Regularity and Latency of Units in Ventral Cochlear Nucleus: Implications for Unit Classification and Generation of Response Properties

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SUMMARY AND CONCLUSIONS

1. The responses of neurons in the ventral cochlear nucleus (VCN) of decerebrate cats are described with regard to their regularity of discharge and latency. Regularity is measured by estimating the mean and standard deviation of interspike intervals as a function of time during responses to short tone bursts (25 ms). This method extends the usual interspike-interval analysis based on interval histograms by allowing the study of temporal changes in regularity during transient responses. The coefficient of variation (CV), equal to the ratio of standard deviation to mean interspike interval, is used as a measure of irregularity. Latency is measured as the mean and standard deviation of the latency of the first spike in response to short tone bursts, with 1.6-ms rise times.

2. The regularity and latency properties of the usual PST histogram response types are shown. Five major PST response type classes are used: chopper, primary-like, onset, onset-C, and unusual. The presence of a prepotential in a unit's action potentials is also noted; a prepotential implies that the unit is recorded from a bushy cell.

3. Units with chopper PST histograms give the most regular discharge. Three varieties of choppers are found. Chop-S units (regular choppers) have CVs <0.35 that are approximately constant during the response; chop-S units show no adaptation of instantaneous rate, as measured by the inverse of the mean interspike interval. Chop-T units have CVs greater than 0.35, show an increase in irregularity during the response and show substantial rate adaptation. Chop-U units have CVs >0.35, show a decrease in irregularity during the response, and show a variety of rate adaptation behaviors, including negative adaptation (an increase in rate during a short-tone response). Irregular choppers (chop-T and chop-U units) rarely have CVs >0.5. Choppers have the longest latencies of VCN units; all three groups have mean latencies at least 1 ms longer than the shortest auditory nerve (AN) fiber mean latencies.

4. Chopper units are recorded from stellate cells in VCN (35, 42). Our results for chopper units suggest a model for stellate cells in which a regularly firing action potential generator is driven by the summation of the AN inputs to the cell, where the summation is low-pass filtered by the membrane capacitance of the cell.

5. Units with primary-like, primary-like-with-notch, and unusual PST histograms give the most irregular discharge (CVs >0.5); the CV is usually constant during the stimulus, or may decrease with time. All primary-like units and many primary-like-with-notch and unusual units show substantial rate adaptation during the stimulus. These irregular unit types have the shortest latencies in the VCN; their mean latencies are usually <1 ms longer than minimum mean AN latencies. The small group of onset and onset-C units studied have short latencies, like primary-like units, and may give regular or irregular discharge (CVs from 0.3–0.7).

6. The regularity and latency of the irregular units (primary-like, primary-like-with-notch, unusual, and some onset units) are all about the same. These unit types are proba-
bly all recorded from bushy cells in VCN, because prepotentials are only seen in the action potentials of these irregular unit types. This conclusion is supported by the results of HRP injection studies (35, 42, 44). The behavior of irregular units probably results from their specialized synaptic connections from small numbers of AN fibers. Their irregularity is consistent with a model in which each arriving AN spike is capable of producing a spike in the VCN cell. One difference among units in this group is the sharpness or precision of their onset responses, as measured by the standard deviation of first spike latency. This difference can be explained by assuming a convergence of different numbers of AN fibers onto bushy cells, with the sharpness of the onset response increasing rapidly as more inputs converge. A difference of only two to three in the number of inputs is sufficient to cover most of the range of latency standard deviations found in this study.

INTRODUCTION

The cochlear nucleus (CN) is the terminal zone of the fibers of the auditory nerve (AN; 24, 30, 34). There are at least six major classes of principal cells in the CN, most of which can be subdivided into two or more subtypes (see Ref. 7 for a review). Correspondingly, single unit studies of the CN have revealed a rich variety of different response types that recode the discharge patterns of AN fibers in various ways (see Ref. 54 for a review). Significant progress has been made over the last 10 years in associating the various physiological response types with morphological cell types. This effort has been driven by the assumption that the widely divergent morphologies of various CN cell types should correspond to significantly different patterns of recoding of AN spike trains (18, 27). It follows from this assumption that knowledge of the correspondence of morphological cell types and physiological response types should be helpful in formulating hypotheses about the information processing functions of CN cells and in interpreting the results of studies of signal processing in the CN.

The responses of cells in the ventral cochlear nucleus (VCN) are usually divided into three classes: chopper units, primary-like units, and onset units. There is general agreement that chopper responses are recorded from one of the VCN principal cell types, the stellate cells (1, 35, 42). There is more uncertainty about the relationships of the remaining response types to cell types. A second principal cell type, the bushy cells (3, 24), have been shown to give primary-like responses (1, 31, 35, 42) as well as some varieties of onset responses (42, 44). On the basis of this apparent diversity of response types from bushy cells, it has been suggested that the basic assumption of a close correspondence of structure and function in VCN may need to be reexamined (42). Moreover, there is evidence that onset responses are recorded from other cell types, including octopus cells, stellate cells, and giant cells in the posteroverentral cochlear nucleus (PVCN; 13, 35, 37, 42).

Part of the uncertainty in correlating physiological response types with morphological cell types is that the techniques for characterizing physiological response types have not kept pace with morphological techniques, particularly intracellular HRP injection, for identifying details of cellular anatomy. Physiological characterizations are based primarily on PST histograms of responses to short tone bursts (1, 13, 32). Although there is little reason to doubt the fundamental validity of many of the distinctions based on PST histograms, such as the distinction between chopper and primary-like units and the identification of the primary-like-with-notch subclass of primary-like units, there are situations in which ambiguities in the PST scheme become problematic. The ambiguities derive from the arbitrary nature of some of the distinctions that are made. In most cases, distinctions between PST histogram types are made on the basis of features that consistently appear in PST histograms. Although some of these features, such as chopping and notches, have been as-

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1 We use the term "stellate" to refer to cells that are called stellate cells in Golgi studies (3) and multipolar cells in Nissl studies (29). These seem to be the same cells (6, 48). The term "stellate" has been used generally in studies correlating morphology and physiology (35, 47, 53) because HRP injection gives a Golgi-like image of the neurons.
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associated with physiological properties of cells, others, such as the distinction between onset units with high sustained discharge rates and primary-like units with low sustained discharge rates, are arbitrary. These arbitrary distinctions are treated differently by different workers and have not been associated convincingly with physiological or morphological characteristics of cells. Moreover, there appear to be marginal cell types that are not easily fit into any one of the standard classes. The problems raised by ambiguities in the PST classification scheme are especially severe in studies, such as those in which cells have been marked with intracellular HRP injection, where it is critical to classify the responses to sound of particular units, as opposed to generalizing about the properties of large groups of units.

The characterization of CN units would be improved if additional tools for the analysis of response properties were available to supplement PST histogram analysis. Ideally, these tools should reveal features of responses that can be related to morphological and membrane properties of cells. In this paper, we present characterizations of VCN unit responses using two measures, regularity of discharge and first-spike latency, that seem to reveal aspects of synaptic processing in cells that are not revealed by PST histograms.

Regularity is a property of spike trains that varies significantly between AN fibers, which are irregular (19), and CN units, which can be either regular or irregular (33). Thus regularity is a direct measure of a major change in response properties between AN and CN. Previous investigations have demonstrated differences in regularity correlated with subdivision of the CN, PST histogram response type, and receptive-field type (1, 12, 13, 15, 38, 46). Similar results have been obtained in the superior olivary nuclei (17, 50). Moreover, regularity seems to be a stable property of units' responses that changes little with changes in stimulus frequency or sound level (14, 16, 50). Thus regularity promises to be both a sensitive and stable characterization of units' responses. Previous studies have analyzed regularity by constructing interval histograms of, usually, steady responses. In this paper we use a new method, suggested by Bourk (1), that can track the temporal evolution of regularity in nonstationary responses. This method allows establishment of a direct relationship between regularity of discharge and PST histogram pattern, where both measures are computed from transient responses to brief stimuli.

First-spike latency has also been shown to be a useful way of characterizing units (11–13, 18). In an elegant study, van Gisbergen and collaborators (12) concluded that first-spike latency can be used as an index of a cell's "integration time", meaning the time required to summate input activity to a level sufficient to produce an output spike. Integration time defined in this way is correlated with other response characteristics, such as PST histogram type and response map type. Thus first-spike latency promises to be another useful probe of input/output processing in cells.

In this paper we show that regularity and latency can be used to clarify the definitions of the major VCN response types, as based on PST histograms. Regularity and latency are shown to be powerful tools for analysis of issues such as the interrelationships of the various PST response types that are recorded from bushy cells. Finally, regularity and latency are shown to provide new insights into the response characteristics of all types of VCN units.

METHODS

Preparation, recording methods, and histological reconstruction

The data for this paper are taken from the same 21 experiments as the data used in an earlier paper on CN response types (43). The preparation is described in that paper. Briefly, adult cats with clean ears were decerebrated while maintained in a state of areflexia with ketamine. Anesthesia was then discontinued and the animals were not paralyzed. In the first eight experiments, the bulla was not opened but was vented with a length of small-bore polyethylene tubing. In the remaining experiments, the bulla and septum were opened to allow electrical stimulation of the AN with extracochlear electrodes. The CN was exposed from a posterior approach in all but five experiments; this approach allows direct exposure of the CN without aspirating any cerebellum. In the remaining experiments, the bulla and septum were opened to allow electrical stimulation of the AN with extracochlear electrodes. The CN was exposed from a posterior approach in all but five experiments; this approach allows direct exposure of the CN without aspirating any cerebellum. In three experiments, the CN was approached dorsally after some cerebellum was aspirated to allow a direct approach to the anteroventral CN (AVCN). In the remaining two experiments, recordings were
made in the AN after exposing it by retracting the cerebellum. One AN experiment was done on a decerebrate cat and the other on a cat anesthetized with pentobarbital sodium.

Platinum-iridium microelectrodes with platinized tips were used to record in the CN. In most experiments, the electrodes entered the CN at the surface of the dorsal cochlear nucleus (DCN) and passed through the nucleus from caudal to rostral along a sagittal plane, eventually reaching the VCN. In experiments in which cerebellum was aspirated, the electrodes entered the AVCN directly in a dorsoventral direction. Glass micropipettes filled with 3 M NaCl were used to record from AN fibers.

After the recording session, the cats were anesthetized with pentobarbital sodium and killed by transcardial perfusion with 10% Formalin. The CN was prepared histologically as has been described previously (43). Where possible, electrode tracks were reconstructed and recording sites localized. In cases where recording tracks could not be reconstructed histologically, they could usually be divided into a DCN portion and a VCN portion on the basis of depth from the surface and tonotopic organization (2, 41). Data reported in this paper come only from units in the VCN. Columns 2-4 of Table 1 give the locations of 77 units that were histologically localized. Thirty-four additional units were localized only to the extent of being in the VCN (5th column of Table 1).

Acoustic stimuli

An electrostatic driver was coupled to the ear through a 13-cm-long eartube (45). In each experiment acoustic calibrations were done at the ear-drum using a calibrated probe tube. The acoustic system has a flat frequency response, which typically fluctuates ±5 dB over the frequency range 20 Hz–20 kHz. Examples of acoustic calibrations for this system have been published previously (9, 52). The stimuli used for the analyses in this paper are 25-ms tone bursts at the best frequency (BF) of the unit. The rise/full times of the tone bursts’ trapezoidal envelopes are 1.6 ms; the 25-ms duration stretches from the beginning of the rise of the envelope to the beginning of its fall. Tone bursts are presented once every 200 ms. The electronic switch is turned on at constant stimulus phase, so phase-locking can be seen in PST histograms. The acoustic system has a delay of 0.55 ms between the synchronizing pulse used to mark the start of the stimulus and the beginning of the rise of the envelope of the tone bursts (measured at the tip of the eartube with the eartube terminated by an acoustic resistance approximately equal to the characteristic impedance of the eartube). This delay is mostly acoustic delay in the eartube, but also includes an 0.1-ms delay in the electronic switches. Because of the delay, the stimulus envelope begins at 0.55-ms latency on the abscissa of the PST histograms shown below, and 0.55 ms should be subtracted from the latency measurements in this paper, in order to calculate the true latency of response.

When a unit was isolated, its BF and threshold were estimated. BF is the frequency at which the unit gives a response, either excitatory or inhibitory, at the lowest sound level. Data for plots of discharge rate versus sound level (rate-level functions) for BF tones and noise bursts were taken. Next, the unit’s pattern of response to tone bursts at BF was studied using the short tone burst stimuli described above. Usually, 500 repetitions of

<table>
<thead>
<tr>
<th>PST Type</th>
<th>AVCN</th>
<th>ANR</th>
<th>PVCN</th>
<th>Other VCN*</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chop-S</td>
<td>10</td>
<td>2</td>
<td>9</td>
<td>13</td>
<td>34</td>
</tr>
<tr>
<td>Chop-T</td>
<td>3</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Chop-U</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>Other chopper†</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Primary-like</td>
<td>14 (9)</td>
<td>0</td>
<td>5 (1)</td>
<td>4</td>
<td>23 (10)</td>
</tr>
<tr>
<td>Pri-N</td>
<td>4 (3)</td>
<td>4 (4)</td>
<td>3</td>
<td>3 (3)</td>
<td>14 (10)</td>
</tr>
<tr>
<td>Unusual</td>
<td>3 (2)</td>
<td>0</td>
<td>3 (1)</td>
<td>0</td>
<td>6 (3)</td>
</tr>
<tr>
<td>Onset‡</td>
<td>4</td>
<td>0</td>
<td>1</td>
<td>4 (1)</td>
<td>9 (1)</td>
</tr>
<tr>
<td>Onset-C</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Phase-locked</td>
<td>4 (1)</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>5 (1)</td>
</tr>
<tr>
<td>Total</td>
<td>45 (15)</td>
<td>6 (4)</td>
<td>26 (2)</td>
<td>34 (4)</td>
<td>111 (25)</td>
</tr>
</tbody>
</table>

Nos. in parentheses are nos. of units with prepotentials. AVCN, anteroventral cochlear nucleus; ANR, auditory nerve root; PVCN, posteroventral cochlear nucleus. *Other VCN means location not determined histologically, but unit localized to VCN (as opposed to DCN) using tonotopic organization and depth from surface; †other choppers are choppers with very low discharge rates (chop-L of Ref 1); ‡does not include 5 onset units with type IV response characteristics.
each stimulus were presented. Sound levels covered the range from 10 dB above threshold to 50 dB above threshold.

Unit classification, prepotentials and PST histograms

AN fibers are classified according to spontaneous rate (23), as follows: low spontaneous rates are < 1 spike/s; medium spontaneous rates range from 1 to 19 spikes/s; and high spontaneous rates are above 19 spikes/s.

The action-potential waveform of each CN unit was digitized at a sampling rate of 50 kHz and averaged. The averaged waveform was examined for prepotentials (1, 31). Prepotentials are (usually) positive deflections that precede the action-potential discharge of a cell by roughly 0.5 ms. They vary in size from large potentials that can be individually triggered to small potentials that can only be revealed by averaging. Examples of averaged prepotentials are shown by the arrows at upper right in Fig. 5 and in Fig. 6, B, E, and F. Prepotentials are thought to be the discharge of the presynaptic terminals on bushy cells (1, 22, 31) and are used in this study as evidence that a unit recording is made from a bushy cell. The numbers in parentheses in Table 1 show the numbers of prepotential units of each response type.

PST histograms are computed from the short tone burst data using a bin width of 0.1 or 0.2 ms. The discharge patterns revealed in these PST histograms are classified according to the definitions given by Bourk (1), Godfrey et al. (13), and Rhode and Smith (38). Figures 2–6 and 8 show examples of the classes used; these figures illustrate typical modes of response for units in the different classes. The following definitions are used in this paper. Primary-like PSTs show an onset response peak followed by a smooth decline in rate to a more or less steady value that exceeds 100 spikes/s (Figs. 2C and 6A). A similar group of units have PSTs with a notch, or short cessation in firing, immediately after the onset peak; the notch is brief, lasting from 0.5 to 2 ms. This pattern is called primary-like with notch (1) and is abbreviated pri-N below (Figs. 5, B, C, and D and 6, B and C). Chopper PSTs show regularly spaced peaks of discharge that are not related to the stimulus waveform, i.e., are not phase-locking (Figs. 2D, 3, and 4). Onset PSTs have a sharp peak at stimulus onset that is followed by little or no sustained activity (<100 spikes/second). Onset-C units exhibit a precisely timed onset spike, which is followed by brief chopping and then by a steady discharge (37, 38). Onset-C units have very wide dynamic ranges (up to 80 dB) and respond at discharge rates well above 100 spikes/s. Few onset-C units were encountered; data from onset-C units are shown in population plots but are otherwise not discussed in detail. Unusual PST histograms have onset peaks and a sustained response >100 spikes/s; they show a variety of behaviors during the transition between onset and steady state (Fig. 6, D, E, and F) which are, strictly speaking, neither primary-like nor chopper. This classification was used in a previous paper (43) to refer to a group of units whose PST histograms do not fit into any of the other categories. We do not feel that unusual units are a separate class, and evidence will be offered that these units are closely related to pri-N units. A small number of units could not be classified into any of the above groups because of phase-locking (5 units). The rows in Table 1 summarize the unit types in the data sample of this paper.

The criterion for the onset response type used here (steady-state rate <100 spikes/s) is arbitrary; we have chosen to assign a unit to the onset group only if its steady-state discharge rate is too low to allow regularity analysis. An arbitrary criterion was used because there appears to be a continuum of response types between pri-N and one kind of onset response, called On-L; units are differentiated along this continuum only by steady-state discharge rate (38, 44). Moreover, both pri-N and On-L response types are recorded from bushy cells (38, 42, 44). Therefore, it does not seem possible to make a meaningful sharp distinction between onset and pri-N. The evidence does not support lumping all onset units with pri-N units, however, and that is not the intent of this classification scheme; rather, because onset units are not a concern in this study, no attempt has been made to subdivide them further. Units classified as onset in this study correspond to very low-rate On-L units and to onset types with essentially no steady discharge, such as the On-I (13, 38), On-A, On-G, and On-P (1) categories.

Data were not recorded from units that were injured, as evidenced by high rate injury discharges or substantial fluctuations in response properties during the recording time. However, action-potential waveshapes differ for the various response types, raising the possibility of electrode effects on response characteristics. Primary-like, pri-N, and unusual units usually have negative, monophasic action potentials (83% of units), whereas chopper units frequently have positive-negative biphasic action potentials (61% of chop-S

2 The numbers of various response types in Table 1 of this paper differ slightly from the numbers in Table 1 of our previous paper (43). Five onset units with type IV response maps were deleted from the sample because they resemble dorsal cochlear nucleus units in most of the features of their responses. Seven primary-like, unusual, and onset units were reclassified as pri-N units. Finally, two units originally classified as unusual and one onset unit were moved to the onset-C category, which was not used in our previous paper.
units, 36% of chop-T and chop-U units). However, there is no difference between the regularity properties (analyzed as in Fig. 7) of chopper units with negative monophasic action potentials and those with positive-negative biphasic action potentials. Because there is no difference, we conclude that action-potential shape differences reflect electrophysiological differences between neuron types and do not necessarily imply incipient injury; data are included in this paper regardless of action-potential waveshape.

For our previous study, units were classified in terms of the prevalence of excitatory and inhibitory regions in their response maps. These classes are not considered in this paper, but units' response map types are given in figures. The classes relevant to this paper are as follows: type I—no inhibitory sidebands; type III—inhibitory sidebands present; and type I/III—insufficient spontaneous activity to allow testing for inhibitory sidebands (see Refs. 43 and 54 for detailed definitions of these types).

**Regularity analysis**

The regularity analysis is illustrated schematically in Fig. 1; it is based on an analysis first reported by Bourk (1). In this analysis, the mean and standard deviation of interspike intervals are computed as a function of the time of occurrence of the first spike in the interval. The calculation is done as follows. The time axis is divided into 0.1- or 0.2-ms bins with the first bin starting at the stimulus synchronizing pulse. Interspike intervals \( i_j \) are computed and interval values are placed in time bins according to the latency of the first spike in the interval. This process is repeated for a large number of stimulus presentations (500 in this paper). The mean \( \mu_R \) and standard deviation \( \sigma_R \) of the \( i_j \) in each bin are computed using Eq. 1 below. The interval values are numbered differently in Eq. 1 and Fig. 1. For Eq. 1, let \( i_{ij}, i = 1, \ldots, N_j \) be the intervals falling in the \( j \)th bin, i.e., the intervals whose initial spikes have latencies between \((j - 1) \Delta \) and \( j \Delta \), for a histogram with binwidth \( \Delta \). In the histogram of Fig. 1, for example, \( i_3 \) would be number 111, \( i_5 \) would be numbered 115, \( i_8 \) would be numbered 125, etc. The mean and variance for the \( j \)th bin are then

\[
\mu_{Rj} = \frac{1}{N_j} \sum_{i=1}^{N_j} i_{ij} \tag{1a}
\]

and

\[
\sigma_{Rj}^2 = \frac{1}{(N_j - 1)} \sum_{i=1}^{N_j} (i_{ij} - \mu_{Rj})^2 \tag{1b}
\]

The regularity plots in Figs. 2–6 show \( \mu_{Rj} \) and \( \sigma_{Rj} \) plotted as functions of time. Data are plotted only from bins containing at least three intervals \( (N_j > 3) \). For units with spontaneous activity, there is a substantial transient in regularity plots associated with the increase in discharge rate at stimulus onset. This transient is not shown in the plots in this paper; instead, regularity data are plotted only for latencies at and beyond the onset peak in the PST histogram.

A useful measure of regularity (actually of irregularity) is the coefficient of variation \( \text{CV} \), which is the ratio of the standard deviation of a random variable to its mean. In this case \( \text{CV} = \sigma_R/\mu_R \). \( \text{CV} \) is larger for irregularly discharging neurons and is smaller for regularly discharging neurons. Plots of CV versus time \( (\text{CV}_j = \sigma_{Rj}/\mu_{Rj}) \) are computed and displayed in the insets of the regularity analysis figures.

Intervals are included in the analysis if they are completed, i.e., the second spike in the interval occurs, with a latency of <50 ms. This means that some intervals that span the end of the 25-ms tone burst are included in the averages. Examples of this end effect are shown later in the paper (Fig. 2); the end effect produces a bias in the values of \( \mu_R \) and \( \sigma_R \), moving their values away from accurate estimates of values for driven activity toward values appropriate for spontaneous activity. The results of the end effect depend on the amount of spontaneous activity. In units without spontaneous activity, there are no intervals spanning the end of the response, so the main effect of the finite burst duration is to place a limit on the length of intervals included in the analysis; that is, there can be no intervals in an analysis bin at time \( t_j \) longer than \( T - t_j \), where \( T \) is the time at which the response to the stimulus terminates. The elimination of these long intervals results in underestimates of \( \mu_R \) and \( \sigma_R \). In units with spontaneous activity, the effect of finite burst duration is to increase \( \mu_R \) and \( \sigma_R \) in later bins, because of contamination of the interspike interval samples by longer intervals occurring partially at the spontaneous discharge rate.

The end effect is largest for irregular units firing at low discharge rates. The interspike interval distributions in these cases have long tails that are curtailed by the finite analysis window. Simulations of irregular spike trains using a Poisson process with deadtime (14, 47, 55) were used to estimate the magnitude of the bias in irregular units. Although effects on \( \mu_R \) and \( \sigma_R \) can be large (up to

3 Irregular spike trains are simulated by a deadtime modified Poisson process (14, 47, 55). Spike trains from a Poisson process are modified by deleting spikes that occur within a deadtime \( t_D \) of a previous spike. The deadtime models refractoriness and is chosen to be 1.2 ms for all the simulations in this paper. This model duplicates many features of the interspike interval statistics of AN fibers responding to short tone bursts (47, 55). AN fibers are as irregular as the most irregular CN units (Fig. 7).
Figure 1. Top: a stimulus burst. Second and third lines show spike trains that result from presentation of 2 stimulus bursts. Spikes occur at times $t_i$; intervals between spikes, $4$, are indicated by $\Delta t$. Bottom line shows accumulation of interval values in a histogram. Tick marks delineate histogram bins, which are 0.1 or 0.2 ms wide (bins not shown to scale in this figure). Interval $i_j$ is placed in histogram bin in which the interval's initial spike $t_j$ is located, as long as the interval is completed by another spike at time $t_{j+1}$, such that $t_{j+1} < 50$ ms. This process is repeated for (usually) 500 repetitions of the stimulus, then mean and standard deviations of the $i_j$ values in each bin are computed (Eq. 1).

In interpreting the results of regularity analysis, it is useful to know something about the underlying interval distributions. For example, a large $\sigma_R$ can result either from an irregularly discharging neuron with a Poisson-like interval distribution or from a neuron with a very regular discharge, which alternates between two interval lengths, a long one and a short one, giving a bimodal interval histogram. All the units analyzed in this paper have unimodal interval histograms of the types described previously for the cochlear nucleus (1, 26, 33, 38).

The unit types analyzed in this paper respond at steady discharge rates over the course of long stimulus sequences of the type used here. Substantial nonstationarity of discharge rate, meaning rate changes exceeding $\pm 10\%$, is seen in only 7% of the cases analyzed in this paper (21/309). The largest rate change is $-31.6\%$. In all but one case, the change is a rate decrease, consistent with adaptation. These rate decreases are accompanied by increases in $\mu_R$ and $\sigma_R$, as expected. However, no consistent effect (increase or decrease) on $CV = \mu_R/\sigma_R$ is observed, probably because the small change in CV expected from an increase in $\mu_R$ and $\sigma_R$ (16) is masked by scatter in the data. Data from all cases, including cases with the nonstationarities described above, are included in the scatter plots of this paper.

Latency analysis

The latency analysis is based on the first spike occurring in response to each tone burst. The measures used in this paper are the mean ($\mu_{lat}$) and standard deviation ($\sigma_{lat}$) of first spike latencies (not corrected for acoustic delay). In units without

+17% or $-45\%$ for rates at the lower end of the range in Fig. 7), the effects on $CV$ are smaller (up to $+16\%$ or $-25\%$). The end effect is small or nonexistent in regularly firing units, because these units usually do not have spontaneous activity (1) and because their regularity allows few intervals that are substantially longer than the mean interval to occur, so there is less limiting of the interval histogram by the finite analysis window.

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Latency analysis

The latency analysis is based on the first spike occurring in response to each tone burst. The measures used in this paper are the mean ($\mu_{lat}$) and standard deviation ($\sigma_{lat}$) of first spike latencies (not corrected for acoustic delay). In units without
spontaneous activity, the first spike in the response can be taken to be the first spike occurring after the stimulus onset synchronizing pulse. In spontaneously active units, however, a spontaneous spike may occur during the latent period. To eliminate these spikes, a cursor is aligned by eye on the beginning of the rise of the onset peak of a PST histogram of the response; $\mu_{\text{lat}}$ and $\sigma_{\text{lat}}$ are computed from the first spikes occurring after the time marked by this cursor. A potential problem with this method is that the latency may be prolonged by refractoriness in cases where a spontaneous spike occurs immediately before the cursor. To check for a refractory effect, latency calculations are done two ways: using the first spike after the cursor for all stimuli and using the first spike after the cursor only when there is no spike (i.e., no spontaneous spike) during the time between the stimulus onset synchronizing pulse and the cursor. These two measures differ by $<5\%$.

More sophisticated approaches to the problem of measuring latency have been devised (11, 12, 25). These are based on the cross-correlation of a pseudorandom noise stimulus, or modulation of the stimulus, and the response. The result is an impulse response or first Weiner kernel for the unit from which latency can be determined as the time of occurrence of the first noticeable rise of the cross-correlation function. The cross-correlation methods do not seem to measure the same time delay as first-spike latency, in that they show little change in latency with stimulus level (12, 25) and do not seem to include the temporal integration period that is important in differentiating unit types in VCN (12). Thus first-spike latency is a better measure for the purposes of this paper.

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**FIG. 2.** A and B show regularity analyses for a primary-like unit (left) and a chopper unit (right). C and D show PST histograms for the same units. In regularity plots, $\mu_R$ is the mean interspike interval, $\sigma_R$ is the standard deviation of interspike intervals, and CV is the ratio $\sigma_R/\mu_R$; $\mu_R$, $\sigma_R$, and CV plots smoothed with a 3-bin wide triangular filter. Bins plotted only if they contain at least 3 spikes; bins plotted from the onset peak of the PST histogram out to latency of 27 ms only. i in CV plot of A marks change in CV associated with end effect.
RESULTS

Differences between primary-like and chopper units

Figure 2 shows data from a primary-like unit and a regularly firing chopper unit, which illustrate the major differences between these two response types. Figure 2C is the PST histogram of the primary-like unit and Fig. 2D is the PST histogram of the chopper. The regularity analyses for these two units are shown in Fig. 2A and B, on the same time scale as the PST histograms.

The regularity analysis of the primary-like unit (Fig. 2A) clearly shows the irregularity of discharge of this unit. The standard deviation of intervals (dashed line) is between 60 and 100% of the mean (solid line) throughout the burst. Although the values of mean and standard deviation increase significantly during the stimulus burst, their ratio stays roughly constant, except for an onset transient, for latencies between the beginning of the response and ~20 ms.

At 20 ms, there is an increase in CV, due mainly to an increase in $\sigma_R$; the point of the increase is marked by an arrow in the inset CV plot. This increase is caused by the end effect discussed in METHODS, i.e., by intervals that span the end of the response to the stimulus and therefore represent a mixture of responses at two different discharge rates. To see that such composite intervals are included, assume that the average values of $\mu_R$ and $\sigma_R$ between 12 and 20 ms latency are accurate measures of interspike intervals during the steady portion of the response. These average values are 4.99 and 3.91 ms, respectively. The PST histogram shows that the response ends at a latency of ~28 ms, and the increase in variability occurs about one mean interval plus one standard deviation ($4.99 + 3.91 = 8.9$ ms) before that. Thus, at about 19–20 ms latency, intervals more than 1 SD longer than the mean interval must extend beyond the end of the response. For times beyond 20 ms, intervals that span the end of the response are an increasing fraction of the total in each bin, and the portion of each interval generated at the spontaneous rate of the unit, i.e., the portion of the interval extending beyond the end of the response, also increases. By the end of the response, $\mu_R$ and $\sigma_R$ approach estimates of the parameters of spontaneous activity. The increase in $\mu_R$ and $\sigma_R$ after 20 ms reflects the lower discharge rate of spontaneous activity.

The regularity analysis for the chopper unit (Fig. 2B) shows a regular discharge: $\sigma_R$ is around 20% of $\mu_R$ throughout the burst. Once again, the CV (inset) is fairly constant, although a small increasing trend is apparent. There is also an end effect due to intervals reaching the end of the response, which shows up as a decrease in $\mu_R$ and $\sigma_R$ at approximately the points indicated by the arrows in Fig. 2B. In this case, the decrease in $\mu_R$ and $\sigma_R$ occurs because of the lack of spontaneous activity, so that longer intervals are eliminated from the computation of $\mu_R$ and $\sigma_R$ near the end of the response.

The end effects shown in Fig. 2 are seen, to some extent, in all units. To minimize the influence of end effects on the results, analyses are routinely done only up to 20 ms latency, and regularity data are shown only up to a latency of 20 ms in the remainder of this paper. This limit makes the end effects small, in the sense that the analysis window is at least $\mu_R + \sigma_R$ away from the end of the response, for an irregular unit (e.g., CV = 0.7) discharging at rates >212 spikes/s and for a regular unit (e.g., CV = 0.3) discharging at rates >163 spikes/s (in both cases, we assume that the response lasts to ~28 ms latency). It will be clear from the results presented below that the end effect does not limit the usefulness of regularity as a means of discriminating CN unit types. The end effect mainly limits the accuracy of estimation of true parameters of spike trains.

Figure 2 shows a number of characteristics of primary-like and chopper responses, other than their degree of regularity. The mean interval plots ($\mu_R$) show that there is a difference in the degree of rate adaptation in the two units. The mean interspike interval of the primary-like unit increases substantially through the burst (Fig. 2A), whereas the mean interval of the chopper increases only slightly (Fig. 2B). The mean interval curve for the primary-like unit is roughly equal to the inverse of the PST histogram, up to 20 ms latency; thus these two measures of discharge rate agree as to the behavior of adaptation. In contrast, the chopper’s mean interspike intervals change only slightly up to the end effect, showing that there is little adapta-
tion of instantaneous discharge rate. The lack of adaptation is not immediately evident from the chopper's PST histogram where the clustering of spikes at certain latencies appears to give a higher discharge rate near the beginning of the stimulus burst.

Note that the mean interspike interval for the chopper in Fig. 2B is between 3 and 3.5 ms, which is approximately equal to the time interval between peaks in the PST histogram in Fig. 2D. This correspondence suggests that a spike occurs in each peak in the PST histogram during each stimulus burst. This one-spike-per-peak behavior can be verified by direct calculation. In the case of the unit in Fig. 2, there was a spike during the first peak in the PST histogram (latencies between 3.2 and 5.8 ms) on 100% of the stimulus bursts; there was a spike in the second peak (5.8–8.8 ms) on 96.8% of trials and a spike in the third peak (8.8–11.8 ms) on 91.1% of trials. This calculation shows that the chopper response pattern is very repeatable, in that it consists of an almost identical pattern of spikes, one in each peak in the PST histogram, during every stimulus burst. Responses to successive bursts differ in that interspike intervals, and therefore spike latencies, are jittered slightly, as is measured by \( \sigma_R \). The jittering is reflected in the PST histogram by the decay of chopping during the burst. Chopping is not observed in the PST histogram after the third or fourth peak because the accumulated jitter of interspike intervals makes the variance of the latency of the fifth and later spikes large enough to blur the chopping.

The data in Fig. 2 are typical of primary-like units and of a large subgroup of choppers. This group of choppers correspond to the chop-S category of Bourk (1); they are called chop-S units or regular choppers in this paper. The differentiation of regular and irregular choppers is discussed below.

**Characteristics of chopper units**

Figure 3 shows data at four sound levels from another regular chopper unit. At the higher sound levels, these data are very similar to those shown for the chopper in Fig. 2. In fact, they are typical of the whole group of regular choppers recorded in the VCN. Regularity (values of \( CV \) <0.35) and small amounts of rate adaptation (i.e., only slight increases in \( \mu_R \) during the response) are the defining characteristics of regular choppers.

Of the 51 choppers included in this study, 34 are regular choppers.

At low sound levels, regular choppers may or may not show chopping in their PST histograms. In the case of the unit in Fig. 3, chopping is not observed at 10 dB above threshold (\( \theta +10 \); Fig. 3A) but is seen at higher levels. Even though the PST histogram does not show chopping at \( \theta +10 \), the unit gives a regular discharge, as measured by \( CV (CV = 0.32) \). Because of the low rate of this unit, it is possible that the regularity analysis is incorrect because of the end effect and that this unit actually has an irregular discharge at \( \theta +10 \). The size of the end effect can be estimated by comparing \( \mu_R \) with the inverse of the discharge rate in the steady portion of the PST histogram. The inverse of average rate should be an unbiased estimator of \( \mu_R \) (10). In Fig. 3A, the average discharge rate in the PST histogram between 12 and 20 ms is 65.7 spikes/s, giving a "true" mean interval of 15.2 ms. \( \mu_R \) from the regularity analysis averages 11.2 ms over the same time, showing that there has been limitation of long intervals by the finite duration of the response. By comparison, the true interspike interval for the data in Fig. 3B, where intervals are short enough to minimize the end effect, is 3.64 ms (1/275 spikes/s) versus \( \mu_R = 3.84 \) ms from the regularity analysis.

An indirect check on \( \sigma_R \) can be made by assuming that the unit is irregular and using the unbiased estimate of \( \mu_R \) derived from average discharge rate to simulate an irregular discharge. Values of \( \mu_R \) and \( \sigma_R \) can then be computed from the simulated spike trains for comparison with the values obtained from the neural data. In the case of Fig. 3A, \( \mu_R \) and \( \sigma_R \), measured by regularity analysis from simulated spike trains with mean rate 64.8 spikes/s (theoretical \( \mu_R = 15.4 \) and \( \sigma_R = 14.2 \) ms), are 5.92 and 3.01 ms, showing the strong end effect expected for a low-rate irregular discharge. By contrast, the values determined from the chopper's spike train are 11.2 and 3.55 ms, confirming that the unit is not irregular in this case.

Forty percent (12/30) of the regular choppers in our sample did not show chopping PST histograms at \( \theta +10 \), but all of these had regular discharge, as judged from their CVs (\( \leq 0.4 \)). This behavior suggests that regularity
FIG. 3. PST histograms and regularity analyses for a regular chopper unit at 4 sound levels. Sound levels given as dB re $\theta$. Organization of plots same as in Fig. 2. Regularity data plotted only up to a latency of 20 ms.
FIG. 4  PST histograms and regularity analyses for 4 irregular chopper units. These illustrate the 2 major patterns of behavior of irregular choppers: chop-T units in A and B; chop U units in C and D. Figure layout as for Fig. 2.
of discharge is a characteristic of choppers' spike trains that can be independent of precision of first-spike latency, which is necessary to observe chopping in a PST histogram.

Figure 4 shows four examples of irregular choppers. Two broad subtypes of irregular choppers are seen in our sample. Data from the first type are shown in the top row of Fig. 4. These units are characterized by rapid chopping in their PST histograms. They differ from regular choppers in that they show substantial rate adaptation and increases in irregularity (CV) during the stimulus burst. They differ from primary-like units in that the choppers' CVs are not as large as those of primary-like units and in that the choppers' CVs increase substantially during the stimulus burst, whereas the CVs of primary-like units are usually approximately constant after a brief onset transient. Although Bourk (1) did not explicitly compute CVs, it is clear that this type of irregular chopper corresponds to his chop-T category and they will be referred to as chop-T units below. Six of 51 choppers in our sample were of this type.

The lower half of Fig. 4 shows data from two irregular choppers of a different type. This is a rather diverse group of units. They may or may not show rate adaptation; in fact they may show substantial increases in instantaneous rate (decreases in pR) during the stimulus. Out of nine units of this type, four showed rate adaptation in some stimulus conditions and two showed rate increases. These units differ from chop-S and chop-T units in that their discharge is most irregular near the onset of stimulation and their CVs decrease during the stimulus. The regularity behavior of these chopper units is similar to that of some pri-N and unusual units (Fig. 6, C and F). These choppers are differentiated from pri-N and unusual units by the fact that they show chopping in their PST histograms and by their latencies (discussed below). Bourk did not describe units of this type; they are called chop-U units in this paper. Nine of 51 choppers in our sample are chop-U units.

Chop-U units also differ from chop-S units in that chop-U units do not show the pattern of 1 spike/PST histogram peak characteristic of chop-S units. Table 2 summarizes the results of computations to demonstrate this point. Peaks in chopper PST histograms were marked off at the minima between peaks; only clearly defined peaks were used. The fraction of stimulus trials during which a spike occurred in each peak was then counted. Table 2 shows the means and standard deviations of those fractions for regular choppers (chop-S) and irregular choppers (chop-T and chop-U). All three types give close to 1 spike/stimulus trial during the first PST peak. The fraction of bursts containing a spike stays near 1 for chop-S units out to the 4th or 5th peak, whereas for chop-U units, there is a substantial drop in the fraction of bursts containing a spike starting at the second peak. Chop-T units behave more like chop-S units.

### Characteristics of primary-like and other irregular units

Primary-like, pri-N, and unusual units show irregular discharge (CV > 0.5). A variety of patterns are seen, the range of which is illustrated in Figs. 5 and 6. The responses of

### Table 2. Fraction of bursts in which PST peaks contain a spike

<table>
<thead>
<tr>
<th>Unit Type</th>
<th>Peak Number</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Chop-S</td>
<td>0.997 ± 0.0463 (87)</td>
</tr>
<tr>
<td>Chop-T</td>
<td>0.983 ± 0.0423 (13)</td>
</tr>
<tr>
<td>Chop-U</td>
<td>0.993 ± 0.0994 (17)</td>
</tr>
</tbody>
</table>

Values are means ± SD. No. in parentheses are no. of PST histograms included in each average.
FIG. 5. PST histograms and regularity analyses at 4 sound levels for a primary-like with notch (pri-N) unit with a small prepotential in its action potential (inset at upper right). Figure layout as for Fig. 2.
these units are not as stereotyped as those of chopper units, so the patterns shown here are typical, but not universally representative.

Figure 5 shows PST histograms and regularity data for a pri-N unit at four sound levels. This unit's action potential has a small prepotential (inset). The behavior of this unit is similar to that of the primary-like unit in Fig. 2, in that the unit is irregular (CV > 0.5) at all sound levels and shows adaptation at the lower three sound levels. However, the pattern of regularity is somewhat more variable in this unit; it has roughly constant CV, like a primary-like unit, at the lowest three

![PST histograms and regularity analyses](image)

**FIG. 6.** PST histograms and regularity analyses for 6 units with primary-like, primary-like with notch (pri-N), or unusual PST histograms. Units in B, E, and F have prepotentials in their action potentials (inset). Figure layout as for Fig. 2. In regularity plots, dashed lines show \( \sigma_R \), solid lines show \( \mu_R \).
sound levels, but has a decreasing CV at the highest sound level (θ + 40). Another difference between this unit and the primary-like unit in Fig. 2 is that the instantaneous rate, inferred from the inverse of  μR, does not correspond to the rate estimate of the PST histogram at short latency. This is clearly seen in the data at θ + 20 and θ + 30 in Fig. 5. The onset peaks in the PST histograms are produced by the precise latency of the unit's first spike and suggest “rates” of 1,600 and 2,500 spikes/s in these two cases, whereas the mean interspike intervals at the corresponding times are ~2 ms, indicating considerably smaller instantaneous discharge rates. Thus the rate estimate provided by the onset peak of a PST histogram is not necessarily an accurate reflection of the unit's instantaneous discharge rate at this time, as determined from the mean interspike interval.

Figure 6 shows PST histograms and regularity data for six units with primary-like, pri-N, and unusual PST histograms. These illustrate the range of responses observed among primary-like and unusual units. The primary-like and pri-N units in the top row are most typical of irregular units in the VCN. Although the units in Fig. 6 show a variety of behaviors during the first 10 ms of the response, they all eventually produce a steady discharge at rates of 100–500 spikes/s. The steady discharge is irregular, with CVs of 0.5 or more. Three of the units in Fig. 6 have prepotentials in their action potentials, indicating that they were recorded from bushy cells. There are 25 prepotential units in our sample; 23 of these give primary-like, pri-N, or unusual PST histograms and none give chopper PST histograms (Table 1). All 25 prepotential units are irregular (CVs >0.5), like the units in Fig. 6.

Distribution of regularity in the population of units

Figure 7 shows a scatter plot that summarizes the regularity results for all units in our sample. Each point is a measure of regularity for one PST histogram, and data from all BF-tone PST histograms are included, regardless of stimulus level (except for cases with low discharge rates that do not fit on the axes). The value of standard deviation plotted on the ordinate and the value of mean interval on the abscissa are average values of μR and σR computed from regularity plots like those in Figs. 2–6, where the average is taken over all bins between 12 and 20 ms. This range is chosen to limit the effects of adaptation; 12–20 ms is a region where both μR and σR are roughly constant with time in most data.4 The symbols indicate the PST type of the unit from which a point is taken and are defined in the legend. Note that all data from a unit are plotted with the same symbol in Fig. 7, even if the unit shows different PST histograms at different stimulus levels (e.g., Figs. 3 and 5). The PST type for a unit is taken as the predominant PST type it displays at 20–40 dB above threshold.

Figure 7 shows clearly the difference in regularity of the different populations of units. Chop-S units (regular choppers) are the most regular units. Primary-like, pri-N, and unusual units are the most irregular. The dashed line shows where CV = 0.5. Almost all primary-like, pri-N, and unusual units are above the line and all chop S units are well below the line. The irregular choppers (chop-T and chop-U) are intermediate; most of them fall just below the CV = 0.5 line. The primary-like, pri-N, and unusual units have a degree of irregularity that is similar to that of AN fibers. The solid lines show the region containing regularity data from 76 AN fibers from two experiments. The small number of data points from onset-C units scatter in the region of irregular choppers, with the exception of one more irregular point. However, four of the six data points from onset-C units come from low discharge rate data, where end effects may be reducing the CV value.

4 For units with stable rates over the averaging interval (12–20 ms), there is a small statistical bias in computing the standard deviation by averaging bins. A theoretically better means of computing standard deviation is to compute it directly from the interspike intervals themselves. The error made by averaging bins is small, as determined from comparison of the two calculations for cases with relatively steady μR and σR. However, for cases with significant adaptation or other nonstationarity, the averaging method used for Fig. 7 is probably preferable. Computing σR directly from the intervals results in an overestimate of σR due to the component of variance contributed by rate change. This extra variance is not recruited by the μR and σR estimates, as long as the profile of average rate is repeatable from response to response.
First spike latency

It is well-known that first-spike latency decreases significantly as stimulus level increases over the dynamic range of CN units (13, 15, 20, 25, 38). Therefore, latency can only be compared across units if stimulus level is controlled. To this end, we use data from stimulus levels between 25 and 35 dB re 0. The results of the latency analyses described below are the same at other stimulus levels.

Figure 8 shows examples of the distributions of first-spike latency for AN fibers and for various response types in the CN. There are two histograms for each unit in this figure; the bottom histogram is a PST histogram and the top histogram shows the distribution of first-spike latencies for the same data set. The data in Fig. 8 are taken from units with BFs between 10 and 30 kHz, where latency changes little with BF and at ~30 dB re 0. These data illustrate, by examples, two features of the behavior of latency in the AN and CN: the shortest latencies are found in the AN and in primary-like, pri-N, and unusual units in the CN; and the dispersion of latency, meaning the scatter in the latency histograms, is largest for AN fibers and primary-like CN units.

The data shown in the top row are typical of results for AN fibers, whose latency distributions show considerable scatter for the tone burst stimuli used here. Data are shown for a high spontaneous rate fiber (Fig. 8A) and a low spontaneous rate fiber (Fig. 8B). The difference in PST histogram shape, i.e., the difference in sharpness of the onset peak, illustrated here is typical of the high and low spontaneous rate groups (36). This difference in sharpness of the onset peak corresponds to substantially larger values of $\mu_{lat}$ and $\sigma_{lat}$ in low spontaneous rate fibers (Figs. 9 and 11). The latency measures of medium spontaneous rate fibers are only slightly larger than those of high spontaneous rate fibers.

The vertical dashed lines in Fig. 8 show the minimum first-spike latencies estimated from PST histograms; these are a rough
Aesthetic nerve
High spont.
26.5 kHz.

Primarylike
17.0 kHz.

Chop S
11.5 kHz.

Chop T
18.9 kHz.

Auditory nerve
Low spont.
19.6 kHz.

Primary notch
14.6 kHz.
measure of the shortest latency at which spikes that are responses to the stimulus are observed. The values of minimum latency for the data in Fig. 8 are given in the figure legend. CN units have latency distributions whose minimum latencies are a fraction of a millisecond longer than those of AN fibers, as expected for a synaptic delay. However, this does not mean that AN fibers always fire their first spike at a shorter latency than CN units. Because of the large latency dispersions of AN fibers, a substantial part of the distribution of first spike latency in an AN fiber can be beyond the entire latency distribution for a pri-N or other small-\(\sigma_{\text{lat}}\) CN unit. In Fig. 8, for example, half the spikes in the latency distribution of Fig. 8B are beyond the right-hand edge of the latency distribution in Fig. 8D, even though the minimum latency of the AN fiber is 0.6 ms shorter than that of the pri-N unit.

The properties of latency are shown for populations of units in Figs. 9, 10, and 11. Figure 9 shows \(\mu_{\text{lat}}\) versus BF for AN fibers responding to BF tone bursts 25–35 dB above threshold. High spontaneous rate fibers, plotted with Xs, have the shortest mean latencies, whereas low and medium spontaneous rate fibers have longer mean latencies. Similar results were obtained by Rhode and Smith (36). The line is a smooth curve drawn through the shortest latency units by eye. This line describes the systematic dependence of latency on BF and is an accurate summary of minimum latency data at other sound levels, if it is shifted vertically.
Figure 10 shows $\mu_{\text{lat}}$ versus BF for CN units; PST types are represented by different symbols, identified in the legend. The solid line is redrawn from Fig. 9 and shows that the shortest CN mean latencies are approximately the same as the shortest mean AN latencies. The shortest latencies in the CN arc found in primary-like, pri-N, onset-C, and unusual units. Choppers, both regular and irregular, have longer latencies; the dashed line is a repetition of the solid line shifted vertically by 1 ms. Most primary-like, pri-N, onset-C, and unusual units are below the dashed line and almost all choppers are above the line. Notice that the irregular and regular choppers do not seem to show different mean latencies, but rather scatter together, mainly above the dashed line.

As was shown in Fig. 8, there is a substantial difference in the dispersion of first-spike latencies ($\sigma_{\text{lat}}$) among different PST histogram types. This shows up in PST histograms in the sharpness and amplitude of the onset peak; large-amplitude onset peaks are observed in units with precisely timed onset spikes, meaning small values of $\sigma_{\text{lat}}$. Figure 11 shows histograms of $\sigma_{\text{lat}}$ for various populations of units. AN fibers and primary-like units (top two histograms) have the largest latency dispersions and the largest range of latency dispersion. Pri-N and unusual units have smaller latency dispersions. Choppers, both regular and irregular, also have precise first-spike latencies. In most chopper units, the first-spike latency histogram is identical to the first peak in the PST histogram.

For the pri-N/unusual and chopper histograms in Fig. 11, there are a few data points with large values of $\sigma_{\text{lat}}$ that are separated from the main cluster. The clusters with smaller values of $\sigma_{\text{lat}}$ are typical of the behavior of these unit types. The scattered larger
REGULARITY AND LATENCY IN VCN

Values of \( \sigma_{\text{lat}} \) come from cases in which most first spikes have latencies that fall within a typically narrow distribution, but a few spikes occur with substantially longer latencies. \( \sigma_{\text{lat}} \) is increased by those few long-latency spikes and therefore is a misleading indicator of latency dispersion in these cases.

DISCUSSION

Classes of CN units based on regularity and latency

Figure 12 is a summary of the results. This figure shows a scatter plot of units with their regularities (CVs) on the abscissa and their latencies on the ordinate. In this plot, CN units cluster into three groups: a regular group of chop-S units with long latencies; an irregular group of pri, pri-N and unusual units with short latencies; and an intermediate group of chop-T and chop-U units with long latencies. If a third axis showing \( \sigma_{\text{lat}} \) were added to Fig. 12, then a fourth group, primary-like units, would separate from the rest (as is shown in Fig. 11). The principal result of this paper is the separation of the nononset units in the CN into these four groups: primary-like, pri-N/unusual, regular choppers (S), and irregular choppers (T, U). The following approximate rules can be given to separate these populations: choppers have latencies \( >1 \text{ ms} \) re the minimum AN latency; chop-S units have CVs \( <0.35 \), and chop T and U units have CVs \( >0.35 \) and \( <0.5 \); irregular units have CVs \( >0.5 \) and latencies shorter than \( 1 \text{ ms} \) re minimum. Onset-C units are a fifth group that was not adequately sampled in this study; those onset-C units that were studied have latencies comparable to the irregular unit group and regularities comparable to those of irregular choppers.

The scatter plots in Figs. 7, 10, and 12 show that there is overlap of the characteristics of neighboring unit types. The rules of thumb given above describe typical characteristics of each unit type; they do not provide absolute borders between response types. Because regularity and latency values form a continuum, these measures are not as useful taken individually as they are when considered as part of a battery of measures of units' response characteristics. The units in Fig. 6, D and F provide examples of the usefulness of regularity and latency in characterizing CN units. The PST histograms of these two cases are not clearly of either chopper or primary-like type. However, both units are more irregular (CVs of 0.66 and 0.62) than choppers and have latencies (0.13 and 0.22 ms re minimum) that are shorter.
than those of choppers; therefore these two units have spike trains with the properties of primary-like units. Similarly, the unit in Fig. 4D is confirmed as an irregular chopper by its CV (0.48) and latency (1.13 ms re minimum).

The distinction between chopper units and irregular units (primary-like; pri-N, and unusual) has a morphological correlate in that chopper responses are recorded from stellate cells and irregular response types are recorded from bushy cells. These conclusions follow from studies in which cells were marked with intracellular injections of HRP (35, 42, 44), from correlation of recording sites with CN cytoarchitecture (1), and from the fact that prepotentials are only recorded from primary-like, pri-N, and other irregular response types (31, 43, Table 1 of this paper). There is evidence, to be discussed below, for a further correspondence between subtypes of the major CN morphological cell types and subgroups of the chopper and irregular response types.

The major exceptions to the rules of thumb offered above are irregular primary-like units with long latencies. Five such units are plotted above the dashed line in Fig. 10, three of which appear in Fig. 12. These units may be related to the long-latency, phase-locked, irregular unit tentatively called primary-like by Rhode and collaborators (35) and recorded from an apparent small cell.

**Dependence of latency and regularity on stimulus conditions**

All the data shown in this paper were obtained using BF tones as the stimulus. It is clear from other investigations that latency depends strongly on both stimulus frequency and intensity: latency is usually shortest at BF and usually increases rapidly away from BF (20, 38); latency also increases as stimulus level decreases (13, 15, 20, 38). Finally, latency values vary from laboratory to laboratory because of differences in stimulus generation equipment. Because of this variability, latency is a useful measure of unit type.
only if stimulus conditions are carefully controlled. The expedient of subtracting the minimum AN latency function from CN unit latencies, as was done in going from Fig. 10 to Fig. 12, is a useful way to correct for most of the confounding factors in latency measurements.

By contrast, regularity averaged over 12-20 ms appears to be a fairly stable property of VCN unit discharge, in that this measure of regularity is relatively insensitive to changes in stimulus level. This point has been considered in detail for neurons in the cochlear nucleus and superior olive (14, 16, 50). In plots like Fig. 7, the data from a single unit tend to move along a slightly curved trajectory of roughly constant CV as stimulus level and discharge rate change.

Small changes in CV are expected as discharge rate changes because of the effects of refractoriness (14). The behavior of a model of irregular unit discharge illustrates this point. In this model, a spike train is generated from a Poisson process with rate R, which is modified by a refractory process, meaning that spikes occurring within a deadtime $t_D$ of a previous spike are eliminated from the train (14, 47, 55). With this assumption, the mean interspike interval $\mu_R$ is related to the standard deviation $\sigma_R$ as

$$\sigma_R = \mu_R - t_D$$  \hspace{1cm} (2)

In a plot like Fig. 7, data from this model should scatter around a line of unity slope that intersects the abscissa at $\mu_R = t_D$. This is approximately the behavior of AN fibers (with $t_D = 1.2$ ms), except for the influence of the end effect artifact in the regularity analysis (J. Li, E. D. Young, and L. I. Hellstrom, unpublished data). The refractoriness model predicts that as $\mu_R$ decreases and discharge rate becomes higher, CV should decrease, i.e., the ratio

$$CV = \frac{\sigma_R}{\mu_R} = 1 - \frac{t_D}{\mu_R}$$ \hspace{1cm} (3)

becomes smaller. The model predicts that CV should range from 0.8 when $\mu_R = 6$ ms to 0.52 when $\mu_R = 2.5$ ms (with $t_D = 1.2$ ms). This change is not large enough to obscure the differences between irregular units and chopper units. However, it does produce a convergence of data from all unit types at high discharge rates, so the scatter in the regularity measure results in overlap of data from different unit groups. This can be seen in Fig. 7 where, for discharge rates greater than $\sim 400$/s ($\mu_R < 2.5$ ms), the data from different unit groups begin to merge together.

A limitation on the use of regularity as a guide in distinguishing unit types follows from the discussion above. Because of the convergence of the regularity of different unit types at short mean intervals, regularity calculations are only revealing when they are done using data at discharge rates below about 400 spikes/s ($\mu_R \geq 2.5$ ms). This limitation was observed in constructing Fig. 12.

A second limitation on the regularity analysis is the end effect, which biases measures of $\mu_R$ and $\sigma_R$ at low discharge rates. End effects can be reduced by the simple expedient of using longer stimulus durations. The choice of 25 ms, which has been standard since the pioneering work of Pfeiffer (32), is unfortunately just short enough to yield significant bias for commonly encountered discharge rates. When simulations of irregular unit discharges are conducted with 50-ms response durations, the regularity measures computed from the standard analysis window (12-20 ms) are very close to theoretical values.

**Chopper units**

The discussion in this section is based on the assumption that chopper units are recorded from stellate cells in the VCN. The evidence for this has been cited above. Three features of stellate cells are of interest in this discussion. First, AN fibers form bouton terminals, not endbulb terminals, on stellate cells (4, 49). Second, there are two varieties of stellate cells in AVCN, where most of our recordings were made: type II cells in anterior AVCN have AN terminals on their somas and dendritic trees, whereas type I cells in anterior AVCN and most stellate cells in posterior AVCN have few terminals on their somas (4, 49). Third, stellate cells have membrane characteristics that favor regular discharge (28, 53). In in vitro preparations, stellate cells respond to depolarization produced by intracellular electrical currents with a regular discharge whose rate is determined by the extent of depolarization (28). The stellate cell spike trains produced
by intracellular currents resemble those pro-
duced by chopper units in response to acous-
tic stimuli (35, 39, 40). This similarity sug-
gests that the regularity of chopper units is 
produced by membrane mechanisms of the 
kind that produce repetitive discharge in a 
variety of neurons (e.g., 8).

The morphology and arrangement of AN 
inputs to stellate cells may also be important 
in producing regular discharge. Bouton ter-
mental inputs on stellate cells should support 
a regular discharge for two reasons. First, as-
suming that the boutons on a stellate cell 
come from many AN fibers, the postsynaptic 
effect of each fiber should be small, requiring 
summation of many inputs to produce a 
spike. This sort of averaging has been shown 
to lead to a regular discharge in modelling 
reviews, under appropriate conditions (26, 
51). The necessity to integrate a number of 
inputs to reach discharge threshold could 
also lead to a longer first-spike latency. Sec-
ond, postsynaptic membrane capacitance 
has a low-pass filtering effect on postsynaptic 
potentials with a cutoff frequency of 
\( \sim 100-200 \text{ Hz} \) (assuming a membrane time 
constant of 5 ms; 21, 56). Although the fil-
tering effect is seen for inputs applied to the 
soma, the cutoff slope of the low-pass filter 
increases as inputs are applied farther out on 
the dendritic tree. Thus type I stellate cells 
might show a sharper low-pass filtering effect 
than type II stellate cells. As a result of the 
filtering, high-frequency temporal fluctua-
tions in the input, such as AN fiber phase-
locking, should be filtered out, leaving the 
low-frequency, or DC, components of the 
input to predominate in driving the stellate 
cell’s spike generator. The fact that phase-
locking in CN chopper units begins to drop 
off at 200-300 Hz, whereas phase-locking in 
AN fibers, primary-like units, and pri-N 
units does not begin to drop off until 1 kHz is 
consistent with this argument (Ref. 1; Black-
burn and Sachs, personal communication; 
note that Rhode and Smith, Ref. 38, report a 
qualitatively similar result, but with a 
smaller difference between the cutoff fre-
quencies of chopper and primary-like popu-
lations).

A simple model for chopper units that fol-
loows from the considerations above is that 
choppers respond to the summed, low-fre-
quency components of their inputs, produc-
ing a regular spike train whose rate is deter-
mined by the average value of the summed 
inputs. Both the membrane-determined reg-
ularity and the membrane low-pass filtering 
serves to limit the ability of choppers to follow 
the temporal patterns of their inputs.

One advantage of the regularity analysis 
used in this paper is its ability to show tem-
poral changes in regularity during a response. 
A distinction that is clearly made in terms of 
the temporal evolution of regularity is the 
difference between the subvarieties of choppers. Chop-S and chop-T response types 
were originally differentiated in terms of PST 
histograms and the behavior of mean inter-
spike interval (1). The results of regularity 
analysis clearly support this distinction and 
allow the definition of another possible 
chopper subtype, chop-U. Although typical 
PST histograms for chop-S and chop-T units 
can be specified, the distinction of chop-S, 
chop-T, and chop-U units on the basis of 
PST histograms alone is difficult in practice. 
Regularity analysis is more informative 
about chopper subtypes.

The existence of three types of chopper 
units raises the question of the relationship 
between the subvarieties of choppers, de-
finite physiologically and the subvarieties of 
stellate cells, defined morphologically. One 
possibility, for example, is that regular chop-
ners (S) are recorded from type I stellate cells 
(few inputs on the soma) and irregular chop-
ners are recorded from type II stellate cells 
(many inputs on the soma). This conclusion 
is suggested by Bourk’s (1) report that chop-
T units tend to be recorded in the anterior 
AVCN where type II stellate cells are seen 
(4), whereas chop-S units tend to be recorded 
in the posterior AVCN where stellate cells 
seem to be mostly type I (49). An association 
of irregular chopper units with stellate cells 
having inputs on the soma is consistent with 
models of the effects of dendritic trees on 
regularity (51). Excitatory synaptic inputs on 
the soma should produce larger EPSPs than 
inputs on the dendritic tree, and larger 
EPSPs should produce more fluctuation in 
discharge rate. This hypothesis also suggests 
that chop-T units should have shorter laten-
cies than chop-S units because of reduced 
electrotonic conduction time. No such la-
tency difference is observed and there is also 
no correlation between latency and irregular-
ity in the chopper population (Fig. 12). The lack of latency difference suggests that the long latencies of chopper units do not derive from electrotonic conduction time but rather from the membrane mechanisms of spike initiation. The question of the generation of action potentials in chopper units requires further study.

Not all evidence favors the association of irregular choppers with type II stellate cells and regular choppers with type I stellate cells. Bourk (1) was able to antidromically activate both chop-S and chop-T units from the central nucleus of the inferior colliculus; in contrast, Cant (5) has reported that type II stellate cells are not labeled with HRP following injections in the colliculus, whereas type I stellate cells are labeled. Thus the intriguing question of the morphological correlate of the regular/irregular chopper distinction cannot be answered without further evidence.

Primary-like and related irregular unit types

Regularity analysis allows clarification of a number of issues surrounding primary-like, pri-N, and unusual response types. All of these response types are found to be irregular, with CVs exceeding 0.5 (Fig. 7). This means that, except for the transient period near the beginning of the burst, these response types give the same sort of irregular action-potential trains. The similarity of steady-state spike trains in primary-like, pri-N, and unusual response types suggests that they share common mechanisms of spike train generation.

Many onset units should also be included in the irregular unit group (44). Onset units in the present study have been defined as having average discharge rates <100 spikes/s, so regularity analysis of their BF tone responses is equivocal due to end effect bias. However, a maintained discharge at a rate >100 spikes/s was obtained in 6 out of 10 onset units tested by using broadband noise (range 140–350 spikes/s). These maintained discharges offer the opportunity of examining the regularity of onset units; however, the results must be regarded with caution, because the regularity of unit discharges can be different for tones and noise (15). In four cases, data for the regularity analysis were taken and all but one of these shows an irregular discharge (CVs of 0.39, 0.51, 0.51, and 0.73). Moreover, six out of nine onset units tested with BF tone bursts 25–35 dB re θ show short first-spike latencies (<1 ms re minimum) with small values of \( \Delta t_{\text{lat}} \) (0.08–0.42); the short-latency units include all four units tested for regularity. These latency values are similar to those of pri-N and unusual units and, along with the regularity data, suggest that a subpopulation of onset units shares the physiological mechanisms of irregular units. Bourk (1) obtained similar results, in that many onset units in his sample have short latencies and good phase-locking. These onset units are similar to primary-like units and different from chopper units in both measures.

The preponderence of evidence indicates that the primary-like, pri-N, and unusual units, as well as some onset units, are recorded from bushy cells. Intracellular HRP injections into physiologically classified cells have produced examples of bushy cells that give primary-like, pri-N, and onset (on-L) responses (35, 42, 44). Moreover, prepotentials are seen only in irregular units and in occasional onset units (Table 1). Thus a common characteristic of bushy cell responses, regardless of PST histogram type, is irregularity of discharge. The various PST response types associated with bushy cells do not seem to have consistently different regularities, except for the transient period near the beginning of the response to a stimulus burst. The degree of irregularity of these units is comparable to that of AN fibers and it is likely that irregular CN units inherit irregularity from AN fibers because of the security of the large synapses they receive from AN fibers. Intracellular analyses of bushy cells have revealed large EPSPs consistent with the large synaptic terminal (28, 35, 44). In most cases, each EPSP seems to be capable of firing the postsynaptic cell by itself, although this is not always true (44). Thus bushy cells give irregular responses because they tend to fire in a nearly one to one fashion in response to the irregular action-potential trains they receive from AN fibers.

Variability of first-spike latency

There is considerable diversity in the irregular unit group in their behavior near stimu-
lus onset. Part of this diversity may result from triggering problems due to the small action potentials of many irregular unit recordings and the evoked potentials frequently associated with them. Even given the triggering problems, one clear distinction that can be made is between primary-like units, which have rather variable first-spike latencies similar to AN fibers and the other unit types, which have precise first-spike latencies (Fig. 11). This difference has been explained as due to convergence of different numbers of AN fibers on bushy cells of different types (1, 38, 44). Bushy cells receive a small but variable number of endbulb terminals, as few as one per cell in rostral AVCN (24, 34). The effect of convergence of a small number of AN fibers on a CN cell can be shown quantitatively by the following model. Assume that there are $N$ AN fibers contacting a CN cell and assume that each AN fiber is capable of producing an action potential in the CN cell. Further assume that the probability density function of the first-spike discharge in each AN fiber is given by

$$P_A(t) = \begin{cases} 0 & t < t_1 \\ R e^{-R(t-t_1)} & t \geq t_1 \end{cases}$$

where $t_1$ is the minimum latency of the fiber and $R$ is the decay rate of the first-spike latency distribution.\(^5\) Equation 4 is an approximation of the behavior of the first-spike latency distributions in Fig. 8, A and B. If the fibers' spike trains are statistically independent and each fiber can cause a discharge in the CN unit, then the probability density function of the first-spike latency of the CN unit is

$$P_N(t) = \begin{cases} 0 & t < t_1 + t_s \\ N R e^{-N R(t-t_1-t_s)} & t \geq t_1 + t_s \end{cases}$$

where $t_s$ is the synaptic delay. The mean and standard deviation of first-spike latency are then

$$\mu_{lat} = t_1 + t_s + \frac{1}{NR}$$

and

$$\sigma_{lat} = \frac{1}{NR}$$

Equation 6B shows that the dispersion of first-spike latency ($\sigma_{lat}$) decreases as $1/N$, i.e., inversely with the number of AN fibers that converge on the cell. Referring to Fig. 11, the median values of $\sigma_{lat}$ are 0.71, 0.8, and 0.28 for AN fibers, primary-like units, and pri-N/unusual units, respectively. This difference in median values can be accounted for by assuming a convergence of two to three times as many AN fibers on a pri-N/unusual unit compared with a primary-like unit. This model also predicts a shorter mean latency for pri-N/unusual units, because of the $1/NR$ term in Eq. 6A. No such trend is apparent in Fig. 10, suggesting that there are additional differences between primary-like and pri-N/unusual units that are not captured in the model of Eqs. 4-6.

Latencies of AN fibers and CN units

An unexpected result in Figs. 9 and 10 is that the shortest AN fiber latencies (solid line) are not a synaptic delay shorter than those of CN units. Rhode and Smith (38) show a similar result in Fig. 12 of their paper, although the overlap is not as large in their data. The overlap of AN and irregular CN unit latencies for tone bursts seems to contradict earlier results obtained with clicks (1, 18), in which AN fibers have first-spike latencies that do not overlap those of CN units; the two populations have mean click latencies that are at least 0.5 ms different.

Click latencies were measured in one AN (decerebrate) preparation. Fibers with BFs above 3 kHz have click latencies $<2.1$ ms, which agrees with earlier AN data (18, 19), once differences in acoustic delay are taken into account. The problem of overlap of AN and CN latencies therefore arises only for responses to tone bursts. A difference between latencies in the unanesthetized decerebrate preparations used for CN recording and the anesthetized preparations used for AN recording was eliminated by recording AN fibers in two animals, one anesthetized and one decerebrate. The results are identical and these two populations are plotted together in Fig. 9. Another possibility is that AN fiber latencies are prolonged in experimental
preparations by the stretching of the nerve that is necessary for its exposure. Although this possibility cannot be eliminated entirely, it seems likely that it is of secondary importance. For one thing, it is inconsistent with previous results on click latencies (1, 18), which should show the same effect.

The most likely explanation for the long latencies in AN fibers is that they result from using the mean of the latency distribution as the measure of latency. If the shortest spike latency is considered instead of the mean, then AN fibers always have shorter latencies than CN units. The CN units whose latencies are comparable to AN fibers are primary- like, pri-N, and unusual units (Fig. 9). As discussed above, these units are probably recorded from bushy cells, so that the model of Eqs. 4-6 applies. The mean latency of AN fibers is $l/R + t_1$, from Eq. 4, whereas the latency for a CN unit that receives N converging AN inputs is $1/NR + t_1 + t_s$ (Eq. 6A). The CN latency is increased by the synaptic delay $t_s$, but the increase is counteracted by the decrease in the first term in the mean latency expression ($1/R$ to $1/NR$). If we assume that $1/R = 0.71$ ms, from the discussion of $\sigma_g$ above, a convergence of three AN fibers decreases the mean latency by 0.47 ms, which is almost enough to make up for a synaptic delay of 0.6 ms. Thus the apparent similarity of latencies in AN and CN results from the reduction of latency dispersion produced by convergence of AN fibers in the CN and the statistical properties of mean latency.

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