Physiology of the Cochlear Nuclei

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1. Introduction and Overview

Most of our knowledge concerning auditory signal processing is based on the response of auditory nerve fibers. To a certain degree, these peripheral fibers function as bandpass filters, relaying the spectral analysis performed in the cochlea to higher nervous centers. However, the auditory coding of acoustic signals involves far more than just frequency analysis. For example, the sensation of low pitch associated with musical melody and speech prosody appears to be relatively independent of spectral analysis since different portions of the spectrum can give rise to this percept. The ability to focus upon a single signal among many concurrently presented also involves mechanisms which lie beyond the reach of the auditory periphery. Thus, many properties of acoustic signals are processed in parallel, providing information not only concerning the spectrum per se, but about certain “ecological” aspects of the signal source, including its location, approximate size and trajectory.

All afferent auditory nerve fibers from the cochlea synapse on neurons in the cochlear nucleus (Powell and Cowan 1962; Lorente de Nó 1933; see Cant 1992). The cochlear nucleus (CN) is divided into distinct regions based on both physiological and anatomical criteria. At least three major divisions of the nucleus can be distinguished on the basis of morphology (Lorente de Nó 1981; Osen 1969; Brawer, Morest, and Kane 1974), each of which contains a complete representation of the audible frequency range (Rose, Galambos, and Hughes 1959). Along with the known projections of the principal cells and intranuclear pathways, the evidence indicates a parallel organization of the auditory system at the level of the cochlear nucleus. At least 22 different types of neurons have been anatomically distinguished (Brawer, Morest, and Kane 1974; Lorente de Nó 1981), thus constituting a natural site for the initiation of this parallel acoustic processing.

Since the seminal work of Rose, Galambos, and Hughes (1959), Pfeiffer (1966), Godfrey, Kiang, and Norris (1975a,b) and Bourk (1976), it has been known that this morphological diversity is accompanied by appreciable differences in physiological response properties. For example, Pfeiffer (1966) distinguished 13 different response types based on patterns of response to short tone bursts, including primarylike (PL), primarylike-with-notch (PLN), choppers (C), onset lockers (OL), onset choppers (OC), pausers (P) and buildups (B). Primarylike units are so named because their temporal response patterns and their interspike interval statistics are remarkably similar to those of primary afferents—the auditory nerve fibers. Onset units are those that have a well-timed initial spike followed by a low or null discharge rate. Onset choppers are characterized by two to four modes in the initial response to a tone. Choppers are characterized by several modes in their temporal response pattern that are unrelated to the stimulus frequency. A pauser unit has one (or possibly two) initial spikes, followed by a 5 to 100-msec silent period which, in turn, is followed by a buildup pattern. Buildup units are similar to pauser units, but lack the initial discharge at stimulus onset.

Evans and Nelson (1973a, b) devised an alternative classification scheme based on both excitatory and inhibitory properties, as well as on the presence of spontaneous discharge, to classify CN neurons. This alternative classification was modified by Young and Brownell (1976) to include a cell’s response to wideband noise. These different schemes have been jointly employed to categorize and correlate unit responses (Shoemaker and Young 1985; Blackburn and Sachs 1989). Several excellent reviews of CN physiology, each with a different perspective, are available (e.g., Evans 1975; Young 1984; Young et al. 1988).

Within the past decade there has been some emphasis placed on correlating physiological response properties with the underlying morphology, as a consequence of the application of intracellular horseradish peroxidase (HRP)-labeling techniques (Rhode, Oertel, and Smith 1983a; Rhode, Smith, and Oertel 1983b; Smith and Rhode 1983, 1987, 1989; Rouiller and Ryugo 1984; Rhode and Smith 1986a,b). These studies have identified the morphological correlates of most of the major CN unit types. These data, as well as other findings to be described in this chapter, were obtained from the cat, unless otherwise indicated.

Complementary studies by Oertel and colleagues (Wu and Oertel 1984, 1987; Hirsch and Oertel 1988a, b) in a mouse CN brain-tissue-slice preparation have served to elucidate the membrane properties of several morphological classes, including bushy, stellate and fusiform cells. This work, combined with the multunit studies of Voigt and Young (1980, 1988, 1990) and information derived from anatomical tract tracing studies (e.g., Adams 1977; Roth et al. 1978), provide a solid empirical foundation upon which to speculate on the functional role of individual cell types. Many biological signals, including animal vocalizations and human speech, are spectrally complex and possess a large degree of amplitude and frequency modulation. Møller (1981) summarized the signal pro-
cessing in the lower auditory CNS as the enhancement of "changes in a complex sound, rather than conveying spectrally analyzed information about the absolute distribution of energy." Unfortunately, the response of cochlear nucleus neurons to such stimuli is little understood, particularly when presented in background noise. Since natural sounds are too complex to study systematically, most studies of complex signal processing in the cochlear nuclei have focused on sinusoidally amplitude-modulated (AM) tones. Such studies provide some insight into the mechanisms underlying the processing of speech due to the presence of amplitude modulation in speech and the similarities between voice pitch and modulation frequency (see Section 7 on Coding of Complex Signals in the Cochlear Nucleus).

1.1 Afferent Projections of the Auditory Nerve into the Cochlear Nucleus.

The auditory nerve enters the cochlear nucleus and bifurcates into an ascending branch that innervates the anteroventral cochlear nucleus (AVCN) and a descending branch that innervates both the posteroverentral (PVCN) and the dorsal cochlear nucleus (DCN). The terminals of many auditory nerve fibers (ANFs) projecting to the AVCN contain large endbulbs of Held, which provide a secure synaptic connection with the large spherical bushy cells of that region, and which are important for preserving frequency information encoded in the precise temporal discharge pattern of ANFs. Because of this secure synaptic connection, the firing behavior of primarylike units resemble ANFs in most respects, sufficiently so for Rose et al. (1974) to have recorded from PL units as a means of monitoring of cochlear function. The synaptic connections are not limited to those of the AN, which contain only large round vesicles. Also found are synaptic structures that contain either small-round, flat or pleomorphic (oblong) vesicles. Each of these arises from a different cell type, whether from within the CN or from a more rostral part of the auditory system. The relative density of these synaptic types often varies on the soma and on the proximal and distal dendrites.

The exact form of synaptic relation between ANFs and the postsynaptic element onto which they project varies markedly in different regions of the CN (e.g., Lorente de Nó 1981; Cant and Morest 1984). Thus, the density and size of AN synaptic projections varies widely across the CN. For example, cells in the molecular layer of the DCN receive very few, if any, synaptic contacts. In contrast, fusiform cells in the DCN have relatively few AN synapses on their somas, with the majority located on the basal dendrites underlying the molecular layer. Perhaps the clearest example of synaptic specialization is the occurrence of a single large synapse on the large spherical, bushy cells in the AVCN. In the nerve root region, one to four modified (smaller) endbulbs will generally synapse on each globular-bushy cell (see Cant 1992 for more detail on the anatomy of the cochlear nuclei).

Traditionally, the response properties of ANFs have been thought to be relatively homogeneous with respect to such features as threshold, dynamic range, rapid adaptation, frequency selectivity, lateral suppression and phase-locking capabilities. (See Chapter 2 by Ruggero.) However, within the past decade, it has become increasingly clear that there is a considerable amount of diversity in these parameters that is correlated with the spontaneous background activity of the fibers (e.g., Liberman 1978; Young and Sachs 1979; Rhode and Smith 1985; Greenberg 1986; Winslow, Barta, and Sachs 1987; Rhode and Greenberg 1992a,b). Such response diversity may have important consequences for information processing in the CN. Although the projection sites of the low, medium, and high spontaneous rate (SR) fibers are still not definitively known, there is some evidence, based on intracellular marking of ANF axons with horseradish peroxidase (HRP), that these classes may segregate with respect to their CN projections (Fekete et al. 1982; Liberman 1982; Rouiller et al. 1986).

There is also preliminary evidence that some ANFs have an exceedingly broad dynamic range, two to three times that of the typical ANF. These fibers have been observed by Winter, Robertson, and Yates (1990) in the guinea pig. However, it is unclear whether such fibers occur in other mammalian species. If they do, then such fibers may be of fundamental significance for understanding intensity coding in the CN. In particular, it would be of interest to ascertain whether the projection of these extended dynamic range AN fibers is segregated from that of other ANFs. Preliminary evidence does indeed suggest that such segregated projections occur, at least in that low-SR ANFs appear to segregate their projection to bushy cells (Sento and Ryugo 1989).

2. Physiological Response Characteristics to Sinusoidal Stimuli

2.1 General Response Patterns Derived from the Post-stimulus-Time and Interspike-Interval Histograms

The most popular method of physiological classification in the CN is derived from the poststimulus-time histogram (PSTH), which is the averaged response to sinusoidal signals of brief duration (25–50 msec), presented at the cell's most sensitive, or characteristic frequency (Rose, Galambos, and Hughes 1959; Pfeiffer 1966; Godfrey, Kiang, and Norris 1975a,b; Bourk 1976; Rhode and Smith 1986a,b; Blackburn and Sachs 1989). The PSTHs of neurons representative of the major response types are illustrated in Figure 3.1, along with their subtypes. Also indicated is
the region of the CN with which the cell type is primarily associated. There is a great diversity of cellular morphology in all CN regions, and conversely, most response classes can be found in regions outside their primary locus, though their numbers in these secondary regions may be rather small. It should be noted that the PSTH alone does not always provide a means for unambiguous classification of the response type, for there are intermediate patterns, and some cells, especially in the DCN may show more than one PSTH type for different stimulus conditions (Godfrey, Kiang, and Norris 1975b). In most instances, the shape and statistics of the InterSpike Interval Histogram (ISIH) are usually sufficient to resolve any ambiguity in classification.

The ISIH is valuable for gaining insight into the mechanisms underlying the generation of neuronal activity. It is simply a frequency distribution of the intervals between successive neuronal discharges (spikes). Figure 3.2 illustrates ISIHs typical of eight CN unit classes, based on the temporal response pattern as seen in the PSTH. The ISIH for a PL unit has an exponential shape similar to that observed among ANFs, and approximates the distribution of a Poisson process. For low-frequency stimuli, phase locking is seen in the unit response, as represented by modes in the ISIH, spaced at integral multiples of the stimulus period. The ISIH of Oc units is often similar to that of PLs for mid- and high-frequency stimuli. Onset units are capable of phase locking with a remarkably high degree of precision to low-frequency signals. This is manifested in the ISIH as a single, narrow mode corresponding to the stimulus period, and usually occurs for stimulus frequencies less than 1 kHz. In these instances the unit fires once per stimulus cycle, in contrast to PLs and ANFs which generally fire at a rate considerably less than the stimulus frequency. For this reason these units are sometimes referred to as “lockers,” for they respond on a very precise phase of every cycle of the stimulus waveform, responding as if each cycle is an effective excitatory stimulus. This behavior is also referred to as “entrainment,” and has been observed for frequencies up to 1050 Hz (Rhode and Smith 1986a).

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**Figure 3.1.** Response diversity of cochlear nucleus units. Representative temporal response patterns (poststimulus-time histograms) for the major physiological unit classes in the ventral and dorsal cochlear nuclei of the cat. The PSTHs were computed from responses to brief tone bursts at the unit CF. For most cells the stimulus duration was 25 msec, with each stimulus repeated 250 times, once every 105 msec. For some DCN units the stimulus duration was lengthened to 100 msec due to the buildup (buildup and pauser/buildup units) or complexity (Ov4/T4, IN-inhibitory) of response. In these instances the stimuli were repeated once every 400 msec. Stimulus sound pressure level was generally 60 dB, approximately 30-40 dB above unit rate threshold. Histogram binwidth was μsec. See list of abbreviations for key to unit type classification indicated in each panel. (Based on data from Rhode and Smith 1986a,b.)

**Figure 3.2.** Temporal response properties of selected CN unit types. The interspike-interval histograms for six unit types in response to CF tones presented at 60 dB SPL. For two unit classes (PL and Oc) a contrast is illustrated between the response to low- and high-frequency stimuli. Phase locking is restricted to frequencies below 4-5 kHz. See text for discussion of these responses.
It is sometimes difficult to unambiguously assign these locker units to a specific response class as a consequence of their phase-locked behavior. On the basis of its PSTH, a locker could fall into either the chopper, O₁, O₂, or PL class. However, it is usually possible to make a definitive assignment on the basis of several other response criteria, such as the statistics of the ISIH, frequency response area, first-spike latency and dynamic range.

The ISIHs of transient choppers (C₁) differ from those of sustained choppers (Cₛ). While sustained choppers exhibit a single, narrow, symmetric mode in the ISIH, C₁ units generally have an asymmetric, broader ISIH. The discharge of C₁ units can be considerably lower than Cₛ units after the initial 10–20 msec response. Regularity is measured as the coefficient of variation (CV) of the ISIH computed for the last half of the stimulus duration (CV = \( \sigma_{\text{isih}} / \text{mean}_{\text{isih}} \)) or as a function of stimulus time. A value of CV = 0.34 is a useful reference to use to separate the Cₛ (<0.34) from the C₁ (>0.34) response pattern (Bourke 1976; Young et al. 1988; Rhode and Greenberg, unpublished observations).

The regularity of onset-chopper units also changes through the time course of the response (Young et al. 1988). During the initial portion of the response, typically 10–20 msec, the firing is highly regular, conforming to the classic chopping pattern. This chopping is reflected in the first, relatively narrow mode of the ISIH. The second mode is much broader, and reflects the much less regular discharge pattern during the remainder of the response. Over a certain intensity and discharge-rate range the two modes may merge.

The ISIH of the buildup unit contains a single mode, similar in form to choppers. However, the modal period is typically longer and the ISIH is sometimes much broader than that of chopper units. The coefficient of variation can be as small as that characteristic of sustained choppers. However, in contrast to Cₛ units, DCN cells generally have a (much) lower sustained discharge rate—usually less than 100 spikes/sec.

2.2.1 Primary-Like and Primary-Like-with-Notch Units

In the AVCN the responses of spherical-bushy and globular-bushy cells exhibit PL and PLₙ response patterns, respectively, and closely resemble those of auditory nerve fibers (Rhode and Smith 1986a). The large endbulbs of Held found in the rostral AVCN are secure synapses that largely function to pass the ANF spike stream to the spherical bushy cells. These axons, in turn, project to the superior olivary complex (SOC) via the trapezoid body (Cant and Morest 1984). This pathway is probably involved in the transmission of information subserving binaural mechanisms underlying localization of sound, and possibly includes afferents to other auditory brainstem nuclei as well. Globular bushy cells project to the ipsilateral lateral superior olive (LSO), the contralateral medial nucleus of the trapezoid body (MNTB) and to the contralateral lateral lemniscus (Frauf and Ostwald 1988; Smith et al. 1991). The globular bushy cells are part of a pathway that likely serves several functions, given its rich axonal collateralization. In particular, its contact with periolivary groups implies involvement in an efferent loop for gain adjustment, with the cochlea being a prime, though not exclusive, target (Spirou, Brownell, and Zidanic 1990).

The PL discharge pattern typically consists of an initial rapid adaptation of the discharge declining to a maximum rate of approximately 250 spikes/sec. A second pattern, PLₙ, is similar to the PL PSTH, but does not exhibit the initial rapid adaptation. This pattern is also observed among low-SR ANFs (Rhode and Smith 1983). These patterns are seen most frequently in the AVCN but are seen occasionally throughout the CN. Another primarylike response pattern observed among cells in the region of the nerve root is the primarylike with notch. Immediately after the initial spike a discharge pause of 0.5–2 msec occurs. This pause is generally attributed to refractory effects of the neuron.

Pfeiffer (1966) and Bourk (1976) observed among the PL unit population a small potential preceding the main component of the action potential by 0.5 msec. This “prepotential” is presumed to reflect the activity of the presynaptic element, the large endbulb of Held (Fig. 3.3). A second category of smaller prepotentials (type 2) was recorded in the nerve root area of the CN where globular bushy cells are concentrated. This is where smaller, modified endbulbs of Held are found, and where the prepotentials are also smaller, and the PLₙ response pattern is observed. Averaging of spike activity is often required to see the (type 2) prepotentials, on account of their smaller size (see Fig. 3.3).

Although the spontaneous activity of CN units is generally lower than that of the majority of ANFs, a large proportion of PLₙ units exhibit spontaneous discharge activity considerably higher than observed in the auditory nerve. The mean spontaneous rate of these units is about twice that of ANFs (Rhode and Smith 1986a), though this observation remains controversial as it has been recently reported that there is a marked dependency on unit CF (Spirou, Brownell, and Zidanic 1990). Units with CFs below 6 kHz had a mean SR of 7.5 spikes/sec while units with higher CFs had a mean SR of 31 spikes/sec for recordings made from trapezoid body fibers. There were large standard deviations in the SR for both studies.

The mechanism(s) underlying this high level of background activity remains obscure. There are two likely possibilities. PLₙ (as well as some PL) units may be preferentially innervated by high-SR fibers. However, if this were the primary basis of the higher spontaneous activity one would expect that there would be no other significant differences in basic discharge behavior. However, the maximum driven discharge rate is also greater among PLₙ units (mean = 313 spikes/sec) compared to ANFs.
deviation of the first-spike latency is extremely small, approaching 100 µsec in some units (Rhode and Smith 1986a). Their preferential response at stimulus onset pertains principally to signals whose frequencies are higher than 1.5–2 kHz. In response to low-frequency, sinusoidal signals, many of these onset units phase lock to low-frequency stimuli with a precision far greater than observed in the auditory nerve.

Most onset units reside in the posterior portion of the ventral division of the CN. However, a small proportion of these cells is found in the AVCN, as described by Pfeiffer (1966), Bourk (1976) and Blackburn and Sachs (1989). There are several patterns that are somewhat different from those found in the more extensively studied PVCN. One pattern observed in the AVCN consists of several peaks during the initial portion of the response, with little activity thereafter. This type of response could be a variant of the O_c pattern common to the PVCN. A second pattern is that of a graded onset, in which the discharge rate reduces to zero over a 25 to 50-msec time interval after an initial burst of activity. This pattern is similar to the O_s responses recorded from the deep layer of the DCN. The AVCN onset cells (as well as perhaps some of their PVCN counterparts) are thought to project to the superior olivary complex via the trapezoid body, although there is no firm anatomical evidence yet to confirm this.

Rhode and Smith (1986a) distinguish three subclasses of onset unit in the PVCN (Fig. 3.1, row two). The two most common types, comprising 80% of the onset population, are the onset-locker and onset-chopper units. The former appear to be large “octopus” cells (Kane 1973; Rhode, Oertel, and Smith 1983a), which are concentrated in the octopus cell area (OCA) of the PVCN. The latter are large, multipolar, stellate cells, which principally populate the multipolar cell region just anterior to the octopus cell area (Rhode, Oertel, and Smith 1983a; Cant and Morest 1984). Although these two types of onset unit share many response properties this similarity appears to be based more on functional convergence than on morphological kinship, in that their dendritic structures differ considerably. O_c units share more in common with ANFs than with O_s in terms of their PSTH and ISIH patterns, dynamic range, threshold, spontaneous rate, and maximum driven rate. O_c units have a wide dynamic range (up to 80 dB), with some units remaining unsaturated even at 100 dB SPL, and exhibiting a very fast rise time for the initial onset discharge. These features are consistent with the hypothesis that their response properties are the result of convergence of several (possibly many) afferents. The onset choppers may project to the contralateral lateral lemniscus via the intermediate acoustic stria (Adams 1991).

O_s (onset-inhibitory) units are less frequently seen than other onset response types. Using a decerebrate preparation, Ritz and Brownell (1982) found units in the PVCN that displayed an on-off response but observed no O_s units, possibly because of the anesthetic. In a barbiturate-anaesthetic
tized animal these units discharge little after the onset spike (Godfrey, Kiang, and Norris 1975a,b), except when their response entrains to low-frequency stimuli (up to a maximum frequency of 0.5–1 kHz). One of their prominent features is a response preference for a particular direction of the sweep in a frequency-modulated (FM) signal. Occasionally, these units will respond exclusively to one direction of the FM sweep, even when the sweep rate is very slow. Although the tuning of O₁ units is very broad, comparable to O₂ units, they exhibit a very small dynamic range of response in contrast to the O₂ units (10–20 dB vs 30–70 dB). The mechanisms underlying the O₂ response pattern remain obscure. The directional sensitivity of their response to FM sweeps has been ascribed to the orderly tonotopically determined depolarization of large dendrites on octopus cells (Szentagothai and Arbib 1975). These cells may play a role in setting up directionally sensitive coding of FM signals in the CN, and may be the basis of the FM-specific channels studied by Kay and Mathews (1972). They may also play a role in the temporal coding of low-frequency complex stimuli.

2.1.3 Chopper Units

Chopper units comprise the other major physiological class in the PVCN, but are also found, in fewer numbers, in the other divisions of the CN. In response to high-frequency sinusoidal stimulation, choppers discharge at regular intervals, independent of stimulus frequency and phase. The modal interval of discharge typically ranges between 1.5 and 10 msec, with most choppers capable of firing at sustained rates up to 200–500 spikes/sec. Because their firing rate is intensity dependent, increasing from threshold levels up to saturation (over about a 30-dB range), the mode of the ISIH also changes over this intensity range. At supersaturation levels the mean interval is generally the reciprocal of the firing rate.

Choppers phase lock to low-frequency sinusoidal signals poorer than any other VCN unit type. Their ability to follow waveform modulations is severely diminished for stimulus frequencies above 1 kHz. Their frequency selectivity is comparable to that of ANFs. When chopper units have spontaneous activity, tones presented above or below CF result in a reduction or elimination of spontaneous activity, manifested as inhibitory sidebands in a frequency-intensity map of unit activity. One possible function of the inhibitory sidebands is to preserve spectral selectivity when there is a convergence of afferent fibers. Morphologically, choppers are stellate cells (Rhode, Oertel, and Smith 1983a). Oertel (1983) has found that such cells in the mouse brain tissue slice display linear voltage characteristics, consistent with the response of an integrator with a finite time constant of approximately 2 to 5 msec.

Two distinct stellate morphologies have been identified—one with tapering dendrites that branch little and produces the C₁ pattern, while the second is characterized by greater branching and dendritic appendages (Rhode, Oertel, and Smith 1983a), and produces the C₁ pattern. There are, as well, two distinct types of stellate cells with respect to synaptic density on the soma (Cant 1981). Those with a large number of somatic synapses project to the contralateral inferior colliculus, while the projection sites of the others are not definitively known.

Blackburn and Sachs (1989) suggest that these two projection patterns correspond to C₁ and C₂ units, respectively. However, it is not entirely clear whether one of these innervation patterns corresponds to AVCN onset units (Pfeiffer 1966; Bourk 1976). This issue will have to be resolved through intracellular labeling of physiologically characterized cells.

Figure 3.4 illustrates several properties of sustained choppers. Figure 3.4A illustrates the response area (a set of isointensity curves) delineating the extent of the excitatory and inhibitory (when the unit is spontaneously active) regions. If the unit is not spontaneously active (as in Fig. 3.4A), a “background” activity level is produced by presenting a wideband noise (WBN) during the collection of a response area (i.e., a “masked” response area, or MRA as in Fig. 3.4D). A reduction of activity below the background level reflects either suppression of cochlear origin or neural inhibition arising from the cochlear nucleus. The receptive fields can be derived from the MRA by computing an isorate curve for a predefined criterion of response. Typically this criterion is set at ±20% of the driven rate (Maximum discharge rate—spontaneous rate). The positive portion of the isorate curve corresponds to the excitatory region and the negative component to the inhibitory/suppression region (Fig. 3.4F). The rate-intensity curve (RC), typically obtained in response to a sinusoidal stimulus presented at CF (solid line in Fig. 3.4B), provides an estimate of threshold, dynamic range, maximum discharge rate, response latency and degree of monotonicity. The same set of parameters can be obtained from presentation of WBN (dashed line in Fig. 3.4B). When noise is combined with the tonal RC, the resultant “masked” rate curves describe the response of the unit to CF stimuli at various sound pressure levels and signal-to-noise ratios (Fig. 3.4C). This provides a method of assessing how well signals are encoded by spike rate in a noisy environment where the threshold increases and there is a shift to higher SPLs of the entire rate-intensity function.

C₁ units exhibit chopping for only a few milliseconds. The discharge regularity decreases as a function of time during stimulus presentation (Young et al. 1988). These units often exhibit lower maximum discharge rates and larger peak-to-steady-state discharge rates than C₂ units. However, there often isn't a clear distinction of C₁ and C₂ units based solely on the PSTH pattern. A coefficient of variation of 0.34 is a convenient dividing point that agrees with the visual interpretation of the PSTH patterns. One can also plot the CV as a function of time, and observe which units show a steady CV over time, and which show a marked
Figure 3.4. Spectrotemporal characterization of a sustained chopper unit. (A) Response area of a $C_4$ unit. Contours are derived from data points representing the rate response (in spikes/sec) to 50-msec tone bursts presented once every 300 msec at the indicated sound pressure levels. The frequency space was sampled at a resolution corresponding to approximately CF/20. For this unit the CF = 4.8 kHz, and its rate threshold at CF = 20–25 dB SPL. Note the large response to low frequencies at 70 and 80 dB SPL. The intensity space was sampled in 10-dB steps, ranging from 0 to 80 dB SPL. Contours for 0 and 10-dB SPL signals are omitted. (B) Rate-intensity curves in response to a CF tone (solid line) and to a wideband noise (dashed line). The stimulus duration was 100 msec, presented once every 300 msec. The intensity space was sampled in 5-dB steps. The noise rate curve is shifted horizontally by a constant amount (35 dB) so as to align the average noise and tone thresholds. The symbols on the noise rate-intensity function are key to the corresponding levels in the masked rate curve in 4C. (C) Three masked rate-intensity curves, in which the CF tone is presented concurrently with wideband noise of variable spectrum level (indicated by the symbols in B (35, 45, 55, dB/Hz). (D) A masked response area obtained by concurrent presentation of tonal stimuli with a wideband noise. The noise spectrum level is set to 45 dB/Hz, which corresponds to the level at which the evoked discharge rate is half of the maximum noise-driven rate. Several intensity-level contours have been omitted for display clarity. Note the presence, particularly above CF, of discharge suppression induced by the sinusoidal signals. (E) The PSTH (PST) and ISIH (IH) in response to a CF tone presented at 60 dB SPL. Stimulus duration = 50 msec. Stimulus repetition interval = 300 msec. Histograms computed from 250 repetitions. The PSTH shows the classic chopping pattern, particularly evident during the initial 15 ms of response. The ISIH reveals the regularity of response, showing the successive discharges cluster around a single mode. Both properties are type characteristics of $C_4$ units. (F) An isorate curve derived from the MRA shown in D. The contours shown are based on an excitatory criterion of 20% above the noise-driven rate and a suppression criterion (shaded areas) of 30% below the noise-driven rate. Note the difference in frequency scaling between panels D (linear) and F (log). In F the low-frequency region is expanded and the high-frequency region is compressed relative to the display in D.
increase. A histogram of CVs for all choppers during the last half of the stimulus (approximates steady-state activity) is unimodal (Rhode and Greenberg, unpublished data), making a separation based on CV alone somewhat arbitrary.

In terms of spectral selectivity, dynamic range, thresholds, spontaneous rates, Q1/2, and maximum discharge rates, C7 and C8 units don’t differ very much. Both unit types exhibit prominent and comparable suppressive sidebands. However, there is a difference between the two chopper types in terms of the variance of the first-spike latency. C7 units have a much smaller latency variance. As a consequence, it is sometimes difficult to distinguish the PTH of these units from O2 units except by virtue of their dynamic range and phase-locking behavior. In addition, the spontaneous rate of choppers is inversely proportional to the magnitude of their CV, suggesting that inhibition may play a significant role in the behavior of C7 units.

2.1.4 Pauser-Buildups Units (DCN)

Neurons in the dorsal cochlear nucleus, principally the “buildup” and “pauser” units, have extensive inhibitory sidebands, which are quite sensitive to the effects of barbiturate anesthesia (Evans and Nelson 1973a,b; Rhode and Kettner 1987) and often display nonmonotonic, inhibitory rate-intensity functions to sinusoidal signals, while showing excitatory responses to wideband noise (Young and Brownell 1976). The DCN is noteworthy for a prominent inhibitory input to the majority of cells studied. Under conditions of no anesthesia (Evans and Nelson 1973a; Young and Brownell 1976) one encounters units that show only inhibitory responses over a wide range of frequencies and intensities (Type V units), a response pattern rarely observed in the anesthetized preparation.

The responses of a DCN pauser cell are shown in Figure 3.5. The unit had a nonmonotonic rate curve for tones at CF (Fig. 3.5B, solid line) but didn’t respond to noise (dashed line). However, when a response area was collected during simultaneous presentation of a wideband noise (MRA in Fig. 3.5D), the nonmonotonicity below 60 dB was eliminated (Figs. 3.5D, 3.5C). Typically, the presence of the noise reduces the maximum discharge rate and may narrow the frequency extent of the excitatory region (Rhode and Greenberg 1992b). The isorate curves in Figure 3.5 indicate there is no inhibitory region below CF, a common finding for low-CF units. However the frequency extent of the inhibitory sideband extended several octaves above CF—even beyond 20 kHz at 70 dB SPL. It is not unusual for the inhibition to extend more than an octave above CF, and for spontaneous and noise-evoked discharge to be completely suppressed.

Pauser and buildup response patterns are often seen in the same DCN unit under varying stimulus conditions (Rhode and Smith 1986b; Godfrey, Kiang, and Norris 1975b). Stimulus intensity, frequency and duty cycle for tone burst repetition can alter the temporal response pattern. In addition, a chopper pattern is often superimposed on the buildup pattern. In one intracellular study (Rhode and Smith 1985b) it was demonstrated that the intracellular resting potential level could change the response pattern. As a cell depolarized, its response pattern usually changed to that of a chopper. By hyperpolarizing the cell the original pauser pattern could be restored (Rhode and Smith 1985b). Manis (1990) has performed a similar experiment in the DCN tissue slice through manipulation of the intracellular resting potential, and demonstrated the prominent role played by the intracellular potential in determining whether the pattern is pauser, buildup, or chopper.

Units recorded from the second layer of the DCN can be thought of as “late-steady” responders (i.e., buildup units). They often have extremely narrow response areas and isorate functions. Their thresholds are often as low (or lower) than other cell types in the CN. They may have nonmonotonic rate curves and/or respond strongly to noise. These cells demonstrate prominent inhibitory sidebands that can extend an octave or more above and, less frequently below CF. The function performed by these CN units is not well understood.

The essential features of pauser/buildup units are several: (1) the long-lasting hyperpolarization induced by prior stimulation has a marked effect in the temporal response (Rhode, Smith, and Oertel 1983b), (2) inhibitory sidebands enhance or preserve spectral selectivity, and combined with sensitive thresholds, may play a role in spectral pattern detection at low sound pressure levels and (3) inhibitory sidebands may also play a role in biasing the cell’s discharge rate downward so as to improve the signal-to-noise ratio and the dynamic range of encoding preserved in the presence of spectrally complex signals. The significance of these nonmonotonic rate-intensity functions is difficult to assess at this time, but their role may be crucial for complex signal processing.

The DCN is probably the most complex region of the CN with respect to cellular morphology. It has been called the “cortex” of the cochlear nucleus by Lorente de Nó (1981), and Mugnaini, Warr, and Osen (1980) have suggested that this region has many structural similarities to the cerebellum. For instance, the granule cells, which are found in seven different regions of the cochlear nuclei, are similar in many respects to their cerebellar counterparts. In addition, these cells give rise to a parallel-fiber system that makes extensive contacts with the spines of cartwheel cells, and the apical dendrites of the fusiform cells, and which enters mossy fiber glomeruli. Granule cells do not receive primary auditory input but may receive input from type II ANFs arising from the outer hair cells (Brown, Berglund, and Kiang 1988). The region they occupy is contacted by multisensory inputs, particularly those of somatosensory origin (Itoh et al. 1987), of potential significance for attentional mecha-
isms in noisy backgrounds. It has also been shown that the saccule projects to several granule cell regions in the CN of Mongolian gerbils (Kevetter and Perachio 1989).

Despite the complexity of this intrinsic circuitry, only the fusiform cells and the giant cells of the deep layer of the DCN project to higher auditory centers (see Cant 1992). Few cells in the DCN, other than fusiform cells, have been both physiologically characterized and labelled. Fusiform cells constitute one element of the ascending auditory system and must complement the role of those fiber systems arising in the AVCN and PVCN.

2.2 Unit Response Classification Based on Excitatory/Inhibitory Activity

An alternative classification scheme to the one described above was proposed by Evans and Nelson (1973a,b), based on the constellation of excitatory and inhibitory inputs. Their classification scheme comprises five distinct classes, derived from the receptive field (RF) or frequency-intensity-response pattern. The classification was modified by Young and Brownell (1976) to incorporate information concerning the response to wideband noise. Shofner and Young (1985) have used this receptive-field-based metric to classify the response of neurons in various areas of the CN. These different schemes have been jointly employed to categorize and correlate unit responses (Shofner and Young 1985).

A condensed view of the five RF types is illustrated in Figure 3.6. A "central" excitatory area is common to RF classes I, II, and III. RF type I units contain only this central excitatory region. The RFs of both type II and III units contain lateral inhibitory sidebands. Type IIIs are distinguished from type IIIIs in that they exhibit little or no spontaneous activity and are generally unresponsive to wideband noise. Although there is little

**Figure 3.5.** Spectro-temporal characterization of a DCN pauser unit. General stimulus parameters are as indicated in Fig. 3.4. (A) Response area. CF = 2 kHz. TH = 0 dB. Several contours omitted for display clarity. (B) Rate-intensity curve to CF tone (solid line) and wideband noise (dashed line). Note that the CF-tone rate-intensity function is highly nonmonotonic, particularly above 70 dB. Wideband noise effectively shuts the cell's response down. (C) Set of masked rate curves at the indicated spectrum levels (N0) derived from B. (D) A MRA with the noise level set at 40 dB point from the noise rate curve in B. (E) PSTR and ISIH in response CF tone presented at 10 dB SPL. The PSTR shows a 20-msec dead interval between response onset and resumption of firing, a diagnostic characteristic of pauser units. (F) The IRC for the excitatory (+20%) and suppressive (−50%) regions derived from the MRA in D. The upper extent of the suppression region was computed from a separate MRA (not shown), which indicated that the upper suppression sideband extends beyond 20 kHz.
or no response to noise among type II units, the presence of WBN suppresses the response to CF tones in the anesthetized cat (Rhode and Greenberg 1992a). The dotted line in the type II panel indicates that some of these units have a nonmonotonic rate curve and may be silent at higher intensities. Types II and V units are confined to the DCN. Type IV receptive fields contain mostly inhibitory regions, but may also have a few small excitatory areas with a prominent, low-threshold excitation region. Type V units lack a sensitive excitatory region. At low sound pressure levels only inhibitory responses are evident. At higher SPLs both excitatory and inhibitory responses are observed. Type IVs exhibit a nonmonotonic rate-intensity function or simply a rate-intensity function (RC) in response to CF tones (in which the unit increases its discharge with increasing SPL at low levels and decreases its firing rate with stimulus level increases at higher SPLs). Voigt and Young (1980) found that the type IV units have an excitatory region displaced to frequencies higher than CF. Based on their multiunit studies it appears that type II units provide an inhibitory input to type IV cells at CF. Type V units exhibit a monotonically decreasing RC (increasing inhibition of spontaneous ac-

### 2.3 Classification Based on Other Response Properties

Several other physiological response measures are useful for distinguishing among different unit classes in the CN. Among these are the rate intensity function to CF-tone and WBN stimulation, the variance of first-spike latency, the phase-locked response to sinusoidal and amplitude-modulated signals and the $Q_{10}$ measured 10 dB above rate threshold. Although it can be difficult to unambiguously classify CN units on the basis of a single measure, classification based on multiple features of the neuronal response correlate highly with both PSTH and cell morphology.

### 3. Multiunit Studies

The rationale for multiunit studies lies in the fact that brain cells operate in consonance. The importance of this work is in setting constraints on models of CN activity. The way to understand neural ensembles that interact in a nonlinear manner is to record simultaneously from the same
members of an ensemble, a difficult but necessary study. The principal method of analyzing the strength and timing of the interaction has been cross-correlational analysis (Perkel, Gerstein, and Moore 1967). These techniques have been exploited most successfully in the cochlear nucleus by Voigt and Young (1980, 1988, 1990; Young and Voigt 1982). Their early studies recorded activity with a single microelectrode and employed a spike separator to distinguish individual spike trains from the joint record, which could then be cross-correlated. It was found that type II units had an inhibitory relation with type IV units in many cases. The extent of the excitatory type II area was within the inhibitory area of the type IVs, suggesting that type II/III units are interneurons in the DCN that contribute inhibitory terminals to type IV units. The interneuron status was verified by stimulating antidromically via the dorsal acoustic stria. Type IV cells could be so driven, implying they are projection neurons (i.e., fusiform and giant cells), while type II units were almost never excited.

In an experiment where two independent electrodes were used (Voigt and Young 1988), it was demonstrated that type IV units have shared inputs only when their CFs are relatively close (<1/3 octave). The stimulus-driven correlation was hypothesized to be induced by a common shared input from type II units or from ANFs rather than derived from direct functional interconnection. The type II units are located predominantly in the deep DCN.

4. Comparative Studies

There are some interesting properties of the barn owl auditory system that have made it an exciting model for the study of sound localization, even in the mammalian auditory system (Knudsen and Konishi 1978). This is due to the importance of acoustic cues in the barn owl’s remarkable ability to localize prey in the dark. Having asymmetrical shaped ears, the barn owl auditory system has separate pathways for processing interaural timing and intensity information. These pathways begin in the avian homologues of the cochlear nuclei, nucleus magnocellularis (specialized for processing timing information used for lateralization along the horizontal azimuth) and nucleus angularis (adapted for intensity coding used for the determination of elevation). This has been demonstrated by Takahashi, Moiseff, and Konishi (1984) by first injecting lidocaine, an anesthetic, into nucleus magnocellularis and noting that while temporal coding disappeared, intensity coding in the neurons of the nucleus mesencephalalis lateralis dorsalis, the avian homologue of the inferior colliculus, was unaffected. The analogous experiment, conducted in nucleus angularis, indicated that this region is responsible for coding intensity, and has no effect on temporal activity. Nucleus magnocellularis has cells analogous to bushy cells, while nucleus angularis contains cells similar to chopper/stellate cells (Sullivan 1985). These choppers showed little or no phase locking and appear to resemble mammalian Cβ, rather than Cγ units in their response pattern. These differences suggest that stellate cells could possibly play a role in intensity encoding in mammals.

Certain ecologically specialized mammalian species, such as bats (Suga 1989), and nonmammalian families such as birds (Manley 1990), turtles, fishes, and insects (Popper and Fay 1980, 1991) offer valuable insights into the relationship between the structure and function of the hearing apparatus, including the cochlear nucleus and its phylogenetic homologues.

5. Physiological–Morphological Correlations

5.1 Overview

In much of the early work on CN physiology, population studies were combined with a knowledge of the cell-type distribution to infer physiological-morphological correlations (e.g., Morest et al. 1973). Over the past decade there has been an increasing emphasis placed on directly correlating physiological response properties of CN units with the underlying morphology. Although it was possible to infer some functional-morphological correlations in the past, firm correspondence between physiological response and cellular morphology in the CN was not fully established until the development of intracellular HRP-labeling techniques (Rhode, Oertel, and Smith 1983a; Rhode, Smith, and Oertel 1983b; Rouiller and Ryugo 1984; Smith and Rhode 1985, 1987, 1989). These studies demonstrated that the PL units correspond to spherically-bushy cells, PLα, globular bushy cells, choppers to stellate cells, onset units to multipolar, stellate cells (PVCN), and pauser-buildup units to fusiform cells. Rhode and colleagues based their conclusions on the physiological analysis of over 1200 neurons, all of which had complete response information (with attendant data on unit CF, Q10 threshold, etc.). Of this population, 80 were intracellularly labelled with HRP, making the physiological-morphological correspondence nearly definitive. These associations are supported, in general, by the results of Rouiller and Ryugo (1984), as well as by the tissue-slice studies of Oertel and colleagues (1988). A pictorial summary of the morphological correlations in the cochlear nuclei is shown in Figure 3.7 in three transverse sections through the CN. A couple of cells are superimposed in each section, along with the axon pathway.

5.1.1 Primary-Like (VCN)

Spherical bushy cells are the predominant cell type in the AVCN. Large spherical cells are located in the rostral pole of the AVCN and appear to be primarily low-CF units. The reason for this low-frequency bias is
by virtue of the "secure" endbulbs of Held (the AN-spherical cell synapse). Therefore, it is likely that their activity plays an important role in localization based on interaural time cues (Erulkar 1972).

Rhode, Oertel, and Smith (1983a) succeeded in labeling spherical bushy cells. All of them were classified as primarylike units on the basis of their physiological responses. Roullier and Ryugo (1984) reported that some of the bushy cells that they labelled were not primarylike. One was physiologically a chopper unit. Two others were classified as "on" units. Thus, it is possible that the correspondence between cellular morphology and physiological response may not be as straightforward for the spherical bushy cells as Rhode, Smith, and Oertel (1983b) originally suggested. However, there is ancillary evidence from tissue-slice studies in support of the bushy cell/primarylike correspondence. A large number of cells have been labelled by Oertel and colleagues in the mouse AVCN (e.g., Wu and Oertel 1984). The bushy cells always displayed a characteristic current-voltage or I–V relationship that is quite distinct from that exhibited by stellate cells. In view of the relationship between the I–V curve and physiological response properties described above, it would appear that most, if not all, busy cells respond like PL units.

The "on" units studied by Roullier and Ryugo (1984) may, in fact, correspond to globular bushy cells which are concentrated in the nerve-root area of AVCN. The globular bushy cells exhibit a PLw response pattern (Smith and Rhode 1985). These cells can have a large onset-to-steady-state ratio, which makes them appear similar to onset units. However, they can be distinguished by large intracellularly recorded EPSPs that are considerably greater in magnitude than observed in onset units. The large EPSPs correlate well with the large presynaptic structures, which are modified (reduced in size) calyces. The number of ANF afferents innervating a globular bushy cell appears to vary between one and four, based on both physiological (spontaneous and maximum discharge rate, see Figure 13 in Rhode and Smith 1986a) and morphological criteria (Lorente de Nó 1981). It is also known that the large calyces of Held, the ultrasecure synaptic connections onto cells in the MNTB, originate from these cells, the axons of which project to the LSO (Friau and Ostwald 1988; Smith et al. 1990). An alternate estimate of the convergence of ANFs onto globular bushy cells, based on the count for each, is 17:1 (Spirou, Brownell, and Zidanic 1990). This estimate would suggest that modified calyces are rather small, and assumes that every ANF has approximately three modified endings (Roullier et al. 1986) and contact globular bushy cells.

5.1.2 Choppers

Chopper units appear from the morphological evidence to be stellate cells. Rhode, Oertel, and Smith (1983a) found there to be at least two distinct stellate morphological patterns. For one of these the dendritic arboriza-
tion branched quite heavily. The other type had little branching and smoother dendrites. The first type of dendritic pattern is associated with physiological chopping responses that are considerably less regular (i.e., the ISIH modes are relatively broad and have higher CVs) than those derived from the small branched variety of cells in which the ISIH mode is narrow. These differences may correlate with the $C_4$ and $C_6$ response patterns respectively. Oertel, Wu, and Hirsch (1988) and Wu and Oertel (1984) have found in the brain-tissue slice that stellate cells exhibit a chopping response when activated by intracellular depolarization. The chopping behavior almost certainly originates in the membrane properties of the soma and in the integrative properties of the dendritic arborization (Young et al. 1988).

5.1.3 Onset Units

Several distinct physiological response patterns can be distinguished among onset units in the PVCN ($O_b$, $O_c$, $O_{cb}$, $O_{hb}$), the DCN ($O_{bc}$, $O_b$) and in the AVCN, based on the response to sinusoidal stimuli. The correlation between physiological behavior and cellular morphology is, in general, less secure than for primarylike and chopper cells, due to the small number of labelled cells. We have recently noted that there are some cells in the deep layer of the DCN that exhibit a pauser pattern with a precisely timed first-spike response (Rhode and Greenberg 1992a). The PSTH pattern of these units looks similar to onset units. However, they differ from onset units in that their dynamic range of response is very large, similar to that of $O_b$ units of the PVCN. However, they differ from $O_c$ in that they lack an early chopper pattern. Instead, they exhibit a pauser pattern and have prominent inhibitory sidebands. On the basis of these distinctions we are fairly confident that this unit population represents a separate physiological class. However, none of these $O_c$ units have been labelled, and thus the underlying cellular morphology remains unknown. One HRP-labeled octopus cell from the OCA of the PVCN responded like an $O_b$ unit (Rhode, Oertel, and Smith 1983). Only one other octopus cell has been reported as labelled from this region. This neuron exhibited an $O_b$ pattern of response (Rouiller and Ryugo 1984), and its soma was considerably smaller than that of the $O_b$ unit. Together with the extracellular recordings of Godfrey, Kiang, and Norris (1975a,b) in the OCA, the correspondence between octopus cells and onset pattern appears to be relatively secure, though more labelled cells are required to place this association on firmer ground.

The firmest morphological-physiological correspondence among the onset units has been established for the $O_{bc}$s. These units are morphologically associated with the large, multipolar, stellate cells of the anterior portion of the PVCN. The $O_c$ units are distinctive in several respects. They are much less frequency selective than other CN neurons, indicating that they receive a broad tonotopic range of AN inputs. Their dynamic range of response is considerably greater than ANFs and other CN units. These properties suggest that these cells receive a projection of ANFs with CFs spanning a broad range of frequencies, in contrast to all other CN unit types whose frequency selectivity is comparable to ANFs.

$O_{bc}$, like other onset units are capable of phase locking to low-frequency sinusoids with exquisite precision, having synchronization coefficients (SC) as high as 0.99. An SC of zero implies no phase locking whatever and a value of one implies perfect synchrony (see Goldberg and Brown 1969). Some of these units are capable of firing once per stimulus cycle up to frequencies of 1.1 kHz (although the upper limits of temporal entrainment are more typically 400–600 Hz). A subset of onset cells, generally with high CFs, do not entrain to low-frequency sinusoids, and may be a function of the unit's filter characteristics or isointensity response curve (i.e., the tail component of the response area receives too little input from the low-frequency afferents to produce the necessary coherent temporal excitation). $O_c$ cells appear to be unique in their ability to integrate synaptic activity over a wide dynamic range. The EPSPs are small with maximum amplitude of 4 mV, and the membrane time constant is very short. Both of these properties may determine entrainment capability.

A large, multipolar stellate cell, along with response measures that physiologically classify it as an $O_c$, are illustrated in Figure 3.8. Often, any one of the three features illustrated in Figure 3.8A's response area (receptive field), PSTH, or rate-intensity function at CF is sufficient to classify a cell as an onset chopper. The dendrites of the cell extend from the ventral border of the CN all the way to the granule cap region of the DCN, in a manner that contacts ANFs spanning a broad range of CFs. The topographic organization of the CN appears to be based on isofrequency bands that are located in the horizontal plane of the PVCN as indicated by the dashed lines (viewed in transverse sections of the CN, e.g., Leake and Snyder 1989). The $O_c$ dendrites cut across a range of frequencies, but not across the entire tonotopic axis.

The dendrites of $O_c$ multipolars are of large diameter (4–8 µm) and are relatively unbranched, suggesting that synapses on dendrites are electrotonically close to the soma. EM studies show that round, pleomorphic, and flat vesicle synapses cover the soma, and synapses with pleomorphic vesicles predominate on the initial segment (Rhode and Smith 1986a). The dendrites do not appear to be heavily covered with synapses. However, the size of the dendritic tree indicates that there is 10–20 times more surface area on the $O_c$ dendrites than on the soma. Even if the AN synaptic density on $O_c$ dendrites appears significantly less than on the soma, the large dendritic field can provide a prominent ANF input via this pathway. The axons of large, multipolar stellate cells have an extensive collateral field in both the PVCN and DCN, and exit the nucleus.
via the intermediate acoustic stria. The synaptic boutons originating from the axons contain pleomorphic vesicles, which may indicate that these cells serve to inhibit the activity of cells onto which they project. Interestingly, $O_C$ units, show no evidence of inhibitory inputs nor of discharge suppression or hyperpolarization of the membrane potential.

Because of their low degree of frequency selectivity (i.e., small $Q_{10}$ values) $O_C$ units probably do not play an important role in frequency coding in the traditional sense. However, on the basis of their extended dynamic range, these cells are capable of encoding intensity information across much of the biological range of SPLs on the basis of discharge rate. They have been shown to cover the entire tonotopic range in their CFs (Rhode and Smith 1986a). Onset choppers can also exhibit an exceptionally high degree of phase locking to low-frequency signals, as well as excellent temporal coding of amplitude modulation, even at high intensity levels (Rhode and Greenberg 1991b). Thus, these units may play an important role in encoding pitch and spectral maxima of complex signals, including speech (see Section 7).

5.1.4 Pauser/Buildup Units

The correspondence between physiological response and the cellular morphology of fusiform cells is, at first glance, less robust than for the other CN cell types. Of the 22 cells labelled by Rhode and Smith (1986b) 16 exhibited a buildup or pauser pattern of response. However, a number of units displayed PSTH patterns sensitive to such parameters as sound pressure level, duty cycle, stimulus offset, stimulus frequency and the level of the intracellular resting potential. It is likely that any fusiform cell is capable of exhibiting response behavior typical of pausers, buildups or choppers under appropriate stimulus conditions. For example, a chopper pattern is frequently superimposed on the buildup portion of the response. With sufficiently long recovery time between stimulus presentations (i.e., hyperpolarization reduced) many units respond like pausers. When the recovery time is reduced, the response pattern becomes similar
Table 3.1. Summary of morphological-physiological correlations in the cochlear nuclei.

<table>
<thead>
<tr>
<th>Location</th>
<th>Cell type</th>
<th>PSTH</th>
<th>RF type</th>
<th>Projection route</th>
<th>Target</th>
<th>Functional role</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVCN</td>
<td>Spherical/bushy</td>
<td>PL</td>
<td>I</td>
<td>VAS</td>
<td>cLSO, iLSO</td>
<td>localization</td>
<td>Adams (1976); Rhode, Smith, and Oertel (1983)</td>
</tr>
<tr>
<td></td>
<td>Stellate</td>
<td>C</td>
<td>III</td>
<td>VAS</td>
<td>DCN, ICC</td>
<td></td>
<td>Adams (1976), Cant (1981)</td>
</tr>
<tr>
<td></td>
<td>Stellate</td>
<td>O</td>
<td>I</td>
<td>VAS</td>
<td></td>
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<td>Roth et al. (1978)</td>
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<td>Smith et al. (1991)</td>
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<td>Rouiller and Ryugo (1984)</td>
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<td>Smith and Rhode (1989)</td>
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<td>Rhode, Smith, and Oertel (1983)</td>
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<td>Rhode, Smith, and Oertel (1983)</td>
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<td></td>
<td>Rouiller and Ryugo (1984)</td>
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<tr>
<td>PVCN</td>
<td>Multipolar</td>
<td>O, C</td>
<td>I</td>
<td>IAS</td>
<td></td>
<td></td>
<td>Rhode, Oertel, and Smith (1983)</td>
</tr>
<tr>
<td>Stellate</td>
<td>C</td>
<td></td>
<td>III</td>
<td>VAS</td>
<td></td>
<td></td>
<td>Smith and Rhode (1985)</td>
</tr>
<tr>
<td>Octopus</td>
<td>O, (O,?)</td>
<td>I/III</td>
<td></td>
<td>VAS/IAS</td>
<td></td>
<td></td>
<td>Kane and Finn (1977)</td>
</tr>
<tr>
<td>DCN</td>
<td>Fusiform</td>
<td>P/B/C</td>
<td>III, IV, V</td>
<td>DAS</td>
<td>cTCC</td>
<td></td>
<td>Lorente de Nó (1981); Mugnaini, Warr, and Osen (1980)</td>
</tr>
<tr>
<td>Giant</td>
<td>C</td>
<td></td>
<td>III</td>
<td>DAS</td>
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<td></td>
<td>Lorente de Nó (1981); Mugnaini, Warr, and Osen (1980)</td>
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<tr>
<td>Stellate</td>
<td></td>
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<td>II</td>
<td></td>
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<td>Lorente de Nó (1981); Mugnaini, Warr, and Osen (1980)</td>
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<tr>
<td>Vertical</td>
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<td></td>
<td>Lorente de Nó (1981); Mugnaini, Warr, and Osen (1980)</td>
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<td>Granule</td>
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<td>Lorente de Nó (1981); Mugnaini, Warr, and Osen (1980)</td>
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<td>Cartwheel</td>
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<td></td>
<td>Rhode and Greenberg (1991b)</td>
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<tr>
<td>Golgi</td>
<td></td>
<td>O,</td>
<td>II</td>
<td></td>
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</table>

*Based solely on physiological criteria*
(i.e., the lowest threshold population of ANFs) distributed over a relatively narrow CF range. Thus, it may be that fusiform cells serve as spectrally selective detectors of sound, optimized to respond at sound pressure levels below the threshold of other units in the CN and AN.

Fusiform cells also display interesting response properties in the presence of noise. Specifically, these units are capable of shifting the dynamic range of their response in the presence of relatively broadband noise signals, probably as a consequence of prominent inhibitory input on the flanks of the central frequency response region (Palmer and Evans 1982; Gibson, Young, and Costalupes 1983). Such response properties suggest that these DCN units also play a role in analyzing spectrally complex sounds in noisy backgrounds.

Fusiform cells project to the central nucleus of the inferior colliculus, a region thought to play an important role in binaural processing of sound (Adams 1976; Roth et al. 1978). The exquisite, spectrally selective sensitivity of these units is consistent with their playing a role in sound localization. In addition, it appears that certain acoustic features derived from pinna cues, such as frequency-specific, steep spectral notches, may provide important information for localization of sound (Musianct and Butler 1985). Many cells in the DCN are capable of precisely encoding such spectral notches as a consequence of their prominent inhibitory sidebands (Young et al. 1991). Thus, it is plausible that fusiform cells play some role in sound localization derived from monaural cues.

It is known from electron microscopic studies that the primary AN input to fusiform cells is on the basal dendrites, while the soma and axon hillock receive extensive inhibitory input (Smith and Rhode 1985). In the cat, all of the fusiform cell axons appear to send collaterals coursing through the DCN, projecting to the high-CF cells of that division. The synaptic boutons of these projections contain round vesicles, suggesting that these projections are excitatory in nature. In the mouse (Oertel, Wu, and Hirsch 1988) and guinea pig (Manis 1990) there are no such collaterals. The basis for this difference in cytoarchitecture remains obscure.

Rhode and colleagues (1983, 1986) administered sodium pentobarbital to anesthetize the cats used in their studies. This anesthetic is known to affect the function of inhibitory circuits, and therefore it was of interest to determine whether the response of DCN units were in any way changed in its absence. Rhode and Kettner (1987) found relatively little change in the responses of VCN units due to anesthesia. In the DCN, the range of unit response types recorded from without anesthesia were about the same as in the barbiturate preparation. However, the proportion of units showing strong inhibitory responses (type IV and V) was significantly higher in the unanesthetized preparation. Such observations are consistent with previous studies (Evans and Nelson 1973a,b; Young and Brownell 1976).

5.2 In Vitro Studies

In vivo intracellular studies of the cochlear nucleus have provided significant new information concerning morphological-physiological relationships (e.g., Rhode, Oertel, and Smith 1983a; Rhode, Smith, and Oertel 1983b), but are technically difficult to successfully execute, and produce relatively small amounts of data per experiment.

One means to obtain similar information, but with a much higher yield, is to record from tissue slices in vitro. Oertel and her colleagues have pioneered the use of this technique in the mouse cochlear nucleus, and have made a number of important observations about the membrane properties, cellular identity and neuropharmacology of CN cells in the process. The ability to record intracellularly for several hours from a single cell, while maintaining a stable physiological environment, is crucial for determining the membrane properties of CN cells.

The current-voltage (I-V) relation is fundamental for characterizing cell membrane properties. Oertel and colleagues (1988) have studied this relation for several cell types in the CN. In the AVCN, they found two distinct types of I-V characteristics. The first is relatively linear and is associated with stellate cells. These neurons discharge in a regular fashion when a depolarizing current is injected. From the physiological-morphological studies of Rhode, Oertel, and Smith (1983a), we know that these stellate cells correspond to chopper units.

The second form of I-V function is, in contrast, highly nonlinear. It would appear that ion channels open and lower the membrane resistance, thus shortening the membrane time constant and effectively maintaining the membrane voltage near the resting level so that the cell can respond to a second input rapidly. These cells have been identified as bushy cells corresponding to primary-like units (Rhode, Oertel, and Smith 1983a). These cells encode the temporal fine structure of the low-frequency waveforms quite accurately.

Representative I-V curves for a bushy and stellate cell are shown in Figure 3.9 along with the I-V curve for a DCN fusiform cell (Hirsch and Oertel 1988a,b). For the fusiform cell, a persistent sodium current was identified that outlasts EPSPs by a factor of ten. There are also prolonged after hyperpolarizations that extend the effects of synaptic activity. Such properties suggest that these cells are not particularly well adapted for encoding temporal fine structure of acoustic signals, although they do appear to encode waveform envelope information, as described below.

Tissue-slice experiments suggest that there may be a fast-acting inhibitory projection from the dorsal to the ventral division of the CN. Wickesberg and Oertel (1990) have suggested that this intrinsic circuit may be involved in the suppression of echoes. However, it will be difficult to test this hypothesis with current physiological techniques.

In a study of the parallel fiber system of the DCN originating in the granule cell layer, Manis (1989) used the tissue-slice preparation to es-
Within the past decade it has become increasingly common to use compartmental models in neuronal simulations (e.g., Segev, Fleshman, and Burev 1985). Banks and Sachs (1991) have presented a compartmental model for a chopper unit that employs voltage-sensitive conductances, and in which the ratios and locations of excitatory and inhibitory inputs may be manipulated.

As an increasing amount of information is available from both extracellular and intracellular recording, along with the detailed morphology and connectivity, these models will be increasingly important for providing a synthesis of available data and for spotting shortcomings in our knowledge. Young et al. (1988) have likened the initial period of study of the cochlear nucleus to “stamp collecting,” in that the focus has been on amassing a database of facts without much concern for integrating these data into a unified theoretical framework. The time may now be ripe for assembling information from anatomical, physiological and behavioral perspectives to provide a more coherent view of the functioning of the cochlear nucleus (e.g., Ainsworth, Hackney, and Evans 1991).

7. Coding of Complex Signals in the Cochlear Nuclei

Most of our knowledge concerning the coding of sound in the auditory periphery and cochlear nuclei has been based on the response of single neural elements to such noneoleological signals as sinusoids, clicks, and wideband noise. The sounds normally encountered by most vertebrates differ appreciably from these signals both spectrally and temporally. For example, amplitude and frequency modulation are common acoustic elements of the vocal repertoire of most vertebrate species (Sebeok 1968). Rapid changes in spectral maxima and overall intensity convey important information, both in animal communication and in human speech. The response patterns to such stimuli are difficult to infer from the response to spectrally simpler signals, as a consequence of various nonlinearities, such as lateral suppression, inhibition and rapid adaptation. To date, there have been relatively few studies of complex signal coding in the cochlear nucleus. Most of these have focused on amplitude modulation. However, spectral selectivity needs to be considered before temporal coding is discussed.

7.1 Spectral Selectivity in the Cochlear Nuclei

Spectral selectivity is traditionally measured by measuring a unit’s $Q_{10}$
Rhode and Smith (1986a,b) showed that the $Q_{10}$s of CN units are comparable to those of ANFs except for $O_C$ and $O_I$ cells. One may thus conclude that afferent convergence, per se, does not degrade spectral selectivity, as long as the inputs are from the same CF region of the auditory

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**Figure 3.9.** Current-voltage curves for three cell populations in the CN of the mouse. Each cell class has a distinctive I-V curve that is likely to reflect intrinsic membrane properties characteristic of its class. (Data adapted from Oertel, Wu, and Hirsch 1988.)

6. Models and Computational Simulations

Computers have come to play an increasingly important role in simulating the behavior of single neurons and neuronal ensembles. Early studies exploring the effect of afferent convergence on postsynaptic response properties demonstrated that several fibers synapsing on a postsynaptic element could result in regular discharge characteristics typical of choppers (Molnar and Pfeiffer 1966). In addition, it was demonstrated that the location and sequence of synaptic activation could reproduce CN unit response preference for one direction of frequency-modulated swept tone (Fernald and Gerstein 1972).
nerve. $O_c$ and $O_t$ units, by virtue of their poorer selectivity, receive inputs from ANFs of widely different CFs.

There are probably several mechanisms accounting for spectral selectivity in the CN. One factor is a narrow distribution of dendrites along the tonotopic axis, as has been reported for fusiform cells (Blackstad, Osen, and Mugnaini 1984). A second factor is the presence of inhibitory sidebands which restrict the extent of the excitatory frequency region, as has been demonstrated for some DCN units (Rhode and Greenberg 1991a). The high-frequency slope of the tuning curves of some DCN units can exceed 2000 dB/octave, a value far exceeding that observed in ANFs of comparable CF. The high-frequency slope increases in the presence of a background noise in some units, suggesting activation of an inhibitory input, particularly for Type II units (Rhode and Greenberg 1991a).

There is another possible role for inhibition in CN units, to effect a dynamic range shift in the presence of noise. With the limited dynamic range found in the majority of ANFs, it has always been difficult to explain how hearing occurs over the known psychoacoustic range (see Evans 1981), though Gibson, Young, and Costalupes (1985) and Viemeister (1988), among others, have developed models incorporating low-SR ANFs that have wider dynamic ranges and higher thresholds than the more populous high-SR ANFs. The presence of noise presents a further confounding factor since it has the effect of limiting the dynamic range of ANFs by effectively increasing their background discharge rate. There is some degree of dynamic range shift that probably results from lateral suppression in the cochlea. However, these latter effects may not be sufficient to solve the dynamic range problem. Neural inhibition may act to bias the output of a CN cell so that suitable signal-to-noise ratios will result in functional rate encoding of signals. For example, the masked rate curves for an AN fiber and a $C_T$ unit are compared in Figure 3.10. Noise doesn't cause much of a response shift to higher intensities in the ANF, in contrast, the $C_T$ unit does shift in proportion to the noise level. Various shift patterns in rate-intensity function are seen (Fig. 3.5C, 3.6C), with some $O_t$ and PL units showing no range shift and others, notably type II (which respond weakly to noise), exhibiting either large range shifts (Fig. 3.10B) or no shift at all in the operating point, as seen for the $O_c$ (type II) unit in Figure 3.10C.

**Figure 3.10.** Masked rate-intensity curves for two CN units and an auditory nerve fiber evoked by CF tones. Noise spectrum level ($N_o$) in dB/Hz is varied as indicated. (A) MRCs for a high-SR ANF (89026-3). CF = 27 kHz, TH = 22 dB SPL, $R_{sp}$ = 75 spikes/sec. (B) MRCs for a $C_T$ unit (88384-15). CF = 18 kHz, TH = 10 dB, $R_{sp}$ = 0 spikes/sec. $C_T$ unit showed a weak response to wideband noise. (C) MRCs for an $O_c$ unit (88355-2). CF = 1.35 kHz, TH = 47 dB SPL, $R_{sp}$ = 0 spikes/sec.
These results are largely in agreement with those of Palmer and Evans (1982), and sharply contrast with the results of Gibson, Young, and Costalupes (1985). The latter used a different paradigm, consisting of a continuous noise background that was gated on 20 sec before data collection. Other outstanding factors include the fact that a decerebrate animal was used, the intensity was varied in a pseudorandom fashion and 200-msec tones were presented. They found under these conditions that (1) ANFs exhibited a sufficient range adjustment to explain CN behavior, (2) only DCN type IV units showed a significantly enhanced dynamic range shift, and (3) discharge rate is an adequate code for conveying fine intensity discriminations in the presence of noise maskers. This disparity in results could be the consequence of the difference between decerebrate and anesthetized preparations, or the possible activation of the efferent system.

7.2 Amplitude-Modulated Tones

The response of onset and chopper units to amplitude-modulated, non-speech signals appears to be generally consistent with their responses to low-frequency sinusoidal signals (e.g., Moller 1972, 1974, 1976; Fernald and Gerstein 1972). Frisina, Smith, and Chamberlain (1990a) computed the modulation transfer function (MTF) for onset and chopper units in the PVCN by recording the response of neurons to sinusoidally amplitude-modulated tones and noise.

The MTF is a measure of the coding of the AM envelope, or modulation frequency. In this chapter, we use the MTF based on the synchronization coefficient as defined by Goldberg and Brown (1969). A distribution with the shape of a halfwave rectified sinewave would have a value of .785, while one corresponding to the envelope of a 100 percent sinusoidally modulated signal would have an SC of 0.5.

MTFs vary as a function of intensity, modulation and carrier frequency, unit type and background noise. Six sets of MTFs are illustrated in Figure 3.11. The modulation transfer functions for ANFs are low pass in shape, with a maximum value around 0.75, and cutoff frequency (defined as the modulation frequency at which the SC drops below 0.1) between 2.0 and

(Figure 3.11, continued) tones, where the carrier was equal to the unit CF. The modulation depth = 100%. Stimulus duration = 100 msec. Repetition interval = 300 msec, unless otherwise indicated. (A) High-SR AN fiber, unit 8893-128, CF = 9.3 kHz, TH = 27 dB, Rsp = 0 spikes/sec. (B) Primary-like, unit 89001-34, CF = 13 kHz, TH = 30 dB, Rsp = 82 spikes/sec. (C) Sustained chopper, unit 91039-19, CF = 10.6 kHz, TH = 12 dB, Rsp = 0.8 spikes/sec. (D) Transient chopper, unit 88043-20, CF = 9.2 kHz, TH = 22 dB SPL, Rsp = 0 spikes/sec. (E) Onset chopper, unit 89001-41, CF = 11 kHz, TH = 40 dB, Rsp = 0 spikes/sec. (F) Buildup, unit 88899-14, CF = 7.3 kHz, TH = -4 dB, Rsp = 0 spikes/sec.
2.5 kHz (e.g., Fig. 3.11). For ANFs the magnitude of the MTF is greatest at low intensities, and systematically decreases as the AM level increases. Usually the magnitude of the MTF drops below significance (SC < 0.1) by 40–50 dB above threshold for ANFs, with the MTFs decreasing faster for high-SR ANFs. The peaks of the MTFs are lower for high-SR ANFs than for low-SR units (Rhode and Greenberg 1992a). The waveform envelope is uniformly well encoded across modulation frequencies ranging up to 1.0–1.5 kHz (depending on unit CF and filter bandwidth).

Many CN units have lowpass MTFs at low stimulus intensities. However, the MTFs of most CN units become bandpass as intensity increases. This is apparent for the PL unit in Figure 3.11. This pattern is often seen for PL_n and O_l units. However, there are also PL, PL_n and O_l units that have low-pass MTFs at all intensities.

Chopper units phase lock poorly to pure tones, yet may phase lock very well to the AM envelope (f_m). They are more likely than any other unit response type to exhibit a bandpass MTF. The MTFs of nearly all C_s units and 50 percent of C_T units are bandpass in shape (see Fig. 3.11C,D). The MTFs are more likely to be bandpass as the intensity is increased to more than 20 dB above threshold. C_s units generally have broader bandpass MTFs than sustained choppers.

C_s units exhibit the narrowest bandpass MTFs of any unit response class in the CN (Kim, Siriani, and Chang 1990; Rhode and Greenberg 1992b). For many of these units there appears to be a high correlation between Best Modulation Frequency (BMF = f_m) and the chopping frequency of the cell under sinusoidal stimulation (Greenberg and Rhode 1986; Kim, Siriani, and Chang 1990). However, the relationship does not apply to all C_s units (Blackburn and Sachs 1989; Rhode and Greenberg 1992b). Among C_s units, BMF often varies with SPL at low and moderate intensities, a fact that has potential implications for models of AM encoding based on spatiotopic location.

O_l units have lowpass MTFs and cutoff frequencies nearly as high as those of ANFs (Fig. 3.11E). O_c units also exhibit the least reduction in the magnitude of their MTF and higher SPLs. However, this statement should be qualified since O_c, C_s, and C_T units are all nearly equal in this respect (see Fig. 3.12). O_c units encode AM better at high intensities than other unit types, a possible consequence of their wide dynamic range and higher rate threshold.

The pauser-buildup units of the DCN can phase lock exceedingly well to low-frequency AM signals, which is surprising in view of their poor synchronization to sinusoidal stimuli of comparable frequency. While the absolute magnitude of the MTFs is generally lower for DCN units, they often exhibit little degradation at higher SPLs (Fig. 3.11F), perhaps as a result of the prominent inhibition seen in the DCN.

The relative sensitivity to increasing AM level can be determined by comparing the magnitude of MTFs at either the BMF or a frequency lower than the corner frequency (for a low-pass MTF) as a function of normalized intensity. This is shown in Figure 3.12 for six unit categories, where the average SC across units is shown. There is almost no overlap in the values between the CN units and the AN curves, even if one considers only the low-SR ANFs. The other major point to note is that O_c, C_s, and C_T units cluster together, with O_l showing superior performance near their threshold. Modulation sensitivity for O_l, (and PLs, which are not shown) lie between the ANF curves and that of the O_c and chopper units. On average, they are less sensitive to increasing stimulus levels, and can encode AM at higher levels than ANFs. The average SC level for DCN units is about 0.5 and varies little with intensity. We may thus specify a hierarchy of low-frequency AM encoding capability among these different unit types as: O_c > C_s > C_T > DCN > O_l > PL = low-SR ANF > high-SR ANF.

One of the more remarkable aspects of hearing concerns the ability to process accurately sounds in background noise and under competitive
acoustic conditions. Thus, we can attend to and decode a single voice out of many, focus on an individual acoustic element against a cascade of noise, etc. It is therefore of interest to ascertain the AM encoding capabilities of CN units and ANFs under conditions which approximate the everyday acoustic conditions in which we typically listen.

The AM-synchronized response of ANFs is appreciably reduced in the presence of intense noise. In Figure 3.13 is shown the effect of presenting increasing levels of a wideband noise concurrently with an AM tone on the MTF of an O\textsubscript{c} unit. When the SPL of the AM signal is relatively low (30 dB SPL in Fig. 3.13A) increasing the noise level has the effect of decreasing the overall level of the MTF. At higher AM intensities, the noise has virtually no effect on the temporal response over the range of noise levels shown in the inset of Figure 3.13B. In contrast, rate saturation induced by the noise, in combination with the signal, will blur or obliterate any peaks in the cochlear place dimension. Thus, AM synchronization will generally be more resistant to potentially disruptive effects of noise than a rate-place representation would be, thus being more capable of preserving information in a noisy environment (Rhode and Greenberg 1992b).

An alternate perspective on this phenomena is shown in Figure 3.14. By comparing AM spike-rate curves to SC rate curves it would appear that even after the rate-intensity function has been flattened by the noise background signal, phase locking continues to provide precise temporal information about the signal’s modulation characteristics. This noise immunity for modulation encoding is seen in other unit types as well, especially among choppers and DCN units.

The robust encoding of AM information in CN units probably relies on very different mechanisms. Onset choppers generally have a wide dynamic range of response, are not very frequency selective, and manifest little or no lateral inhibition. Thus, O\textsubscript{c} units are probably capable of encoding AM at high SPLs for two reasons. First, as a consequence of their extended dynamic range there will be little or no rate saturation to compress the modulation-synchronized component of the response. Second, because of the broad tonotopic range of AN projections there will typically be a significant number of unsaturated ANF afferents encoding the modulation characteristics across a wide range of intensities. These two mechanisms are probably related. DCN units, on the other hand, have a limited dynamic range of response, and are relatively sharply tuned

(Figure 3.13 continued) of the AM signal = 30 dB. At this intensity the level of the wideband noise has an appreciable effect on the ability of the unit to synchronize to the modulation frequency. (B) Sound pressure level of the AM signal = 70 dB. At this higher intensity level the noise has virtually no impact on the unit’s MTF.
The AM encoding capability of three major CN unit response classes is compared with that of ANFs in Table 3.2. There does not appear to be a unique pattern of features, such as synapse location, dynamic range, inhibition, etc., that is correlated with superior AM encoding capability. However, there is generally superior AM coding CN compared to the AN. Two outstanding AM coding features among CN units are: (1) the improved coding at higher SPLs and (2) the preservation of temporal information among many units in the presence of intense background noise.

### 7.3 Frequency Modulation

Frequency modulation (FM) is a common property of vocal communication signals. In human speech, frequency modulation is observed in the formant transitions between consonantal and vocalic segments (e.g., Flanagan 1972). FM rates of 10 kHz/s are common in speech formant transitions. Human listeners appear to be exquisitely sensitive to FM. For a center frequency of 2 kHz the difference limen (Δf/f) is approximately 0.17 percent (Kay 1982). Zwicker (1952) found that FM detectability is poorer than that of amplitude modulation at low FM rates, but is superior to AM at higher modulation frequencies. Kay and Mathews (1972), based on psychophysical studies using adaptation techniques, suggest that amplitude and frequency modulation are processed in separate channels for human listeners. They have also suggested that there may be separate mechanisms for FM rates above and below 100 Hz.

Frequency modulation coding has been studied in the cochlear nucleus by Moller (1972) and by Fernald and Gerstein (1972). There is some

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**Table 3.2. Summary of morphological and physiological properties for three principal cochlear nucleus unit response classes.**

<table>
<thead>
<tr>
<th>Location</th>
<th>Onset choppers</th>
<th>Choppers</th>
<th>Pauser/buildup</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cell type</td>
<td>PVCN Multipolar</td>
<td>Throughout CN Stellate</td>
<td>DCN Fusiform</td>
</tr>
<tr>
<td>AN synapse location</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soma</td>
<td>+ + +</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Dendrites</td>
<td>+ +</td>
<td>+ +</td>
<td>+ + (Basal)</td>
</tr>
<tr>
<td>Q0, re AN</td>
<td>&lt;</td>
<td>=</td>
<td>&gt;</td>
</tr>
<tr>
<td>Dynamic range</td>
<td>30–80</td>
<td>20–30</td>
<td>Nonmonotonic</td>
</tr>
<tr>
<td>Inhibition</td>
<td>0</td>
<td>+ +</td>
<td>+ + +</td>
</tr>
<tr>
<td>Synchrony (re AN)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max freq (sinusoid)</td>
<td>&lt;</td>
<td>&lt;</td>
<td>&lt;&lt;</td>
</tr>
<tr>
<td>Max synth (sinusoid)</td>
<td>&gt;</td>
<td>&lt;</td>
<td>&lt;&lt;</td>
</tr>
<tr>
<td>Max synth (AM)</td>
<td>&gt;&gt;</td>
<td>&gt;</td>
<td>&gt;&gt;</td>
</tr>
<tr>
<td>Latency (first spike)</td>
<td>+ &lt;</td>
<td>&gt;</td>
<td>&gt;&gt;</td>
</tr>
<tr>
<td>standard deviation</td>
<td>&lt; &lt;</td>
<td>&lt;</td>
<td>&gt;&gt;</td>
</tr>
<tr>
<td>waveform prop encoded</td>
<td>Period</td>
<td>Envelope</td>
<td>Envelope</td>
</tr>
</tbody>
</table>
degree of variability among unit types in response to FM stimuli. However, only the O₁ and O₂ units exhibit a marked difference to the direction of an FM, linearly swept tone (Rhode and Greenberg, unpublished observations). The directional asymmetry in the response can be as much as 30 to 1, and in either direction. It is difficult to ascertain the significance of this asymmetrical sensitivity to FM in these units due to the relatively small number of units studied.

7.4 Speech

7.4.1 Rate-Place Information

In their original study of the auditory nerve response to speech, Sachs and Young (1979) concluded that rate-place information was unlikely to play an important role in encoding the vocalic spectrum, as a consequence of rate saturation among the majority of ANFs at moderate-to-high sound pressure levels. They have more recently reassessed their dismissal of rate-place encoding (Sachs et al. 1986; Winslow, Bart, and Sachs 1987) on the basis of the responses of fibers with low (<10 spikes/sec) spontaneous activity. The response of these low-SR fibers does not show pronounced rate saturation. The rate-place profile of the formant pattern based on this restricted population of fibers (~35 percent) provides a representation in which spectral peaks are more clearly delineated than in the case for high-SR units, perhaps as a result of lateral suppression (Schalk and Sachs 1980). Despite their relatively small numbers (16 percent), the lowest SR group (<0.5 spikes/sec), may exert a significant influence on the response of cochlear nucleus neurons if their innervation pattern is more extensive than that of their high-SR counterparts (Fekete et al., 1982). Blackburn and Sachs (1990), in fact, suggest that the rateplace representation observed in the response of AVCN choppers at high sound pressure levels may reflect the predominant input of the low-SR fibers, with perhaps some further sharpening of the spectral representation derived from lateral inhibitory interactions. The crossed olivocochlear bundle may also serve to increase the dynamic range of the ANF input, particularly under conditions of low signal-to-noise ratio (Winslow, Bart, and Sachs 1987) and thereby sharpen the rate-place-based spectral representation in the unanesthetized animal.

7.4.2 Synchrony-Place Information

Blackburn and Sachs (1990) have compared the synchrony-place (average localized synchronized rate—ALSR) representation of PL and chopper units in the AVCN with that obtained in the auditory nerve (Young and Sachs 1979) for the synthetic vowel [ε].

The temporal representation of the vocalic spectrum (formants one through three) observed in the auditory nerve was relatively well pre-served in the response of PL units, but not in choppers, which failed to synchronize to frequencies above 1 kHz (in the range of the second and higher formants for most vowels). Although there does appear to be an ALSR representation in the response of AVCN chopper units it does not appear to be as well delineated as in the auditory nerve. This degradation may be the result of a number of extraneous factors, such as the smaller samples size and pooling results across animals imposed on recording conditions in the cochlear nucleus.

The limited phase-locking potential of central auditory neurons raises a number of questions concerning the relevance of temporal information for the encoding of the speech spectrum. Beyond the MSO, neurons rarely synchronize to frequencies above 1 kHz (Yin and Kuwada 1984). What happens to synchrony information associated with frequencies in the range of the second and higher formants, which is so well encoded in the activity of ANFs? Perhaps this information is used solely for binaural analysis associated with sound localization and is dispensed with at higher levels. But is it not also conceivable that such temporal information is transformed into a different representational form, perhaps at the level of the cochlear nucleus? What is the manner in which such timing information is transmitted to the chopper and onset units of the VCN, and what is the nature of the stimulus transformations which occur as a result of these neurons' "emergent" properties?

7.4.3 Synchrony- and Rate-Based Information Derived from Onset Units

Onset units typically respond to low-frequency signals as if each waveform form were a separate stimulus, each spike being precisely timed with respect to the stimulus period. The variance of discharge relative to the stimulus cycle is comparable to that of the first-spike latency (τ ~ 100 μsec). This precision of firing, coupled with relatively low frequency selectivity suggests that these units may act as coincidence detectors, sensitive to the precise timing of multiple inputs.

If onset units act as coincidence detectors, they would be particularly responsive to an input driven by common synchrony over a relatively broad tonotopic range. With the probability of discharge proportional to the number of synchronous inputs (and these inputs derived from fibers covering a broad CF range), the spike rate would increase, up to some limit, as the tonotopic extent of the common synchrony (or latency) increased. The frequency of the formant could be recovered from the interspike interval (due to entrainment, the interspike interval would almost always be the reciprocal of the stimulus frequency). Evaluation of this model awaits detailed systematic study of the onset unit response to speech. Preliminary studies indicate that among the onset population of the PVCN, O₂ and O₃ units typically phase lock to f₀ and first formant
8. Development

It is of interest to establish whether the neuronal response properties observed in the mature cochlear nucleus are the result of genetically programmed hard wiring, or are rather the result of experiential learning and adaptation to the acoustic environment during the earliest weeks of life. If such properties as filter bandwidth, inhibitory sidebands, phase locking, temporal response patterns and receptive field types are present in the immature CN then it would appear that these features of auditory function are determined by preprogrammed neuronal wiring and membrane properties. On the other hand, the extent to which these properties change over the course of the early stages of life provides some measure of the importance of external stimulation on shaping the detailed aspects of auditory function.

In this regard, it is interesting to note that the basic shape of neural response areas and their associated temporal response patterns for chopper, pause, buildup and onset units appear as early as the second postnatal week (Brugge, Javel, and Kitzes 1978; Brugge and Connor 1984). From these observations Brugge and Connor (1984) concluded that only ANFs and a few interneurons and centrifugal fibers in the CN are necessary to account for the response patterns in the adult. If this speculation proves correct this would raise some serious questions concerning the role played by late-developing descending and intrinsic inputs in the functioning of the CN.

There are several general principles in auditory development, some of which have been established in extensive studies of the avian auditory system by Rubel (1985). He states, “the major central nervous system pathways for the processing of auditory information are established, and probably become functional, independent of tonic peripheral influences. Following the onset of receptor function, normal CNS development requires an intact cochlea and auditory nerve. The onset and maturation of peripheral auditory function does not appear to be activated by a single event, or trigger. Instead, there seems to be a highly regulated synchrony of the final stages of differentiation both at the cochlea and in the central nervous system.” There is also some evidence of a correlation between behavioral and physiological measures of sensory coding.

Rubel has also presented a model for the development of tonotopic organization in the avian cochlea and higher auditory stations. Initially the cochlea responds only to low-frequency stimuli, but as the system develops over the first weeks of life the basal region responds to progressively higher frequencies and at the same time the lower frequencies progressively simulate more apical regions of the cochlea. Harris and Dallos (1984) have added evidence that an analogous principle of tonotopic development occurs in the mammalian auditory system. Using glucose uptake in the auditory nucleus of gerbils Ryan, Woolf, and Sharp (1982) showed that the region that responded maximally to 3-kHz tone shifted in a manner compatible with the Rubel model.

9. Summary

The last ten years have witnessed a significant expansion of our knowledge concerning the physiology and morphology of the cochlear nuclei. Physiological response properties have been defined along two dimensions: temporal response patterns and receptive field analysis. Neither appears to be uniquely correlated with specific cellular field analysis. Within the context of Lorente de Nó's (1981) morphological descriptions, the correlations are relatively modest in number. However, many of the cell types in Lorente de Nó's work are small intrinsic interneurons and difficult to label. It is the projection neurons of the CN that are of greatest interest since they are the conduit for the information transmitted to the higher centers. Most of the projection neurons have been extensively studied, though a more extensive database of physiologically characterized and labelled cells would be valuable.

Spectrotemporal characterizations of neuronal behavior have been obtained from all divisions of the CN. In addition, there have been forays into the study of complex signal processing. Responses to AM signals
indicate that the pitch of a harmonic complex can be temporally coded by the nervous system. In fact, nearly every neuron in the CN is capable of encoding modulation information in terms of temporal response properties. Envelope information must be important for signal/source identification. Further, many CN cells encode envelope information better than ANFs, both in quiet and in noise.

Some of these features probably arise from lateral inhibitory mechanisms and/or the convergence of ANFs over a range of CFs. Lateral inhibition must play a role in preserving frequency selectivity of the peripheral system or possibly improving on it. The inhibition is also likely to affect the dynamic range shift seen in several cell types, especially DCN neurons and many PVCN choppers. This dynamic-range adjustment allows these cells to rate-encode stimuli by shifting their operating range above the background noise, in a manner analogous to the way the retina adjusts to the ambient light level.

Some of these response properties are undoubtedly crucial in the processing of complex signals such as, species-specific vocalizations, environmental sounds, and speech. They could also be important for the localization of wideband stimuli. However, at this stage of our knowledge, we are far from understanding the actual mechanisms that underlie these complex processes.

Key studies are being conducted that will identify many of the membrane channels and receptor types. These studies employ brain slice and dissociated cell preparations. Voltage and patch clamping of identified cells may also lead to a fundamental expansion of our knowledge.

The CN offers a complex neuronal structure at a relatively peripheral level for study. It may play a role in acoustic processing analogous to that of the retina in vision. It has both a parallel and a hierarchical structure, with multiple intrinsic pathways and multiple inputs originating from lower and higher levels in the auditory pathways.

Abbreviations

Anatomical Regions

AN auditory nerve
AVCN anteroventral cochlear nucleus
CN cochlear nucleus
DAS dorsal acoustic stria
DCN dorsal cochlear nucleus
IAS intermediate acoustic stria
LSO lateral superior olive
MNTB medial nucleus of the trapezoid body
MSO media superior olive

OCA octopus cell area
PVCN posteroventral cochlear nucleus
SOC superior olivary complex
VAS ventral acoustic stria
VCN ventral cochlear nucleus

Physiological Response Types

ANF auditory nerve fiber
B buildup
C chopper
C₅ sustained chopper
C₇ transient chopper
O₀ onset chopper
O₁ onset graded
O₂ onset inhibitory
O₇ onset locker
Oₓ onset-like (DCN)
P pauser
PL primarylike
PLₙ primarylike-with-notch
PLₙₕ sustained primarylike

Physiological Response Parameters

ALS average localized synchronized rate
BMF best modulation frequency
BW₁₀ bandwidth at 10 dB above rate threshold
CF characteristic frequency
CV coefficient of variation = σₛ⁄μₛ
DR dynamic range = saturation SPL—threshold SPL
FTC frequency threshold curve
L-V current—voltage
ISIH (IH) interspike interval histogram
IRC isorate contour
M monotonic
MRA masked response area
MRC masked rate curve
MTF modulation transfer function
NM nonmonotonic
NRC noise rate-intensity curve
PSTH poststimulus-time histogram
Q₁₀ CF/BW₁₀
RA response area
RC rate-intensity curve
RF  receptive field
R_{max}  maximum discharge rate
R_{n}  noise-induced rate
R_{sp}  spontaneous discharge rate
S_{sup}  suppression bandwidth
SC  synchronization coefficient
spikes/sec  spikes per second
SR  spontaneous rate
TH  threshold
WBN  wideband noise

Stimulus Parameters
AM  amplitude-modulated or amplitude modulation
dB  decibel
FM  frequency-modulated
F_{mod}  modulation frequency
Hz  hertz = cycle per second
N_{s}  noise spectrum level in units of dB/Hz
SPL  sound pressure level re 20 pascals
msec  milliseconds
\mu sec  microseconds

Miscellaneous
HRP  horseradish peroxidase
mV  millivolt
nA  nanoamp

References

3. Physiology of the Cochlear Nuclei


