RANDOM WALK MODELS FOR THE SPIKE ACTIVITY OF A SINGLE NEURON

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ABSTRACT Quantitative methods for the study of the statistical properties of spontaneously occurring spike trains from single neurons have recently been presented. Such measurements suggest a number of descriptive mathematical models. One of these, based on a random walk towards an absorbing barrier, can describe a wide range of neuronal activity in terms of two parameters. These parameters are readily associated with known physiological mechanisms.

INTRODUCTION

A prominent characteristic of the electrical activity in the nervous system is the prevalence of spontaneous activity, both at the level of the spatially summed potentials observed with a gross electrode and at the level of the action potentials of a single neuron. In a recent paper Rodieck, Kiang, and Gerstein (1962), using examples recorded in the cochlear nucleus of anesthetized cats, set forth some quantitative methods that may be used to study the statistical properties of the train of action potentials associated with spontaneous activity of a single neuron. It was shown in that paper that three types of measurements are particularly useful in order to establish a statistical description of the spike train:[1]

(*a*) The interval histogram—a histogram of the distribution of time intervals between successive spikes. This measurement estimates the probability density of intervals.

(*b*) The joint interval histogram—a histogram of the joint distribution of two successive interspike intervals. This measurement estimates the joint probability density of successive intervals.

(*c*) The scaled interval histogram—a histogram of the intervals between every $2^{m\text{th}}$ spike when m is a positive integer. (For $m = 0$ this description is identical with the interval histogram.) This measurement estimates the probability density

[1] We shall use spikes and action potentials interchangeably.

of particular intervals that are themselves the sum of 2, 4, 8, . . . successive interspike intervals.

In the present paper we shall use some of the data and measurements of Rodieck *et al.* (1962) as a basis for several mathematical models of the neuron. We shall show that the parameters in these models can be given significance in physiological terms, and that these models can generate many of the observed characteristics of spike trains from single neurons.

SOME BASIC OBSERVATIONS

The Poisson Model

Whenever one deals with a sequence of events that seem randomly spaced in time, it is usual to assume as a first approximation that the probability for the event to occur during a time increment dt is equal to $R\ dt$, independently of the past history of the process. Here, R is a constant that defines the average time rate of occurrence of the events. If the events are action potentials, these conditions cannot be met fully because the interspike interval has a lower bound, D, resulting from the refractory time of the neuron. If there are no other constraints, the interspike intervals will be distributed with a probability density

$$\begin{aligned} I(\tau) &= R \exp [-R(\tau - D)] \quad \text{for} \quad \tau \geq D \\ &= 0 \qquad\qquad\qquad\quad \text{for} \quad \tau < D, \end{aligned} \tag{1}$$

where τ is the duration of the interspike interval.

In this type of model successive interspike intervals are independent random variables, so that the joint probability density for interval τ_1 followed immediately by interval τ_2 can be written

$$\begin{aligned} I(\tau_1, \tau_2) &= R^2 \exp [-R(\tau_1 - D + \tau_2 - D)] \\ &= R^2 \exp [-R(\tau_1 + \tau_2 - 2D)] \quad \text{for} \quad \tau_1 \geq D, \quad \tau_2 \geq D \end{aligned} \tag{2}$$

It follows that the lines of equal probability density in the joint distribution of τ_1 and τ_2 will be straight lines that are parallel to the second bisectrix $\tau_1 + \tau_2 = 0$.

Consider also the probability density $I_k(\tau)$ for the interval between a spike and the k^{th} spike that follows it. (This represents a slight generalization of the measurement defined by the scaled interval histogram, in which k was restricted to be of the form 2^m, when m is a positive integer.) In the present case of an exponential distribution, each such interval is the sum of k independent exponential random variables. The resulting probability density is called the gamma distribution of order k:

$$I_k(\tau) = R^k \tau^{k-1} \exp (-R\tau)[\Gamma(k)]^{-1}, \tag{3}$$

where Γ represents the gamma function. As k increases, this distribution rapidly becomes peaked, symmetric, and tends towards the Gaussian.

Thus, in order to test empirically the conjecture that a spike train may be de-

scribed as a Poisson process, one must examine the basic distribution of interspike intervals $I(\tau)$, the joint distribution of successive intervals $I(\tau_1, \tau_2)$, and, finally, the distribution of scaled intervals $I_k(\tau)$. It is clear that there are indeed cases in which all three theoretical predictions of the Poisson process are verified. For example, consider the data given by Rodieck *et al.* (1962) for Unit 259-2 which show an exponential distribution of intervals.[2] We show in Fig. 1*a* that for this unit the lines of constant probability density in the joint interval histogram are indeed parallel to $\tau_1 + \tau_2 = 0$. In Fig. 2*a* we see that the scaled interval histograms for this unit tend rapidly toward a narrow and symmetric shape.

The simple Poisson type of model has been used previously in neurophysiology (Kuffler, Fitzhugh, and Barlow, 1957; Grossman and Viernstein, 1961). Unfortunately, it is a purely descriptive model that does not contribute much to our understanding of the detailed mechanisms that may be involved in the firing of a neuron. It is also clear that many units produce spike trains for which the three fundamental predictions based on a Poisson model are grossly incorrect. In this paper we shall study two such examples, one rather briefly, the other in detail.

The Gaussian Model

Consider a train of action potentials which exhibits appreciable periodicity so that there are only relatively small fluctuations in the durations of interspike intervals. Here, the probability density of intervals may "look" very much like that of a sample from a Gaussian population. If this is indeed the case, and if successive intervals τ_1 and τ_2 are independent, then the joint density of successive intervals would be the product

$$I(\tau_1, \tau_2) = (2\pi\sigma^2)^{-1} \exp\{-(2\sigma^2)^{-1}([\tau_1 - E(\tau_1)]^2 + [\tau_2 - E(\tau_2)]^2)\}. \quad (4)$$

Here, $E(\tau_1)$ is the expectation value, or mean duration, of the first interval of the pair and σ^2 is the variance of either interval. According to equation (4), the contours of equal density are circles with a common center at the coordinate point $E(\tau_1), E(\tau_2)$.

The sum of k successive interspike intervals will be a sum of k independent Gaussian variables. According to the well known properties of the Gaussian distribution, this sum will itself be a Gaussian variable with a mean value $kE(\tau)$ and a variance equal to $k\sigma^2$. (Here, $E(\tau)$ and σ^2 refer to the probability density of the basic interspike intervals.)

We may find cases that are in reasonable agreement with these theoretical predictions. As an example, consider the data of Rodieck *et al.* (1962) for Unit *R*-4-10 which show an interval histogram that looks like a Gaussian distribution.[3] In Fig. 1*b* of the present paper we demonstrate that lines of constant probability density in the joint interval histogram are approximately circular. The scaled interval

[2] See Rodieck, Kiang, and Gerstein (1962), Fig. 5*a*.

[3] See Rodieck, Kiang, and Gerstein (1962), Figs. 4*b* and 5*b*.

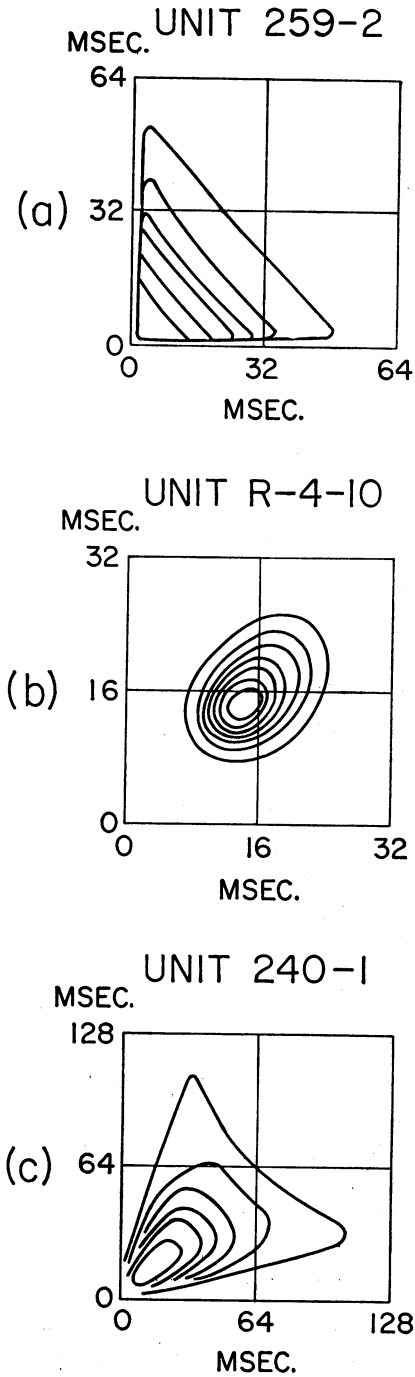


FIGURE 1 Lines of constant density in joint interval histograms for the three units discussed here. (*a*) Unit 259-2; (*b*) Unit R4-10; (*c*) Unit 240-1.

histograms of Fig. 2*b* show that the mean value and variance of the sum of intervals indeed behave as predicted. (Note that the time scale of each successive order of scaled interval is adjusted by a factor of 2, and that this keeps the center (mean) of the successive scaled interval distributions at the same location on the abscissa.)

Long Interspike Intervals

The exponential and the Gaussian distributions share an important property: The asymptotic decrease of the probability density function is quite rapid for large values of τ. In other words, long interspike intervals are extremely rare. However, there are experimental situations in which the density of intervals behaves very differently. In qualitative terms, there may be, in comparison with the number of intermediate length intervals, an excessive number of both fairly short and very long interspike intervals. An example of such data is given by Rodieck *et al.* (1962) for Unit 240-1: their Fig. 5*d* clearly shows an upward curvature of the semilogarithmic plot of the interval histogram. It is interesting to note that similar behavior has been observed by one of the authors (B. B. M.) in several fields of study that are quite remote from neurophysiology (Mandelbrot, 1960, 1963 *a* and *b*; Berger and Mandelbrot, 1963).

Another important characteristic of the data from Unit 240-1 is shown in Fig. 2*c*: with the indicated changes in time scale, the shape of each of the first few successive orders of scaled interval histogram remains approximately the same. This means that a sum of successive interspike intervals has the same probability density—to within a scale factor—as the basic interspike intervals. If we make the simplifying assumption that the lengths of successive intervals are independent (this is not quite true for the short intervals in the data), successive orders of scaled interval histogram are related by $I_2(\tau) = I(\tau) * I(\tau)$. Then the observed invariance of shape under the scaling transformation means that the density of interspike intervals must obey

$$I(\tau) * I(\tau) = (1/2) I(\tau/2). \tag{5}$$

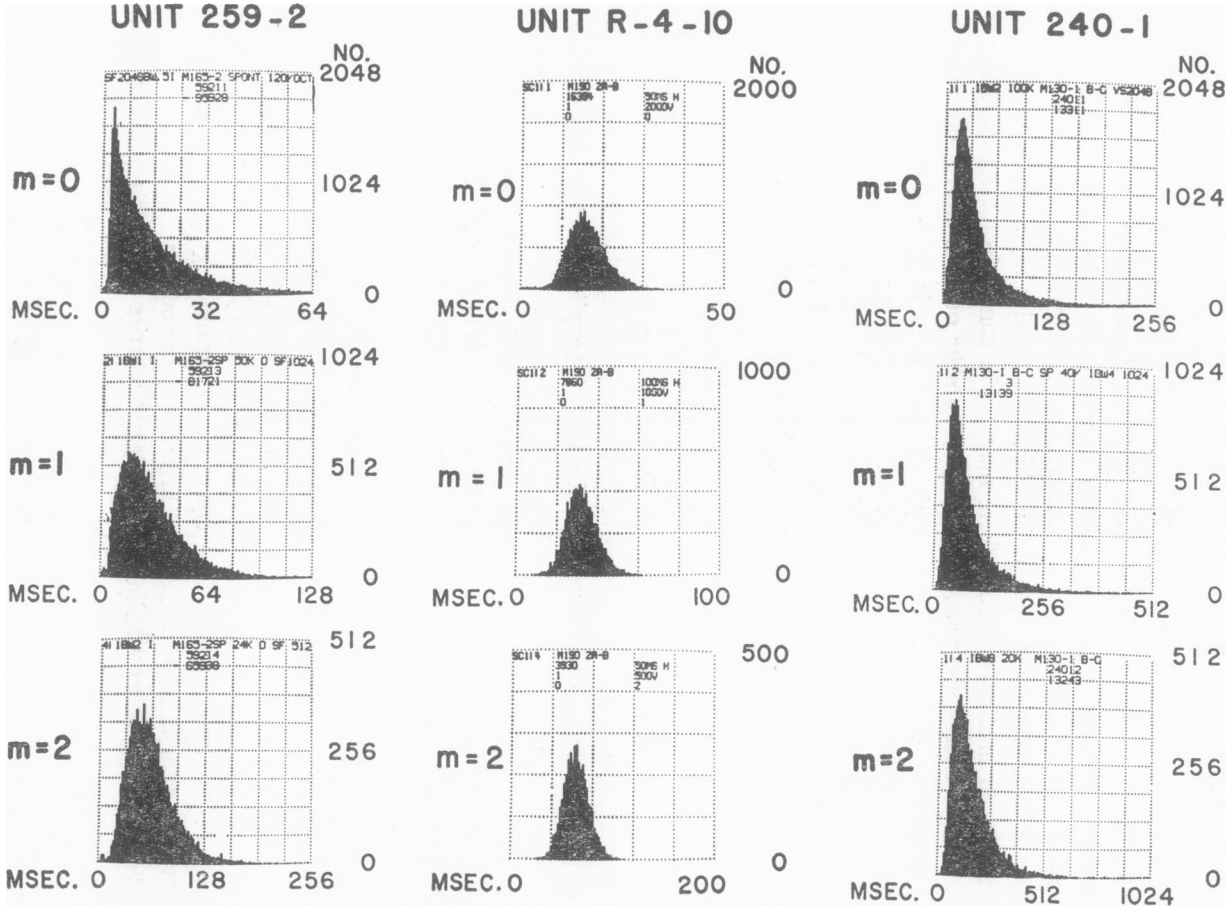
Here, the symbol * denotes the operation of convolution. This extremely restrictive condition may be stated as follows: When the probability density is convolved with itself, the result must have the same functional form, with only a particular change of the time scale. In the conventional terminology of probability theory, the "type" of the interspike interval is invariant under addition.

These properties, as we shall show, suggest a series of models that can describe the spike activity of a single neuron.

THE SIMPLE RANDOM WALK MODEL

Development of the Model

Distribution functions whose densities obey a general relation that is similar to


UNIT 259-2
UNIT R-4-10
UNIT 240-1
NO.
2048
2000
1024
1000
512
500
256
0
m=0
m=1
m=2
MSEC. 0
32
64
50
128
100
200
256
512
1024

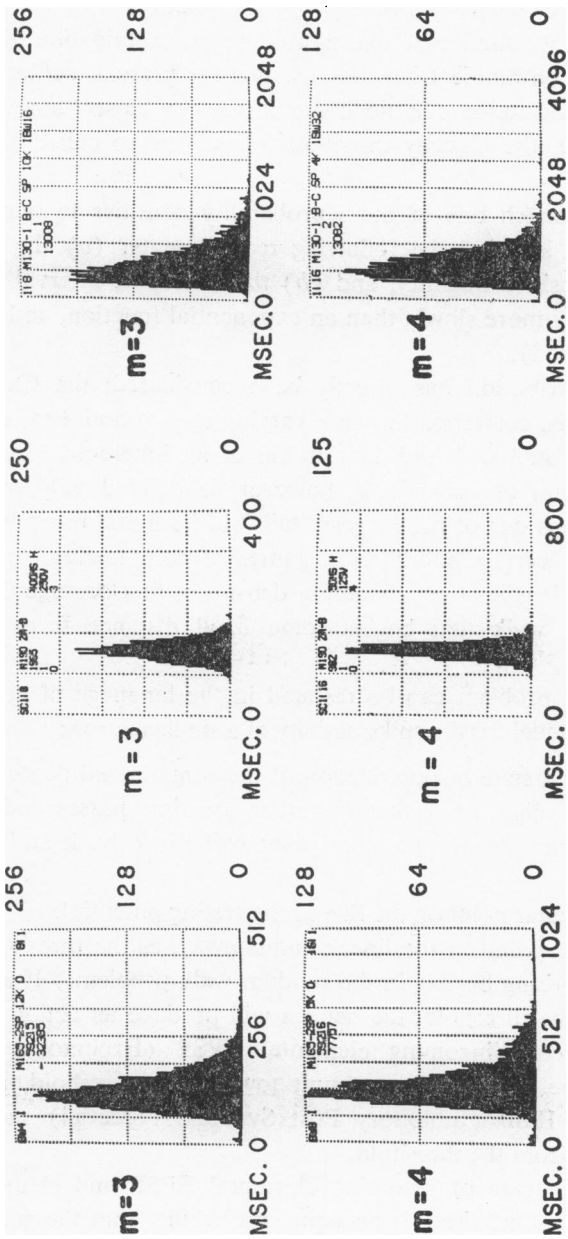


FIGURE 2 Scaled interval histograms for the same units as in Fig. 1. (*a*) Unit 259-2; (*b*) Unit R4-10; (*c*) Unit 240-1.

equation (5) are known as stable distribution functions. The stability property refers to the invariance of the functional form of the distribution function under convolution; in general, there may be a linear change of scale in the variable. These functions have been extensively studied (Lévy, 1940; Gnedenko and Kolmogorov, 1954); we shall postpone more detailed examination of their properties until the section on Stable Distributions. For the present, suffice it to say that only three stable distribution functions are known in closed analytic form: the Gaussian distribution, the Cauchy distribution, and the so called stable distribution of order 1/2.

In attempting to match one of these probability densities to our experimental data, we must keep in mind the following requirements: (*a*) the interspike interval is always a positive quantity, and (*b*) the interspike interval histogram decreases asymptotically more slowly than an exponential function, and is asymmetric about its mode (skewed).

The Gaussian distribution has already been considered; the Cauchy distribution has two long tails, corresponding to τ varying to $-\infty$ and $+\infty$, and thus could not readily be associated with the distribution of an inherently positive quantity. The stable distribution of order 1/2, however, is defined only on the interval $(0, +\infty)$, and also has one of the longest "tails" to be found in probability theory. It is associated with certain solutions in games of coin tossing, or with random walks. In particular, it gives the probability density of first passage times in a one-dimensional random walk that begins some fixed distance from an absorbing barrier.

The random walk problem can be restated in the language of neurophysiology in order to define a model for the spike activity of a single neuron:

1. Let the electrical state of polarization of the somatic and dendritic membrane of the neuron be specified by a single number. As time passes and the electrical state of the membrane varies, the state point will move back and forth along a straight line.

2. Choose a particular point on the line as the resting potential.

3. Choose another point on the line, z_0 units away, as the threshold. (This corresponds to the absorbing barrier in the random walk problem.) If at any time the state point reaches the threshold, the neuron will produce an action potential.

4. Assume that each incoming elemental EPSP (Excitatory Post Synaptic Potential) moves the state point one unit toward the threshold, and that each incoming elemental IPSP (Inhibitory Post Synaptic Potential) moves the state point one unit away from the threshold.

5. Let the average rate of incoming elemental EPSP and elemental IPSP be the same; *i.e.*, at any time there is an equal probability that the state point move either a unit toward or a unit away from the threshold.

6. Immediately after the state point has attained the threshold and caused the

production of an action potential, it returns to the resting potential, only to begin again on its random walk.

Some basically different neuron models which also utilize a state point and a threshold have been previously described. Our random walk model should be compared, for example, with the additive noise models of Viernstein and Grossman (1961) and Verveen (1961). These authors postulate fluctuations of the membrane state (or alternatively of the threshold) which have a Gaussian distribution of amplitudes. They also assume that there is no correlation between successive fluctuations, so that there may be arbitrarily large sudden transitions of the state point. In contrast, transitions in our model are the result of many small steps and may be compared with the lag or lead of the number of heads in the repeated tossing of a coin. Thus the probabilistic characteristics of our model are a reflection of the rate and order of incoming elemental EPSP and IPSP, and do not explicitly require the introduction of a "noisy" membrane or noisy threshold.

Even if the membrane state fluctuations in the additive noise models are band width-limited so as to produce smooth transitions, our random walk model differs by its use of the reset to resting potential. This fundamental distinction causes the two types of model to have quite different densities for reaching threshold. There is, of course, neurophysiological evidence that at least for some neurons reset does take place after the occurrence of an action potential (Eccles, 1957, particularly chapter 2).

It should also be pointed out that the precise rules that govern the motion of the state point in the random walk do not seriously affect the calculation of first passage time. In the model described thus far we have considered a "membrane" with infinite time constant and identical excitatory or inhibitory steps occurring at regular increments of time. Recently work has been done (Fetz and Gerstein, 1963) on models which utilize an exponential time distribution of excitatory and/or inhibitory steps together with finite time constants for the membrane. Even with time constants shorter than typical interspike times, such models can exhibit most of the properties discussed for the random walk model of the present paper. We may conclude that the microscopic rules of a random walk model cannot be uniquely determined from physiological data on spike trains. More detailed intracellular potential measurements than presently available would be needed in order to set such details in the model.

Interval Densities

In order to make theoretical predictions that can be compared with data on the probability density of interspike intervals, we must, in terms of our random walk model, calculate the probability density for first attaining the threshold. If we assume that each elemental movement of the state point in the model is small in comparison with the distance z_0 between the resting potential and the threshold, and if

we do not need a description of the detailed motion of the state point, then the problem may be treated with high accuracy as a diffusion process with an absorbing barrier. The normal diffusion current at the absorber will correspond to the probability density of first passage times (interspike intervals) (Chandrasekhar, 1943).

This density has the form

$$I(z_0, \tau) = (4\pi)^{-1/2} z_0 \tau^{-3/2} \exp(-z_0^2/4\tau) \qquad \tau \geq 0$$
$$= 0 \qquad \tau < 0 \tag{6}$$

where τ is the duration of an interspike interval and z_0 has been defined.

Long intervals are so probable in this model that the variable τ has no population moments of any order. Even its mean value is infinite. In other words, a sample mean interval calculated on a finite sample of data would be expected to grow without bound as the sample size increases. These characteristics of the model may be made more intuitively acceptable by considering the random walk: the state point is free to wander arbitrarily far from the threshold, thus allowing an extremely long first passage time. We illustrate this behavior in Fig. 3, which shows a computer simulation of several random walks. With the resting potential 32 steps from the threshold (or absorber), the state point has frequently not reached the firing threshold even after 2560 steps.[4]

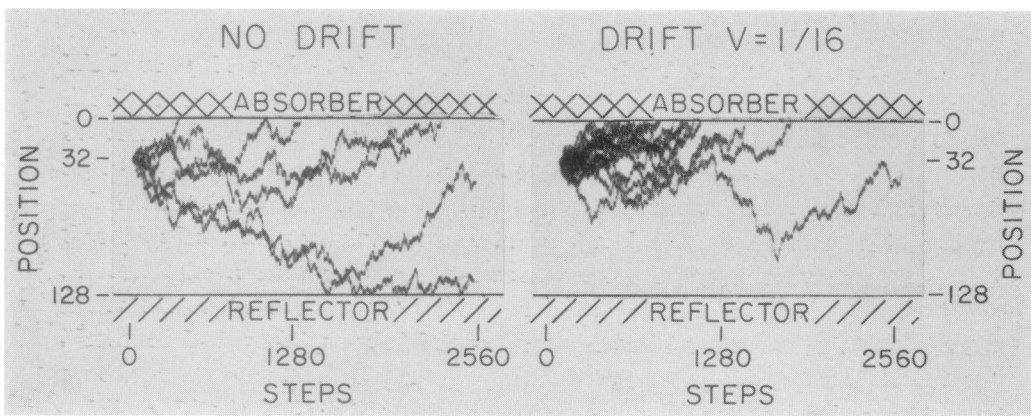


FIGURE 3 Typical random walks in one dimension in a computer simulation of the model.

For the simple random walk model, successive interspike intervals are independent. The joint density of successive intervals, when both τ_1 and τ_2 are large enough to discard the exponential, is of the form

$$I(\tau_1, \tau_2) = C^2 \tau_1^{-3/2} \tau_2^{-3/2} = C^2 (\tau_1 \tau_2)^{-3/2}. \tag{7}$$

[4] We have, for convenience, introduced a reflecting barrier into the illustration, which corresponds to some maximum hyperpolarization. This limits the maximum distance that the state point may be from the firing threshold. However, as long as this distance is large compared with z_0, the density of first passage times remains as we have described above.

Clearly, the lines of equal probability are hyperbolae. Their curvature contrasts qualitatively with the straight contour lines of the Poisson (or exponential) model and with the circular contour lines of the Gaussian model.

One may easily verify that, under addition of successive interspike intervals, the density of equation (6) shows the shape invariance required of a stable function. By direct integration, we obtain

$$I(\tau)*I(\tau) = (1/4)I(\tau/4). \tag{8}$$

More generally, for the density of equation (6), the sum of k successive interspike intervals, weighted by k^{-2}, will have the same probability density as the fundamental interspike intervals.

It is not surprising that the simple model that we defined above does not quantitatively fit the data, and that it is necessary to make the model more complex. A number of discrepancies exist between the predictions of the simple model and the data. Perhaps most striking is the fact that the experimentally observed scaling invariance (Fig. 2*c*) implies a weighting factor k^{-1} in contrast with the k^{-2} weighting factor of the simple random walk model.[5] This difference is also made evident by comparing the experimental convolution relation (equation (5)) with the prediction of the simple random walk model in equation (8). Thus, although the model predicts invariance of shape under the scaling transformation, it does so with the wrong change of time scale.

A second discrepancy between data and model is, experimentally, that as k becomes large, the scaling invariance no longer applies (see the last few scaled interval histograms at the bottom of Fig. 2*c*). In other words, the asymptotic decrease of the experimental interval density is much faster than the $\tau^{-3/2}$ decrease predicted by the simple random walk model.

A third discrepancy is that the observed joint density of successive interspike intervals $I(\tau_1, \tau_2)$ does not clearly exhibit the hyperbolic contour pattern that we derived in equation (7). (See Fig. 1*c*.)

We shall now demonstrate that a relatively small modification of the simple random walk model will allow a far better fit of the data.

THE RANDOM WALK WITH DRIFT

Calculation of Interval Density

In the section on The Simple Random Walk Model it was assumed that the average rates of incoming elemental EPSP and elemental IPSP are identical: there was no "bias toward" either input. But it is far more reasonable in a physiological model to assume that these two rates are different, and that there is some excess of either

[5] If $I(\tau)$ were a Gaussian density with zero mean, the required weighting factor would be $k^{-1/2}$.

EPSP or IPSP input. In this case, the probability for the state point to move one unit toward the threshold will be different from the probability for it to move away from the threshold.

In terms of a diffusion process, the difference between these probabilities can be considered a "drift velocity," either toward or away from the threshold. Taking the origin of our coordinate system at the threshold, we must solve

$$\frac{\partial \omega}{\partial t} = \frac{\partial^2 \omega}{\partial z^2} - c \frac{\partial \omega}{\partial z}$$

subject to the boundary conditions

$$\omega = \delta(z - z_0) \quad \text{at} \quad t = 0; \quad \omega = 0 \quad \text{at} \quad z = 0 \qquad \text{all} \quad t \geq 0.$$

Here, c represents the drift velocity, and we have taken the diffusion coefficient to be unity. The quantity ω represents the spatial density of the diffusing particles: each such particle represents the state point of our neuron model during the time between some two action potentials. The normal diffusion current at the absorber corresponds to the probability density of first passage times in the model. Thus we find

$$\begin{aligned} I(z_0, c, \tau) &= (4\pi)^{-1/2} z_0 \tau^{-3/2} \exp\left\{-\frac{(z_0 + c\tau)^2}{4\tau}\right\} && \tau \geq 0 \\ &= 0 && \tau < 0. \end{aligned} \tag{9}$$

We have again used τ to indicate the duration of a first passage time, z_0 to indicate the distance between resting potential and threshold, and c to express the difference between the rate of elemental EPSP and elemental IPSP input to the neuron. Clearly, for $c = 0$ this result reduces to equation (6).

The probability density given in equation (9) is, unfortunately, such that convolution with itself does produce change in the functional form. However, it is easy to show that for a certain range of parameters there is approximate shape invariance under the convolution operation with a 2× expansion of the time scale. This is illustrated in Fig. 4 by scaled interval histograms in a computer simulation of the random walk model with draft.

When drift is included in the random walk model, successive intervals remain independent. The joint density of successive intervals $I(\tau_1, \tau_2)$ is thus given by a product of two terms like equation (9). For reasonable choice of parameters, a numerical evaluation quickly shows that the contours of equal density are less curved than the hyperbolas of equation (7).[6] The contour lines return to near the origin through regions close to the τ_1 and τ_2 axes. The over-all contours are therefore roughly right "triangles" with an inward curved hypotenuse. This curvature be-

[6]Because of the linear term in the exponential of equation (9) for very large values of τ_1 and τ_2 (far beyond values which are experimentally observed), the contour lines become straight lines parallel to $\tau_1 + \tau_2 = 0$.

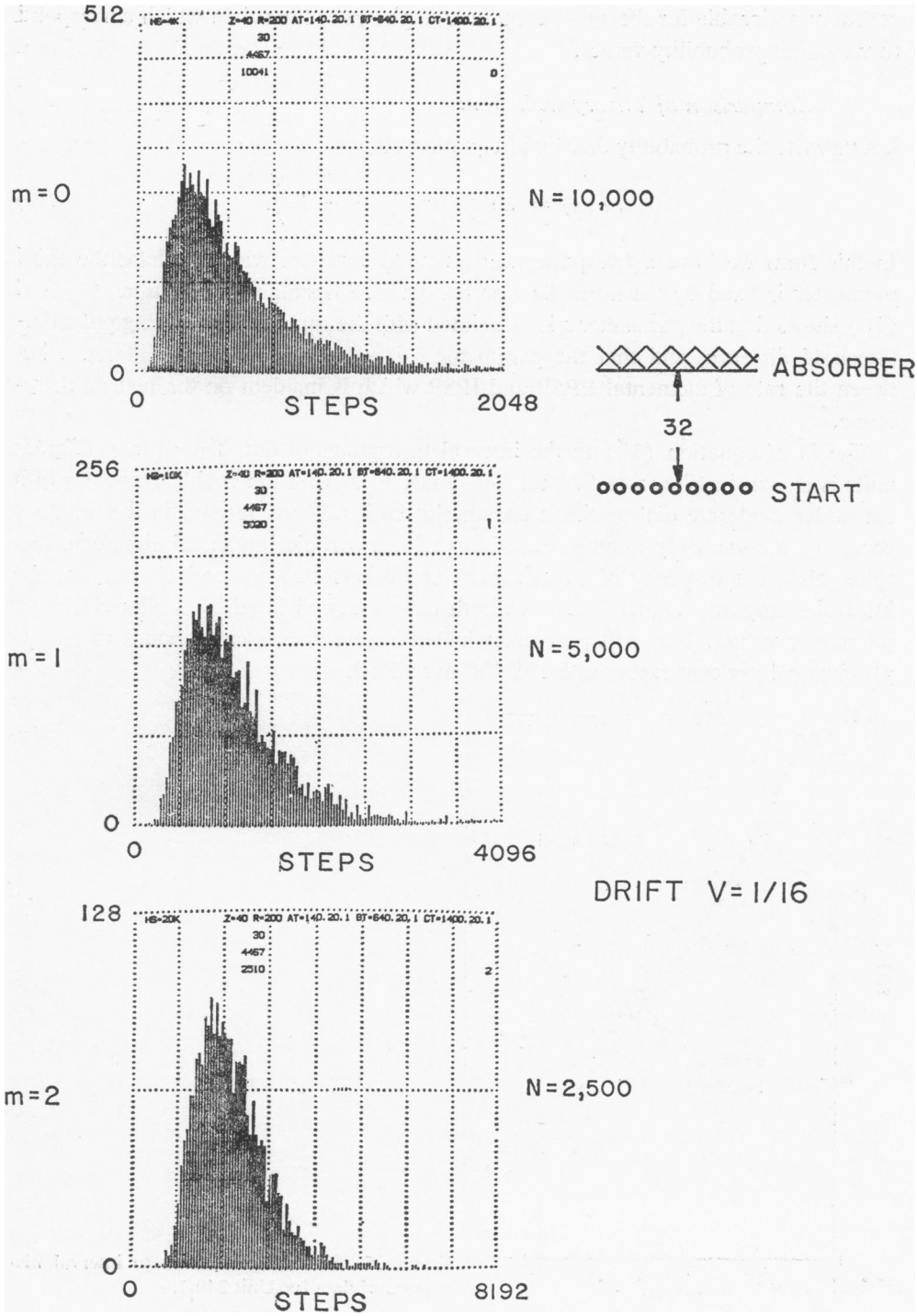


FIGURE 4 Scaled interval histograms for the computer simulation of the model.

comes unnoticeable for the small contour triangles near the origin which correspond to very high probability values.

Comparison of Theory with Data

Let us write the probability density of equation (9) as

$$I(a, b, \tau) = K\tau^{-3/2} \exp\left(-\frac{a}{\tau} - b\tau\right). \tag{10}$$

In this form we have a two-parameter curve to compare with the data; the third parameter is fixed by the normalization condition. Inspection of equations (9) and (10) shows that the parameter a is associated with the square of the resting potential-threshold distance, and that the parameter b is associated with the difference between the rate of elemental EPSP and IPSP which is incident on the neuron membrane.

The fit of equation (10) to the interval histograms of data from three different units is shown in Figs. 5 to 7. Unit 240-1 was located in the cochlear nucleus of a cat under moderate dial-urethane anesthesia; Unit 6-2 was located in the auditory cortex of a completely unanesthetized cat with a chronic implanted electrode. Despite this great disparity of experimental conditions and anatomical location, the interval histograms of the data from both units are well fitted by similar choice of parameter values. The drift parameter in both these causes corresponds to an approximate 4 per cent excess rate of EPSP over IPSP.

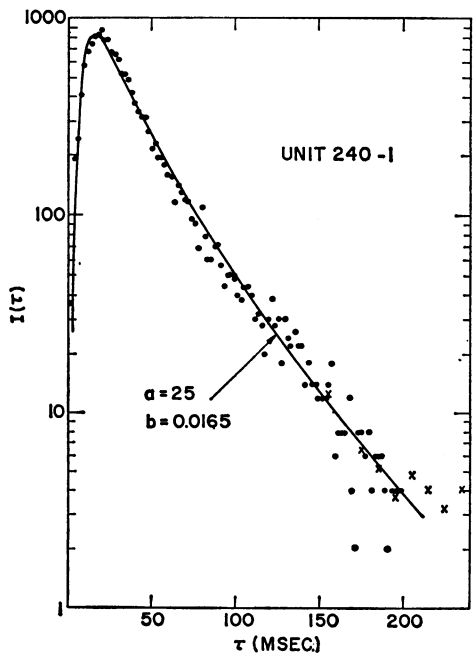


FIGURE 5 Fit of equation 10 to interval histogram of data for Unit 240-1.

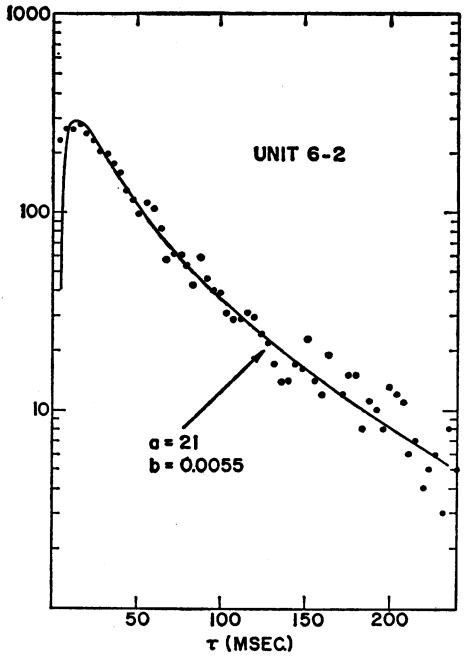


FIGURE 6 Fit of equation 10 to interval histogram of data for Unit 6-2.

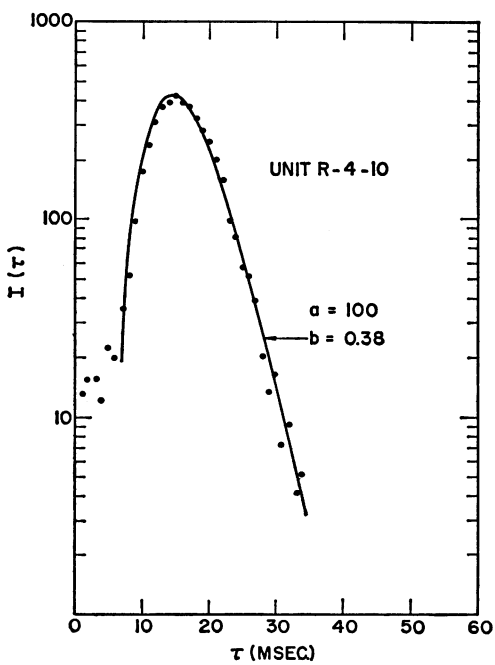


FIGURE 7 Fit of equation 10 to interval histogram of data for unit R4-10.

Reasonably good agreement between model and experiment is also observed for the joint density of successive interspike intervals from these two units. The contour pattern of the data from Unit 240-1 (Fig. 1*c*) differs from the theoretical prediction (page 52) mainly in that the vertex angle of the contour triangles is less than the predicted 90°. The source of this discrepancy is that in the model successive interspike intervals are completely independent, while in the data there is some correlation between successive intervals when they are short.

In Fig. 7 we show that the Gaussian-like data of Unit R-4-10 can also be fitted by equation (10), but require a very different set of values of a and b: In comparison with the values used in Figs. 5 and 6, we have here increased the a parameter by a factor of 4, and the b parameter by a factor of 23. Physically, this change means that the model for this particular neuron has a higher threshold than in Figs. 5 and 6 and a much larger excess rate of EPSP over IPSP. It is intuitively obvious that under such conditions of high drift velocity the state point of our model will reach the threshold frequently and in an almost periodic way.[7] In order to choose between this fit and the fit by the Gaussian density, we shall have to determine whether, for a large number of units, the parameters of the model exhibit a continuous range of values or tend to cluster in some significant way. Again for this case there is good agreement between model and experiment for the contour lines in the joint density of successive interspike intervals.

A TIME-VARIANT MODEL

In most physiological experiments data are taken not only during spontaneous activity, but in the presence of transient stimuli that are often periodically presented. In recordings from single units one frequently observes correlation between the pattern of action potentials and the instants at which the stimulus is presented (Gerstein and Kiang, 1960). Unless the unit is firing very rapidly in comparison with the rate of stimulus presentation, an interval histogram of the activity should show some evidence of the interval between stimuli. This situation is illustrated in Fig. 8, which shows interval histograms for the activity of a unit from the cochlear nucleus of an anesthetized cat during presentation of clicks at various rates. The mode of the interval histogram of spontaneous activity lies at approximately 10 msec. When clicks are presented at 10/sec., the neuron fires "spontaneously" several times in the course of the 100 msec. between stimuli; thus no evidence of 100 msec. periodicity

[7] Since the distance between the points that represent the resting potential and the threshold is experimentally found to be quite similar for most cells, we should point out that an alternate physical interpretation of the parameters of Fig. 7 is possible. In the foregoing development we have assumed that the variance of EPSP-IPSP rate fluctuations has been taken at some fixed value, and accordingly have set the diffusion constant at unity. If this limitation is removed, we may interpret the change in parameter values in Fig. 7 as follows: variance of the EPSP-IPSP rate fluctuations is smaller, there is a large excess of EPSP rate, and the threshold remains at some "normal" value.

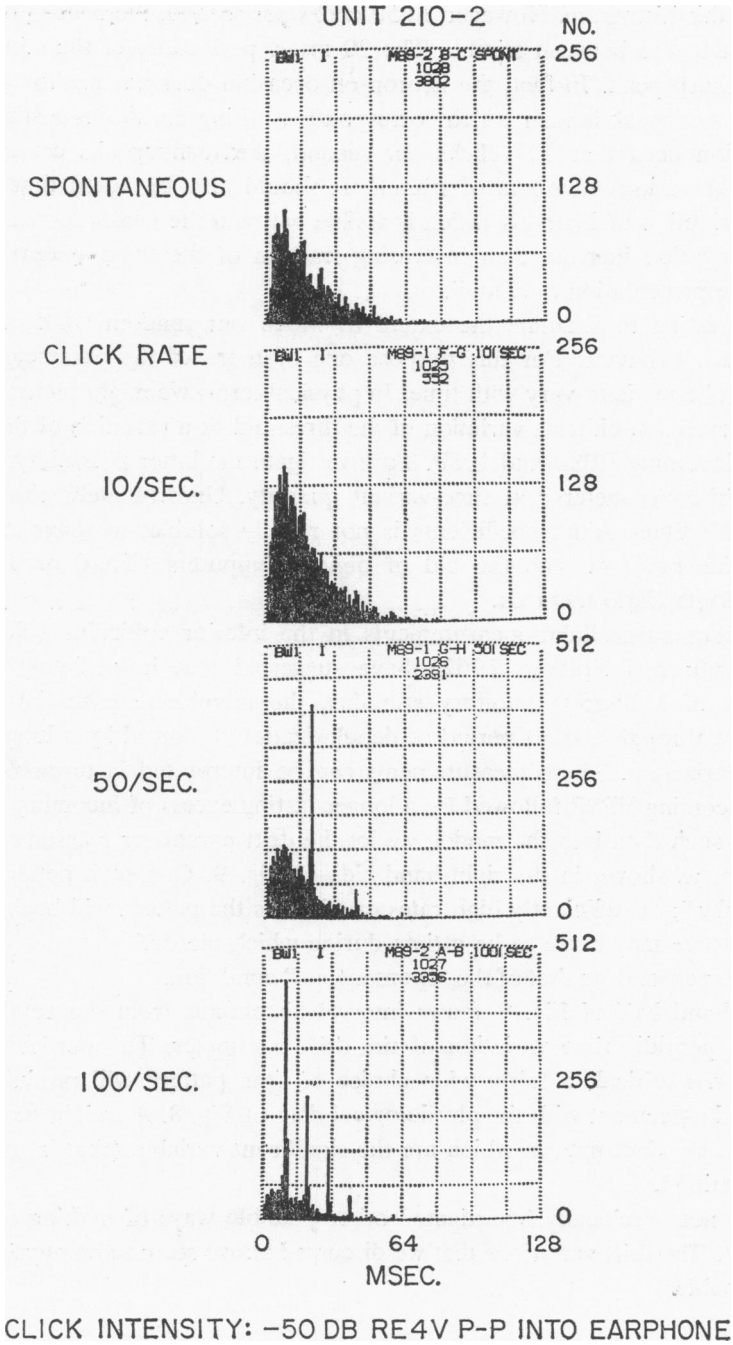


FIGURE 8 **Interval histograms for a cochlear nucleus unit during stimulation by clicks at various rates. (courtesy of N.Y-S. Kiang)**

is visible in this histogram. However, at 50 clicks per second, the neuron frequently does not get to fire between stimuli. The 20 msec. periodicity of the stimulus appears as a sharp peak. In fact, the neuron on occasion does not fire for 40 msec., so that a second peak is seen which corresponds to firing on alternate stimuli. The same situation occurs at 100 clicks per second; the many peaks correspond to "skipping" of various numbers of stimuli. It should also be noted that the continuous distribution of intervals which is visible between the peaks decreases as the rate of stimulation increases; an increasing fraction of the firing pattern is time-locked to the presentation of stimuli.

It is interesting to examine the extent to which our random walk model can duplicate such behavior. For this purpose one or more of the parameters in the model might be made to vary with time. In physical terms we might picture the corresponding events at either a variation of the threshold or a variation of the relative amount of incoming EPSP and IPSP. To investigate the latter possibility, we must make the drift parameter c at time-variant quantity. Unfortunately, the diffusion equation with time-variant coefficients is not readily soluble; we have, therefore, examined this problem with the aid of digital computers (TX-0 or TX-2) by means of Monte Carlo methods.

Some recent intracellular measurements in the inferior colliculus (Nelson and Erulkar, 1960; and Erulkar, 1962) have suggested that immediately after the presentation of a discrete auditory stimulus, the membrane potential of many neurons goes through a short period of depolarization, followed by a longer period of hyperpolarization. These measurements can be interpreted in terms of a short excess of incoming EPSP followed by a longer lasting excess of incoming IPSP. To incorporate such data into the model, we let the drift parameter c assume a similar time pattern, as shown in the right-hand side of Fig. 9. One such pattern follows each "stimulus"; at sufficiently high rates of stimulus the pattern will begin to overlay so that there may cease to be a time during which the drift parameter is at the value that corresponds to that of the "spontaneous" condition.

The left-hand half of Fig. 9 shows interval histograms from our random walk model with periodic time variation of the drift parameter. The particular values chosen are not critical; a fairly wide choice of time pattern will produce almost equally good agreement with the physiological data of Fig. 8. As might be expected, it is areas in the drift pattern which are the significant variable (that is, strength of drift $\times$ duration).

We have not specifically investigated other possible ways of making our model time-variant. The drift variations that we discussed above seem to be physiologically quite reasonable.

DEFECTS OF THE RANDOM WALK MODEL

Although the model that we have described does seem to fit a wide variety of

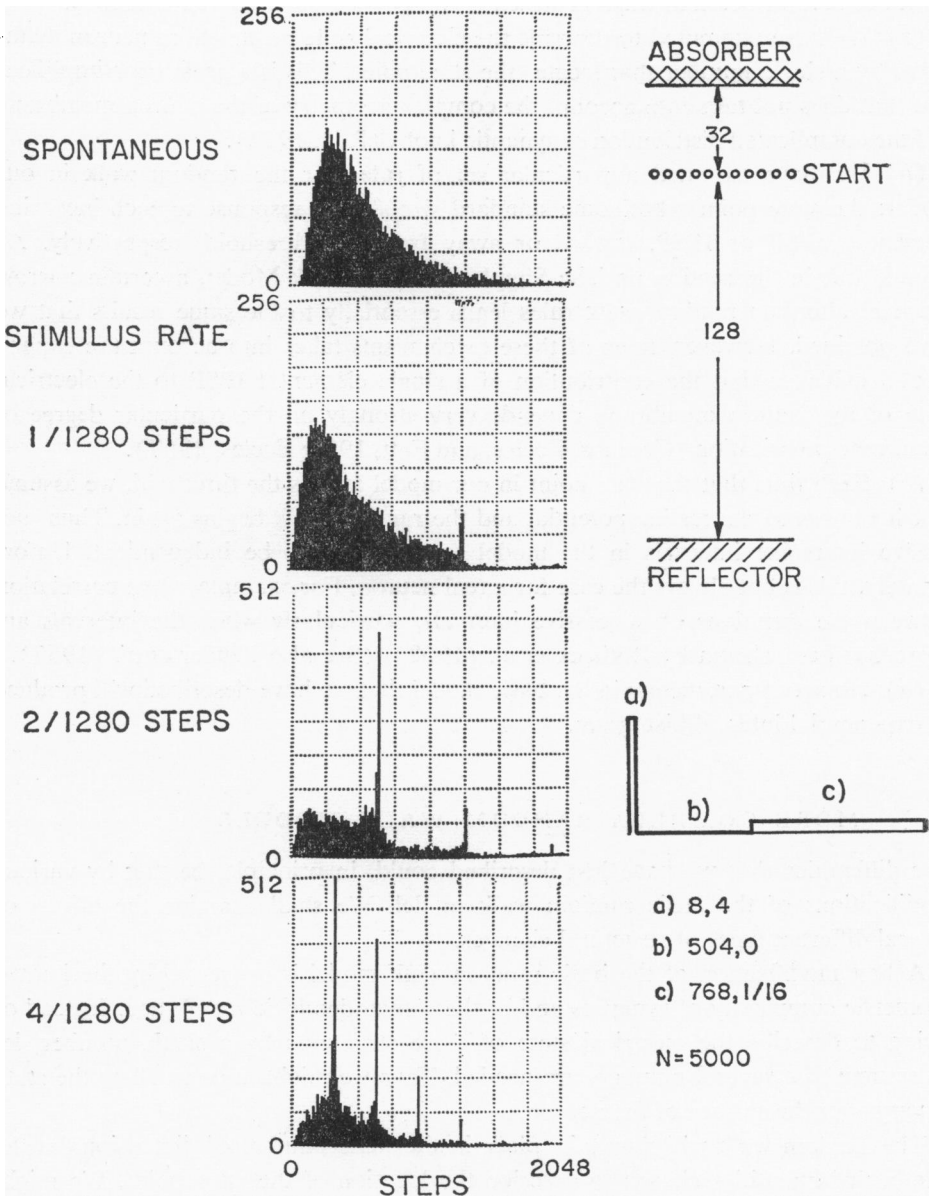


FIGURE 9 Interval histograms for the time-variant random walk model; periodic drift changes. Upper inset, the model's boundaries. Lower inset, time course of the drift parameter corresponding to 1 stimulus per 1280 steps; values for each portion are given in the form: duration, drift velocity towards absorber.

neurophysiological observations, there are a number of obvious defects in its formulation and also in its predictions. By examining these limitations, we shall be able to point out several possible ways in which this type of model may be extended.

(*a*) We have attempted to describe the electrical state of the entire neuron membrane by a single number that locates the state point. This is a gross oversimplification that does not take into account the complex geometry of the neuron membrane and the complicated distribution of synaptic knobs (Rall, 1962).

(*b*) We have assumed a particular set of rules for the random walk in our model: the state point takes some standard size step in response to each incoming elemental EPSP or IPSP, toward or away from the threshold, respectively. As pointed out in the section on The Simple Random Walk Model, a certain narrow range of alternate random walk rules leads essentially to the same results that we have obtained. However, none of these mechanisms takes into account the experimental evidence that the contribution of a single elemental IPSP to the electrical state of the neuron membrane depends very strongly on the particular degree of membrane polarization (Coombs, Eccles, and Fatt, 1955; Eccles, 1957).

(*c*) Each time that the state point in our model attains the threshold, we assume that it returns to the resting potential and the random walk begins again. Thus successive interspike intervals in the model are assumed to be independent. Unfortunately, this is not always the case for a real neuron. For example, some correlation between the durations of successive intervals, particularly when the intervals are short, has been shown by Rodieck *et al.* (1962). (See also Kuffler *et al.* (1957).)

(*d*) No set of parameters in the basic model that we have described will produce an exponential interval histogram.

MORE COMPLEX RANDOM WALK MODELS

The difficulties that we have just described could, in principle, be met by various modifications of the basic random walk model. We shall examine the effects of several different types of structural changes.

A first modification of the basic random walk model is suggested by the known geometric complexity of synapses and of the somatodendritic membrane. Instead of trying to describe the electrical state of these structures by a single number, let us assume that several numbers are needed. Thus we might hope to allow the state to vary over the surface of the neuron.

The random walk will now take place in the same number of dimensions as the number of quantities chosen to describe the location of the state point. We might postulate that such a multidimensional walk be along some set of orthogonal directions, so that the state point can move from point to point in some multidimensional lattice. The simple absorber that we have associated with a threshold now must be taken to be some surface that bounds the region of the lattice in which

the state point is allowed to move. As before, whenever the state point reaches the absorber, the model produces an action potential, and the state point is reset to its resting location.

In this guise, it is clear that the particular choice of absorbing surface exerts a profound effect on the behavior of the model. For example, consider the absorbing surface to be some array of the orthogonal coordinate planes. Then, in effect, the model will behave as if several competing but independent one-dimensional random walks are proceeding simultaneously; the one-dimensional walk that first reaches its absorber plane would produce the action potential and reset the state point. In physiological terms this type of model might correspond to a neuron that has two (or more) functionally independent trigger zones or dendritic trees, each of which can, when properly depolarized, initiate the spike discharge.

A concrete example of this type of model is the following: consider a two-dimensional random walk along Cartesian coordinates which is restricted to a single quadrant by choosing the absorbing boundary on the x axis and y axis. If we assume that the resting position of the state point is at $x_0 = y_0$ and that there is no drift, then the density of first passage times takes the form:

$$I(\tau) = \pi^{-1/2} x_0 \tau^{-3/2} \exp(-x_0^2/4\tau)\Phi(x_0/2\tau^{1/2}) \tag{11}$$

where

$$\Phi(y) = \frac{2}{\sqrt{\pi}} \int_0^y e^{-u^2}\, du.$$

The corresponding result obtained by simulating this two-dimensional random walk on a computer is shown in Fig. 10. Qualitatively, at least, this form of the model produces an interval distribution that is similar to that produced by the simple one-dimensional model: the tail of the interval histogram falls off more slowly than would an exponential. Thus, little is gained by increasing the complexity of the model in this way.

A quite different situation is obtained if we choose the absorbing boundary so that it is a more complex function of the coordinates. In such a case the several simultaneous one-dimensional random walks along the orthogonal coordinates will interact. The position of the state point along one coordinate will modify the effective boundary conditions of the random walks along the other coordinates. In physiological terms, this situation might represent a neuron with several interacting trigger zones, or perhaps with several interacting dendritic trees.

We have investigated two random walk models that exhibit this type of interaction: (*a*) a two-dimensional random walk inside a circular absorbing boundary, and (*b*) a three-dimensional random walk inside a spherical absorbing boundary. Each of these problems can, of course, be analytically solved by standard methods. However, the resulting solutions are in the form of series, and are extremely un-

wieldy for our purposes. Thus, for example the three-dimensional walk spherical boundary yields a probability density of first passage times

$$I(\tau) = \frac{a}{b}\left[\frac{1}{4\pi\tau^3}\right]^{1/2} \sum_{n=-\infty}^{+\infty} [(2n+1)a - b] \exp\left\{-\frac{[(2n+1)a-b]^2}{4\tau}\right\}, \quad (12)$$

where the resting position of the state point is at radius b and the absorbing boundary at radius a. We assume there is no drift, and set the diffusion constant equal to 1. Clearly, the form of equation (12) is not conducive to a study of the tail of the density, nor of how it behaves in the convolution process of equation (5).

Again we have turned to Monte Carlo methods and have obtained the required probability density of intervals from the TX-2 digital computer. Under these circumstances it was also possible to study the effects of drift, which was arbitrarily chosen along one of the Cartesian axes.

Results from these particular two- and three-dimensional models are shown in Figs. 11 and 12. The tails of these probability densities fall off exponentially (or perhaps even somewhat more rapidly). As in all other cases that we examined, a drift parameter can be used to adjust the general slope of the density's tail. The behavior of both probability densities under the convolution of the scaling process is approximately stable, that is, qualitatively similar to that shown in Fig. 4 for the one-dimensional random walk with drift.

Interesting results can be obtained from a fundamentally different type of two-

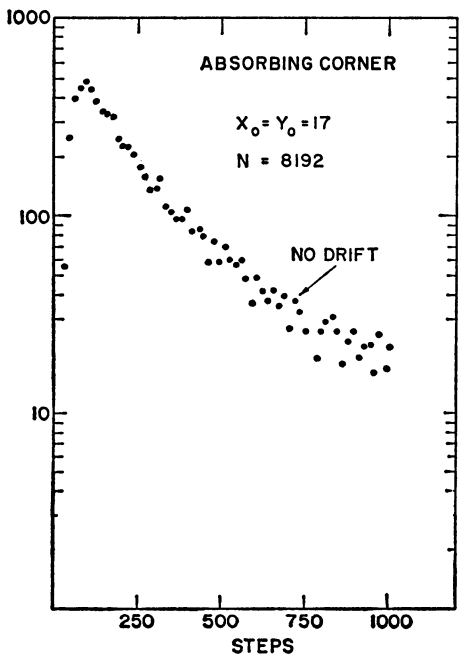


FIGURE 10 Interval histogram of two-dimensional random walk with absorbing 90° corner.

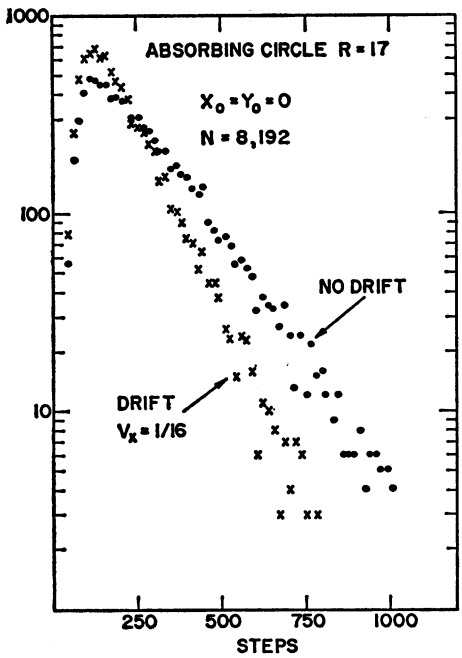


FIGURE 11 Interval histogram of two-dimensional walk with absorbing circle.

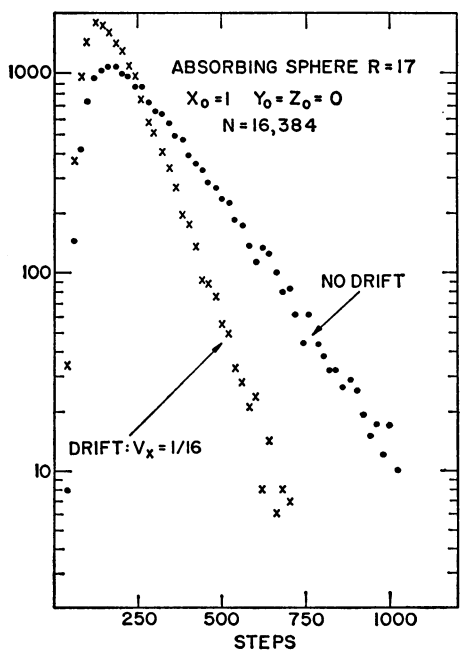


FIGURE 12 Interval histogram of three-dimensional walk with absorbing sphere.

dimensional model that is specified by the following rules: We allow the state point to perform two independent random walks. However, the model will give rise to a firing only after both random walks have reached threshold value; both coordinate numbers of the state point then return to their resting values. (One returns from threshold, the other from some random value after having attained the threshold.) Since the two walks are independent, the probability that the interspike interval is longer than τ will be equal to the product of the probabilities that the two random walks reach the threshold values after a time longer than τ. For large τ

$$Pr\,(\min\cdot(\tau', \tau'') > \tau) \sim [\tau^{-1/2}]^2 = \tau^{-1}.$$

This probability distribution function exhibits the precise invariance property—with a weighting factor k^{-1}—that is required by the experimental data of Unit 240-1. On the other hand, this model is less convincing from a physiological viewpoint and depends critically upon formulation in two dimensions.

In the course of this investigation we tried a number of other modifications of the basic random walk model. In particular, we have examined the one-dimensional case in which the size of the step toward threshold is a constant, while the size of the step away from threshold is a function of the location of the state point. This model results in a density of interspike intervals with an exponential tail, but which differs qualitatively from a Poisson-like distribution. We have also examined a one-dimensional model in which the drift contains a term proportional to the distance of the state point from some point z_1 on the z axis. (Mathematically, this model is reminiscent of the Brownian motion of an elastically bound particle.) Again, this more complicated model yields a density of interspike intervals with an exponential tail.

We have not tried a model with explicit correlation between successive random walks which corresponds to the experimentally observed correlation between successive interspike intervals. This could be done, for example, by letting the threshold value take some physiologically reasonable time course after the production of each spike. We should point out that the concept of absolutely refractory time is built into all the random walk models that we have described, since the state point cannot reach threshold in less than z_0 units of time.

STABLE DISTRIBUTIONS

Properties

In this section we shall examine briefly the general properties and peculiarities of stable distributions. (See Lévy, 1940; and Gnedenko and Kolmogorov, 1954.)

We limit ourselves to the k-fold summation of identically distributed variables (as in scaled interval histograms, for example). Distributions that are invariant to

within scale under this type of transformation are called stable and are defined through a relation of the form

$$f(x)*f(x) = f(Ax + B)$$

where A and B are constants.

This process may be iterated to give the desired k-fold summation; in this case A and B can be functions of k only.

We pointed out in the section on The Simple Random Walk Model that for the Gaussian distribution $A(k) = k^{-1/2}$ and for the stable distribution of order 1/2, $A(k) = k^{-2}$. Also, it is known that the Cauchy law yields $A(k) = k^{-1}$.

In general, stable density functions have thus far only been specified in terms of a Fourier characteristic function that involves four parameters. Three of the parameters are measures of "location," "scale," and "skewness" and "peakedness" that replace the usual measures based upon moments. The fourth parameter, usually called α, is limited to $0 < \alpha \leq 2$. The value $\alpha = 2$ corresponds to the Gaussian distribution; $\alpha = 1$, to the Cauchy distribution, and $\alpha = 1/2$, to the stable distribution of order 1/2.

The form of the characteristic function precludes inversion into densities of closed analytic form for any values of α but the three examples given. Numerical methods may, of course, be used to obtain the stable distributions for any other values of α.

An interesting theorem may be proved about the moments of a stable distribution function (Gnedenko and Kolmogoroff, 1954, p. 182). A stable distribution with characteristic exponent α $(0<\alpha<2)$ has finite absolute moments only of order $\delta(0<\delta<\alpha)$. (Note that the first inequality circumvents the Gaussian case.) Thus, while the Gaussian distribution has first, second, (and all higher) moments, the Cauchy distribution and the stable distributions of order 1/2 do not even have a first moment.

These intuitively unpleasant ideas are illustrated in Fig. 13, in which for a random walk process we have plotted sample means as a function of sample length. The non-convergent quality of these measurements is apparent.[8]

A Phenomenological Model

During another investigation, several of the stable densities of non-analytic form were computed numerically (Mandelbrot and Zarnfaller, 1961). In order to avoid

[8] Direct simulation of the random walk model must be carried out with an upper limit for the duration of the walk, because of computer time limitations. Under these conditions, even without drift ($c = 0$), the sample mean and sample variance of the first passage times do converge fairly rapidly. In order to avoid this practical difficulty the values used to produce Fig. 13 were obtained in the following way: Uniformly distributed random numbers between zero and one were chosen, and the corresponding values τ_i were read from the known probability distribution function.

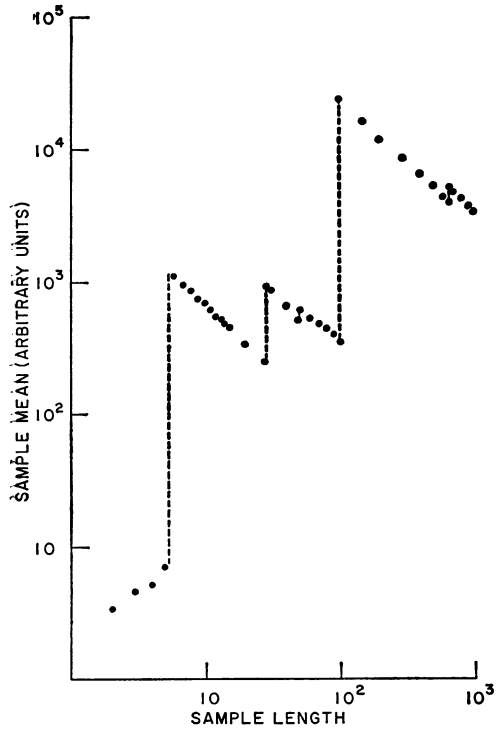


FIGURE 13 Sample mean of the first passage time in the random walk model without drift as a function of sample length. See footnote 8.

a heavy investment in mathematical notation, we shall only mention here that one of these stable densities, a skew form of the Cauchy law, has essentially the same invariance property as that found for the density of interspike intervals of Unit 240-1. The invariance property holds with the desired constants only for small m, just as in the data of Unit 240-1; asymptotically the density decreases as τ^{-2} (just as the Cauchy law itself).

In spite of close agreement with certain mathematical properties of the data, this phenomenological model for the spike activity of the neuron is intrinsically unsatisfactory. We know of no mechanism that would generate this stable probability density; hence this "model" can provide, at best, a mathematical shorthand for the data.

CONCLUSION

In this paper we have presented a series of random walk models for the spike activity of a single neuron. More generally, in making use of stable distributions, we have introduced a type of statistics into electrophysiology which offers a new interpretation of the striking "irregularity" of electrical activity in the nervous system. Usually such "irregular" phenomena have been explained in terms of some well behaved

process whose properties happen to vary in time; such an explanation requires many more parameters for a description in terms of the usual statistical measures. In contrast, the irregularity is a fundamental property of a variable that is described by a stable distribution; there is no need to invoke properties that vary in time. We have pointed out that all stable variables (except the Gaussian) lack a second moment and many lack even the first moment. We have shown in computing sample mean or sample variances for a stable variable, that the major portion of the calculated quantity can be contributed by a very few data points. Thus, in contradiction to our intuitive feelings, increasing the length of available data for such processes does not reduce the irregularity and does not make the sample mean or sample variance converge.

The general properties of stable distribution functions would seem to make these functions useful statistical tools in neurophysiology. However, it is clear that our measurements and data are not enough to suggest unique models. A more detailed study of the applicability of the stable distributions must await more critical and restrictive types of measurements on neurophysiological data.

We wish to thank the technical staffs of the TX-2 computer, of the TX-0 computer, and of the Research Laboratory of Electronics, Massachusetts Institute of Technology, for their assistance. We are grateful to Professor W. A. Rosenblith for his support and continued interest in this project.

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