N-71-14917

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A METHOD OF DESCRIBING THE SPONTANEOUS ACTIVITY OF NERVE UNITS THAT EXHIBIT A STOCHASTIC DEAD TIME

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November 1970

A METHOD OF DESCRIBING THE SPONTANEOUS ACTIVITY OF NERVE UNITS THAT EXHIBIT A STOCHASTIC DEAD TIME

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SUMMARY

A method is presented for describing the statistical characteristics of the spontaneous electrical activity of nerve units that have stochastic dead times following an impulse. The method is based on the determination of the possible functional forms of the marginal cumulative distribution of the interspike times that result from a concept of the nerve unit behavior suggested by the work of Harris and Flock. For the purpose of illustration, the method is applied in the appendix to an observed series of electrical impulses originating spontaneously from an isolated vestibular nerve unit of the frog.

INTRODUCTION

This paper presents a method of empirically modeling the statistical structure of a time-dependent series of electrical impulses spontaneously emitted by nerve units that have a stochastic dead time following each impulse. Examples of such nerve units are the Xenopus laevis lateral line units studied by Harris and Flock (ref. 1), who showed that a pronounced dead time or refractory period following the occurrence of an electrical impulse is characteristic of the observed interspike times. The approach is developed within the framework of a stationary stochastic point process and is based on the possible functional representations of the marginal distribution function which defines the probability that an interspike time is less than or equal to a given length of time.

Moore, Perkel, and Segundo (ref. 2) pointed out that neuronal spike trains (series of electrical impulses) may be analyzed within the context of stochastic point processes. Characteristically, these processes are time dependent and the events of interest are discrete, for example, particle emissions of a radioactive source where the observed event is a particle emission at some point in time (ref. 3). One common method of representing the characteristics of such a series of impulses is to define the ordered sequence of interval times $\tau_1, \tau_2, \tau_3, \ldots,$ where τ_i denotes the interval between the (i - 1)st and ith impulse. A typical interval time process associated with a given series of impulses is shown in figure 1. In the particular case of electrical neuronal activity, the observed event would be the electrical impulse or action potential measured at a point in time.

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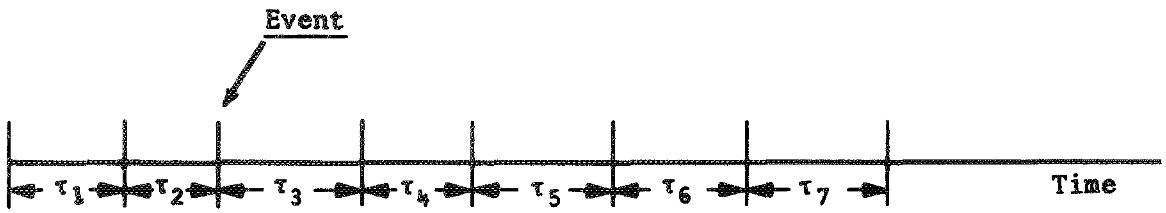

Figure 1.- Series of events and its associated interval time process. The variation τ_i indicates the time between the (i-1)st and the ith event where the hash marks indicate the events.

In a neuronal unit a pronounced dead time following an impulse will most certainly be reflected in the interspike (interval time) process. Hence, any method used to describe the activity of nerve units that exhibit a dead time should take this characteristic into account. Therefore the approach used in this paper includes a stochastic dead time in the conceptualization of a given interspike time which in turn provides a means of examining how such a dead time can affect the marginal distribution function of the interspike times. This function determines many of the statistical characteristics of the interval time process exhibited by neuronal units, such as discussed above, and under certain conditions it completely defines the process. Moreover, the method presented here utilizes the explicit forms of the marginal distribution function that result from the conceptualization of a given interval time as possible empirical models that may be useful in characterizing the spontaneous electrical activity of neuronal units heretofore discussed.

The factors considered in the conceptualization are discussed, and for illustrative purposes, the method developed here is applied in the appendix to the observed spontaneous activity of an isolated vestibular nerve unit of the frog.

APPROACH

Factors Considered in the Conceptualization of the Interspike Time

In order to simplify the problem of statistically describing the spontaneous electrical activity of neuronal units that exhibit a dead time, the general factors considered here are essentially those suggested by the work of Harris and Flock. The problem can then be idealized in the following manner.

The unit is considered to be comprised of several interacting sensory cells, and the observed spike (action potential) is regarded as originating from one of the cells. Harris and Flock regarded the unit as capable of generating a spike by spontaneous depolarization of a cell membrane defined here as *event 1*, or by the random excitation of the sensory receptors of the cell defined as *event 2*. Although they concluded that spontaneous depolarization is the more likely, both hypotheses are considered here for the purpose of developing methods of characterizing the general situation.

Moreover, if an observed spike is due to the spontaneous membrane depolarization (event 1), the unit enters a prolonged dead period resulting from some form of inhibitory interaction and is defined to be in *condition 1*. If, however, the spike results from the random excitation of the sensory receptors of the cell (event 2), the unit enters a dead period whose duration is a function of the refractory period of the nerve fiber, and the unit is then defined to be in *condition 2*.

The possible unit conditions following the Mth and (M+1)st spike and the associated events that must be accounted for in the statistical characterization of the interval time process are shown in figure 2.

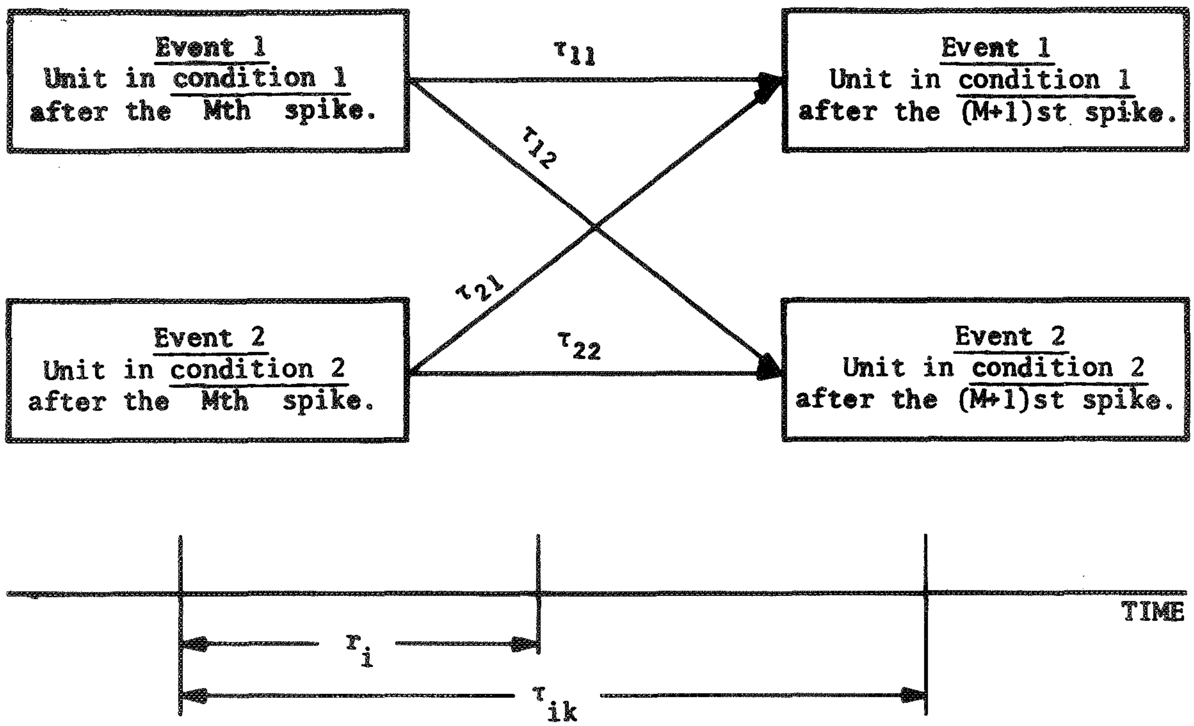

Figure 2.- Possible unit conditions following the Mth and (M+1)st spike. The variable τ_{ik} denotes the inter-spike time if the Mth spike is due to event k where i and k = 1 or 2, while r_i denotes the dead time if the unit following the Mth spike is in condition i where i = 1 or 2.

In this figure a given interval of time is defined by one of four possible intervals denoted by the variables τ_{11}, τ_{12}, τ_{21}, and τ_{22}. A given interval, say τ_{12}, is defined by two adjacent spikes, denoted by subscripts, in this case 12. The first subscript denotes that the first spike is due to spontaneous depolarization and the second indicates that the second spike is due to the random excitation. Thus the original interval time process, denoted by the ordered sequence of interval times $\tau_1, \tau_2, \tau_3, \ldots$, may be redefined in terms of the four possible interval types. For example, the interval time process may be given by $\tau_{11}, \tau_{21}, \tau_{12}, \tau_{22}, \ldots$. Consecutive intervals are restricted because only interval type τ_{12} or τ_{11} can follow τ_{11} or τ_{21}, while only τ_{21} or τ_{22} can follow τ_{22} or τ_{12}. Also, the interval types denoted by τ_{11} and τ_{12} contain the dead time associated with the spontaneous depolarization hypothesis, whereas τ_{21} and τ_{22} exhibit the dead time associated with the random excitation hypothesis.

Thus, it is evident that the marginal distribution function of the interval times, a function of particular use in describing the statistical characteristics of the interval time process, and defined as $F_\tau(t) = \text{Prob}\ (\tau \leq t)$ where τ denotes a given interval time or, equivalently, the probability density function $f_\tau(t) = dF_\tau(t)/dt$ is dependent on the statistical characteristics of the four possible types of interval times and the manner in which they are related in the interval time process. It should be noted that although conceptualizations such as used here are generally not unique, they are important as an economical means of studying the possible forms of the various statistical functions that may have use in empirically modeling the observed behavior of the process under investigation. To this end, the marginal distribution function (henceforth referred to as the distribution function) that results from the characterization of the interval time process shown in figure 2 is outlined in the following section.

Derivation of Distribution Function and Statistical Description of the Interspike Times

In general, the statistical characteristics of any stochastic point process cannot be adequately described by simple functions, such as the distribution function, unless the process is stationary; that is, the joint distribution of the number of events in k fixed time intervals is invariant under time translations. This implies that the number of events occurring in a period of time is proportional to the time length of the period, and, moreover, that the distribution of the interval times is identical for all the interval times contained in the process if the origin is defined by an arbitrarily chosen spike. For these reasons stationarity will be assumed and the origin of the interval time process is taken to be an arbitrary spike. Within this framework, the distribution function ($F_\tau(t)$, or, equivalently, the probability density function $f_\tau(t)$, of the interval time process may be derived as follows.

The following variables describe the statistical characteristics of the Mth interval time (interval time between the (M-1)st and Mth spike). If it is assumed that the (M-1)st spike is due to *event 1* (spontaneous depolarization) and, hence, the unit is in *condition 1* (dead time associated spontaneous depolarization), then

τ_{1k} the time length of the Mth interval if the Mth spike is due to event k where $k = 1,2$

r_1 the dead period following the (M-1)st spike

s_k $\tau_{1k} - r_1$, the waiting time, measured from the end of the dead period, to the Mth spike which may be due to *event k*; k = 1 or 2

Similarly, assume that the (M-1)st spike is due to *event 2* (random excitation) and the unit is now in *condition 2* (dead time associated with random excitation), and define

τ_{2k} the time length of the Mth interval if the Mth spike is due to *event k* where k = 1,2

r_2 the dead period following the (M-1)st spike

s_k $\tau_{2k} - r_2$, the waiting time, measured from the end of the dead period, to the Mth spike which is due to *event k*, k = 1 or 2

Further, define the conditional transition probabilities associated with the two possible events (1 or 2) and the resulting four types of possible interval times τ_{11}, τ_{12}, τ_{21}, τ_{22} by

β_{11} probability that the Mth spike is due to event 1 given that the (M-1)st spike was due to event 1 (The associated interval time is denoted by τ_{11}.)

β_{12} $(1 - \beta_{11})$ probability that the Mth spike is due to event 2 given that the (M-1)st spike was due to event 1 (The corresponding interval time is given by τ_{12}.)

β_{21} probability that the Mth spike is due to event 1 given that the (M-1)st spike was due to event 2 (The corresponding interval time is given by τ_{21}.)

β_{22} $(1 - \beta_{21})$ probability that the Mth spike is due to event 2 given that the (M-1)st spike was due to event 2 (The corresponding interval time is given by τ_{22}.)

The probability density function of the interval times may now be derived in terms of the transition probabilities β_{11}, β_{12}, β_{21}, β_{22} and the probability density functions $f_{\tau_{11}}(t)$, $f_{\tau_{12}}(t)$, $f_{\tau_{21}}(t)$, $f_{\tau_{22}}(t)$ of each interval type from the possible relationships of interval types between the (M-1)st interval and the Mth interval as schematically shown in figure 3.

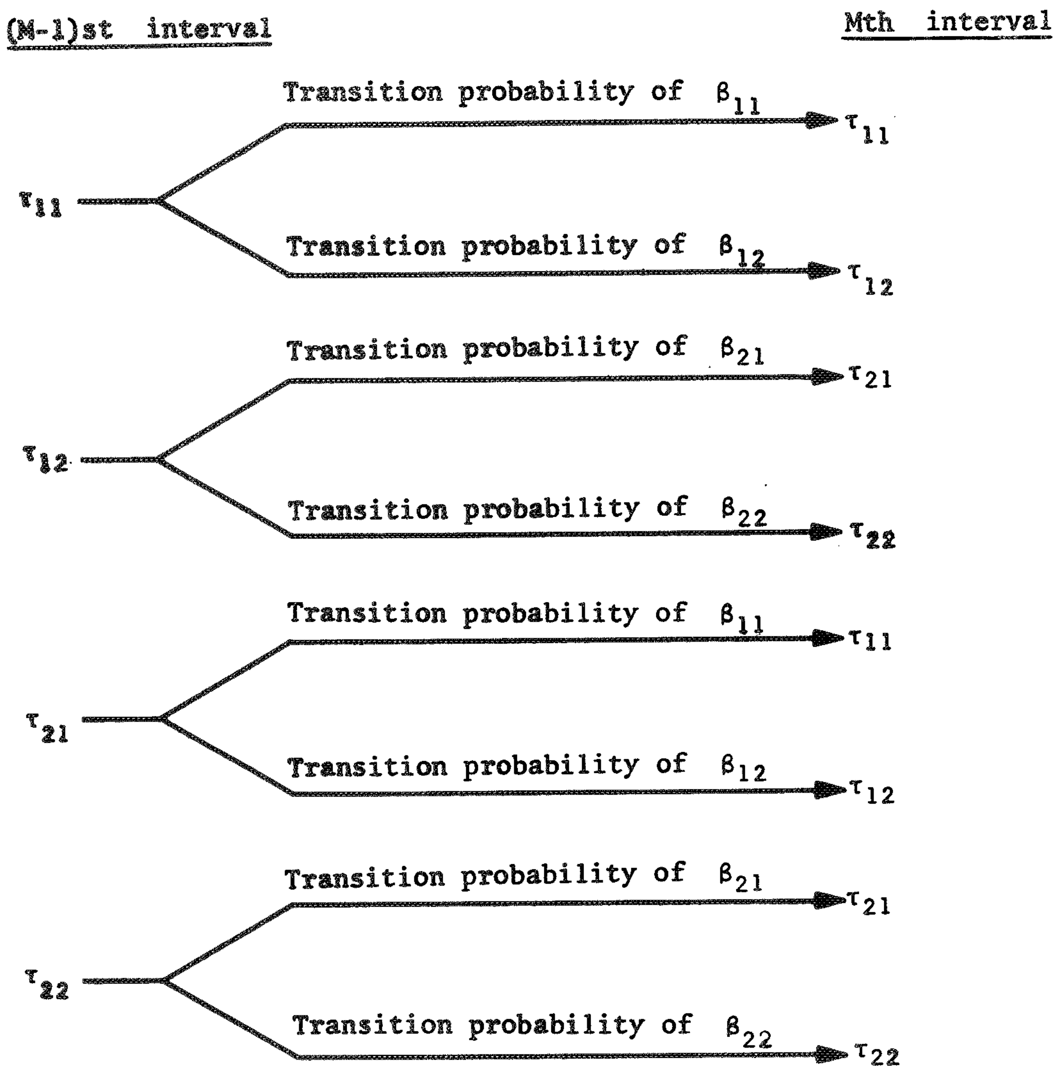

Figure 3.- Possible interval types at adjacent intervals. Quantities β_{ij} denote the transition probability that the second interval will be of a specified type.

If

p_1 probability that the next interval to occur in the interval time process is defined by the variable τ_{11}

p_2 probability that the next interval to occur is defined by τ_{12}

p_3 probability that the next interval to occur is defined by τ_{21}

p_4 probability that the next interval to occur is defined by τ_{22}

where $p_1 + p_2 + p_3 + p_4 = 1$, the probability density function of the interval time process is

$$f_\tau(t) = p_1 f_{\tau_{11}}(t) + p_2 f_{\tau_{12}}(t) + p_3 f_{\tau_{21}}(t) + p_4 f_{\tau_{22}}(t), \quad t \geq \min(\tau_{11}, \tau_{12}, \tau_{21}, \tau_{22}) \tag{1a}$$

or, equivalently, the distribution function is

$$F_\tau(t) = \int_{\min(\tau_{11})}^{t} p_1 f_{\tau_{11}}(t)dt + \int_{\min(\tau_{12})}^{t} p_2 f_{\tau_{12}}(t)dt + \int_{\min(\tau_{21})}^{t} p_3 f_{\tau_{21}}(t)dt + \int_{\min(\tau_{22})}^{t} p_4 f_{\tau_{22}}(t)dt \tag{1b}$$

The probabilities p_1, p_2, p_3, and p_4 can be expressed in terms of the transition probabilities β_{11}, β_{12}, β_{21}, and β_{22}, using the relations shown in figure 3, as follows:

$$p_1 = \beta_{11}p_1 + \beta_{11}p_3$$

$$p_2 = \beta_{12}p_3 + \beta_{12}p_1$$

$$p_3 = \beta_{21}p_2 + \beta_{21}p_4$$

$$p_4 = \beta_{22}p_4 + \beta_{22}p_4$$

These relationships show that

$$p_1 = (1 - \beta_{22})\beta_{11}/(2 - \beta_{11} - \beta_{22})$$

$$p_2 = (1 - \beta_{11})(1 - \beta_{22})/(2 - \beta_{11} - \beta_{22})$$

$$p_3 = p_2$$

$$p_4 = (1 - \beta_{11})\beta_{22}/(2 - \beta_{11} - \beta_{22})$$

Thus, the density function, given by equation (1a), can be expressed in terms of the transition probabilities as

$$f_\tau(t) = (1 - \beta_{22})/(2 - \beta_{11} - \beta_{22})[\beta_{11} f_{\tau_{11}}(t) + (1 - \beta_{11}) f_{\tau_{12}}(t)]$$

$$+ (1 - \beta_{11})/(2 - \beta_{11} - \beta_{22})[(1 - \beta_{22}) f_{\tau_{21}}(t) + \beta_{22} f_{\tau_{22}}(t)] ,$$

$$t \geq \min(\tau_{11}, \tau_{12}, \tau_{21}, \tau_{22}) \qquad (1c)$$

Equation (1c) can be somewhat simplified if the probability density function of the random variable X_1 is defined as

$$g_1(t) = \beta_{11} f_{\tau_{11}}(t) + (1 - \beta_{11}) f_{\tau_{12}}(t), \qquad X_1 \geq \min(\tau_{11}, \tau_{12})$$

and the probability density function of the random variable X_2 as

$$g_2(t) = (1 - \beta_{22}) f_{\tau_{21}}(t) + \beta_{22} f_{\tau_{22}}(t), \qquad X_2 \geq \min(\tau_{21}, \tau_{22})$$

Letting

$$\alpha = (1 - \beta_{22})/(2 - \beta_{11} - \beta_{22})$$

we can write the density function of the interval time τ as

$$f_\tau(t) = \alpha g_1(t) + (1 - \alpha) g_2(t), \qquad t \geq \min(X_1, X_2)$$

which is seen to be the form of the density function derived from a two-state semi-Markov process model (ref. 4).

The average interval time length, the variance, and the serial correlation function are descriptive characteristics of the process that can be derived immediately from the probability density function as given by equation (1a) or (1c). The average interval time length of the process is given by

$$E(\tau) = \alpha E(X_1) + (1 - \alpha) E(X_2) \qquad (1d)$$

and the variance by

$$\mathrm{Var}(\tau) = \alpha \mathrm{Var}(X_1) + (1 - \alpha) \mathrm{Var}(X_2) + \alpha(1 - \alpha)[E(X_1) - E(X_2)]^2 \qquad (1e)$$

where

$$E(X_1) = \beta_{11} \int_{\min(\tau_{11})}^{\infty} t f_{\tau_{11}}(t) dt + (1 - \beta_{11}) \int_{\min(\tau_{12})}^{\infty} t f_{\tau_{12}}(t) dt$$

$$E(X_2) = (1 - \beta_{22})\int_{\min(\tau_{21})}^{\infty} tf_{\tau_{21}}(t)dt + \beta_{22}\int_{\min(\tau_{22})}^{\infty} tf_{\tau_{22}}(t)dt$$

$$\mathrm{Var}(X_1) = \beta_{11}\int_{\min(\tau_{11})}^{\infty} [t - E(X_1)]^2 f_{\tau_{11}}(t)dt(1 - \beta_{11})$$

$$\times \int_{\min(\tau_{12})}^{\infty} [t - E(X_1)]^2 f_{\tau_{12}}(t)dt$$

$$\mathrm{Var}(X_2) = (1 - \beta_{22})\int_{\min(\tau_{21})}^{\infty} [t - E(X_2)]^2 f_{\tau_{21}}(t)dt$$

$$+ \beta_{22}\int_{\min(\tau_{22})}^{\infty} [t - E(X_2)]^2 f_{\tau_{22}}(t)dt$$

Finally, the serial correlation function of lag k, which measures the linear dependence between every kth interval time contained in the process, is shown by Cox and Lewis (ref. 4) to be

$$\rho_k = \frac{[E(X_1) - E(X_2)]^2 \alpha(1 - \alpha)(\beta_{11} + \beta_{22} - 1)^k}{\alpha \mathrm{Var}(X_1) + (1 - \alpha)\mathrm{Var}(X_2) + \alpha(1 - \alpha)[E(X_1) - E(X_2)]^2} \qquad (1f)$$

It is seen that equation (1a) or (1c) expresses the probability density of the interval time in terms of the density functions of the four intervals τ_{11}, τ_{12}, τ_{21}, τ_{22}, while equation (1b) establishes the same type of relationship for the distribution function. Also, equations (1d), (1e), and (1f) show how the descriptive characteristics as given by the mean, variance, and serial correlation function, depend on the characteristics of the four interval types. Hence, these relationships provide a basis for examining how the characteristics of the four interval types are reflected in a given interval of time. In order to obtain explicit functional forms that define the statistical characteristics of a given interval of time for these equations, plausible forms of the distribution functions of τ_{11}, τ_{12}, τ_{21}, and τ_{22} or, equivalently, r_1, r_2, s_1, and s_2 must be postulated. Since the spontaneous electrical activity exhibited by neuronal units is generally considered to be a random and steady-state type phenomenon, it seems reasonable to assume the null-type hypothesis that the variables r_1, s_1, and s_2 are random and are defined by events that occur according to the Poisson criterion of randomness (ref. 5) or approximately so. In such case, the density functions of these variables are expressed by

$$f_{r_1}(t) = \lambda_{r_1} e^{-\lambda_{r_1}(t-d_1)}, \qquad t \geq d_1$$

$$f_{s_1}(t) = \lambda_{s_1} e^{-\lambda_{s_1}(t)}, \qquad t \geq 0$$

$$f_{s_2}(t) = \lambda_{s_2} e^{-\lambda_{s_2}(t)}, \qquad t \geq 0$$

where d_1 can be considered the absolute minimum dead time of the unit if the last impulse is due to the spontaneous depolarization of the cell membrane (event 1). However, the density function of the random variable r_2 is taken to be

$$f_{r_2}(t) = \delta(t - d_2), \qquad t \geq 0$$

(where $\delta(\ )$ is the Dirac delta function) since r_2 denotes the dead time of the unit if the last spike is due to the random excitation hypothesis which assumes no inhibitory interaction among the cells of the unit. Consequently, the dead time in this case should be directly related to the refractory period of the nerve fiber, denoted here by d_2. Since

$$\tau_{11} = r_1 + s_1$$

$$\tau_{12} = r_1 + s_2$$

$$\tau_{21} = r_2 + s_1$$

$$\tau_{22} = r_2 + s_2$$

it follows that the density function of the variables τ_{11}, τ_{12}, τ_{21}, and τ_{22} is given by

$$f_{\tau_{11}}(t) = \frac{\lambda_{s_1}\lambda_{r_1}}{\lambda_{s_1} - \lambda_{r_1}} \left[e^{-\lambda_{r_1}(t-d_1)} - e^{-\lambda_{s_1}(t-d_1)} \right], \qquad t \geq d_1$$

$$f_{\tau_{12}}(t) = \frac{\lambda_{s_2}\lambda_{r_1}}{\lambda_{s_2} - \lambda_{r_1}} \left[e^{-\lambda_{r_1}(t-d_1)} - e^{-\lambda_{s_2}(t-d_1)} \right], \qquad t \geq d_1$$

$$f_{\tau_{21}}(t) = \lambda_{s_1} e^{-\lambda_{s_1}(t-d_2)}, \qquad t \geq d_2$$

$$f_{\tau_{22}}(t) = \lambda_{s_2} e^{-\lambda_{s_2}(t-d_2)}, \qquad t \geq d_2$$

Further, if $d_2 \leq d_1$, the probability density of an interval of time, from equation (1a) or (1b), is explicitly given by

$$\left.\begin{aligned}
f_\tau(t) &= (1-\alpha)\left[(1-\beta_{22})\lambda_{s_1} e^{-\lambda_{s_1}(t-d_2)} + \beta_{22}\lambda_{s_2} e^{-\lambda_{s_2}(t-d_2)}\right], \qquad d_2 \leq t \leq d_1 \\
f_\tau(t) &= \alpha\left\{\beta_{11}\frac{\lambda_{s_1}\lambda_{r_1}}{\lambda_{s_1}-\lambda_{r_1}}\left[e^{-\lambda_{r_1}(t-d_1)} - e^{-\lambda_{s_1}(t-d_1)}\right]\right. \\
&\quad \left. + (1-\beta_{11})\frac{\lambda_{s_2}\lambda_{r_1}}{\lambda_{s_2}-\lambda_{r_1}}\left[e^{-\lambda_{r_1}(t-d_1)} - e^{-\lambda_{s_2}(t-d_1)}\right]\right\} \\
&\quad + (1-\alpha)\left[(1-\beta_{22})\lambda_{s_1} e^{-\lambda_{s_1}(t-d_2)} + \beta_{22}\lambda_{s_2} e^{-\lambda_{s_2}(t-d_2)}\right], \qquad t \geq d_1
\end{aligned}\right\} \tag{2a}$$

where

$$\alpha = (1-\beta_{11})/(2-\beta_{11}-\beta_{22})$$

The corresponding distribution function is

$$F_\tau(t) = (1-\alpha)\left[1 - (1-\beta_{22})e^{-\lambda_{s_1}(t-d_2)} - \beta_{22}e^{-\lambda_{s_2}(t-d_2)}\right], \qquad d_2 \leq t \leq d_1$$

(2b)

$$\begin{aligned}
F_\tau(t) &= \alpha\left\{1 - \beta_{11}\frac{\lambda_{s_1}\lambda_{r_1}}{\lambda_{s_1}-\lambda_{r_1}}\left[\frac{e^{-\lambda_{s_1}(t-d_1)}}{\lambda_{s_1}} - \frac{e^{-\lambda_{r_1}(t-d_1)}}{\lambda_{r_1}}\right]\right. \\
&\quad \left. - (1-\beta_{11})\frac{\lambda_{s_2}\lambda_{r_1}}{\lambda_{s_2}-\lambda_{r_1}}\left[\frac{e^{-\lambda_{s_2}(t-d_1)}}{\lambda_{s_2}} - \frac{e^{-\lambda_{r_1}(t-d_1)}}{\lambda_{r_1}}\right]\right\} \\
&\quad + (1-\alpha)\left[1 - (1-\beta_{22})e^{-\lambda_{s_1}(t-d_2)} - \beta_{22}e^{-\lambda_{s_2}(t-d_2)}\right], \qquad t \geq d_1
\end{aligned}$$

The average interval time length, from equation (1d), is expressed by

$$E(\tau) = \alpha E(X_1) + (1-\alpha)E(X_2) \tag{2c}$$

where

$$E(X_1) = \beta_{11}\left(\frac{\lambda_{r_1} + \lambda_{s_1}}{\lambda_{r_1}\lambda_{s_1}} + d_1\right) + (1 - \beta_{11})\left(\frac{\lambda_{r_1} + \lambda_{s_2}}{\lambda_{r_1}\lambda_{s_2}} + d_1\right)$$

and

$$E(X_2) = (1 - \beta_{22})\left(\frac{1}{\lambda_{s_1}} + d_2\right) + \beta_{22}\left(\frac{1}{\lambda_{s_2}} + d_2\right)$$

From equation (1e), the variance is found to be

$$\mathrm{Var}(\tau) = \alpha \mathrm{Var}(X_1) + (1 - \alpha)\mathrm{Var}(X_2) + \alpha(1 - \alpha)[E(X_1) - E(X_2)]^2 \qquad (2d)$$

where $\mathrm{Var}(X_1)$, $\mathrm{Var}(X_2)$ are now explicitly written as

$$\mathrm{Var}(X_1) = \beta_{11}\left(\frac{\lambda_{r_1}^2 + \lambda_{s_1}^2}{\lambda_{r_1}^2\lambda_{s_1}^2}\right) + (1 - \beta_{11})\left(\frac{\lambda_{r_1}^2 + \lambda_{s_2}^2}{\lambda_{r_1}^2\lambda_{s_2}^2}\right)$$

and

$$\mathrm{Var}(X_2) = (1 - \beta_{22})\left(\frac{1}{\lambda_{s_1}^2}\right) + \beta_{22}\left(\frac{1}{\lambda_{s_2}^2}\right)$$

Similarly, the explicit form of the serial correlation function, obtained by substituting the above expressions for $E(X_1)$, $E(X_2)$, $\mathrm{Var}(X_1)$, and $\mathrm{Var}(X_2)$, into equation (1f), is then given by

$$\rho_k = \frac{[E(X_1) - E(X_2)]^2\alpha(1 - \alpha)(\beta_{11} + \beta_{22} - 1)^k}{\alpha \mathrm{Var}(X_1) + (1 - \alpha)\mathrm{Var}(X_2) + \alpha(1 - \alpha)[E(X_1) - E(X_2)]^2} \qquad (2e)$$

Thus, under the null-type hypothesis, the functional form of the distribution function as given by equation (2b), or equivalently, the probability density function given by equation (2c), is seen to be the weighted sum of, at most, three exponential terms and the explicit forms of the descriptive characteristics of a given interval of time expressed by equations (2c), (2d), and (2e). Moreover, special cases of the distribution function, given by equation (2b), may be derived by making various assumptions about the transition probabilities β_{11}, β_{22}. These special cases represent different types of interval time processes with respect to their statistical characteristics, and three such processes of special interest are discussed in the following:

1. If $\beta_{11} = 1 - \beta_{22}$, equation (2b) then represents the probability density function of a renewal process. A renewal process is a stationary process whose interval times are independently and identically distributed. This implies that the interval time process, originally denoted as the ordered sequence of interval times $\tau_1, \tau_2, \tau_3, \ldots$ is not dependent on order. Its serial correlation function, given by equation (2e), is thus equal to zero for lags of all orders.

2. If the random excitation hypothesis of spike generation is not significant, then the variables r_2, s_2 have no effect; thus, $\beta_{11} = 1$, $\beta_{22} = 0$. Since these values of β_{11}, β_{22} satisfy the relationship $\beta_{11} = 1 - \beta_{22}$, the process is renewal and the distribution function given by equation (2b) reduces to

$$F_\tau(t) = 1 - \frac{\lambda_{s_1}\lambda_{r_1}}{\lambda_{s_1} - \lambda_{r_1}}\left[e^{-\lambda_{s_1}(t-d_1)} - e^{-\lambda_{r_1}(t-d_1)}\right], \qquad t \geq d_1, \qquad \lambda_{s_1} \neq \lambda_{r_1} \tag{3a}$$

which is seen to be the distribution function of the simplest generalization of an integral-order Erlang process. When $\lambda_{s_1} = \lambda_{r_1} = \lambda$, the distribution function then becomes

$$F_\tau(t) = 1 - e^{-\lambda(t-d)}[1 + \lambda(t - d_1)], \qquad t \geq d_1 \tag{3b}$$

which is seen to be the Gamma distribution function of order 2 (chi-square, Pearson type III).

3. Finally, if the spontaneous depolarization hypothesis of spike generation is not significant, then the variables r_1, s_1 have no effect; thus $\beta_{11} = 0$, and $\beta_{22} = 1$. Again, since these values of β_{11}, β_{22}, satisfy the relationship $\beta_{11} = 1 - \beta_{22}$, the process is renewal and the distribution function given by equation (2b) reduces to

$$F_\tau(t) = 1 - e^{-\lambda_{s_2}(t-d_2)}, \qquad t \geq d_2 \tag{3c}$$

which is the negative exponential distribution function characteristic of a Poisson process.

These results immediately suggest the possible functional forms of the distribution function that may be useful in empirically modeling the spontaneous spike train activity of neuronal units exhibiting a dead time following each electrical impulse. Specifically, the examination of the null-type situation suggests that the distribution function of the interval time process exhibited by such neuronal units could be possibly described by:

1. The negative exponential as given by equation (3c),

or

2. The generalized Erlang as expressed by equation (3a) or its special case, the gamma of order 2 given by equation (3b), if the process is renewal, and

3. A weighted sum of a mixture of two generalized Erlangs and a mixture of two negative exponential distributions as shown in equation (2b), if the process is renewal or nonrenewal.

The plausibility of these results is somewhat substantiated from the standpoint that the negative exponential, the distribution function of a Poisson process, has been used to fit the observed distribution characteristics of neuronal spike trains by such authors as Rodieck, Kiang, and Gerstein (ref. 6) while a form of the gamma distribution was employed by Kuffler, Fitzhugh, and Barlow (ref. 7).

Therefore, the results of this paper suggest the following procedure for empirically modeling the observed distribution of interval times and thereby describing the statistical characteristics of the spontaneous electrical activity of nerve units exhibiting a dead time:

1. Test the stationarity and renewal characteristics of the interval time process. (For a discussion of actual tests that can be used to examine these hypotheses see refs. 4 and 8.)

2. After determining the stationarity and renewal characteristics, empirically model the observed distribution of interval times in the following manner:

If the process is found to be stationary but not renewal, then the appropriate form of the distribution function to use in empirically modeling or fitting the observed distribution is given by a weighted sum of exponentials of the form

$$\left.\begin{aligned} F_\tau(t) &= 1 - A_1 e^{-\lambda_1 t} - A_2 e^{-\lambda_2 t}, \quad t_0 \leq t \leq t_1 \\ F_\tau(t) &= 1 - A_3 e^{-\lambda_3 t} - (A_1 - A_4) e^{-\lambda_1 t} - (A_2 - A_5) e^{-\lambda_2 t}, \quad t \geq t_1 \end{aligned}\right\} \quad (4a)$$

where A_1, A_2, A_3, A_4, A_5, λ_1, λ_2, and λ_3 are parameters subject to the restrictions that

$$A_1 e^{-\lambda_1 t_0} + A_2 e^{-\lambda_2 t_0} = 1$$

$$A_i \geq 0, \quad i = 1, 2$$

$$A_3 e^{-\lambda_3 t_1} + A_4 e^{-\lambda_1 t_1} + A_5 e^{-\lambda_2 t_1} = 0$$

and

$$\lambda_i \geq 0, \quad i = 1, 2, 3$$

If, however, the process is found to be renewal, then in addition to the weighted sum of exponentials shown above, the functional forms of the distribution that may be used to empirically model the observed distribution are given by the negative exponential,

$$F_\tau(t) = 1 - e^{-\lambda(t-d)}, \qquad t \geq d \tag{4b}$$

the generalized Erlang,

$$F_\tau(t) = 1 - \frac{\lambda_1\lambda_2}{\lambda_1 - \lambda_2}\left[e^{-\lambda_1(t-d)} - e^{-\lambda_2(t-d)}\right], \qquad t \geq d \tag{4c}$$

or its special case, the gamma of order 2,

$$F_\tau(t) = 1 - e^{-\lambda(t-d)}[1 + \lambda(t - d)], \qquad t \geq d \tag{4d}$$

It should be noted that in the case of a renewal process, the distribution function or, equivalently, the probability density function of the interval times completely specifies the statistical characteristics of the interval time process.

CONCLUDING REMARKS

The conceptualization of the spontaneous spike trains originating from neuronal units exhibiting a pronounced dead time as depicted in figure 2, albeit a naive representation of a complex process, enables one to study the possible forms of the marginal distribution function of the interspike times contained in such process. The resultant examination of the null-type case has use in establishing a reference point to determine any deviations from randomness that may be exhibited by an observed interspike (interval time) process. Moreover, the explicit forms of the distribution functions that have been determined in this paper may have use in empirically modeling the observed distribution of the intervals contained in the process. Specifically, if the process is found to be renewal, then the negative exponential (eq. (4b)), the gamma of order 2 (eq. (4d)), the generalized Erlang (eq. (4c)), or the weighted sum of exponentials (eq. (4d)) are the possible functional forms. If the process is nonrenewal but stationary, then the weighted sum of exponentials (eq. (4a)) is the most appropriate form of the distribution function.

The determination of the most appropriate empiric model is important since the distribution function describes many of the statistical characteristics of the spontaneous electrical activity of neuronal units heretofore discussed. Moreover, the functional form of the distribution may be used as a basis for demonstrating how evoked activity differs from spontaneous activity.

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APPENDIX

ILLUSTRATIVE EXAMPLE

The method of empirically modeling the distribution function of the interval times shown on pages 13-15 is applied to the observed interval time process resulting from the spontaneous electrical activity of an isolated vestibular neuronal unit of a frog.[1] The electrical impulses originating from this unit were measured over time and the resulting interval time process consisted of 997 spikes or 996 interval times where the initial spike defined the origin of the process.

STATIONARY AND RENEWAL CHARACTERISTICS

The hypotheses of stationarity and renewal were examined and it was determined by nominal 5 percent level tests that the interval time process could be characterized as being stationary and renewal. The tests used to examine these hypotheses are those suggested by Lewis (ref. 8) on pages 207-208 and 212-213. The stationarity hypothesis was essentially tested by examining whether the mean rate of spike occurrence remained constant over time and is based upon the necessary condition that no trends over time exists in the mean rate of spike occurrence if the process is stationary. Similarly, the test used to examine the renewal hypothesis is based upon the necessary condition of a renewal process that the serial correlation function is zero for all lags.

Empirically Modeling the Cumulative Distribution of Interval Times

The empiric distribution is calculated by first ranking all the interval times in order of magnitude to obtain the ranked series $t_1, t_2, t_3, \ldots$. The observed cumulative distribution function may then be computed by

$$F_T(t) = i/N , \quad 1 \leq i \leq N$$

where N is the total number of intervals contained in the observed process. The resultant empiric distribution, shown in 2 ms increments, and the descriptive statistics of the observed interspike times are shown in the following table.

[1]The data were collected by R. S. Carpenter, Ames Research Center, 1969.

TABLE 1.- OBSERVED DISTRIBUTION OF THE INTERSPIKE TIMES BASED ON A SAMPLE OF 996

Time, ms	Distribution	Time, ms	Distribution	Time, ms	Distribution
10	0.0110	44	0.7701	78	0.9649
12	.0291	46	.7972	80	.9679
14	.0733	48	.8213	82	.9689
16	.1044	50	.8353	84	.9729
18	.1556	52	.8524	86	.9789
20	.2209	54	.8655	88	.9799
22	.2821	56	.8785	90	.9829
24	.3444	58	.8966	92	.9859
26	.4167	60	.9046	94	.9880
28	.4789	62	.9127	96	.9910
30	.5281	64	.9197	98	.9920
32	.5643	66	.9297	100	.9940
34	.6104	68	.9378	102	.9950
36	.6486	70	.9468	104	.9950
38	.6787	72	.9518	106	.9950
40	.7189	74	.9568	108	.9980
42	.7470	76	.9598		
Minimum interval time = 8.1 ms Maximum interval time = 129.0 ms Average interval length = 34.057 ms; variance = 341.957 ms^2					

The procedure outlined on pages 13-15 of this paper shows that if the process is renewal, then the possible forms of the distribution are given by those of the negative exponential (eq. (4b)), the generalized Erlang (eq. (4c)), its special case the gamma of order 2 (eq. (4d)), or the weighted sum of exponentials (eq. (4a)). The method employed here to establish an empiric model of the distribution function was to use sequentially the above forms of the distribution until an adequate fit of the observed distribution was obtained. A nominal 5 percent Kolmolgorov-Smirnoff goodness of fit test (ref. 9) was used to judge the adequacy of the fit and this test is based upon the statistic

$$KS = \max_{1 \leq i \leq N} \left| (i/N) - F_\tau(t_i) \right|$$

where $F_\tau(t)$ is the hypothesized distribution. The 5-percent two-sided critical value of this statistic is given by $1.358/\sqrt{N}$ which in our case is equal to 0.043 since $N = 996$.

Hence, the negative exponential distribution function given from equation (4b) by

$$F_\tau(t) = 1 - e^{-\lambda(t-d)}, \qquad t \geq d$$

was initially used to fit the observed distribution. The method of moments was used to estimate the rate parameter λ and the minimum dead time d. This method involves equating the theoretical moments to the corresponding observed moments; and for the present case, the resulting equations are

$$E(\tau) = 1/\lambda + d = 34.057$$

and

$$\mathrm{Var}(\tau) = (1/\lambda)^2 = 341.957$$

The theoretical form of $E(\tau)$, and $\mathrm{Var}(\tau)$ can be obtained from equations (2c) and (2b) by setting $\beta_{11} = 0$, $\beta_{22} = 1$ while the observed moments are shown in table 1. The estimates of the parameters are then seen to be $\lambda = 0.05408$ spikes/ms and $d = 15.56$. The observed value of the KS statistics was found to be 0.098 which is seen to be greater than the 5-percent critical value of 0.043, thus indicating a significant lack of fit. Hence, the generalized Erlang distribution function, given from equation (4c) by

$$F_\tau(t) = 1 - \frac{\lambda_1\lambda_2}{\lambda_1 - \lambda_2}\left[e^{-\lambda_1(t-d)} - e^{-\lambda_2(t-d)}\right], \qquad t \geq d$$

was then used in the attempt to find an adequate empiric model. Again, the method of moments was employed to obtain estimates of the parameters λ_1, λ_2, d, where the equations involving the first two moments are expressed by

$$E(\tau) = \frac{\lambda_1 + \lambda_2}{\lambda_1\lambda_2} + d = 34.057$$

$$\mathrm{Var}(\tau) = \frac{\lambda_1^2 + \lambda_2^2}{\lambda_1^2\lambda_2^2} = 341.957$$

or

$$\lambda_1,\lambda_2 = \frac{(34.057 - d) \pm \sqrt{2(341.957) - (34.057 - d)^2}}{(34.057 - d) - 341.957}$$

The first and second moments, $E(\tau)$ and $\mathrm{Var}(\tau)$, may be obtained from equations (2c) and (2d) by substituting the values 1 and 0 for β_{11} and β_{22}. For a real solution to exist, d must satisfy the inequality $d \leq 34.057 - \sqrt{683.914}$ or $d \leq 7.905$. Also, since $d \geq \min(t_1 \ldots t_{996})$, where the minimum time from table 1 is seen to be 8.12, it follows that $7.905 \leq d \leq 8.125$. These bounds define well the possible values of d, and the midpoint of the interval was taken to be the estimate of d. Thus $d = 8.01$, and when this value of d is substituted into the above relationships, it is seen that $\lambda_1 = 0.070459$ and $\lambda_2 = 0.084357$. The observed value of the KS statistic was computed to be 0.028, and since this value is less than the 5-percent critical value, it was concluded that the generalized Erlang function given explicitly by

$$F_{\tau}(t) = 1 + 0.42767\left[11.85438e^{-0.084357(t-8.01)} - 14.19265e^{-0.070459(t-8.01)}\right], \quad t \geq 8.01$$

was an adequate empiric model of the observed distribution. For purposes of visual comparisons, the fit given by the negative exponential and the generalized Erlang distribution functions are shown in figure 4.

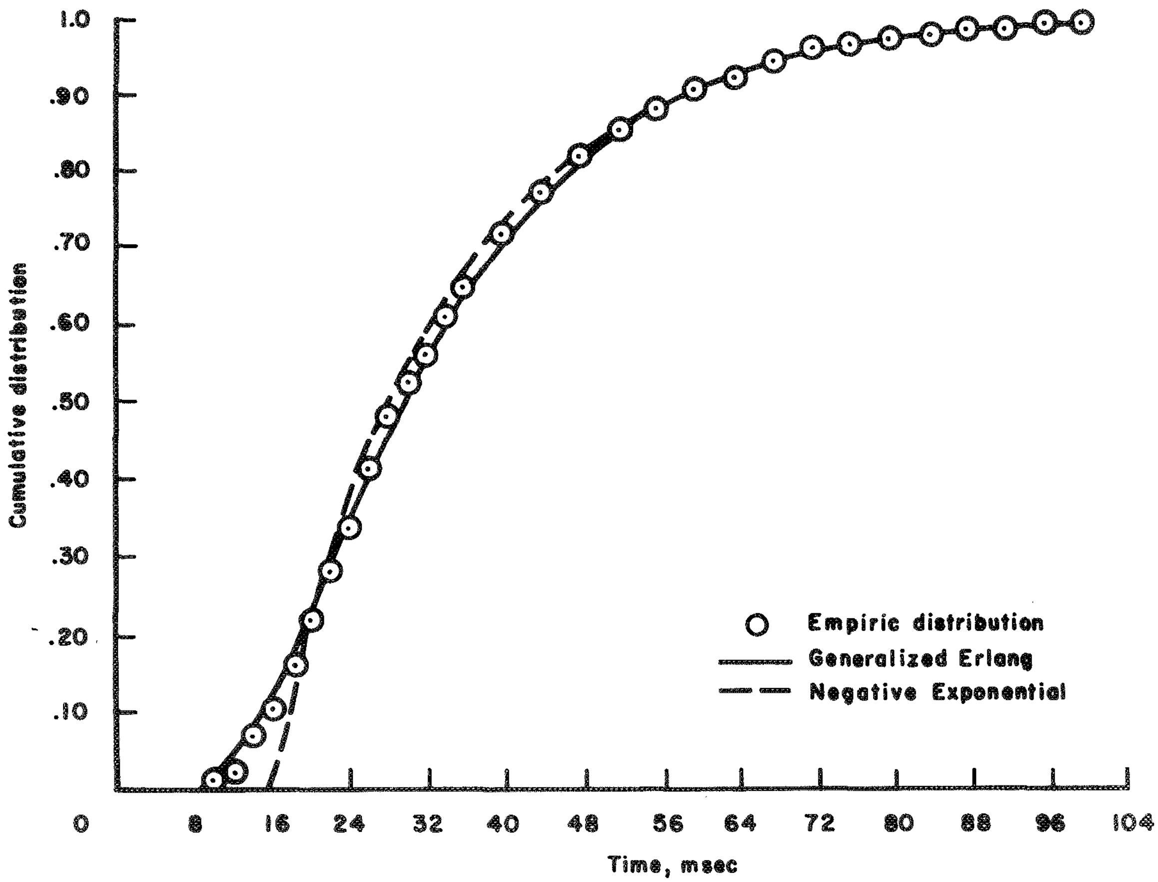

Figure 4.- Interval time distribution.

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