ANALYSIS OF DISCHARGES RECORDED SIMULTANEOUSLY FROM PAIRS OF AUDITORY NERVE FIBERS

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ABSTRACT Spike trains were recorded simultaneously from pairs of auditory nerve fibers in anesthetized cats. Tests for correlation between spike trains were developed for spontaneous activity and for discharge patterns resulting from single-tone stimuli. The application of these tests to the recordings indicates that the responses of auditory nerve fibers to a tone and to silence can be described as statistically independent point processes. This result implies that the initiation of spikes in these fibers is governed by localized processes specific for each fiber.

INTRODUCTION

Spike discharge patterns in mammalian auditory nerve fibers have been extensively studied for one fiber at a time. Very little is known about relationships between discharge patterns recorded simultaneously from several fibers. If each fiber can be considered to be an independent channel whose activity is determined by local conditions at its synaptic contact in the inner ear, one should not be able to find correlations between the activities of fibers, no matter how close their peripheral terminations. It is known, however, that there are mechanical and electrical events which occur over considerable extents of the cochlea (von Békésy, 1960). Should these events influence the discharge patterns in the fibers, significant correlations might exist between the activities in fibers, particularly if they innervate the same general region in the cochlea. This paper presents statistical analyses of discharges recorded simultaneously from pairs of auditory nerve fibers in an effort to determine whether such correlations exist in spontaneous and tone-stimulated activity.

METHODS

The basic techniques for recording from the auditory nerve were as described previously (Kiang et al., 1965). Adult cats were anesthetized with diallyl barbituric acid in urethane solution (75 mg/kg). A closed acoustic system was sealed into the external ear canal and the auditory nerve exposed from a dorsal approach by retracting the cerebellum. The recording electrodes were 2 M KCl-filled micropipets. Two pipets were mounted on separate micro-

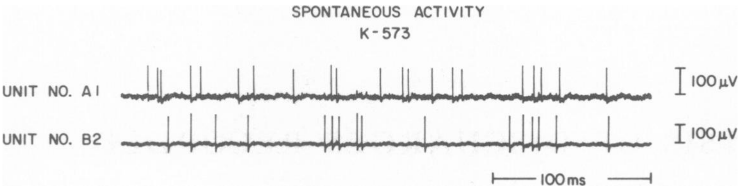

FIGURE 1 Simultaneously recorded spike trains from two auditory nerve fibers. The characteristic frequency of unit A1 is 2.58 kHz and that of B2 is 2.41 kHz. Their spontaneous discharge rates are 44.2 spikes/s and 40.7 spikes/s, respectively. An upward deflection of each trace corresponds to positivity of the recording microelectrode relative to the headholder.

manipulators. No attempt was made to place the pipets close to one another in the nerve. Once contact was established with a single unit or fiber, the characteristic frequency (CF) was determined using 10/s, 50 ms duration tone bursts with 2.5 ms rise-fall times. The second pipet was then advanced until it, too, made contact with a fiber, and its CF was then determined. In some cases a special effort was made to find fibers with similar CF. Recordings were then made of spontaneous discharges of these fibers and their responses to single tones. The activity at both microelectrodes was recorded on FM magnetic tape and processed off-line on a PDP-4 computer. The timing of spikes was measured with a resolution of 100 μs except for the processing of responses to low frequency tones, in which case the resolution was 300 μs. The data-processing methods will be described with the results.

RESULTS

Spontaneous Activity

Fig. 1 shows a sample of spontaneous activity recorded simultaneously from a pair of auditory nerve fibers having similar discharge rates and similar CF. From visual inspection of this record, it is not clear whether there is some correlation between these spike trains.

A quantitative test of correlation depends upon how the individual spike trains are mathematically described. In this paper, a train of spikes will be modeled as a point process, i.e., a sequence of identical, nonoverlapping pulses (Cox and Lewis, 1966). A particular point process is described by the time of occurrence of each pulse. Tests of the correlation between two point processes depend upon whether the point processes are considered to be stationary (which means the statistics of point processes do not vary with time) or nonstationary (the statistics do vary with time). The spontaneous activities of auditory nerve fibers are assumed to be described as stationary point processes.

Two methods have been described for measuring the correlation between stationary point processes (Moore et al., 1966; Perkel et al., 1967). One is based upon the computation of the cross-correlation histogram and the second upon the computation of the cross-interval histogram. The cross-correlation histogram is computed from the intervals between each spike in one train and all spikes in the other train. If the spike trains can be modeled as stationary, statistically independent, point processes, then the

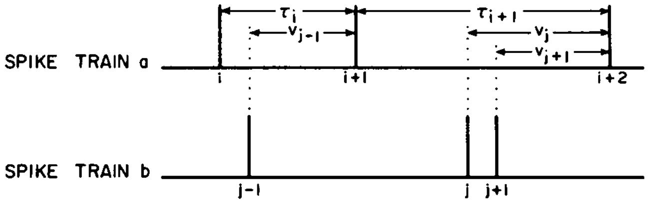

FIGURE 2 Definitions of the quantities used in the recurrence-time test. The quantity τ is a random variable denoting the interval between successive spikes in spike train *a*. τ_i is the measured interval between the i^{th} and $(i + 1)^{\text{st}}$ spike. The random variable v_j denotes the forward recurrence time measured with respect to the j^{th} spike in spike train *b*.

cross-correlation histogram will be a constant (within the limits of statistical fluctuation).

In this study, the cross-interval histogram method will be referred to as the recurrence-time test, because it is based upon measurements of the *recurrence times*. The *forward recurrence time* is a random variable defined to be the interval between a randomly chosen time and the succeeding pulse in a point process (Cox, 1962). The *backward recurrence time* is the interval between a randomly chosen time and the preceding pulse. For a stationary point process, the probability density function (pdf) of the forward recurrence time v is (McFadden, 1962):

$$p_v(v) = \frac{1}{E[\tau]} \int_v^{\infty} p_\tau(\tau)\mathrm{d}\tau \qquad (1)$$

where $p_\tau(\tau)$ is the pdf of τ, the interval between successive pulses in the point process; $E[\tau]$ is the expected value of τ; and $p_v(v)$ is the pdf of the forward recurrence time v.

The pdf of the forward recurrence time v and of the backward recurrence time u are identical (McFadden, 1962). The measurement of the forward recurrence times is illustrated in Fig. 2. These times are denoted by v_j, the time from the j^{th} spike in train *b* to the succeeding spike in train *a*. The forward recurrence-time histogram $N\hat{p}_v$ is computed from the v_j. (N equals the number of recurrence times v_j which comprise the histogram.) A similar computation yields the backward recurrence times u_j, from which the backward recurrence-time histogram $N\hat{p}_u$ is computed. The recurrence-time test consists of comparing the recurrence-time histograms ($N\hat{p}_v$ and $N\hat{p}_u$) with the result of applying Eq. 1 to the measured interval histogram for spike train *a*. The recurrence-time histograms depend upon the mutual relations between the two spike trains; the result of applying Eq. 1 depends only upon the properties of spike train *a*. If these spike trains are stationary and statistically independent, then these histograms will agree within expected statistical variations. Note that an agreement between these histograms does not prove independence; it only indicates *consistency* with an assumption of independence. If, however, the results of these computations disagree, either the spike trains are correlated or they are nonstationary or both. This comparison constitutes the test of independence used in this study. A

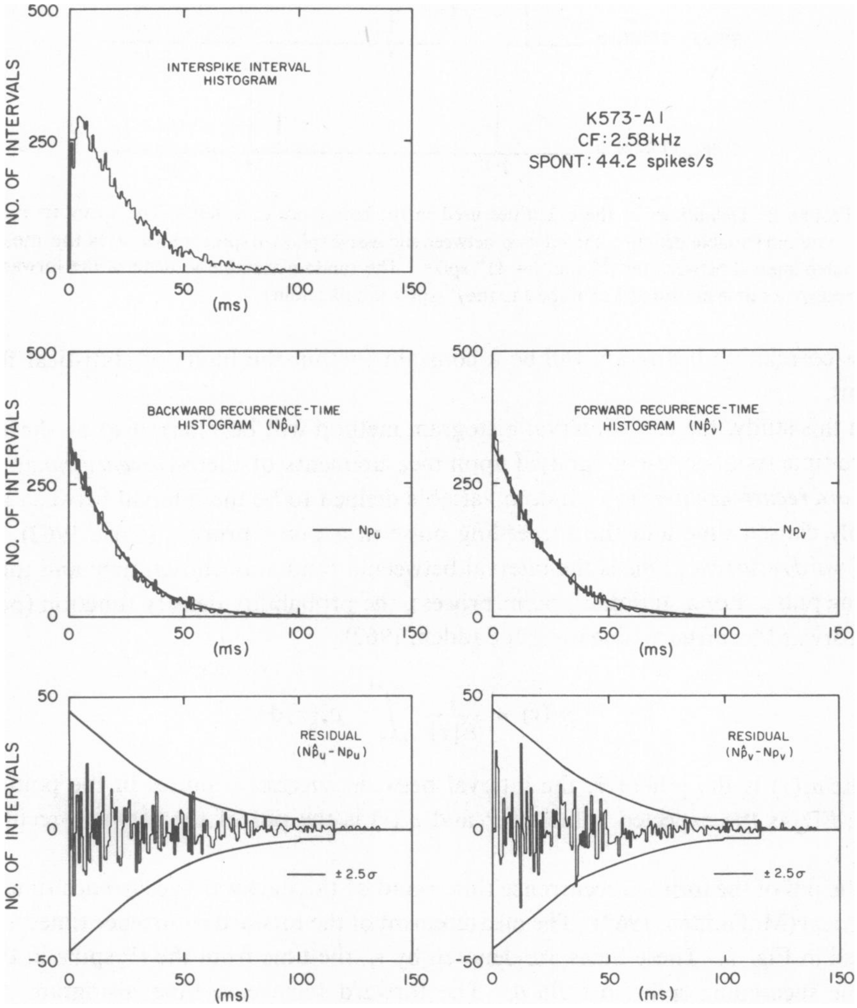

Figure 3 Results of applying the recurrence-time test to the spontaneous activities of the pair of units K573-A1 and K573-B2. In this figure, the activity of unit K573-A1 assumed the role of spike train *a* as defined in Fig. 2 while the activity of unit K573-B2 assumed the role of spike train *b*. These units have similar characteristic frequencies (2.58 kHz and 2.41 kHz) and similar spontaneous discharge rates (44.2 spikes/s and 40.7 spikes/s). The interspike interval histogram for unit K573-A1 is shown at the top of the figure (11,064 intervals). The measured recurrence-time histograms are shown in the middle row as light, jagged lines. The smooth curves superimposed upon these histograms represent the values calculated by assuming the spike trains are describable as independent point processes. The vertical scales of the theoretical curves are adjusted so that the areas below these curves are equal to the total number of spikes in the measured histograms (10,200). The differences between the measured histograms and the theoretical curves, the residuals, are shown by the light, jagged lines in the bottom row. The smooth curves in the bottom row represent $\pm 2.5\sigma$, where σ is the theoretical standard deviation of the measured histograms assuming the two spike trains are independent (Eq. 13). These data represent 250 s of continuous recording.

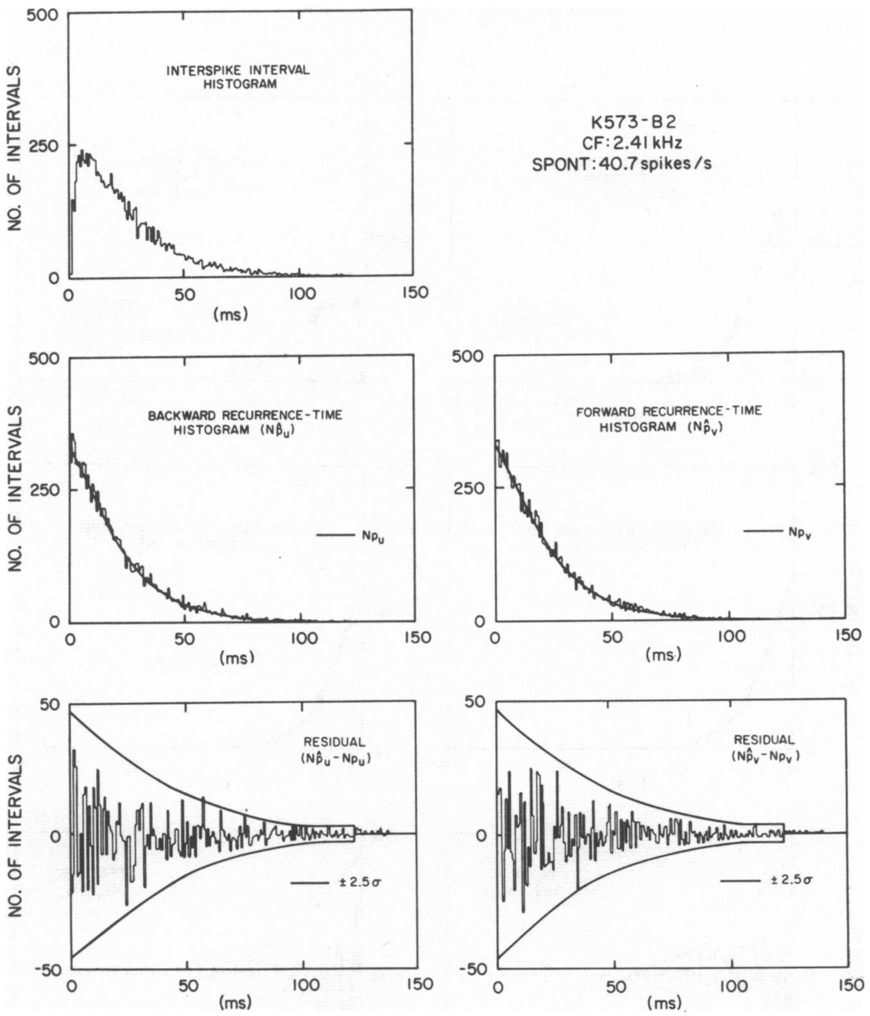

FIGURE 4 Results of applying the recurrence-time test to the spontaneous activities of the pair of units K573-A1 and K573-B2, the same pair of units represented in Fig. 3. In this figure, however, the roles of the spike trains are reversed in performing the recurrence-time test. The interval histogram at the top is measured from the activity of unit K573-B2 (10,181 intervals). The number of spikes used in the formation of the recurrence-time histograms is 11,080.

more precise formulation of the recurrence-time test, leading to a method of obtaining confidence levels for the comparisons, is given in Appendix A.

Figs. 3 and 4 illustrate the application of the recurrence-time test to the simultaneously recorded spontaneous activities of two auditory nerve fibers. The backward ($N\hat{p}_u$) and forward ($N\hat{p}_v$) recurrence-time histograms are shown in the middle rows of these figures. Superimposed upon these histograms are Np_u and Np_v, the estimates of the backward and forward recurrence-time pdfs using Eq. 1. ($N\hat{p}_u - Np_u$) and ($N\hat{p}_v - Np_v$), the residuals for the backward and forward recurrence-time histo-

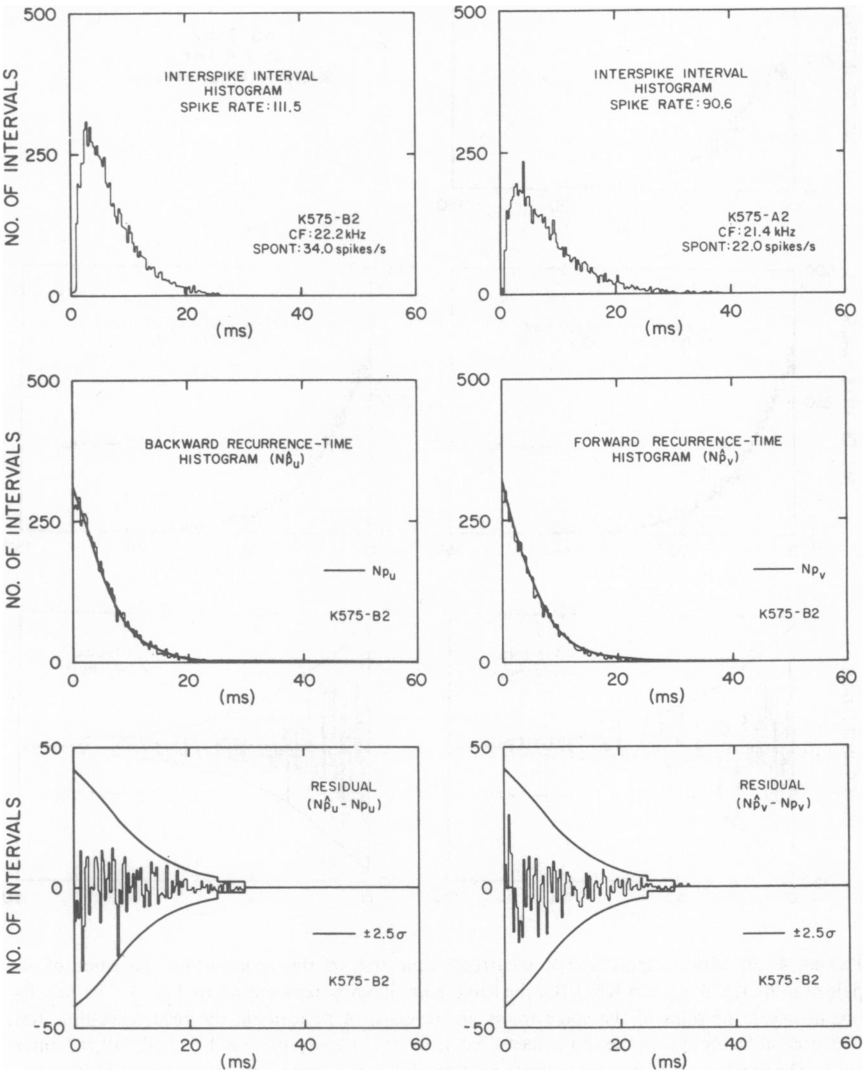

FIGURE 5 Results of applying the recurrence-time test to the activities of two units stimulated by a high frequency tone (21.4 kHz at 52 dB SPL). The interspike interval histograms are shown at the top. Total number of intervals for unit K575-B2 is 7,808 and, for unit K575-A2, the number is 6,342. The recurrence-time histograms shown in the middle row were measured with the activity of unit K575-B2 as spike train *a* and with the activity of unit K575-A2 as spike train *b* (Fig. 2). Total number of intervals in these histograms: 6,350. The residuals are shown in the bottom row of plots and are labeled as in Fig. 3. These data represent 70 s of continuous recording.

grams are shown in the bottom row. The standard deviation of each residual, denoted by σ, is given by Eq. 13. The values of the residuals lie within the $\pm 2.5\sigma$ bound for almost all bins. The results of the test presented in Figs. 3 and 4 are consistent with the view that the spontaneous activities of these units can be described as *independent* point processes.

The spontaneous activities of 20 more pairs of units were similarly analyzed. The spontaneous discharge rates of these units varied from 7.5 spikes/s to 131.5 spikes/s. For units having lower spontaneous discharge rates, it was difficult to obtain sufficient data for a meaningful application of this test. The CF of the units in the tested pairs are shown in Fig. 9*a*. In all of these cases, the residuals lie well within the boundaries $\pm 2.5\sigma$. Thus it appears that the spontaneous activities of pairs of auditory nerve fibers are consistent with an independent point process description.

Responses to Single Tones

Although the spontaneous discharges in pairs of auditory nerve fibers may be uncorrelated, it is still possible that discharges during sound stimulation could be correlated. For a single tone, the responses of an auditory nerve fiber vary with stimulus level and frequency (Kiang et al., 1965). For tone frequencies below a few kilohertz, the discharges tend to occur at preferred phases of the tone (Rose et al., 1967). Under these conditions, the probability of a discharge occurring in a small time interval depends upon the relationship of the interval to the phase of the stimulus. With such time-varying probabilities, the spike trains cannot be modeled as stationary point processes, and the test described in the previous section is inappropriate. As the tone frequency increases, however, the responses become less effectively time-locked to the stimulus (Johnson, 1974) and the recurrence-time test becomes more applicable.

Responses to High Frequency Tones. The results of applying the recurrence-time test to responses elicited by high frequency tones are illustrated in Fig. 5. These data indicate that the spike trains used in computing these histograms may be regarded as statistically independent point processes.

The recurrence-time test was applied to eleven fiber pairs responding to high frequency tones. The CF of these pairs are shown in Fig. 9*b*. In these experiments, the stimulus frequency was usually at the CF of one member of the pair. In all cases the results of this analysis resembled those shown in Fig. 5 for all of the stimulus levels and frequencies used. Therefore, an independent point process model can be used to describe the responses of pairs of auditory nerve fibers to high frequency tones.

Responses to Low Frequency Tones. Fig. 6 illustrates how the spikes of two simultaneously recorded auditory nerve fibers are time-locked to the individual cycles of a tone. The period histograms for the two units in this figure are similar at each stimulus level. Since the periodicities of the preferred times for the occurrence of spikes in each train are clearly related to a common stimulus, the spike trains must be correlated. Whether any correlation exists beyond that attributable to a common stimulus is another matter.

The procedure for resolving this issue begins by removing stimulus-locked periodic-

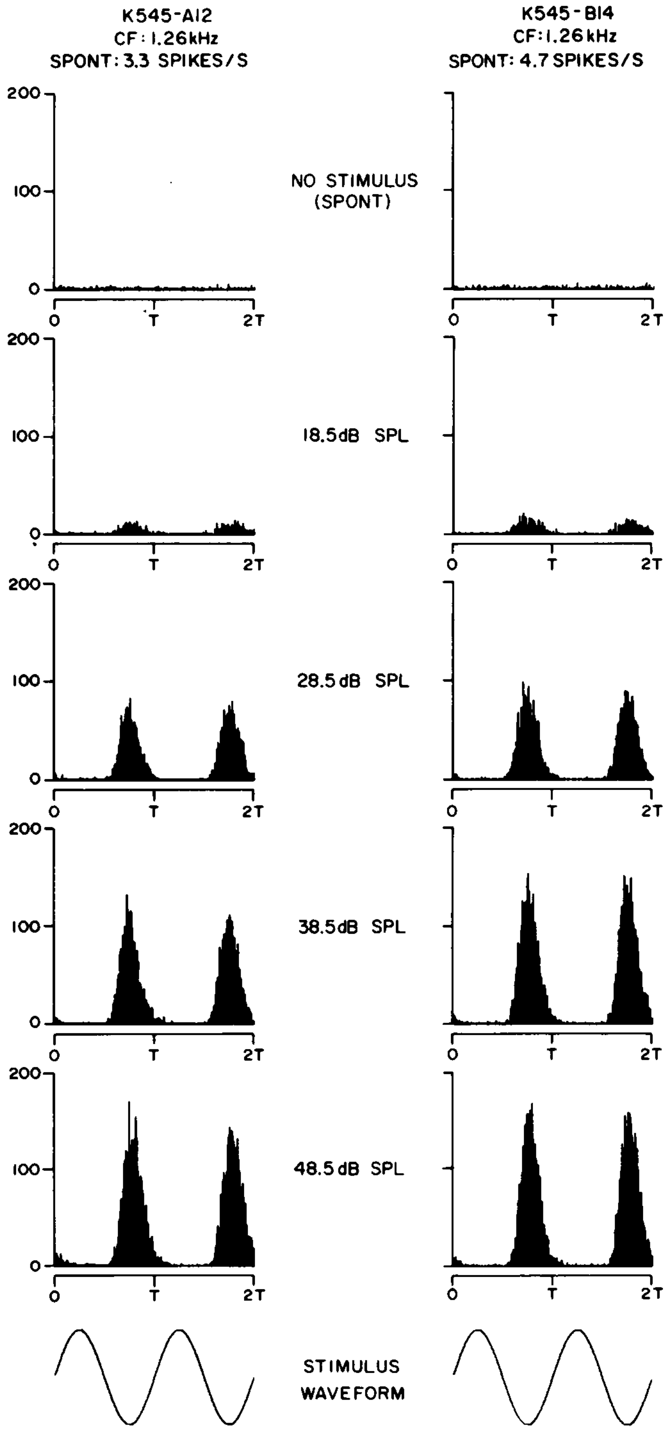

FIGURE 6 Period histograms of the responses to a low frequency tone (1.212 kHz) of a pair of units. The histograms in the left column were computed from the responses of unit K545-A12; the ones on the right were computed from the responses of unit K545-B14. The histograms in descending order along each column correspond to increasing tone levels. Zero time in these histograms corresponds to a positive-going zero crossing of the electric output of the stimulus oscillator. Two cycles of the 1.212 kHz stimulus tone are represented in each histogram. Each histogram represents 1 min of data.

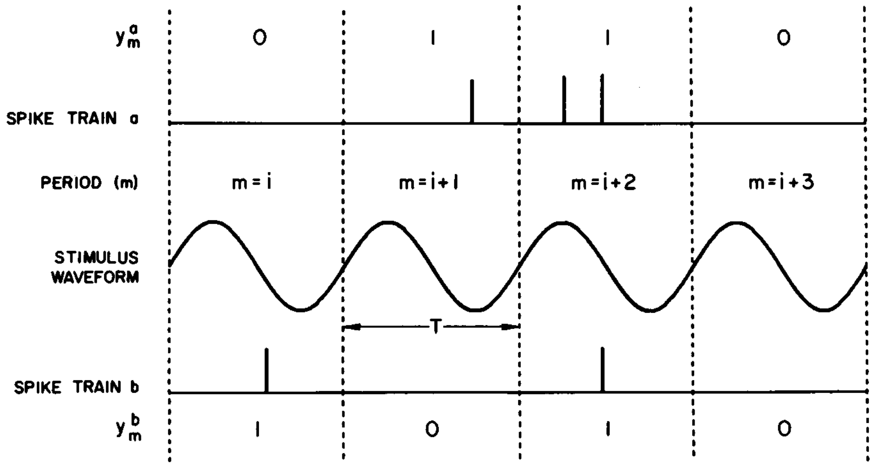

FIGURE 7 Definition of the quantities used in the cross-correlation test. Two spike trains, a and b, are depicted as well as the waveform of the stimulus tone. In performing the cross-correlation test, the time axis is partitioned into intervals equal to the period of the stimulus T. The i^{th} term of the sequence $\{y_m^a\}$ is set equal to either zero (if no spike occurs in spike train a during period $m = i$) or one (if one or more spikes occur). The sequence $\{y_m^b\}$ is computed from spike train b in a similar fashion. The cross-correlation test focuses on the computed cross-correlation of the sequences $\{y_m^a\}$ and $\{y_m^b\}$.

ities in the spike train (Fig. 7). The spike trains are partitioned into equal time segments of duration T, where T is the stimulus period. For spike train a, a binary sequence $\{y_m^a\}$ is defined as:

$$\begin{aligned} y_m^a &= 0 \quad \text{if no spike occurs in train } a \text{ during the } m^{\text{th}} \text{ stimulus period;} \\ y_m^a &= 1 \quad \text{if one or more spikes occur during the } m^{\text{th}} \text{ period.} \end{aligned} \tag{2}$$

A corresponding definition yields the sequence $\{y_m^b\}$ for spike train b. For tone frequencies greater than a few hundred hertz, two or more spikes rarely occur within one stimulus period. Consequently, the sequences $\{y_m^a\}$ and $\{y_m^b\}$ indicate the stimulus periods during which any spike occurs. Thus stimulus-locked periodicities are removed from the spike trains. Assuming that the probability of a spike occurring during a stimulus period does not change with time, the sequences $\{y_m^a\}$ and $\{y_m^b\}$ are stationary. The correlation between these sequences is indicated by the cross-correlation function $R_{ab}(k)$.

$$R_{ab}(k) = E[y_m^a \, y_{m+k}^b]. \tag{3}$$

The test of independence of the sequences $\{y_m^a\}$ and $\{y_m^b\}$ consists of comparing the measured cross-correlation function $\hat{R}_{ab}(k)$ with the result of applying Eq. 3 to the sequences. A more complete analysis of the cross-correlation test is given in Appendix B.

The application of this test is illustrated in Fig. 8. The empirically obtained data points (open circles) lie within $\pm 2.5\sigma$ of $M \cdot R_{ab}(k)$, the result of applying Eq. 3.

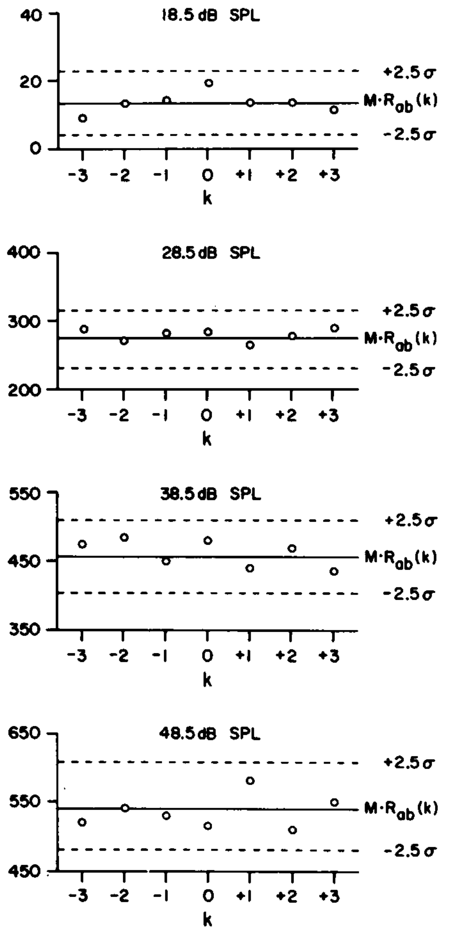

FIGURE 8 Results of applying the cross-correlation test to the activities of a pair of units (K545-A12, B14) having similar characteristic frequencies (1.212 kHz) and similar spontaneous discharge rates. The results depicted in this figure are derived from the same pair of units used in Fig. 6. The measured cross-correlation $M \cdot \hat{R}_{ab}(k)$ of the sequences $\{y_m^a\}$ and $\{y_m^b\}$ (defined in Fig. 7) is shown by the open circles. The cross-correlation $M \cdot R_{ab}(k)$, computed by assuming the sequences $\{y_m^a\}$ and $\{y_m^b\}$ are independent, is shown by a solid line. The dashed lines indicate ±2.5 SD (σ) of the measured cross-correlation (Eq. 20). The four measured cross-correlations are for different stimulus levels. The parameter M represents the number of stimulus periods incorporated into the computation of the cross-correlation; this parameter differs for each cross-correlation shown here. From top to bottom, the values of M are 208,839; 107,471; 126,440; 93,670.

Consequently, $\{y_m^a\}$ and $\{y_m^b\}$ can be modeled as statistically independent sequences. Thus, so long as there are no correlations on a time scale finer than a stimulus period, the spike trains from which the sequences $\{y_m^a\}$ and $\{y_m^b\}$ were derived can be modeled as statistically independent processes.

32 pairs of spike trains were analyzed with this cross-correlation test. The fre-

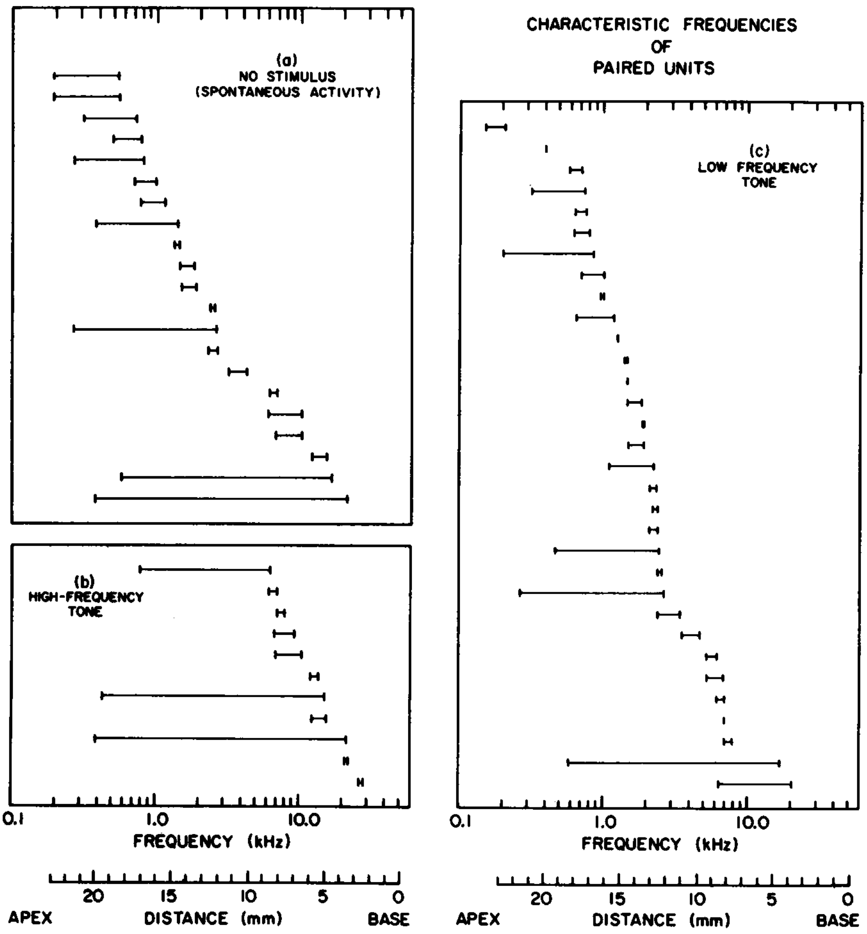

FIGURE 9 Characteristic frequencies of the pairs of units in this study. The characteristic frequency of each unit is represented by a vertical bar with a horizontal line connecting the characteristic frequencies of a simultaneously recorded pair. The figure is divided into three parts according to the stimulus condition. For the upper-left part (*a*), there was no acoustic stimulus. In the lower-left part (*b*), the stimuli were tones at frequencies too high to elicit responses synchronized to the individual cycles of the tone. For the right part of this figure (*c*), the stimuli were tones at frequencies low enough to elicit synchronized responses. The spontaneous discharge rates of these units ranged from 0.2 to 87.4 spikes/s. The recurrence-time test was applied to the activities of the pairs whose characteristic frequencies are shown on the left while the activities of pairs on the right were studied using the cross-correlation test. Spontaneous activity as well as driven activity were recorded for some pairs of units so that some pairs are represented more than once in this figure. In all, 52 pairs of units were used in this study. Two horizontal scales are shown: a frequency scale and a distance scale. The frequency axis represents characteristic frequency on a logarithmic scale. The distance axis represents the presumed number of millimeters along the basilar membrane from the extreme basal end of the cochlea that corresponds to a given frequency (Greenwood, 1961). The dimensions of the cochlea were not measured in this study. Instead, the total length of the cochlear partition was arbitrarily taken to be 23 mm.

quency of the stimulus tone was usually set equal to the CF of one of the fibers. The CF of these pairs are shown in Fig. 9*c*. The stimulus levels ranged from 25 dB SPL to 95 dB SPL. In these data, the empirical cross-correlation rarely exceeded the $\pm 2.5\sigma$ bound and never by a large amount. Thus, both spontaneous and tone-stimulated activity in auditory nerve fibers can be adequately modeled as statistically independent point processes. Whatever correlations exist for the tone-stimulated activity can be attributed to the fact that there is a common stimulus.

DISCUSSION

Several limitations on the interpretations of the data from these experiments should be discussed:

(1) It is possible that the data in this study do not reflect all possible pairs of auditory nerve fibers. In particular, pairs of longitudinal fibers that innervate many hair cells might not be represented in our sample, because longitudinal fibers are said to represent less than 10% of the total number of auditory nerve fibers (Spoendlin, 1966). In that case, any conclusions must perforce be limited to the radial fibers that innervate only a few or even a single hair cell.

(2) The recurrence-time test used in this paper is appropriate only for testing correlations over short time intervals. Correlations that might occur over long time intervals (seconds or even minutes) could be found by using cross-correlation tests (Moore et al., 1966; Rodieck, 1967) but are unimportant for the questions considered in this paper.

(3) It may be that under different experimental conditions such as absence of anesthesia, efferent system activation, or exposure to a wider choice of stimulus conditions, some correlations of activity between fibers would be demonstrable.

As the results stand, they bear on conceptions of how spike trains are generated in auditory nerve fibers. If spike discharges are influenced by excitatory processes that extend over regions covering millimeters in the cochlea, one might have expected to find correlations between fibers that were tuned to similar frequencies and therefore were presumably innervating neighboring regions in the cochlea. Some of the pairs of units in this study had CF that were identical within experimental error (Fig. 9) suggesting that such widespread influences do not exist. Errors in measuring CF were estimated to correspond to less than 0.1 mm along the cochlear partition so that the activity of fibers innervating hair cells separated by at least this distance would appear to be independent. It is of interest to ask whether the activity of fibers innervating the same inner hair cell might be correlated. Unfortunately, present physiological criteria cannot establish whether two nerve fibers innervate the same inner hair cell.

Nevertheless, the results of this study do place some constraints on possible models of the generation of spike activity in auditory nerve fibers. Assuming that spike discharges of each fiber are generated at a specific site, the results make it appear unlikely that there are interactions between nerve fibers central to that site. Moreover, the mechanical and electrical events that are broadly localized in the cochlea do not appear to trigger the spike discharges directly. Instead such events might only modulate the activity of a very localized but noisy excitatory process, and it is this excitatory process that triggers the spike discharges.

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APPENDIX A

The Recurrence-Time Test for the Independence of Two Stationary Point Processes

The recurrence-time test consists of comparing the empirical forward (or backward) recurrence-time histogram with the result of applying Eq. 1 to the measured interval histogram. Although only the forward recurrence-time test is developed here, it is easily seen that a similar analysis applies to the backward recurrence-time test. Let $N\hat{p}_v(k)$ denote the forward recurrence-time histogram computed according to the equation:

$$N\hat{p}_v(k) = \sum_{i=1}^{N_b} \delta(k, v_i, \Delta) \tag{4}$$

where k denotes the bin of the histogram being computed; v_i denotes the i_{th} forward recurrence time in spike train a measured with respect to the i^{th} spike in train b (Fig. 2); Δ denotes the binwidth of the histogram; $\delta(k, v_i, \Delta)$ is a function equaling either zero or one according to whether the measurement v_i lies in the k^{th} bin:

$$\begin{aligned} \delta(k, v_i, \Delta) &= 1 \qquad \text{if } k\Delta \leq v_i < (k+1)\Delta, \\ \delta(k, v_i, \Delta) &= 0 \qquad \text{otherwise;} \end{aligned} \tag{5}$$

N denotes the number of intervals used in the computation of the recurrence-time histogram. N is always equal to N_b, the number of spikes occurring in train b.

Assuming that the binwidth is small compared with the range of variation in $p_v^a(v)$ and that the spike trains are independent, the expected value of $\delta(k, v_i, \Delta)$ is given by:

$$E[\delta(k, v_i, \Delta)] = p_v^a(k\Delta)\Delta, \tag{6}$$

and the expected value of the forward recurrence-time histogram by:

$$E[N\hat{p}_v(k)] = N_b p_v^a(k\Delta)\Delta. \tag{7}$$

The forward recurrence-time histogram is an estimator of $p_v^a(v)$ but requires a second independent spike train.

A second estimator, which does not require a second spike train, is based upon Eq. 1. This estimator $N\tilde{p}_v(k)$ is related to the interval histogram I_n by:

$$N\tilde{p}_v(k) \alpha \sum_{n=k}^{\infty} I_n, \tag{8}$$

where:

$$I_n = \sum_{i=1}^{N_a} \delta(n, \tau_i, \Delta). \tag{9}$$

τ_i denotes the i^{th} interspike interval (Fig. 2).

The expected value of $N\tilde{p}_v(k\Delta)$ is also proportional to $p_v^a(k\Delta)$. The number of responses involved in the computation of any bin of $N\tilde{p}_v(k)$ is much larger than the number of responses used in computing the corresponding bin of $N\hat{p}_v(k)$ so that the second estimator may be considered to estimate $p_v^a(v)$ more exactly than the first. Henceforth $N\tilde{p}_v(k)$ will be assumed to be proportional to $p_v^a(k\Delta)$ and will be written as Np_v.

The test of independence consists of comparing the estimators specified in Eqs. 4 and 8 by considering the residual, the difference between the two estimators ($N\hat{p}_v - Np_v$). (The second estimator is normalized in this comparison so that $N\hat{p}_v$ and Np_v have equal areas.) This residual is nonzero for finite values of N because of the inherent statistical variability of the estimate $N\hat{p}_v$.

Eq. 4 is a special case of the general expression:

$$S = \sum_{i=1}^{N} z_i, \tag{10}$$

where $\{z_i\}$ is a sequence of random variables, each term being either zero or one. This relationship permits the derivation of an expression for the variance of the residual. The statistics of the sequence $\{z_i\}$ are presumed not to vary with i. Letting z_i equal one with probability p, the variance of S is given by:

$$\mathrm{var}[S] = Np(1 - p) + 2\sum_{r=1}^{N-1} (N - r)[R_z(r) - p^2], \tag{11}$$

where $R_z(r)$ denotes the autocorrelation function of the sequence $\{z_i\}$, $R_z(r) = E[z_i z_{i+r}]$. The variance of S can be approximated by the first term of Eq. 11:

$$\mathrm{var}[S] \approx Np(1 - p). \tag{12}$$

Direct application of Eq. 11 yields an expression for $\mathrm{var}[N\hat{p}]$ which by Eq. 7 is equal to the variance of the residual. From Eq. 12 the standard deviation of the residual is approximated by:

$$\sigma = (N_b p_v^a(k\Delta)\Delta[1 - p_v^a(k\Delta)\Delta])^{1/2}. \tag{13}$$

This approximation differs by less than 10% from the exact value found by evaluating Eq. 11.

In Figs. 3, 4, and 5, curves denoting $\pm 2.5\sigma$ are shown with the residuals. Assuming the residuals have Gaussian distributions, the probability of any residual exceeding these curves in one bin is 0.0124. Consequently, in a 200-bin histogram, the residual would, on the average, be expected to exceed $\pm 2.5\sigma$ approximately two times if the spike trains are statistically independent and more frequently if the trains are not.

APPENDIX B

The Cross-Correlation Test of the Independence of Two Binary Sequences

The cross-correlation test is applied here to the binary-valued sequences $\{y_m^a\}$ and $\{y_m^b\}$ defined in Eq. 2. The empirical value $\hat{R}_{ab}(k)$ of the cross-correlation function is computed according to the equation:

$$M \cdot \hat{R}_{ab}(k) = \sum_{m=0}^{M-|k|-1} y_m^a \, y_{m+k}^b, \tag{14}$$

where M is the number of stimulus periods, and k is the lead of the cross-correlation in units of stimulus periods. If the product $y_m^a \, y_{m+k}^b$ equals 1, a spike occurs in spike train a during period m as well as a spike in train b during peroid $(m + k)$. Consequently, the statistic $M \cdot \hat{R}_{ab}(k)$ represents the number of times that spikes occur in both spike trains during stimulus periods that are k periods apart. The expected value of $M \cdot \hat{R}_{ab}(k)$ is given by:

$$E[M \cdot \hat{R}_{ab}(k)] = (M - |k|)R_{ab}(k), \tag{15}$$

where $R_{ab}(k)$ is the cross-correlation function of y_m^a and y_m^b (Eq. 3). For the data analyzed in this study, M, the number of stimulus periods, is of the order of 10^5 and $|k|$ is less than five; consequently, the expected value of $M \cdot \hat{R}_{ab}(k)$ is very nearly equal to $M \cdot R_{ab}(k)$.

Assuming $\{y_m^a\}$ and $\{y_m^b\}$ to be statistically independent, the cross-correlation $R_{ab}(k)$ is given by:

$$R_{ab}(k) = p_a p_b, \tag{16}$$

where:

$$\mathrm{Prob}[y_m^a = 1] = p_a,$$
$$\mathrm{Prob}[y_m^b = 1] = p_b. \tag{17}$$

These probabilities do not depend upon m, as the sequences $\{y_m^a\}$ and $\{y_m^b\}$ are presumed to be stationary. The expected values of $\{y_m^a\}$ and $\{y_m^b\}$ are p_a and p_b, respectively. Estimates of p_a and p_b are obtained by dividing the number of spikes in each train (Σy_m) by the number of stimulus periods (M).

$$\hat{p}_a = \frac{1}{M}\sum_{m=0}^{M-1} y_m^a,$$

$$\hat{p}_b = \frac{1}{M}\sum_{m=0}^{M-1} y_m^b. \tag{18}$$

These estimates do not depend upon how the sequences are related. The second estimate of $M \cdot R_{ab}(k)$ is computed according to:

$$M \cdot \tilde{R}_{ab}(k) = \frac{1}{M}\left(\sum_{m=0}^{M-1} y_m^a\right)\left(\sum_{m=0}^{M-1} y_m^b\right). \tag{19}$$

This estimate is assumed to reflect the correlation function $M \cdot R_{ab}(k)$ which would be obtained if $\{y_m^a\}$ and $\{y_m^b\}$ were statistically independent sequences.

The cross-correlation test, as applied to sequences, consists of comparing this correlation function with the measured correlation function $M \cdot \hat{R}_{ab}(k)$. As in the recurrence-time test, the size of the inherent statistical fluctuation in these measurements must be estimated in order to obtain a meaningful comparison. As $M \cdot R_{ab}(k)$ is a constant (Eq. 19), computing the variance of the residual $M \cdot \hat{R}_{ab}(k) - M \cdot R_{ab}(k)$ is equivalent to computing the variance of $M \cdot \hat{R}_{ab}(k)$. Eq. 14 resembles Eq. 10 with z_m equaling $y_m^a\, y_{m+k}^b$. Consequently, the derivation given in Appendix A for var $[S]$ applies here also (Eq. 11). So long as p (equal to $p_a p_b$ in this instance) is small, the approximation

$$\sigma = [M p_a p_b (1 - p_a p_b)]^{1/2} \tag{20}$$

is valid. The probabilities p_a and p_b are estimated by dividing the average discharge rates of each spike train by the stimulus frequency (Eq. 18). Typically, the error introduced in the standard deviation of $M \cdot \hat{R}_{ab}(k)$ by using Eq. 20 instead of the general equation 11 is less than 10%.