

Auditory-nerve action potentials form a nonrenewal point process over short as well as long time scales

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The firing patterns of auditory-nerve action potentials exhibit long-term fractal fluctuations that do not arise from the distribution of the interevent intervals, but rather from the ordering of these intervals. Using the serial interevent-interval correlation coefficient, the Fano-factor time curve, and shuffling of interevent intervals, it is shown that adjacent intervals for spontaneous firings exhibit significant correlation. The events are therefore nonrenewal over short as well as long time scales.

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INTRODUCTION

It is well known that in mammals, the pathway for the transfer of information from the inner ear to higher auditory centers in the brain is provided by the VIIIth nerve. The neural signal transmitted on individual fibers of this nerve has been studied by many researchers, with the goal of gaining insight into the mechanisms of information encoding (Galambos and Davis, 1943, 1948; Tasaki, 1954; Katsuki *et al.*, 1958; Kiang *et al.*, 1962, 1965; Rose *et al.*, 1967, 1971; Hind *et al.*, 1967; Evans, 1972, 1975; Kiang, 1984; Teich and Khanna, 1985; Young and Barta, 1986; Teich, 1989, 1992). This signal comprises a series of brief electrical nerve spikes, whose amplitude and energy are widely assumed not to be significant variables. Rather, it is generally accepted that the times of occurrences of the spikes carry the auditory information. Randomness is involved, since ensembles of identical single-fiber experiments lead to differing sequences of nerve spikes (Tasaki, 1954; Peake *et al.*, 1962; Rupert *et al.*, 1963; Kiang, 1984).

From a mathematical point of view, the neural activity in a peripheral auditory fiber is perhaps best characterized as an (unmarked) stochastic point process (Parzen, 1962). To take the simplest case, we consider auditory neural firings in the absence of any external acoustic stimulation. Auditory neurons spontaneously fire under such conditions, albeit at a lower rate than if a stimulus were present. Any realistic model of neural spike-train data must include the effects of dead time (absolute refractoriness), which limits the rate at which neurons can fire. After a relatively brief (1–2 ms) dead-time interval, the neuron is ready to fire again, and the time to the next firing event approximates an exponentially distributed random variable. (More precisely, the neuron recovers gradually, over a relative refractory period that lasts tens of milliseconds, rather than abruptly.) Figure 1 provides a histogram of the interevent times for the spontaneous spike train from cat auditory-nerve unit A (which is typical) on a semilogarithmic scale; the curve approximates an exponential distribution after the dead-time period. The dead-time modified Poisson point process (DTMP) (Ric-

ciardi and Esposito, 1966; Prucnal and Teich, 1983; Teich, 1985), which is a renewal point process, also has exponentially distributed interevent times after the dead-time period, and has been used as a zeroth-order approximation to model such data. Two related renewal point processes that provide somewhat better models make use of stochastic dead time (Teich *et al.*, 1978; Young and Barta, 1986) and relative dead time, also called sick time (Gray, 1967; Teich and Diamant, 1980; Gaumond *et al.*, 1982).

I. LONG-TERM CORRELATIONS

However, despite the exponential character of the interevent-time histogram, there now exists compelling evidence that, over long time scales, auditory-nerve spike-train data are not renewal (Teich, 1989; Teich *et al.*, 1990a,b; Woo, 1990; Powers, 1991; Woo *et al.*, 1992; Teich, 1992), but that

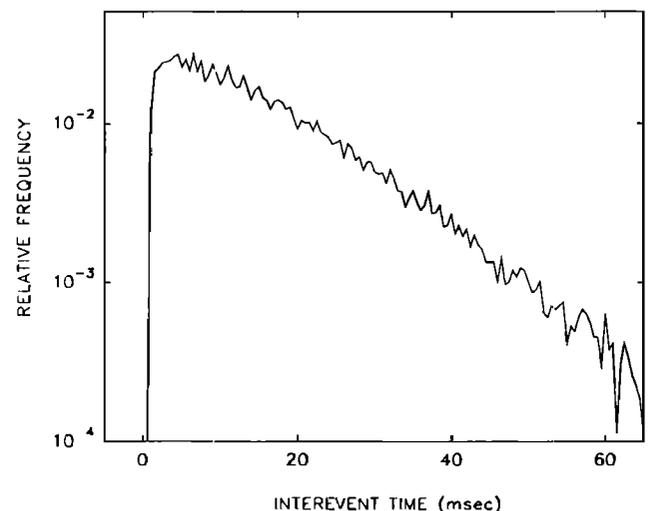


FIG. 1. Semilogarithmic plot of relative frequency of interevent times (interevent-time histogram) for unit A. The data closely follow a straight line for interevent times greater than about 4 ms. Bin width is 0.5 ms. The CF for this unit is 10.2 kHz.

long-term positive correlations are present in the data. One measure of this correlation is the Fano-factor time curve (FFC), defined as the variance of the number of events in a specified counting time T divided by the mean number of events in that counting time. In general, the FFC varies with the counting time T . For a DTMP process, the Fano factor never exceeds unity for any counting time, but for the auditory-nerve spike-train data the Fano factor increases in a power-law fashion beyond unity for large counting times.

Figure 2 shows the experimental FFC for unit A (solid curve). Note that the Fano factor increases steadily for counting times greater than about 100 ms, and exceeds 10 for counting times in excess of 30 s. This monotonic increase indicates the presence of a fractal process, with fluctuations on many time scales, rather than a collection of a few simple processes with single time constants, such as breathing or heartbeat. A plot of the FFC alone does not determine whether this large Fano factor arises from the distribution of the interevent times or their ordering. This issue is resolved by shuffling (randomly reordering) the interevent intervals and then replotting the Fano factor versus counting time. FFCs constructed from shuffled data yield information about the relative sizes of the intervals only; all correlation and dependencies among the intervals are destroyed by shuffling. The nonsolid curves in Fig. 2 illustrate five successive shufflings. The shuffled interevent intervals have FFCs which all approach a value less than unity for large counting times, illustrating that it is the ordering of the intervals that gives rise to the growth in the FCC. All auditory-nerve-fiber data examined to date (for which long-duration spike trains exist) show this type of behavior, both in the presence and in the absence of stimulation.

Thus the auditory-nerve data are more clustered than the DTMP process. The interevent intervals will be relatively more similar *within* a long counting time T than in the

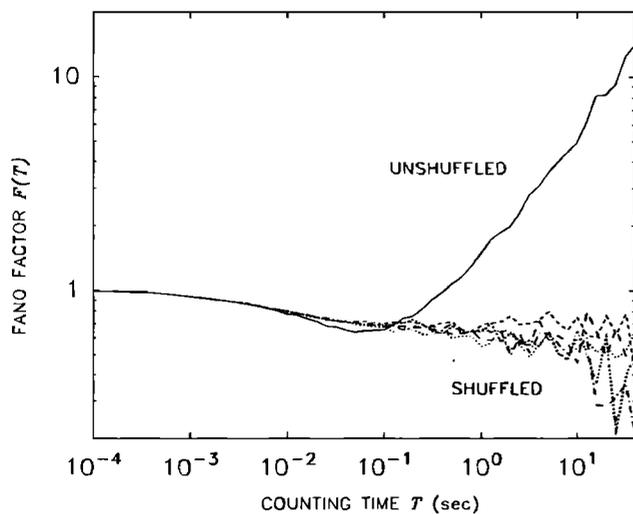


FIG. 2. Doubly logarithmic plot of Fano-factor time curve (FFC) for unit A. The curve for the unshuffled data approximates a straight line of positive slope for counting times larger than several hundred milliseconds, whereas the curve for the shuffled data does not rise. This indicates that the action potentials are clustered.

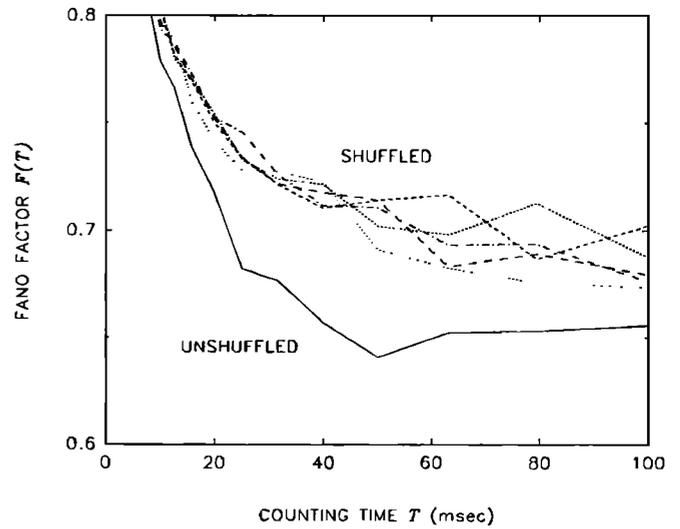


FIG. 3. Doubly linear plot of Fano-factor time curve (FFC) for unit A for counting times less than 100 ms. The curves for the shuffled data resemble each other but are consistently higher than the curve for the unshuffled data.

DTMP process, leading to a larger variation *among* counting times, and a larger Fano factor. The FFC provides a sensitive test for the presence of clusters, detecting them even when they are interleaved and therefore not readily apparent in visual representations of the auditory-nerve firings. Doubly stochastic models, such as the fractal-shot-noise-driven Poisson point process (FSNDP) (Lowen and Teich, 1991) are not renewal, and fit auditory-nerve-fiber data well. The FSNDP model contains interdigitated clusters, much as the auditory-nerve-fiber data appear to. For a variety of statistical measures, the data and simulations of the FSNDP yield nearly identical results, particularly for time scales of 100 ms or larger (Teich *et al.*, 1990b).

II. SHORT-TERM CORRELATIONS

Aside from the positive correlation over long times, there is also a small but significant correlation over time scales on the order of tens of milliseconds. Figure 3, which is a magnification of Fig. 2 (but plotted with linear coordinates), shows this effect. Again, the FFCs for the shuffled intervals are repeatably different from those of the unshuffled intervals, and again they are closer to unity. For this particular unit, and in this range of counting times T , the FFC *increases* with shuffling, indicating anticlustered interevent intervals. Thus for this unit, long intervals are likely to be followed by short intervals and *vice versa*; over long time scales, as with all auditory units, the opposite is true. Many of the units studied exhibit this short-time effect.

This behavior is demonstrated in Table I using another measure, the serial interevent-interval correlation coefficient (SIICC). The SIICC is the correlation coefficient calculated between adjacent intervals, and is defined by

TABLE I. Serial interevent-interval correlation coefficients (SIICCs) for ten data sets recorded from cat auditory-nerve fibers in the absence of stimulation. The average interevent intervals for each unit, in milliseconds, are shown in column 2, and the total number of events in column 3. SIICC values are shown for data both before and after shuffling, in columns 4 and 5. Also shown, in columns 6 and 7, are the likelihoods that an SIICC of that magnitude or larger would be obtained by chance from an identical number of uncorrelated intervals. None of the shuffled data sets exhibits significant correlation, while most of the unshuffled data sets do.

Unit	Average interval (ms)	Number of events	SIICC		Likelihood	
			unshuffled	shuffled	unshuffled	shuffled
A	15.3	26709	-0.03732	-0.00310	1.08×10^{-9}	6.12×10^{-1}
B	15.2	15345	-0.04535	+0.00354	1.93×10^{-8}	6.61×10^{-1}
C	13.5	22575	+0.00441	-0.00731	5.08×10^{-1}	2.72×10^{-1}
D	16.4	37932	-0.03031	-0.00373	3.58×10^{-9}	4.68×10^{-1}
E	27.0	4560	+0.02223	-0.00647	1.33×10^{-1}	6.62×10^{-1}
F	344.	206	+0.02175	+0.08745	7.56×10^{-1}	2.11×10^{-1}
G	28.1	2191	+0.09428	+0.02796	1.02×10^{-5}	1.91×10^{-1}
H	27.3	2603	+0.08855	+0.00082	6.28×10^{-6}	9.67×10^{-1}
I	58.1	1176	+0.08675	-0.00157	2.94×10^{-3}	9.57×10^{-1}
J	15.9	4190	-0.03828	+0.01083	1.32×10^{-2}	4.83×10^{-1}

$$\rho \equiv \frac{(N-2)^{-1} \sum_{i=1}^{N-1} (\tau_i - \langle \tau \rangle)(\tau_{i+1} - \langle \tau \rangle)}{(N-1)^{-1} \sum_{i=1}^N (\tau_i - \langle \tau \rangle)^2},$$

where N is the number of intervals,

$$\langle \tau \rangle \equiv N^{-1} \sum_{i=1}^N \tau_i,$$

is the sample average interevent time, and the τ_i represent the individual interevent intervals. The SIICC ranges from -1 (perfect anticorrelation) to +1 (perfect correlation), and is zero for uncorrelated intervals. The SIICC is calculated for the data before and after shuffling, and is presented in columns 4 and 5 of the table, respectively. Shuffling, i.e., the random rearrangement of the interevent intervals, provides a useful check on the SIICC computation algorithm. A random collection of intervals should exhibit no significant correlation. Similar results for the SIICC (for unshuffled data only) have been reported by Cooper (1989).

These SIICC values do not, by themselves, prove the existence or absence of correlation, so we develop a test of significance. Suppose that a number of independent interevent intervals are drawn from the same distribution, and that the SIICC is calculated for these intervals. Repeating this procedure will in general yield a different SIICC value, depending on the particular intervals selected. Thus the SIICC statistic has a margin of error. For the case of a large number of independent intervals, the SIICC will have a Gaussian distribution with zero mean and a variance proportional to the inverse of the number of intervals. This was verified by estimating the SIICC for 10^4 sets of 10^4 simulated exponentially distributed interevent-time samples, 10^4 sets of 10^3 samples, and 10^4 sets of 10^2 samples, all with the same mean. Exponentially distributed random variables have a finite mean and variance, so that the Central Limit Theorem may be applied.

For each SIICC value, we computed the probability that a random collection of intervals would generate an SIICC of that magnitude or larger. The results are displayed in co-

lumns 6 and 7 of the table for unshuffled and shuffled intervals, respectively. A relatively large probability indicates that the corresponding data set is probably uncorrelated, while a small one indicates the existence of correlation. The results show that the ten shuffled data sets are not significantly correlated, as expected, since shuffling destroys any correlation; however, most of the unshuffled data sets do exhibit significant correlation.

Interestingly, there is no clear trend in the data. Some data sets exhibit significant positive correlation, some significant negative correlation, and some no significant correlation at all. The correlation does not seem to be related to the average interevent interval. Thus no simple model is likely to suffice in describing the relationship between nearby interevent intervals.

The fractal behavior underlying the long-term correlations is almost certainly not related to the short-term correlations. The fractal part of the Fano factor, as an example, scales as T^α , with $0 < \alpha < 1$, and therefore has only minimal variation over the relatively short time scale of a single interevent interval. The FSNDP model we employed to simulate the auditory-nerve spike behavior of unit A yielded an SIICC that was only slightly statistically significant when dead-time effects were removed. For 100 runs, each using a different random-number seed, the computed likelihoods were all greater than 10^{-5} . The FSNDP produced a slight positive correlation in the interval statistics as expected, much less significant than that shown in Table I for unit A. Furthermore, the most significant correlations shown in the table are negative, while the FSNDP and other similar fractal models necessarily introduce a positive correlation. It is likely that the short-term correlation arises from a form of refractoriness with memory that extends over a few interevent times. Such models have been successfully employed for clicks (Gaumond *et al.*, 1983), and tone bursts (Lütkenhöner and Smith, 1986), for which nonrenewal, and indeed nonstationary, behavior would be expected.

III. DISCUSSION

Auditory-nerve firing patterns are not well modeled as a dead-time-modified Poisson process (DTMP), either in the absence or in the presence of stimulation. Over long time scales, the firing patterns exhibit long-term fractal fluctuations that do not arise from the distribution of the interevent intervals, but rather from their ordering. Using the SIICC, shuffling, and the FFC, we have shown that adjacent intervals have significant correlation, and thus the process is also nonrenewal at short times. We computed the SIICC both before and after shuffling, eliminating the possibility that the correlation is an artifact of the interevent-time distribution. Distributions with long tails can generate apparent correlation statistics in finite data samples even when no such correlation exists. The nonrenewal nature at short times is also apparent in higher-order interevent time distributions (Teich and Khanna, 1985). The Fano factor provides a different picture of the relationships between closely spaced interevent times, showing short time correlations as well as long-term behavior simultaneously. The difference between the shuffled and unshuffled FFCs provide further evidence for the nonrenewal nature of the auditory-nerve-fiber data over all time scales. Cognizance of this fact should lead to an improved understanding of the physiology underlying the generation of sequences of auditory-nerve action potentials.

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