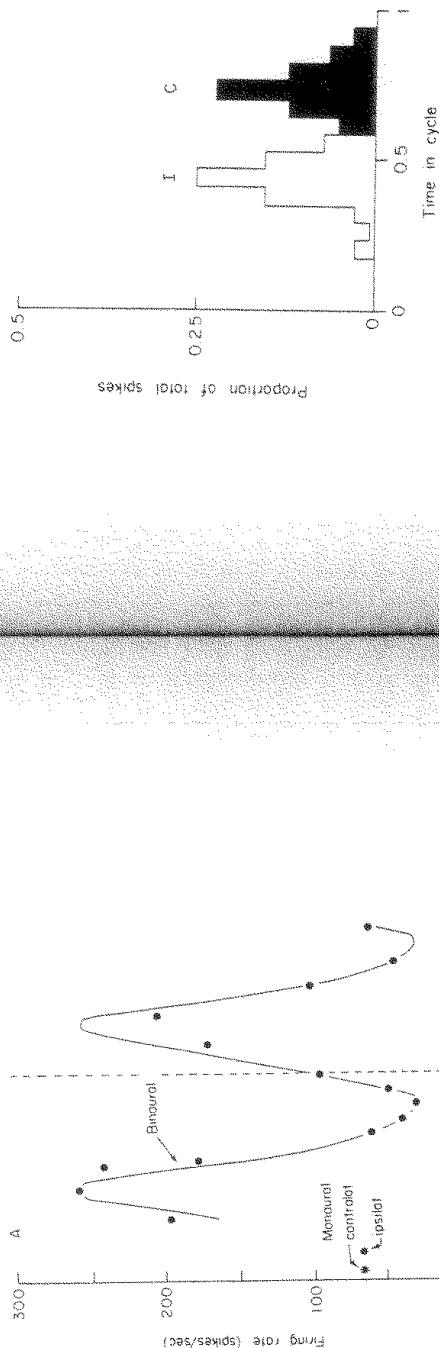


Fig. 6.14 The histograms of latencies of firing to ipsilateral (I) and contralateral (C) stimuli, made with respect to constant phase of the stimulus waveform, indicate different delays in transmission from the two ears. From Goldberg and Brown (1969, Fig. 7).

the neurones far harder than could even more intense monaural stimuli (Fig. 6.15).

Studies in which the uptake of labelled 2-deoxyglucose has been measured, suggest that the MSO is driven most strongly by sounds on the contralateral side (Masterton and Imig, 1984).

We can summarize the role of the LSO and MSO in sound localization as follows. In the LSO most cells are EI cells and so respond to intensity differences between the ears. The majority of the cells are high-frequency cells, and so have characteristic frequencies in the range where a sound source to one side will produce significant interaural intensity differences. In addition, the cells are sensitive to temporal disparities in the time of arrival of the sound waveforms. By contrast, in the MSO the majority of cells are EE cells, and so will not respond to interaural intensity differences. The cells are able to respond to direction only on the basis of interaural temporal cues, and in general are most responsive to low frequencies. Since this is the range in which phase information is preserved, sensitivity to timing differences will be apparent as a sensitivity to interaural phase differences. Anatomical evidence suggests a picture in agreement with this view. Animals with small heads and good high-frequency hearing, who might be expected to favour intensity cues, have large LSO nuclei and small MSO nuclei, whereas animals with large heads and good low-frequency hearing, tend to have the reverse (Masterton and Diamond, 1967).

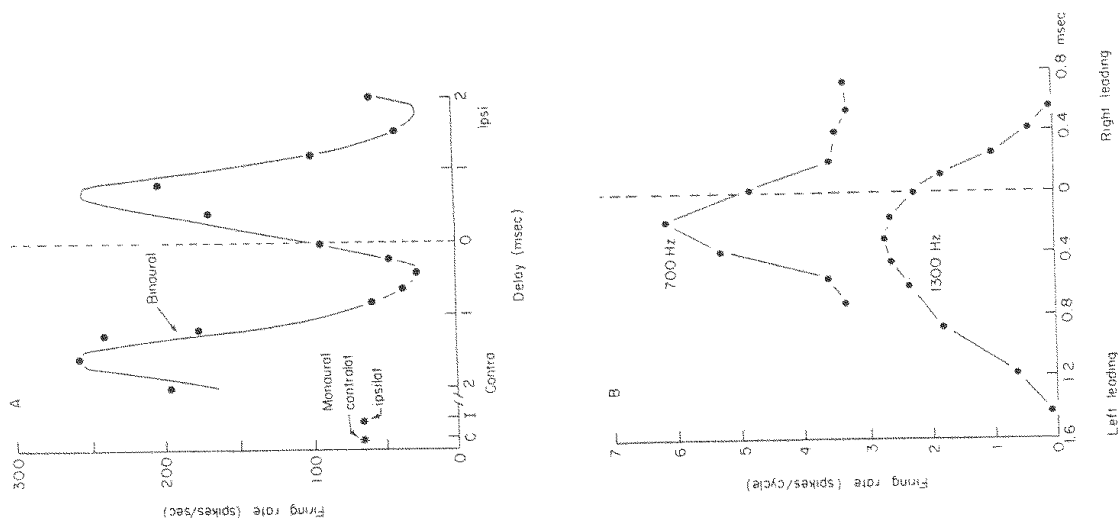


Fig. 6.13 (A) The cyclic function relating firing rate to interaural delay for a cell in the MSO. CF = 444 Hz, period of stimulus = 2.25 ms. From Goldberg and Brown (1969, Fig. 6). (B) Firing rate as a function of interaural delay for sinusoids of two different frequencies. The delay giving the greatest response is independent of stimulus frequency. Kangaroo rat MSO. From Crow *et al.* (1978, Fig. 2).

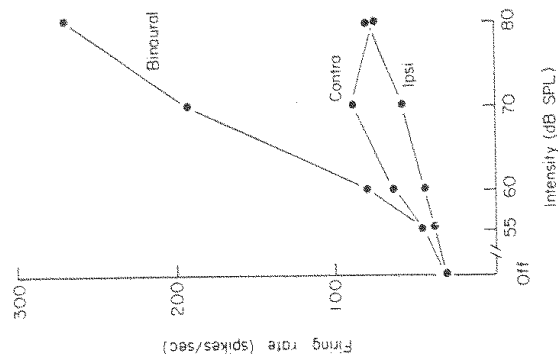


Fig. 6.15 Rate-intensity functions are shown for monaural and binaural stimuli in the dog superior olive. The binaural stimulus was in the optimal phase relation; and could produce a greater firing rate than could either monaural stimulus. From Goldberg and Brown (1969, Fig. 11).

(d) The medial nucleus of the trapezoid body

The medial nucleus of the trapezoid body (MTB) is the relay conveying information from the cochlear nucleus of the opposite side to the lateral superior olive ipsilaterally to the MTB. The afferent axons are the largest fibres of the trapezoid body, and end as large end-bulbs of Held. The principal cells therefore receive secure, short-latency, synaptic inputs, as indeed do the cells of the anteroventral cochlear nucleus from which the axons arise, and so are able to influence the LSO with only a short delay. As we might expect, cells of the MTB have simple discharge characteristics, similar to those seen in the anteroventral cochlear nucleus (Goldberg *et al.*, 1964). In addition to the pathways described above, the nucleus receives projections from the fibres projecting to the LSO, and sends axons not only to the ipsilateral LSO but to the surrounding subnuclei as well. Other types of cell and other types of response have also been described. For instance, the olivocochlear bundle, the centrifugal pathway to the cochlea, with its complex response characteristics, also arises partly from the MTB (Warr, 1975). The olivocochlear bundle will be discussed further in Chapter 8.

D. The Ascending Pathways of the Brainstem

The principal ascending pathways were shown diagrammatically in Fig. 6.9.

The main receiving station for the ascending pathways from the superior olivary complex is the inferior colliculus. The LSO projects bilaterally to the inferior colliculus, whereas the MSO projects only ipsilaterally (Adams, 1979; Elverland, 1978). The fibres run in the tract known as the lateral lemniscus. Some send collaterals to the nuclei of the lateral lemniscus. The ventral nucleus of the lateral lemniscus receives an input from the contralateral cochlear nucleus and projects ipsilaterally to the inferior colliculus, whereas the dorsal nucleus of the lateral lemniscus receives a bilateral input and projects bilaterally to the inferior colliculus (Masterton and Imig, 1984). The inferior colliculus also receives direct afferents from the contralateral dorsal cochlear nucleus, from the contralateral posteroventral nucleus, and to a lesser extent from the contralateral anteroventral nucleus (Adams, 1979). Most paths that cross do so at or near the level of the trapezoid body, although the fibres from the dorsal cochlear nucleus cross further rostrally. There is also a smaller uncrossed projection from these nuclei. Interestingly, the direct projection of the cells with simpler response properties, such as the large spherical cells, the globular cells and the octopus cells, to the inferior colliculus seems particularly small. The inferior colliculus is therefore a site of convergence of projections with complex frequency responses but a monaural input from the dorsal cochlear nucleus, and projections with rather simpler frequency responses but a binaural input, from the superior olive. Because the inferior colliculus is tonotopically organized, fibres from different sources but of the same characteristic frequency apparently manage to meet at the appropriate site. The inferior colliculus is an obligatory relay for practically all the auditory input to the medial geniculate body, since injections of horseradish peroxidase into the tracts leading into the medial geniculate give rise to massive labelling in the inferior colliculus, but very little elsewhere (Aitkin and Phillips, 1984).

E. The Inferior Colliculus

1. General Anatomy

The inferior colliculi form the rear pair of a set of four lobes on the dorsal surface of the brainstem. The anterior pair, the superior colliculi, are an important visual reflex centre. The inferior colliculi are an auditory relay and reflex centre. There are three main divisions to the inferior colliculus. The central nucleus (Fig. 6.16A) was defined by Morest and Oliver (1984) in

Golgi stained sections as being limited to a strongly laminated central region. This definition has superseded an earlier parcellation by Rockel and Jones (1973a), in which the central nucleus stretches more dorsally to include a non-laminated area. Above the central nucleus is a region known as the dorsal cortex, divided into four layers (Morest and Oliver, 1984). This region includes regions which Rockel and Jones described as a pericentral nucleus and the dorsal part of their central nucleus. The lateral nucleus (partly coextensive with the external nucleus of Rockel and Jones) forms part of what Morest and Oliver called the paracentral nuclei. These nuclei are scattered around the central nuclei. In contrast to the rest of the inferior colliculus, the paracentral nuclei are primarily somesthetic and auditory integrative areas rather than an auditory relay (Robards, 1979; Aitkin *et al.*, 1978). The inferior colliculus in man has the same general form as in the cat (Moore, 1987).

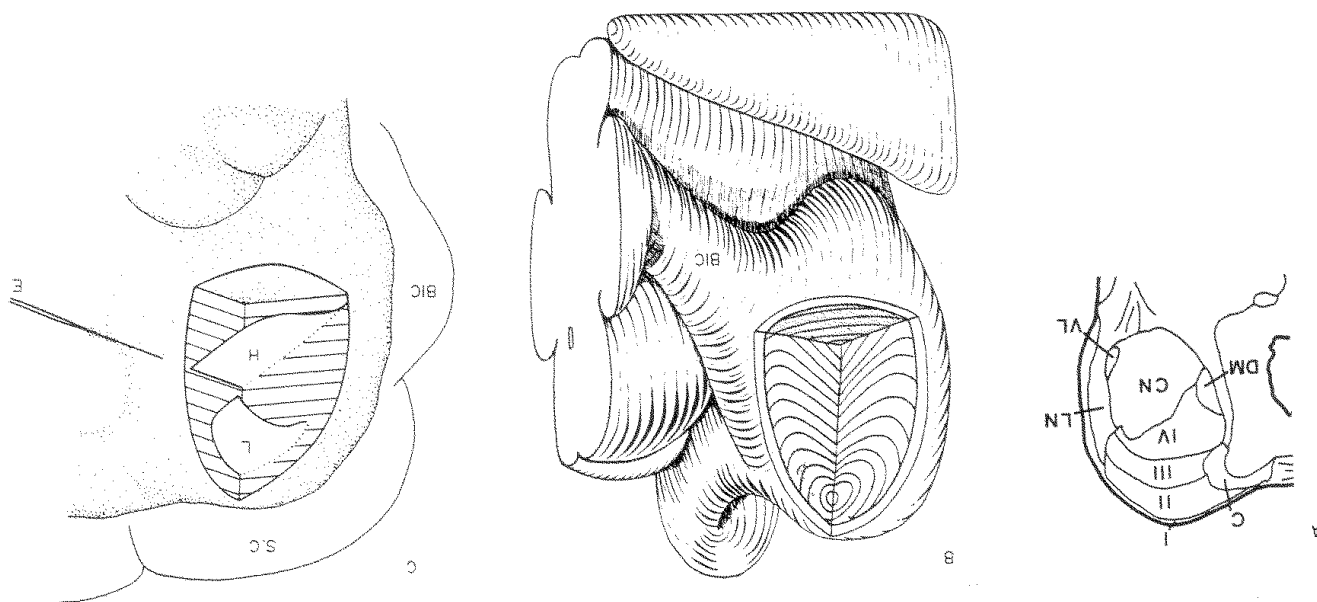
2. The Central Nucleus

(a) The spatial organization of the nucleus and its afferents

Oliver and Morest (1984) have given an authoritative account of the structure of the central nucleus. The nucleus has a pronounced laminar structure. The laminae are strongly tilted, so that as one moves laterally in the central nucleus the laminae move ventrally (Fig. 6.16B). At the lateral edge of the central nucleus, the laminae suddenly turn and sweep dorsally. The laminae are formed by layering of the afferent axons and the dendrites of the intrinsic neurones (Rockel and Jones, 1973a). Semple and Aitkin (1979) associated these sheets with iso-frequency sheets of cells (Fig. 6.16C). Low frequencies were found in the dorsal sheets, and high frequencies in the ventral ones.

Interesting overlaps and segregations have been described in the innervation of the central nucleus. Mention has already been made of the wide range of nuclei that project to the inferior colliculus. Roth *et al.* (1978) showed that any particular injection of horseradish peroxidase (HRP) into a confined area of the central nucleus led to reaction product, transported in a retrograde direction, in only some, but never at once all, of the nuclei labelled by large injections. Aitkin and Shuck (1985) and Maffi and Aitkin (1987) suggested that the different projecting nuclei sent afferents to segregated target zones within the central nucleus. The site of origin of some of the afferents, too, seems to be arranged in a patchy manner (Adams, 1979). Retrograde transport of HRP showed alternate labelled and unlabelled columns of cells in the anteroventral cochlear nucleus. Therefore, while

Fig. 6.16 The inferior colliculus. (A) Transverse section of the inferior colliculus, with nuclei as defined by Morest and Oliver (1984). CN: central nucleus; I, II, III, IV: layers I-IV of dorsal cortex. The paracentral nuclei include: LN: lateral nucleus; C: commissural nucleus; DM: dorsomedial nucleus. It is now recognized that the laminae are not continuous as far laterally as this drawing suggests, and that they do not show the tight curvature dorsally which is shown here. BIC: brachium of the inferior colliculus. From Rockel and Jones (1973a), Fig. 22. (C) Low-frequency (L) and high-frequency (H) iso-frequency sheets in the central nucleus of the inferior colliculus, seen in caudolateral view. BIC: brachium of inferior colliculus; E: electrode; SC: superior colliculus. From Semple and Aitkin (1979), Fig. 5.



there must be a great deal of convergence onto the inferior colliculi, there seems to be a microstructure in the sites of both the origin and termination which could well be of functional significance.

A similar patchiness was found electrophysiologically in the colliculus by Roth *et al.* (1978). It often appeared that groups of adjacent cells had similar response properties, so that a microelectrode might meet groups of several intensity-sensitive EI cells together, then several time-sensitive EE cells, and so on, even if all were of the same characteristic frequency. A corresponding point was made over a larger scale by Semple and Aitkin (1979), who showed that neurones with different types of binaural interaction were segregated into different parts of the iso-frequency sheet. EE neurones were most common medially, whereas EI neurones were most common rostrally. Monaurally driven units were encountered more caudally, ventrally and laterally. Binaural time-sensitive neurones were almost completely segregated from the ones sensitive to intensity differences, and were encountered rostrally, dorsally and laterally. It seems that there is a considerable segregation of function within each iso-frequency sheet, both generally across the nucleus and on a much smaller scale.

(b) Electrophysiology

In response to single tones, tuning curves and temporal response patterns can be described. Tuning curves show a wide range of bandwidths, some being very broad and some very narrow. Aitkin *et al.* (1975) showed extraordinarily high Q_{10} values of 25–40 for a frequency range around 10 kHz. Such tuning is unrivalled elsewhere in the auditory system. The whole question of a progression to sharper and sharper tuning at higher levels of the auditory system has been controversial. Katsuki *et al.* (1959) suggested that tuning curves became sharper and sharper from the auditory nerve to the medial geniculate body, after which they became broader. Kiang (1965) and Aitkin and Webster (1972) contradicted this progression at the levels of the cochlear nucleus and the medial geniculate body respectively. It should be pointed out that when we analyse frequency resolution it is important to distinguish the frequency resolving power shown by the tip, described by the Q_{10} measure, from that shown well above threshold. Q_{10} 's indicate, except for the above report of Aitkin *et al.* (1975), similar or deteriorating tuning at the higher levels of the nervous system. Any such increase in resolution could be produced only by as yet unknown mechanisms that increased the fundamental resolving power of the auditory system. In contrast, well above threshold, some high-level neurones show narrow bandwidths of excitation to tones, much narrower than for instance those shown by primary auditory nerve fibres. Here it seems that a simple

mechanism of lateral inhibition could help preserve at high intensities the resolution seen at low intensities, by narrowing down the response area. Katsuki *et al.* (1959) may have sampled such neurones selectively in their report; other reports indicate that the proportion of broadly tuned neurones increases at higher levels of the nervous system.

Complex excitatory-inhibitory interactions have been found in the inferior colliculus, although they have been described in less detail than in, say, the cochlear nucleus (e.g. Ryan and Miller, 1978). Half of the neurones show the nonmonotonic rate-intensity functions suggestive of complex excitatory-inhibitory interactions. Temporal patterns of response show many onset and pauser types (Rose *et al.*, 1963), with transitions between the types as the stimulus intensity is varied (Ryan and Miller, 1978). For instance, Ryan and Miller describe a common transition from primary-like to pauser, and then to onset, with changes in intensity. Unanaesthetized animals may show sustained excitatory and inhibitory responses rather than onset or pauser ones (Bock *et al.*, 1972), although this has since been disputed (Ryan and Miller, 1978). Some neurones are found to be sensitive to amplitude or frequency modulation and are specifically responsive to a certain speed or direction of modulation (Nelson *et al.*, 1966). As in the dorsal cochlear nucleus, the response to time-varying stimuli cannot necessarily be predicted from the response to tones. But we do not have enough information to decide whether the processing of complex monaural stimuli in the inferior colliculus shows significant advances over that in the dorsal cochlear nucleus.

As in the various nuclei of the superior olive, many neurones are sensitive to interaural timing or intensity differences (Rose *et al.*, 1966; Yin *et al.*, 1986; Caird and Klinke, 1987). As in the MSO, many of the low-frequency time-sensitive neurones seem to have a characteristic delay which is independent of stimulus frequency (Yin and Kuwada, 1983). Most of the neurones are predominantly sensitive to sounds on the contralateral side. This is the same as the predominant representation in the MSO, which sends its outflow mainly to the ipsilateral colliculus. The contribution from the superior olive is more puzzling, since this nucleus, which represents the ipsilateral side, sends bilateral projections to the colliculus (e.g. Roth *et al.*, 1978). A solution was suggested by Glendenning and Masterton (1983), who showed that the main ipsilateral projection from the LSO arose from the lateral side of the LSO, and the main contralateral projection arose from the medial side. Since the medial side codes high frequencies, and since we would expect the high-frequency EI cells of the LSO to code sound direction particularly well, this suggests that the main laterality-specific outflow is crossed, in agreement with the representation in the colliculus.

The sensitivity to interaural timing and intensity differences suggests that

neurons should be able to represent the direction of a sound source. By moving a speaker around a cat's head, Aitkin *et al.* (1984, 1985) found that many of the neurons could indeed represent the direction of a real sound source. There seems to be some mapping of source direction, with sources to the midline represented caudally, and those to the side represented rostrally. For high frequency stimuli some of the directional selectivity arose from the directionality of the pinna, since for such stimuli the selectivity could be altered by manipulating the pinna nearest the sound source (Aitkin *et al.*, 1984). However, and in contrast to the position in mammals, an apparently detailed map of auditory space has been found in the barn owl, in its homologue of the inferior colliculus, the lateral dorsal mesencephalic nucleus (Knudsen and Konishi, 1978). Neurons in the lateral rim of the nucleus coded the direction of a real sound source. Points high in space were represented high in the nucleus, and points low were represented low. Points forward were represented anteriorly, and points to the side were represented posteriorly. Each nucleus represented space on the contralateral side, although in front the field crossed 15° over to the ipsilateral side. The owl achieves this map with two specializations which do not appear in the mammal. Firstly, the two ears are set at different heights on the head, and this, combined with the ruff feathers around the head, means that elevation of the source is coded as an interaural intensity difference. Secondly, the owl is sensitive to far smaller interaural time differences than are mammals (Moiseff and Konishi, 1983). The representation of auditory space will be examined in more detail in Chapter 9.

The inferior colliculus therefore seems to combine the complex frequency analysis of the dorsal cochlear nucleus with the sound localizing ability of the superior olive. Very little is known of the details of the interactions between the inputs from the two sources. The convergence may, however, give us a clue to a special function for the inferior colliculus. Localizing sound by interaural time disparities requires the preservation of accurate time relations. These are lost in the dorsal cochlear nucleus by the circuitry needed for complex amplitude and frequency analysis. It is therefore appropriate that the direction of the sound should be extracted separately. The inferior colliculus, by combining information from both sources, might therefore be able to code simultaneously the complexity of sounds and their direction in space.

The inferior colliculus has an important role in many auditory reflexes. They will be discussed below in Section G of this chapter and in Chapter 9.

3. The Dorsal Cortex and Paracentral Nuclei

The dorsal cortex receives a substantial somatosensory input as well as an auditory input (Aitkin *et al.*, 1981). While the cells have broad or complex

tuning curves to sound, and show responses to somatosensory stimuli, they are nevertheless tonotopically organized (Aitkin, 1979; Aitkin *et al.*, 1975). On the other hand, the paracentral nuclei can be viewed more as somesthetic and integrative areas than as an auditory relay. Tuning curves to auditory stimuli are very broad, so much so that the definition of a best frequency is often arbitrary (Fig. 6.17). Aitkin *et al.* (1978) found that 54%

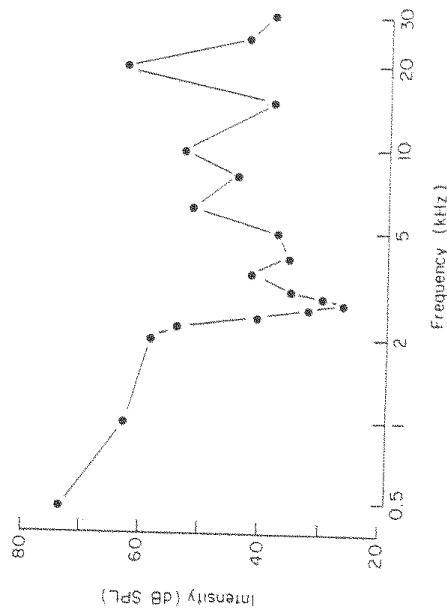


Fig. 6.17 The broad tuning curve of a neuron in a paracentral nucleus of the inferior colliculus. From Aitkin *et al.* (1978, Fig. 5).

of neurons recorded were bimodal, most of these being excited by auditory, and inhibited by somatosensory, stimuli (see also Aitkin *et al.*, 1981). Very little is known about the functions of these nuclei. The nuclei mark the first appearance of a 'diffuse', 'belt', or nonspecific auditory system, which surrounds the specific (or 'core') auditory relay system. This division into specific and diffuse auditory systems is carried up through the medial geniculate body to the auditory cortex.

F. The Medial Geniculate Body

1. Anatomy

The medial geniculate body contains the specific thalamic auditory relay of the auditory system, receiving afferents from the inferior colliculus, and projecting to the cerebral cortex. The medial geniculate body has been divided in different ways by different anatomists. According to the scheme

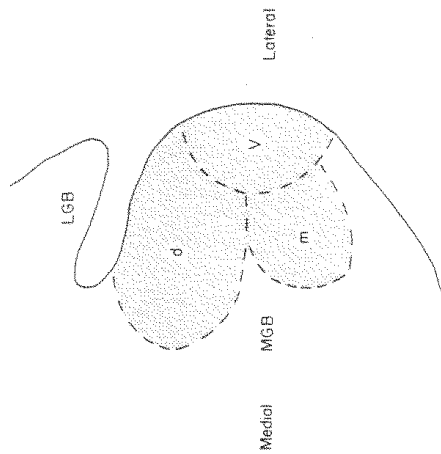


Fig. 6.18 Divisions of the medial geniculate body (MGB). v, ventral (principal) division of MGB; d, dorsal division of MGB; LGB, lateral geniculate body; m, medial division of MGB. From Harrison and Howe (1974a, Fig. 8).

of Mørest (1964), there is a ventral (or lateral) medium-celled principal division (Fig. 6.18), a dorsal division, and a medial, large-celled division. Of these, only the ventral division has any claims to being a specific auditory relay. Its afferents run mainly ipsilaterally from the central nucleus of the inferior colliculus (Calford and Aitkin, 1983). The fibres run in the brachium of the inferior colliculus, a bulge on the lateral surface of the brainstem between the inferior colliculus and the geniculate bodies (Fig. 6.16B). The medial and dorsal divisions receive a multiplicity of inputs, the former receiving auditory afferents from the inferior colliculus and the lateral tegmental system running just medial to the brachium of the inferior colliculus, as well as somatosensory afferents, and the latter receiving afferents from the region medial to the brachium, the superior colliculus, the pericentral nucleus of the inferior colliculus, and the somatosensory system (e.g. Harrison and Howe, 1974a; Calford and Aitkin, 1983). They therefore can be viewed as forming a 'diffuse' or nonspecific auditory system surrounding the specific auditory nuclei.

The ventral division projects principally to the AI area of the auditory cortex, and in addition to the anterior, posterior and possibly also the ventral posterior fields (defined in Fig. 7.1). In contrast, the medial division projects to the auditory cortex in a less specific way, and the dorsal division projects to AII, Ep and I-T. Calford and Aitkin (1983) suggest that the different areas of the medial geniculate are parts of three separate projection pathways to the auditory cortex.

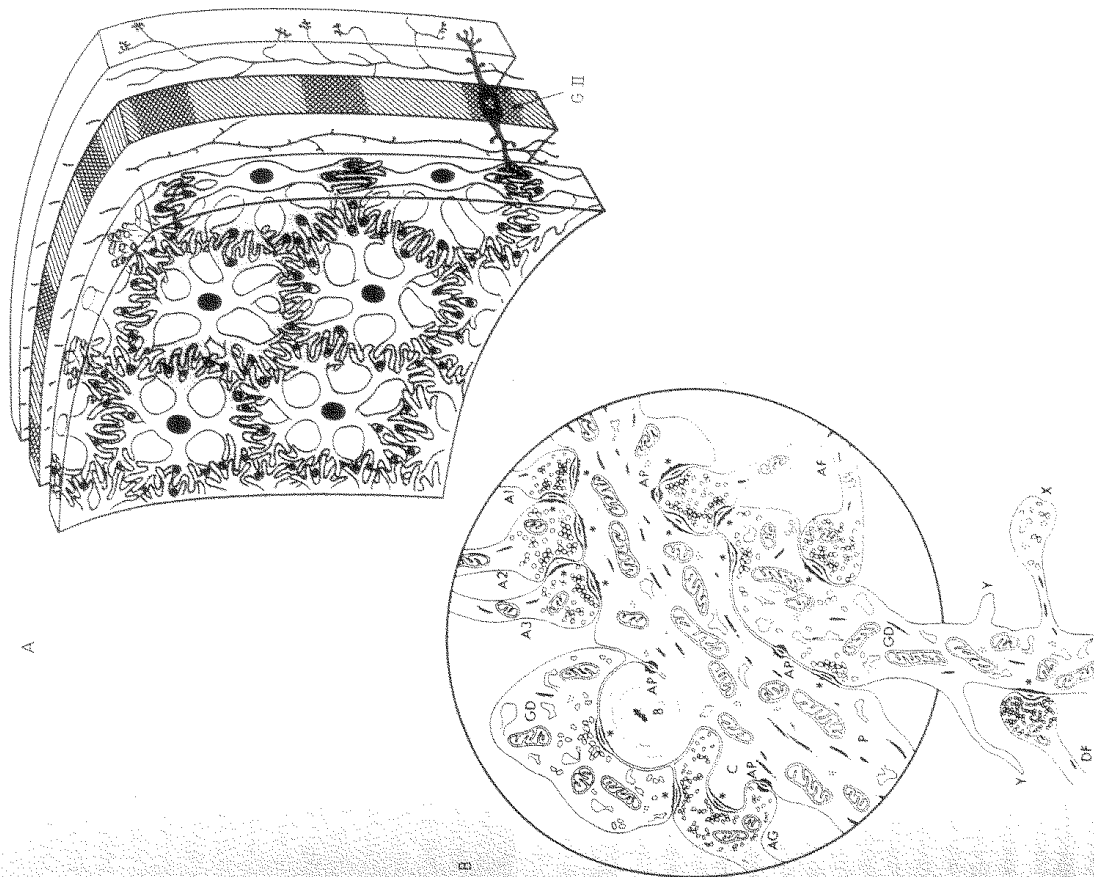


Fig. 6.19 (A) Dendritic trees within the laminae of the medial geniculate body. G II, Golgi type 2 interneurone. From Majorossy and Kiss (1976, Fig. 7). (B) Synaptic contacts in the synaptic nest between the afferent fibre (AF) dendrite of the principal cell (running across the middle of the diagram), and a dendrite of a Golgi type 2 cell (GD). DF, Descending (centrifugal) fibre from cortex. From Mørest (1975, Fig. 22).

The ventral division itself shows a laminar structure, the laminae being flat sheet-like layers consisting of both the afferent fibres and dendrites of the constituent neurones (Morest, 1965). Over much of the nucleus the sheets are curved and oriented vertically. Tonotopic organization in this division of the nucleus produces high frequencies located medially and low frequencies laterally, and it is very likely therefore that the sheets of cells detected anatomically are iso-frequency planes (Aitkin and Webster, 1972; Merzenich *et al.*, 1977). The ventral division contains two cell types, namely the principal cells, which project to the auditory cortex, and Golgi type 2 cells, which are short axon interneurons (Morest, 1975). The principal cells have characteristically tufted dendritic trees (Fig. 6.19A; Majorossy and Kiss, 1976). This comparatively simple cellular complement is, however, associated with a great deal of complexity in the local synaptic and dendritic organization, which has been worked out in detail (Majorossy and Kiss, 1976; Winer, 1985a). The interneurons make dendro-dendritic synapses with the principal neurones in terminal clusters called "synaptic nests", containing three-way synaptic contacts between the different cell types. These could lead to gating by descending fibres from the cerebral cortex, as well as to complex transformations of the afferent activity (Fig. 6.19B).

2. Physiology

Neurones in the ventral division, the specific auditory relay, show responses to sound, with best frequencies tonotopically organized over the majority of the division. Tuning curves are relatively sharp, although only a very small proportion seem more sharply tuned than primary auditory nerve fibres, and then by only a small amount (Aitkin and Webster, 1972). Aitkin and Webster did not report any cells with extraordinarily sharp tuning, as in the inferior colliculus. In their temporal firing patterns, many cells are onset or sustained excitatory types in the anaesthetized preparation, although sustained excitation or inhibition were more common in the unanaesthetized preparation (Calford, 1983; Aitkin and Prain, 1974). Inhibitory sidebands existed in the medial geniculate body as in other brainstem nuclei, and as the stimulus frequency was changed, complex excitatory-inhibitory interactions became visible. In general, the neurones with complex temporal properties have nonmonotonic rate-intensity functions and complex frequency response areas, as would be expected for neurones with a multiplicity of excitatory and inhibitory inputs (Aitkin and Prain, 1974).

As in the inferior colliculus, a high proportion of neurones are binaurally sensitive (Aitkin and Webster, 1972). Some, mainly high-frequency units, are predominantly sensitive to interaural intensity differences. Others,

mainly low-frequency units, are predominantly sensitive to interaural time differences. The tuning curves for stimuli at the two ears separately are approximately similar, although not exactly so (Fig. 6.20). Units sensitive

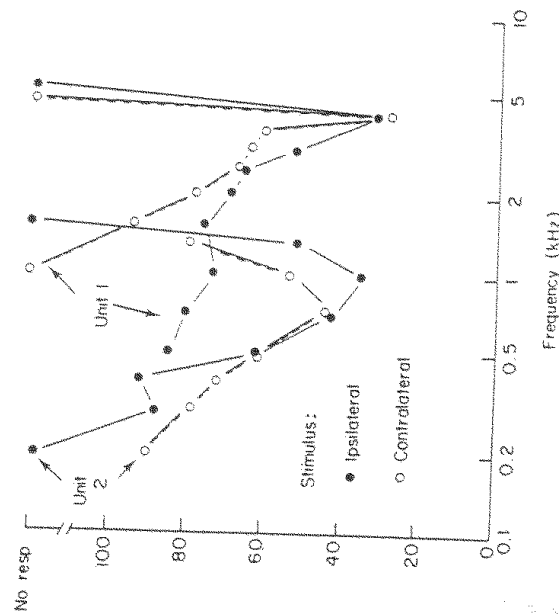


Fig. 6.20 Tuning curves in the ventral division of the medial geniculate body to ipsilateral and contralateral stimuli. From Aitkin and Webster (1972, Fig. 5).

to differences in interaural intensity may show very sharp sensitivity to the intensity differences, sometimes being driven over 80% of their firing range by a change of only 2 dB in interaural disparity.

Such studies, again, give very little idea of the sensory transformations occurring in the medial geniculate body. Thus attempts have been made to find neurones specifically responsive to the features of complex sounds. Whitfield and Purser (1972) reported that some units responded only to complex sounds and not to tones. Smolders *et al.* (1979) compared the responses of both medial geniculate and cochlear nucleus neurones to tones and the complex sounds produced by cats' vocalizations. They reported that, at least for the neurones studied in the posteroventral cochlear nucleus, the response to complex sounds could be predicted reasonably well from the response to tones. This was, however, not the case in the medial geniculate body. David *et al.* (1977) have shown cells in the medial geniculate of the unanaesthetized cat apparently sensitive only to specific speech parameters or to other complex features. It is obvious that such experiments

designed to uncover either specific transformations in a nucleus or specific feature detectors face enormous difficulties. It will be recalled that even as early as the dorsal cochlear nucleus there are neurones that will respond to broadband stimuli but not to tones (Young and Brownell, 1976). Such neurones may have led to reports of neurones in the cochlear nucleus responding only to "complex" stimuli. A great deal of care is needed to distinguish the different types of complex response, and this may be beyond the limits of our present techniques in a nucleus as high in the system as the medial geniculate. It is also obvious that the central state of the animal influences the responses. Thus Whitfield and Purser (1972) noted that in the freely moving animal the responses in the medial geniculate body were labile, with, say, bands of excitation and inhibition appearing and disappearing over time.

In the medial division, part of the "diffuse" auditory system which projects generally to the auditory cortex, Aitkin (1973) in the unanaesthetized cat showed very wide and complex response areas, with many onset responses and much variability and habituation. Three-quarters of the units were binaural. We expect there to be multimodal interactions in the nucleus, and Aitkin suggested that the wide response areas were a reflection of this nonspecificity. Units in the deep division of the dorsal nucleus showed short-latency and sharply-tuned responses to sound in the anaesthetized cat; those situated more dorsally and medially (in the caudodorsal and supragenulate divisions of the dorsal nucleus) responded more weakly and inconsistently, with much habituation (Calford and Aitkin, 1983).

G. Brainstem Reflexes

The brainstem is the main auditory reflex centre of lower vertebrates, and it would be surprising if some of these functions were not retained in man and other mammals.

1. Unlearned Reflexes

One of the most elementary auditory reflexes is the middle ear muscle reflex. The tensor tympani and stapedius muscle contract reflexly to loud sounds. Borg (1973) showed that an arc of three to four neurones was involved, consisting of a projection from the ventral cochlear nucleus to the MSO and then to the motor nuclei of the facial and trigeminal nerves. But in addition to this short-latency pathway, he presented evidence for a slower pathway.

perhaps projecting via the red nucleus or the reticular formation, both of which receive an auditory input.

At a rather higher level, the inferior colliculus has also been implicated in many auditory reflexes. It has been implicated in a reaction known as the auditory startle response, in which a sudden sound produces a characteristic and widespread muscular contraction. Fox (1979) showed that the reaction persisted in rats decerebrated above the inferior colliculus, but that additional lesions of the colliculi abolished the response. While the nervous pathways involved are not known, it was suggested by Willott *et al.* (1979) that the pericentral and external nuclei, rather than the central nucleus were involved, because in unanaesthetized animals the neurones there habituated in the same way as did the startle reflex. Audiogenic seizures also seem to require structures up to the level of the inferior colliculus, but not beyond. In certain susceptible strains of animals, early deprivation of auditory input leads to a hypersensitivity of the central nervous system, so that a later auditory stimulus produces a motor seizure (Saunders *et al.*, 1972). Lesion of the inferior colliculus, or structures below it, reduces the susceptibility to seizure, whereas lesion of higher centres does not (Kesner, 1966). Similarly, auditory influences on spinal reflexes require an intact inferior colliculus (Wright and Barnes, 1972). Wright and Barnes suggested that, of all the brainstem auditory nuclei, the inferior colliculus had the richest projection to the reticular formation. Thompson and Masterton (1978) have also shown that structures in the region of the colliculus were necessary for the initial reflex turning of the head towards a sound source.

The inferior colliculus also seems important for directing the animal's attention to auditory stimuli. Jane *et al.* (1965) trained cats to avoid an electric shock, with a combined tone and light as a warning stimulus. In later testing, the efficacy of the two stimuli separately was measured in unreinforced trials in which only one or the other stimulus was presented; normal animals responded mainly to the tone rather than the light. However, animals in whom the inferior colliculus had been lesioned before training responded primarily to the light. By contrast, lesions in other auditory structures did not have this effect. It seems, therefore, that the inferior colliculus was necessary for establishing the importance of sound in governing the animals' normal behaviour.

2. Learned Reflexes

Modifiability of single-unit auditory evoked responses during training has been seen in the inferior colliculus (e.g. Ryan and Miller, 1977; Birt *et al.*, 1979) and in the medial geniculate body (e.g. Birt and Olds, 1981). While

attempts have been made to ascertain the lowest level of the auditory system at which modifiability occurs during learning, the interpretation of these interesting experiments is fraught with difficulties. For instance, there is the difficulty of stimulus control during the measurements. In addition, the responses may be influenced by pathways descending from the higher levels of the nervous system. Thus it is possible that descending pathways from the cortex affect the responses of the earlier stages of the auditory system according to their significance for the animal. Some learning, even if it requires the presence of the auditory cortex, may be stored subcortically under the influence of descending pathways from the cortex.

The role of the brainstem in sound localization behaviour will be further described in Chapter 9.

H. Summary

1. The electrophysiological analysis of the auditory brainstem is faced with difficulties, because we do not have good ideas of the sensory features to which the auditory system is particularly responsive. It is also quite possible that many of the features extracted are represented not in the activity of single cells, but only in a pattern of activity over many cells. A successful scheme of organization is based on tonotopicity, such that neurones are arranged in ascending order of best frequency across one dimension in each nucleus, with complementary schemes of organization along the orthogonal axes.

2. The cochlear nucleus has three divisions, known as the anteroventral, the posteroventral, and the dorsal cochlear nuclei. Each division of the cochlear nucleus is tonotopically organized, and the best frequencies of the neurones make a spatially ordered map. In the anteroventral division, the neuronal responses are rather similar to those of auditory nerve fibres, with simple tuning curves, no inhibitory sidebands, and monotonic rate-intensity functions. In the dorsal cochlear nucleus, the tuning curves are very complex, with strong bands of inhibition, and rate-intensity functions that are nonmonotonic. Responses in the posteroventral cochlear nucleus have an intermediate form. This is correlated with the form of the post-stimulus-time histograms to tone bursts: those in the anteroventral cochlear nucleus are similar to those of auditory nerve fibres, whereas those more dorsally in the nucleus tend to show inhibitory pauses. It is reasonable to suppose that neurones in the anteroventral nucleus relay the auditory information to the next nucleus with very little transformation, whereas those in the dorsal cochlear nucleus have already

begun some complex sensory analysis. Some neurones in the dorsal cochlear nucleus appear particularly responsive to tones which are amplitude- and frequency-modulated, and others respond only to wide-band stimuli. In addition, inhibitory sidebands may serve to extract signals from background noise over a wide range of stimulus intensity.

3. The anteroventral and posteroventral cochlear nuclei project mainly to the superior olivary complex, which receives an input from the cochlear nuclei of both sides. The superior olivary complex has several component nuclei. The largest, known as the lateral superior olivary nucleus (or S-segment) receives an input from both sides, the ipsilateral input being predominantly excitatory, and the contralateral input predominantly inhibitory. The nucleus is mainly a high-frequency nucleus, is responsive to interaural disparities in intensity and timing, and uses these to code the direction of a sound in space. Another component nucleus, the medial superior olivary nucleus, is mainly a low-frequency nucleus. It is responsive to disparities in interaural timing, and therefore can be said to code the direction of a sound in space on the basis of timing differences.

4. The next major nucleus of the auditory pathway is the inferior colliculus, which receives afferents bilaterally from the superior olivary complex and contralaterally from the cochlear nucleus, mainly the dorsal division. The inferior colliculus therefore combines the spatially coded input from the superior olivary complex with the results of the complex sensory analysis of the dorsal cochlear nucleus. The central nucleus of the inferior colliculus is tonotopically organized, with cells arranged in iso-frequency sheets across the nucleus. Within each sheet, there seems some degree of mapping of sound source position, with cells responding to sources near the midline situated caudally, and those responding to sources at the side situated rostrally. The inferior colliculus seems to play an important part in many auditory reflexes.

5. The medial geniculate body receives its input from the inferior colliculus and projects to the auditory cortex. It has three divisions, only one of which, the ventral division, is a specific auditory relay. Neuronal responses are complex, although it is difficult to judge the extent to which they are in advance of those in the inferior colliculus.

6. Many auditory reflexes are established at the brainstem level, although our knowledge is sketchy. One of the most elementary reflexes is that by which the middle ear muscles contract in response to loud sounds. It involves an arc of three to four neurones, running from the ventral

cochlear nucleus to the medial superior olive and then to the motor nuclei of the facial and trigeminal nerves. The inferior colliculus has also been implicated in many auditory reflexes. It seems important for the startle response to loud sounds, and for the development of audiogenic seizures, a motor response resulting from a central hypersensitivity of the auditory system following early deprivation of auditory input. Auditory influences on spinal reflexes also seem to require an intact inferior colliculus. The inferior colliculus further affects the animal's attention to auditory stimuli. Learning has been shown to produce modification of neuronal responses in the inferior colliculus and medial geniculate body, but we do not know if the modification resulted from neuronal plasticity at those levels, or was due to descending influences from, say, the cortex.

1. Further Reading

The anatomy of the cochlear nucleus has been reviewed by Cant and Morest (1984) and J. K. Moore (1986b). The physiology has been reviewed by Young (1984) and Brugge and Geisler (1978). Neurotransmitters of the nerve and nucleus have been reviewed by Wenthold and Martin (1984), Caspary (1986), and in chapters in *Auditory Biochemistry* edited by D.G. Drescher (Charles C. Thomas, Springfield, 1985). The superior olivary complex has been reviewed by Brugge and Geisler (1978). The inferior colliculus has been reviewed by Aitkin (1986), who also gives a general review of the brainstem. The brainstem in relation to sound localization has been reviewed by Masterton and Imig (1984). An excellent general review of the brainstem is given by Irvine (1986).

7. The Auditory Cortex

The anatomical definition of auditory cortex has been simplified by the introduction of axonal transport techniques, which allow a definition of cortical areas on the basis of thalamic connections, and by detailed electrophysiological mapping, which allows a definition on the basis of tonotopic organization. The anatomical and physiological organization of the auditory cortex will be described, together with what is known of the neuronal responses. The auditory cortex has been a favourite target for behavioural scientists; unfortunately the behaviour-ablation method has in recent years proved to be less powerful for analysing the function of the auditory cortex than it seemed to be 20 years ago. The general functions of the auditory cortex are still not certain, and some hypotheses are listed.

A. Organization

1. Anatomy and Projections

The auditory cortex has been most commonly studied in the cat, where it is displayed on the surface of the brain. Until recently, much less work has been done in primates, where the auditory cortex lies on the superior temporal plane hidden in the lateral or Sylvian fissure.

A framework for analysing the areas of the cat auditory cortex can be built on Rose's (1949) delimitation of the cytoarchitectural areas of the temporal cortex (Fig. 7.1). By defining areas with constant cellular characteristics as seen with the Nissl stain, he described primary auditory cortex (AI), secondary cortex (AII), and a further auditory area on the posterior ectosylvian gyrus (Ep). Primary auditory cortex was described as being cytoarchitecturally similar to other primary sensory cortex, with six layers and a high density of pyramidal and granule cells in layers II, III and IV, but with sparse staining in layer V. The high density of granule cells leads to the term koniocortex, or "dust cortex". Additional auditory areas were