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NEURONAL FIRING AND INPUT VARIABILITY

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Abstract

Asymptotic results are obtained for the mean and variance of the interspike time of a model neuron in which subthreshold depolarizations are represented by an Ornstein–Uhlenbeck process (OUP). The presence of a small amount of noise, even when it has zero mean, always reduces the mean firing time or increases the mean firing rate. The results are used to interpret the effects of jitter on firing rates of crayfish stretch receptors and to predict the effects of noise on pacemaker activity. We also consider the amount of regularization of an input train of spikes effected by the model neuron as it transforms the input to an output spike train. This is done by evaluating the coefficient of variation of the output interspike interval for a wide range of input parameter values. Conditions under which the coefficient of variation of the output is less than that of the input are obtained. The details of the perturbation techniques used to obtain the asymptotic results are contained in an appendix.

1. Introduction

The Ornstein–Uhlenbeck process has often been used to approximate subthreshold depolarizations of a nerve cell receiving random synaptic inputs (Gluss, 1967; Johannesma, 1968; Roy and Smith, 1969; Capocelli and Ricciardi, 1971; Holden, 1976; Ricciardi and Sacerdote, 1979; Tuckwell and Cope, 1980). If the cell receives Poisson excitation and inhibition with rates f_e and f_i and the excitatory and inhibitory postsynaptic potential amplitudes are a_e and a_i ($a_e, a_i \geq 0$), then the random depolarization in the diffusion approximation $X(t)$ satisfies the ordinary stochastic differential equation,

$$(1) \qquad dX(t) = [-X(t) + f_e a_e - f_i a_i]dt + [f_e a_e^2 + f_i a_i^2]^{1/2} dW(t),$$

whenever the depolarization is below threshold for firing, θ. In this equation $W(t)$ is a Wiener process with zero mean and variance t, and time is measured in units

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of the membrane time constant. Of interest to us here is the neuronal firing time problem. This asks for the distribution or moments of the time $\tau_\theta(x_o)$, at which $X(t)$ first reaches threshold θ, given that $X(0) = x_o$. We will always take $x_o = 0$, corresponding to the case of a cell initially at resting level, and set $T = \tau_\theta(0)$.

Exact expressions for the mean and variance of the firing time can be found from the Laplace transform of its density (Roy and Smith, 1969; Ricciardi and Sacerdote, 1979). These expressions, which take the form of infinite series, have been evaluated on the computer for specific values of the basic input parameters

(2) $$a = f_e a_e - f_i a_i,$$

(3) $$b = [f_e a_e^2 + f_i a_i^2]^{1/2},$$

and the parameters θ and x_o. In general, the use of the exact expressions is computationally difficult; but in certain parameter ranges relatively simple asymptotic expressions can be found which give a ready insight into the dependence of the mean and variance of the firing time on input parameters. Ricciardi and Sacerdote obtained such an expression when $b^2 >> \theta^2$ and $a = 0$.

There have been investigations of the first passage time problem for the Ornstein–Uhlenbeck process outside the realm of neurobiology. Early studies include those of Andronov, Pontriagin and Witt (1933), Wang and Uhlenbeck (1945) and Darling and Siegert (1953). Approximate solutions for the moments of the first passage time have been found by Bolotin (1967) and Thomas (1975). Tables of the density and first two moments of the first passage time have been compiled by Keilson and Ross (1975) who used asymptotic expressions for the density and moments when $b^2 << \theta^2$ and $a = 0$.

In this paper we will obtain asymptotic expressions for the mean and variance of the interspike interval in the case of small input variability. The mathematical derivations are contained in the Appendix. We will use these asymptotic results to analyse data on firing rates of slowly adapting stretch receptors (Buno *et al.*, 1978) and to ascertain the quantitative effects of noise on pacemaker activity. We will also obtain by asymptotic and other methods the dependence of the coefficients of variation of output interspike intervals on the input parameters.

2. Asymptotic results

In order to reduce the number of parameters in the problem it is convenient to introduce the two dimensionless quantities,

(4A) $$\varepsilon = \frac{b}{\theta},$$

(4B) $$\alpha = \frac{a}{\theta}.$$

In this section, we limit ourselves to those cases where

$$\varepsilon^2 << 1 \tag{5}$$

so that the standard deviation b, of the input, is small relative to the threshold depolarization θ. In presenting the asymptotic results we consider the following cases separately:

(A). Mean steady state response (α) 'above' threshold so that

$$\alpha - 1 >> \varepsilon.$$

(B). Mean steady state response 'below' threshold so that

$$1 - \alpha >> \varepsilon.$$

(C). Mean steady state response very close to threshold so that

$$|1 - \alpha| = 0(\varepsilon).$$

A. *Results for* $\alpha - 1 >> \varepsilon$

From the results obtained in the Appendix we have the following approximate expressions for the mean and variance of the firing time for $\alpha - 1 >> \varepsilon$:

$$E[T] \sim ln\left(\frac{\alpha}{\alpha - 1}\right) - \frac{\varepsilon^2}{4}\left[\frac{1}{(\alpha - 1)^2} - \frac{1}{\alpha^2}\right] \tag{6}$$

$$\operatorname{var}[T] \sim \frac{\varepsilon^2}{2}\left[\frac{1}{(\alpha - 1)^2} - \frac{1}{\alpha^2}\right] \tag{7}$$

To the extent that var$[T]$ is of order ε^2, we have, to a first approximation, the mean firing time (for $\varepsilon^2 << 1$) being the same as the time at which the mean depolarization reaches θ. Also, for inputs with a small standard deviation so that $\varepsilon^2 << 1$ and for threshold voltages well below the values eventually attained by the mean depolarization so that $\varepsilon^2/(\alpha - 1)^2 << 1$, the first order correction *reduces* the mean firing time.

B. *Results for* $1 - \alpha >> \varepsilon$

For $1 - \alpha >> \varepsilon$, the asymptotic expressions for the solutions of the differential equations for the first and second moments are not as simple as in Case A; but it is still possible to obtain simple approximate formulas for the moments of the firing time as these only require values of the solutions for a nerve cell initially at rest, $X(0) = 0$. It can be shown (see Appendix) that

$$E[T] \sim \frac{\varepsilon\sqrt{\pi}}{1 - \alpha}\, e^{(1-\alpha)^2/\varepsilon^2}, \tag{8}$$

for all $(1 - \alpha)^2 >> \varepsilon^2$. Note that $E[T]$ tends to ∞ as $\varepsilon \to 0$ as it must. When the mean steady state response is below the threshold value ($\alpha < 1$) and there is no noise, it is simply not possible for the depolarization to reach the prescribed threshold in finite time. On the other hand, any amount of noise, however small, makes it possible for the process to cross any threshold, however high relative to the mean steady state response, at some finite time.

We find that the corresponding expression for the variance is,

(9) $$\mathrm{Var}[T] \sim \frac{\varepsilon^2 \pi}{(1-\alpha)^2}\, e^{2(1-\alpha)^2/\varepsilon^2}.$$

for all $(1-\alpha)^2 >> \varepsilon^2$; it becomes unbounded as $\varepsilon \to 0$.

C. *Results for* $|1-\alpha| = 0(\varepsilon)$

When the steady state mean depolarization in the absence of noise is close to threshold so that $\alpha = 1 + \gamma\varepsilon$ where $\gamma = 0(1)$, the previous results do not apply. A different method of solution of the differential equations for the moments is needed as presented in the Appendix. The asymptotic expressions for the mean and variance of the firing time depend on whether α is just below unity ($\gamma \leqslant 0$) or just above unity ($\gamma \geqslant 0$).

For the mean firing time we obtain,

(10) $$E[T] \sim \begin{cases} \ln\left(\frac{1}{\varepsilon}\right) + K_b - K_1(\gamma), & \gamma \geqslant 0, \\ \ln\left(\frac{1}{\varepsilon}\right) + K_b - K_1(-\gamma) + g(-\gamma), & \gamma \leqslant 0, \end{cases}$$

where

(11) $$K_1(z) = 2\int_o^z e^{t^2} \int_t^\infty e^{-s^2}\, ds\, dt,$$

(12) $$g(z) = 2\sqrt{\pi}\int_o^z e^{t^2}\, dt,$$

(13) $$K_b = 0{\cdot}98175501\ldots\quad .$$

The corresponding expressions for the variance of the interspike time are,

(14) $$\mathrm{Var}[T] \sim \begin{cases} [K_b - K_1(\gamma)]^2 + C_2(\gamma), & \gamma \geqslant 0, \\ [K_b - K_1(-\gamma) + g(-\gamma)]^2 + C_3(-\gamma), & \gamma \leqslant 0, \end{cases}$$

where

(15) $$C_2(z) = 2[K_d - K_2(z) + K_b K_1(z)],$$

(16) $$K_2(z) = 2\int_o^z e^{t^2} \int_t^\infty e^{-s^2} K_1(s)\, ds\, dt,$$

(17) $$C_3(z) = 2[g(z) - K_1(z) - \tfrac{1}{2}K_b]^2 - \tfrac{1}{2}[K_b{}^2 - 4K_d],$$

and $K_d = 0{\cdot}134929\ldots$. With $|\gamma| = 0(1)$, the values of $K_1(|\gamma|)$, $g(|\gamma|) - K_1(|\gamma|)$ and $K_2(|\gamma|)$ can be found in Tables 2 and 3 of Keilson and Ross (1975).

For the special case when $\alpha = 1$ we obtain

(18) $$E[T] \sim ln\left(\frac{1}{\varepsilon}\right) + K_b,$$

and

(19) $$\mathrm{Var}[T] \sim K_b^2 + 2K_d.$$

3. Applications of the asymptotic results

The above asymptotic results enable us to readily predict the effects of small amounts of noise on the time between action potentials in the 'leaky integrator' model of neuronal activity when subthreshold depolarizations are represented by an Ornstein–Uhlenbeck process.

A. *Effects of jitter on stretch receptor firing rates*

We see from the asymptotic behaviour of $E[T]$ that the effect of a small amount of noise, *even of zero mean*, is to decrease the expected time between action potentials. This is not obvious from the complicated exact formula obtained for $E[T]$ by Roy and Smith (1969). In those cases where $\alpha < 1$, the reduction of the mean interspike time is from infinite to finite values. Previous computer simulations (Stein, 1967) and exact calculations (Tuckwell, 1976) had shown a similar effect when synaptic excitation caused jumps in membrane potential. In contrast, for the earlier model of Gerstein and Mandelbrot (1964) in which the depolarization can be represented below threshold by $X(t) = mt + \sigma W(t)$, where m and σ are constants depending on the input, a zero mean noise input does not alter the mean interspike time. For that model, it is known that the expected value of the time to reach threshold depends only on the mean value of the input and not on its variability.

The reduction of the mean interspike time in the OUP model by input noise as indicated by the asymptotic results of Section 2 provides a simple theoretical explanation of the effects of jitter applied to slowly adapting crayfish receptors (Buno *et al.*, 1978). For these experiments the effect of the jitter was always to increase the mean discharge rate. In one case, for example, a cell under a steady input current fired at 3·7 impulses per second. In the presence of jitter (assumed zero mean noisy input) the mean firing rate was increased to 6·1 impulses per second. Crude parameter estimates are possible for this experiment. The value of α is estimated to be about 1·98 using the value 150 msec for the membrane time constant at this frequency of firing (A. Kohn, personal communication). The asymptotic expression from part C of the last section then yields the estimate of 0·4 for ε.

B. *Noisy pacemaker cells*

In the ideal situation a pacemaker cell discharges at regular intervals and the density of the interspike time is a delta function centered at the mean value. For the noisy pacemaker one expects the density to be approximately normal with a small spread about the mean value as depicted in MacGregor and Lewis (1977, Ch. 10, p. 235).

A simple model for a pacemaker is a leaky integrator with constant input current such that the steady state depolarization, in the absence of noise, exceeds threshold. Thus $\alpha > 1$ and the time between spikes is $T = ln[\alpha/(\alpha - 1)]$. Now, if there is noise so that the scaled depolarization satisfies

$$dX(t) = (\alpha - X)dt + \varepsilon dW(t), \qquad X(0) = 0, \tag{20}$$

with $X < 1$ and $\alpha >> 1 + \varepsilon$, the results of part A of the last section apply. We then find that the mean interval between discharges, μ_T, is shortened by the presence of noise (even though this has zero mean) to the value given approximately by formula (6). The variance of σ_T^2 of the same interval is given approximately by formula (7). Furthermore, we expect T to be approximately a normal random variable with probability density

$$\phi_T(z) = \frac{1}{\sqrt{2\pi\sigma_T{}^2}} \exp\left[-\frac{(z - \mu_T)^2}{2\sigma_T{}^2}\right]. \tag{21}$$

From normal tables we may find the probability that T lies within prescribed intervals.

4. Coefficient of variation

The coefficient of variation of the interspike time is its standard deviation divided by its mean. It can be employed to quantify the regularity of a spike train. A neuron receiving random synaptic excitation and inhibition has a random input spike train, with time between spikes T_i and a random output spike train with interspike time T_o, as depicted in Fig. 1. With the input train is an associated coefficient of variation C_i and a corresponding quantity C_o is associated with the output train of spikes. A natural question to ask is what effect the neuron produces on the regularity of the spike train as it transforms an input train to an output train? Does it tend, for example, to regularize the train, or equivalently, is C_o less than C_i?

If the excitation and inhibition are both (independent) Poisson processes, with rates f_e and f_i, then the pooled input is also a Poisson process with rate $f_e + f_i$. The coefficient of variation for the interval between events in a Poisson process is unity so that for this model input we have $C_i = 1$ independent of the magnitudes of the synaptic potentials or their frequencies. It is therefore of interest to compute the coefficient of variation of the output train for various values of the input parameters for the model described in the Introduction. After scaling there are two parameters: α, which describes the mean of the input, and ε, which describes its variability.

The kinds of asymptotic analysis employed to find the mean and variance of the interspike time for the case of small variability can also be employed to find the

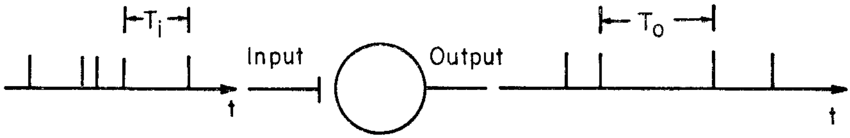

Fig. 1. A neuron, depicted by a circle, receives random inputs and emits a random spike train. T_i and T_o are the corresponding random interevent times.

asymptotic behaviour of $C_0(\alpha, \varepsilon)$. This analysis, more delicate than those for the mean and variance, is explained in the Appendix. Further knowledge of the dependence on the parameters is obtained from the asymptotic behaviour of $C_0(\alpha, \varepsilon)$ for large input variability with a fixed α, and for large mean input with a fixed ε, including those obtained by Ricciardi and Sacerdote (1979). We have supplemented these asymptotic results with direct numerical solution of the relevant boundary value problems. Fortunately the values of α and ε at which the asymptotic methods do not yield accurate approximations are those at which the numerical integrations are not hampered by difficulties due to excessively large numbers. As a check on some of these results the tables of Keilson and Ross (1975) were employed where appropriate.

For small values of ε the following facts emerge from the asymptotic analysis (see Appendix). When $\alpha > 1$, C_o is less than 1 and tends to zero as $\varepsilon \to 0$. For $0 \leqslant \alpha < 1$, C_o is also less than 1 and tends to $\sqrt{K_b^2 + 2K_d}/\ln(1/\varepsilon)$ as α approaches 1 from below. When α is negative we find C_o is less than 1 only for small negative values of α. For larger negative values C_o is greater than 1 but in the limit as $\alpha \to -\infty$, C_o approaches 1 from above. Furthermore there is just one finite value of α at which $C_o = 1$ so C_o must attain a maximum at some negative value of α which depends on ε.

In the limit as $\varepsilon \to 0$, the input becomes deterministic and threshold crossings are only possible when $\alpha > 1$. Then, since the output is also deterministic, the value of C_o is necessarily zero. This is consistent with the above asymptotic results. When ε is very small and $\alpha < 1$, the mean and standard deviation of T_o are, from the results of section 2 part B, approximately equal. That is, $C_o \to 1$ as $\varepsilon \to 0$ for $\alpha < 1$. This is in accordance with the fact that there are only infrequent random threshold crossings so that we have effectively a waiting time for rare events (Poisson process with coefficient of variation unity). Thus the overall result is

$$\lim_{\varepsilon \to 0} C_0(\alpha, \varepsilon) = H(1 - \alpha), \tag{22}$$

where $H(\cdot)$ is the unit step function.

In the case of large input variability and fixed α, C_o increases as the square root of ε and exceeds unity for sufficiently large ε. In the case of large mean input and fixed ε, $C_o \to 0$ as $\alpha \to \infty$ and C_o approaches unity from above as $\alpha \to \infty$. Again, these facts are derived in the Appendix.

In Fig. 2 we give the graphs of $C_o(\alpha, \varepsilon)$ vs. α for various ε using the asymptotic results for small and large ε as well as numerical solutions for moderate ε. We see from these graphs that there are many values of α and ε for which $C_o < 1$, and furthermore we often find C_o close to zero. Recalling that $C_i = 1$, we find somewhat amazingly that the (model) neuron is capable of transforming a 'completely random' sequence of events into a nearly regular sequence and thus can serve to filter out noise.

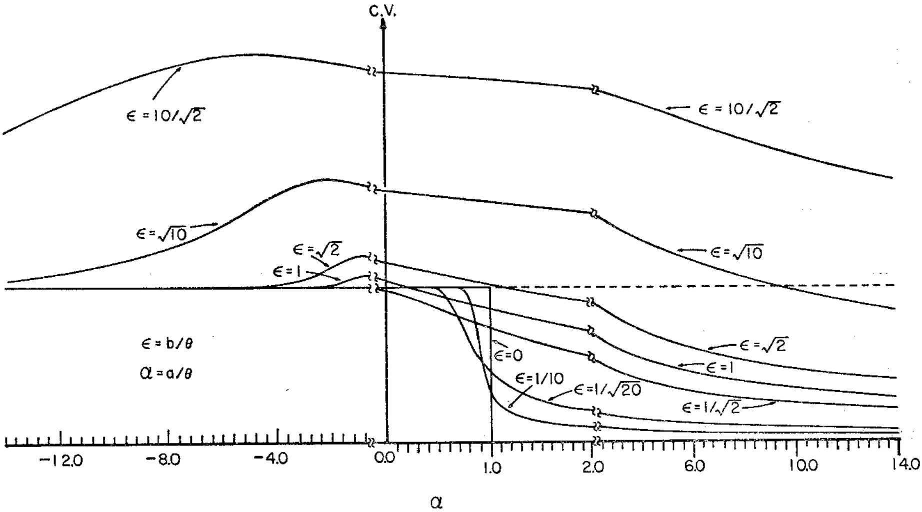

Fig. 2. A sketch of the dependence of the coefficient of variation of the interspike time for the Ornstein–Uhlenbeck model on the parameter a for for various values of the standard deviation of the input process. For $\varepsilon = 0$ a step function is obtained and the C.V. can attain values greater than unity when there is noise and there is sufficient inhibition.

In the case of excitation only, $\alpha = f_e(a_e/\theta)$ and $\varepsilon^2 = f_e(a_e/\theta)^2$. For many cells we have $a_e/\theta << 1$ (synaptic potentials small relative to threshold) so that conditions under which $C_o < 1$ (namely $\varepsilon^2 << 1$ and $\alpha > 1$) may prevail. When inhibitory inputs are introduced α must decrease and ε^2 must increase so that in general the ouput becomes less regular since C_o must generally increase in the parameter ranges of physiological interest.

For Stein's model (Stein, 1965) with excitation only, both computer simulations and exact solutions (Stein, 1967; Tuckwell and Richter, 1978) revealed that C_0 was less than unity. In a following study which included inhibition (Tuckwell, 1979), computer simulations indicated that sometimes a value of C_o greater than unity could be obtained. For that model it was deduced that a value of C_o greater than 1 implied the presence of inhibitory inputs. The results in Fig. 2 of this paper show that there are many instances when the diffusion approximation leads to a value of C_o greater than unity when inhibition is either absent or present. The need for further work with more realistic neuronal models is indicated to ascertain whether a value of C_0 greater than unity strongly suggests that a cell is in fact receiving synaptic inhibition. Unfortunately the models considered thus far, in which the subthreshold depolarization is a Markov process, are those most amenable to analysis.

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APPENDIX

The kth moment of $\tau_\theta(x_o)$, denoted by $T_k(x_o)$ with $T_o(x_o) \equiv 1$, is determined by the boundary value problem (Darling and Siegert, 1953)

$$\text{(1A)} \qquad \tfrac{1}{2}b^2 \frac{d^2T_k}{dx_0^2} + (a - x_o)\frac{dT_k}{dx_o} = -kT_{k-1}, \quad (k = 1, 2, \ldots)$$

$$\text{(1B,C)} \qquad T_k(\theta) = 0, \qquad \lim_{x_o \to -\infty} \left[\frac{dT_k}{dx_o}\right] = 0.$$

An exact solution in terms of double quadratures is possible for the boundary value problem (BVP) (1A)–(1C), but simple asymptotic expressions in different parameter ranges are often more useful than the complicated exact expression. These asymptotic expressions may be obtained directly from the BVP (1A)–(1C) by perturbation methods and the method of matched asymptotic expansions. To carry out the asymptotic analyses, we introduce $\alpha = a/\theta$ and $\varepsilon = b/\theta$ as before and also $x = x_o/\theta$. In terms of α, ε, and x we write the differential equation (1A) as

$$\text{(2A)} \qquad \tfrac{1}{2}\varepsilon^2 \ddot{T}_k + (\alpha - x)\dot{T}_k = -kT_{k-1}, \qquad (k = 1, 2, \ldots)$$

and the auxiliary conditions (1B) and (1C) as

$$\text{(2B,C)} \qquad T_k(1) = 0, \qquad \lim_{x \to -\infty} \dot{T}_k(x) = 0$$

where $(\dot{\ }) \equiv d(\ )/dx$. While our subsequent asymptotic analyses also apply to other types of limiting condition for $x \to -\infty$, the condition (2C) is consistent with the fact that a reflecting boundary condition is appropriate for the corresponding one-sided exit problem over a finite interval.

Asymptotic mean and variance of interspike time for noise with low variability

A. *Low threshold values.*—For low threshold values so that $a/\theta = \alpha > 1$, we have $\alpha - x > 0$ for all $x \leqslant 1$. For a sufficiently small value of b so that $\varepsilon^2 = b^2/\theta^2 << 1$, a singular perturbation solution of the BVP (2A)–(2C) is appropriate (Cole, 1968). Away from the end points of the solution domain, an approximate solution of the BVP can be obtained by expanding $T_k(x; \varepsilon)$ in a regular perturbation series in powers of ε^2:

$$(3) \qquad T_k(x;\varepsilon) = \sum_{n=1}^{\infty} T_k^{(n)}(x)\varepsilon^{2n}$$

and requiring that the system (2) be satisfied identically in ε. In particular, the leading term of the so-called 'outer solution' (3) for $T_1(x)$ is governed by

$$(4) \qquad \begin{cases} (\alpha - x)\dot{T}_1^{(0)}(x) = -1, & (-\infty < x < 1) \\ T_1^{(0)}(1) = 0, & \text{and } \lim_{x \to -\infty} \dot{T}_1^{(0)}(x) = 0 \end{cases}$$

so that we have

$$(5) \qquad T_1^{(0)}(x) = ln\left(\frac{\alpha - x}{\alpha - 1}\right).$$

Note that $T_1^{(0)}(x)$ as given by (5) is a nonnegative monotone decreasing function as x increases. Furthermore, $T_1^{(0)}(x)$ satisfies both boundary conditions in (4) without a supplementary boundary layer solution. In fact, a boundary layer analysis shows that the ODE (4A) does not support a boundary layer solution at $x = 1$ when $a > 1$. The leading term solution (5) for $T_1(x)$ is identical to the passage time for a deterministic input.

We can continue the process to calculate higher order terms in the series (3). For example, we have for the $0(\varepsilon^2)$ term,

$$(6) \qquad \begin{cases} (\alpha - x)\dot{T}_1^{(1)} = -\frac{1}{2}\ddot{T}_1^{(0)} = \frac{1}{2}\dfrac{1}{(\alpha - x)^2} \\ T_1^{(1)}(1) = 0, \qquad \dot{T}_1^{(1)}(-\infty) = 0 \end{cases}$$

which determines $T_1^{(1)}(x)$. Except for $0(\varepsilon^4)$ terms, we have

$$(7) \qquad T_1(x) \sim ln\left(\frac{\alpha - x}{\alpha - 1}\right) - \frac{\varepsilon^2}{4}\left[\frac{1}{(\alpha - 1)^2} - \frac{1}{(\alpha - x)^2}\right] + 0(\varepsilon^4)$$

The two-term perturbation solution (7) provides an accurate approximation of the exact solution whenever $\varepsilon^4/(\alpha - 1)^4 << 1$. This simple approximate solution is considerably more informative than the double quadrature exact solution (given later in (20)).

A similar perturbation solution for $T_2(x)$ can be obtained by the same procedure. To terms of order ε^4, we have

$$(8) \quad T_2(x) \sim \left[ln\left(\frac{\alpha - x}{\alpha - 1}\right)\right]^2 - \frac{\varepsilon^2}{2}\left[ln\left(\frac{\alpha - x}{\alpha - 1}\right) - 1\right]\left[\frac{1}{(\alpha - 1)^2} - \frac{1}{(\alpha - x)^2}\right] + 0(\varepsilon^4)$$

Higher order correction terms for $T_1(x)$ and $T_2(x)$ as well as coefficients for the higher moment series can be calculated similarly. Since the process is straightforward, we will not carry out these calculations but only note that the asymptotic solutions (7) and (8) for the BVP for $T_1(x)$ and $T_2(x)$ are identical to the asymptotic expansions of the corresponding exact solutions to the order obtained. Moreover, these asymptotic solutions are uniformly valid for all $-\infty < x \leqslant 1$.

From (7) and (8), we can get the following asymptotic expression for the variance of the exit time,

$$\text{(9)} \qquad \operatorname{Var}[\tau_\theta(x)] = T_2(x) - [T_1(x)]^2 \sim \varepsilon^2\left[\frac{1}{(\alpha-1)^2} - \frac{1}{(\alpha-x)^2}\right] + 0(\varepsilon^4).$$

B. *High threshold values.*—For the more difficult case of $\alpha = a/\theta < 1$, we note that the coefficient $(\alpha - x)$ of the $\dot{T}_k$ term in (2A) vanishes once inside the solution domain, namely when $x = \alpha$. At and near the 'turning point' (Cole, 1968), the first derivative term no longer dominates the second derivative term in (2A) no matter how small ε is. Thus, the same 'outer solution' (3) is not expected to hold for the whole of the interior of the solution domain. To the left of the turning point, $x < \alpha$, we expect an outer solution to be adequate. For the leading term outer solution for $T_1(x)$, we have again

$$\text{(10)} \qquad T_1^{(0)}(x) = A_l + \ln\left(\frac{\alpha - x}{1-\alpha}\right) \qquad (x < \alpha);$$

but now the constant of integration A_l must be determined by relating this outer solution to a solution valid across the turning point. In particular, it cannot be determined by the boundary condition at $x = 1$ since this solution is only valid for $x < \alpha < 1$ as it becomes unbounded as x tends to α. The leading term outer solution (10) does have the correct behaviour as $x \to -\infty$.

To the right of the turning point, $x > \alpha$, we also have as a leading term outer solution for $T_1(x)$,

$$\text{(11)} \qquad T_1^{(0)}(x) = A_r + \ln(x - \alpha) \qquad (x > \alpha)$$

Evidently, this outer solution should only be used away from $x = \alpha$ as it becomes unbounded there. The only constant of integration A_r is needed for the matching of $T_1^{(0)}(x)$ with a solution valid across α. Therefore, unlike the $\alpha > 1$ case, this outer solution cannot be made to satisfy the boundary condition $T_1(1) = 0$ and we expect a boundary layer (or inner) solution adjacent to $x = 1$ (Cole, 1968).

For this layer solution, we introduce a stretched variable $y = (1 - x)/\varepsilon^2$ and write the ODE (2A) with $k = 1$ as

$$\text{(12)} \qquad \tfrac{1}{2}\hat{T}_1'' - (\alpha - 1 + \varepsilon^2 y)\hat{T}_1' = -\varepsilon^2$$

where $\hat{T}_1(y) \equiv T_1(x)$ and $(\ )' \equiv d(\ )/dy$. We now seek a perturbation series for $\hat{T}_1(y)$ in powers of ε^2; the leading term $\hat{T}_1^{(0)}$ of this series is seen to be

$$\text{(13)} \qquad \hat{T}_1^{(0)}(y) = B_r[1 - e^{-2(1-\alpha)y}] = B_r[1 - e^{-2(1-\alpha)(1-x)/\varepsilon^2}]$$

where one of the two constants of integration has been fixed so that

$$\hat{T}_1^{(0)}(0) \equiv T_1^{(0)}(1) = 0.$$

(Note that there is no decayed exponential solution near $x = 1$ when $\alpha > 1$ and therefore no boundary layer solution there.) The matching of the 'inner solution' (13) and the outer solution (11) in an intermediate region (through an intermediate variable $z = (1 - x)/\varepsilon$, say) requires $A_r + ln(1 - \alpha) = B_r$ so that (11) becomes

$$T_1^{(0)}(x) \sim B_r + ln\left(\frac{x - \alpha}{1 - \alpha}\right) \qquad (0(\varepsilon) \leqslant 1 - x < 1 - \alpha). \tag{14}$$

The remaining constant of integration B_r is to be determined by relating this outer solution to a solution valid across $x = \alpha$. More specifically, an asymptotic solution for $T_1(x)$ valid in a neighborhood of $x = \alpha$ contains two new constants of integration, say C_r and C_l. The four unknown constants A_l, B_r, C_l, and C_r are then determined by matching conditions on $T_1(x)$ and $\dot{T}_1(x)$ in two overlapping regions of validity of the two pairs of contiguous solutions.

Near the turning point $x = \alpha$, the appropriate stretched variable is $x - \alpha = \varepsilon t$ which transforms the ODE (2A) with $k = 1$ into

$$\tfrac{1}{2}\frac{d^2\bar{T}_1}{dt^2} - t\,\frac{d\bar{T}_1}{dt} = -1 \tag{15}$$

where $\bar{T}_1(t) \equiv T_1(x)$. Unfortunately, no simplification is possible for this ODE which is equivalent to (2A) and is effectively the same as the principal ODE in Keilson and Ross (1975) for the first moment of the first passage time; the exact solution of (15) is in the form of a double integral. However, for the purpose of matching $\bar{T}_1(t)$ and $T_1^{(0)}(x)$, we need only the asymptotic behavior of $\bar{T}_1$ for large $|t|$.

It is a straightforward calculation to obtain for large values of $|t|$ (Cole, 1968)

$$\bar{T}_1(t) \sim \begin{cases} \bar{C}_{ro} + C_{r1}\dfrac{e^{t^2}}{t} + ln(t) & (t >> 1) \\[2ex] \equiv C_{ro} + C_{r1}\dfrac{e^{t^2}}{t} + ln\left(\dfrac{x - \alpha}{1 - \alpha}\right) & \\[2ex] A_l + ln\left(\dfrac{\alpha - x}{1 - \alpha}\right) & (t << -1) \end{cases} \tag{16}$$

where the matching of $\bar{T}_1(t)$ and $T_1^{(0)}(x)$ for $x << \alpha$ has been used to determine the two constants of integration in the asymptotic solution of (15) for $t << -1$. The matching of $\bar{T}_1(t)$ and $T_1^{(0)}(x)$ for $x >> \alpha$ can also be used to set $C_{r1} = 0$ and $C_{ro} = A_r$. However, while a term of the form e^{t^2}/t is eliminated in the range $t << -1$ by the auxiliary condition $\dot{\bar{T}}_1(-\infty) = 0$ (see (17)), the same type of term can be retained in the range $t >> 1$ to give a slightly more accurate solution than the leading term outer solution. This additional degree of accuracy will be needed in our analysis of the coefficient of variation in a later section. The solution (16) for $t >> 1$ can actually be made to satisfy the boundary condition $T_1(x = 1) = 0$ by setting $C_{r1} = -C_{ro}t_1e^{-t_1^2}$ with $t_1 = (1 - \alpha)/\varepsilon$ so that

$$\bar{T}_1(t) \sim C_{ro}\left[1 - \frac{t_1}{t}\, e^{(t^2 - t_1^2)}\right]$$

(17)

$$= C_{ro}\left[1 - \frac{1-\alpha}{x-\alpha}\, e^{-(1-x)(1+x-2\alpha)/\varepsilon^2}\right] \qquad (t >> 1)$$

For $x = 1 - \varepsilon^2 y$, we have $\bar{T}_1(t) \sim \hat{T}_1(y)$ (see (13)) if $C_{ro} = B_r$. Having determined C_{r1} (in terms of $C_{ro} = B_r$) we now see that, away from the boundary $x = 1$, the term e^{t^2}/t in (16) for $t >> 1$ is in fact small (of exponential order) compared to the first term in the same expression and hence either (17) or (10) is an acceptable leading term outer solution.

To determine the remaining constants $C_{ro} = B_r$ and A_l in $T_1^{(0)}(x)$, we must consider the local structure of $\bar{T}_1(t)$ near $t = 0$ and relate this local structure to the asymptotic behaviours of $\bar{T}_1^{(0)}(t)$ for $t >> 1$ and $t << -1$. We will not repeat the analysis of Lakin (1972) which establishes the required connection formulas for a general second order ODE (and references to earlier papers such as Ackerberg and O'Malley (1970)) but simply make use of his connection formulae to find $B_r = A_l = g(t_1) \equiv \mathrm{C}$, where

$$g(t) = 2\sqrt{\pi}\int_0^t e^{y^2}dy, \quad g(t) \sim \frac{\sqrt{\pi}}{t}\, e^{t^2} \quad (t >> 1) \tag{18}$$

After some simplifications by the asymptotic behaviour of $g(t)$ for $t >> 1$ given in (18), we have

$$T_1^{(0)}(x) \sim \begin{cases} C + \ln\left(\dfrac{\alpha - x}{1-\alpha}\right) & (\alpha - x >> \varepsilon) \\[2ex] C - \underline{\dfrac{\sqrt{\pi}\varepsilon}{x-\alpha}\, e^{(x-\alpha)^2/\varepsilon^2}} + \underline{\ln\left(\dfrac{x-\alpha}{1-\alpha}\right)} & (\varepsilon << x - \alpha < 1 - \alpha) \\[2ex] C[1 - e^{-2(1-\alpha)(1-x)/\varepsilon^2}] & (0 \leqslant 1 - x = 0(\varepsilon)) \end{cases} \tag{19}$$

Since $t_1 = (1 - \alpha)/\varepsilon$, the underlined terms in (19) are negligibly small compared to $C \sim \sqrt{\pi}e^{t_1^2}/t_1$ and may be omitted in the range $\varepsilon << x - \alpha < 1 - \alpha - \varepsilon$. Retaining them gives a slightly more accurate asymptotic solution, with the additional accuracy needed in some delicate situations such as the dependence of the coefficient of variation on α discussed in a later section. (The advantage of retaining exponentially small terms in a perturbation solution was also encountered in a recent study of D. Ludwig on *Harvesting Strategies in a Randomly Fluctuating (Fish) Population* (University of British Columbia I.A.M.S. Technical Report No. 79–22, May, 1979).) In contrast, the term $\ln[(\alpha - x)/(1 - \alpha)]$ is dominant for a sufficiently large value of $(\alpha - x)$ and cannot be neglected in the range

$\alpha - x >> \varepsilon$. It is not difficult to verify by the asymptotic behaviour of the exact solution of boundary value problem (2),

$$T_k(x) = \frac{2k}{\varepsilon^2}\int_x^1 e^{(\alpha-\eta)^2/\varepsilon^2}\left[\int_{-\infty}^{\eta} e^{-(\alpha-\xi)^2/\varepsilon^2} T_{k-1}(\xi)d\xi\right]d\eta, \tag{20}$$

that (19) gives the correct asymptotic behaviour of $T_1(x)$ for $\varepsilon << 1$ in the entire solution domain except for a small neighborhood of α and that all terms neglected are small of higher order compared to the terms retained.

For $|x - \alpha|/\varepsilon = 0(1)$, a simple approximate expression for $T_1(x)$ may be obtained from a Taylor series solution of (15)

$$\begin{aligned}\bar{T}_1(t) \equiv T_1(x) &= \sum_{n=0}^{\infty} c_n t^n \\ &= c_o + c_1(t + \tfrac{1}{3}t^3 + \tfrac{1}{10}t^5 + \tfrac{1}{42}t^7 + \ldots) \\ &\quad -(t^2 + \tfrac{1}{3}t^4 + \tfrac{4}{45}t^6 + \ldots)\end{aligned} \tag{21}$$

since $t \equiv (x - \alpha)/\varepsilon = 0$ is an ordinary point of the differential equation (15). The series (21) converges for all finite values of t as the linear differential equation (15) has no finite singular points. The two constants of integration c_o and c_1 can therefore be determined by matching the asymptotic behaviour of (21) with the asymptotic solution (19) for $|t| >> 1$ to be $c_1 = -\sqrt{\pi}$ and $c_o \sim C$ for $(1 - \alpha) >> \varepsilon$. (It is actually easier to get these constants from (20) with $c_1 = \bar{T}_1'(0)$ and $c_o = \bar{T}_1(0)$.) Therefore, we have

$$T_1(x) \equiv \bar{T}_1(t) \simeq C - \underline{\sqrt{\pi}g_o(t) - g_e(t)} \qquad \left(|t| \equiv \left|\frac{x-\alpha}{\varepsilon}\right| \equiv 0(1)\right) \tag{22A}$$

where

$$g_o(t) = t + \tfrac{1}{3}t^3 + \tfrac{1}{10}t^5 + \tfrac{1}{42}t^7 + \ldots = \frac{1}{2\sqrt{\pi}}g(t) \tag{22B}$$

$$g_e(t) = t^2 + \tfrac{1}{3}t^4 + \tfrac{4}{45}t^6 + \ldots, \tag{22C}$$

for $(1 - \alpha) >> \varepsilon$, with $g_o(t)$ being the Taylor series for $g(t)/2\sqrt{\pi}$. From (22), we see that $T_1(x)$ is monotone decreasing as x crosses the turning point α. For $|t| = 0(1)$, $T_1(x)$ is effectively a constant as $C \sim \varepsilon e^{(1-\alpha)^2/\varepsilon^2}/(1 - \alpha)$ dominates the rest of the series for $(1 - \alpha) >> \varepsilon$ so that the underlined terms in (22) may be omitted.

The structure of the boundary value problem for $T_2(x)$ is the same as that of $T_1(x)$ except for the forcing term of the differential equation. An analysis similar to that for $T_1(x)$ above yields a leading term asymptotic solution for $T_2(x)$ which may be simplified to read

$$
(23) \qquad T_2(x) \sim \begin{cases} [T_1(x)]^2 + C^2 - \underline{4C\ln\left(\frac{1-\alpha}{\varepsilon}\right)} & (\alpha - x >> \varepsilon) \\ 2C^2\left[1 - \underline{\frac{1}{C}\ln\left(\frac{1-\alpha}{\varepsilon}\right)}\right] & \left(|t| \equiv \left|\frac{x-\alpha}{\varepsilon}\right| = 0(1)\right) \\ [T_1(x)]^2 + C^2 - \underline{[g(t)]^2 - 2[C - g(t)]\ln\left(\frac{1-\alpha}{\varepsilon}\right)} & \\ \qquad + \underline{4g(t)\ln\left(\frac{x-\alpha}{1-\alpha}\right)} & (\alpha + \varepsilon << x < 1) \\ 2C^2[1 - e^{-2(1-\alpha)(1-x)/\varepsilon^2}] & 0 \leqslant 1 - x = 0(\varepsilon^2) \end{cases}
$$

where again we have $g(t) \sim \sqrt{\pi}e^{t^2}/t$. With $(1-\alpha)/\varepsilon >> 1$, the underlined terms in (23) are also small of higher order compared to other terms in the same expression for $(1-x)/\varepsilon > 1$, they are needed only in some delicate situation such as the behaviour of the coefficient of variation discussed in a later section. The variance of the exit time is given asymptotically by

$$
(24) \qquad \mathrm{Var}[\tau_\theta(x)] \sim \begin{cases} C^2 & \left(\frac{1-x}{\varepsilon} > 1\right) \\ C^2[1 - e^{-4(1-\alpha)(1-x)/\varepsilon^2}] & \left(0 \leqslant \frac{1-x}{\varepsilon} = 0(1)\right) \end{cases}
$$

which becomes unbounded, except at $x = 1$, as $\varepsilon \to 0$.

C. *Threshold values near the steady state mean depolarization.*—As noted in Section 2, the case $\theta \approx a$, with $a/\theta = 1 + \gamma\varepsilon$ and $\gamma = 0(1)$, must be treated separately. In this case, the differential equation (2A) for $T_k(x)$ takes the form:

$$
(25) \qquad \tfrac{1}{2}\varepsilon^2\ddot{T}_k + (1 - x + \gamma\varepsilon)\dot{T}_k = -kT_{k-1} \qquad (k = 1, 2, \ldots).
$$

For $k = 1$, this equation admits an outer solution

$$
(26) \qquad T_1(x) \sim A_o(\varepsilon) + \ln(1-x) + \varepsilon\frac{\gamma}{1-x} + \varepsilon^2\frac{1-2\gamma^2}{4(1-x)^2} + \ldots
$$

where A_o is a constant of integration whose dependence on the parameter ε is completely arbitrary since any constant is a complementary solution of (25). Evidently, the outer solution (26) for $\varepsilon << 1$ does not satisfy the boundary condition $T(1) = 0$ though it satisfies the condition $\dot{T}(-\infty) = 0$. The differential equation (25) has a turning point at α which is in the neighborhood of the boundary point. For an inner solution in that neighbourhood, we use a stretched variable $t = (1-x)/\varepsilon$ and write the equation for T_1 as

$$\tfrac{1}{2}T_1'' - (t + \gamma)T_1' = -1, \tag{27}$$

where primes denote differentiation with respect to t.

In terms of the stretched variable t, the boundary conditions at $x = 1$ becomes $T_1(t = 0) = 0$. For the inner solution to match with the outer solution is it necessary to have $T_1'(t) \to 0$ as $t \to \infty$.

For $\gamma \geqslant 0$, this inner solution may be taken in the form

$$T_1 = 2\int_{\gamma}^{t+\gamma} e^{s^2} \int_{s}^{\infty} e^{-u^2}\, du ds \equiv K_1(t + \gamma) - K_1(\gamma) \qquad (\gamma \geqslant 0) \tag{28}$$

where $K_1(z)$ is as defined in (11) of Section 2. For $t >> 1$, we have

$$K_1(t + \gamma) \sim ln(t) + K_b + \frac{\gamma}{t} + \ldots, \tag{29}$$

with $K_b = 0{\cdot}981755 \ldots$. The matching of (26) and (28) in an intermediate range $1 - x = 0(\sqrt{\varepsilon})$ gives $A_o(\varepsilon) = ln(1/\varepsilon) + K_b - K_1(\gamma)$. Therefore, we have for $\gamma > 0$

$$T_1(x) \sim ln\left(\frac{1 - x}{\varepsilon}\right) + C_1(\gamma) + \varepsilon\frac{\gamma}{1 - x} + \ldots, \qquad C_1(\gamma) = K_b - K_1(\gamma). \tag{30}$$

For $\gamma < 0$, and $x \leqslant \alpha$, the inner solution may be written as

$$T_1(x) = K_1(t - |\gamma|) - K_1(|\gamma|) + g(|\gamma|) \qquad (\gamma \leqslant 0) \tag{31}$$

where $g(t)$ is as defined in (18). The matching of (26) and (31) in the intermediate range $1 - x = 0(\sqrt{\varepsilon})$ gives $A_o = ln(1/\varepsilon) + K_b - K_1(|\gamma|) + g(|\gamma|)$ and therewith

$$T_1(x) \sim ln\left(\frac{1 - x}{\varepsilon}\right) + C_1(|\gamma|) + g(|\gamma|) + \varepsilon\frac{\gamma}{1 - x} + \ldots \quad (\gamma \leqslant 0). \tag{32}$$

It should be noted that (28) and (31) are in fact the exact solution of the BVP (2) with $k = 1$ for $\alpha \geqslant 1$ and $\alpha < 1$, respectively, and (30) and (32) are their asymptotic expansions away from α. Thus, the matched asymptotic solution procedure is really not necessary for obtaining the asymptotic behaviour (30) and (32) in the case of O.U. processes. However, we anticipate that this solution procedure will simplify the determination of the corresponding asymptotic behavior for more general stochastic processes and its use for the O.U. process here is intended to illustrate the various ramifications in its application unencumbered by the technical details of the more general case.

The expressions (30) and (32) are to be used only for $t \equiv (1 - x)/\varepsilon >> 1$. For $t = 0(1)$, $T_1(x)$ may be more efficiently evaluated by way of its Taylor series representation (about the boundary point $x = 1$).

$$\begin{aligned} T_1(x) = {} & D_1(\gamma)\left[t + \gamma t^2 + \frac{1 + 2\gamma^3}{3}t^3 + \left(\frac{\gamma}{2} + \frac{\gamma^3}{3}\right)t^4 + \ldots\right] \\ & - \left[t^2 + \frac{2\gamma}{3}t^3 + \frac{1 + \gamma^2}{3}t^4 + \ldots\right], \end{aligned} \tag{33A}$$

instead of the integral representation where

$$(33B) \qquad D_1(z) = 2e^{z^2}\int_t^\infty e^{-s^2}\,ds = \sqrt{\pi}e^{z^2}\left[1 - \frac{2}{\sqrt{\pi}}\int_o^z e^{-s^2}\,ds\right].$$

The series (33) was obtained by the method of undetermined coefficients directly from the ODE (27) and the auxiliary conditions $T_1 = 0$ and $dT_1/dt = D_1(\gamma)$ at $t = 0$, the second condition being a direct consequence of (28).

Similar arguments applied to (25) and the auxiliary conditions (2B) and (2C) for $k = 2$ give the asymptotic expressions

$$(34) \qquad T_2(x) \sim \begin{cases} [T_1(x)]^2 + C_1^2(\gamma) + C_2(\gamma) & (\gamma \geqslant 0) \\ [T_1(x)]^2 + [C_1(|\gamma|) + g(|\gamma|)]^2 + C_3(|\gamma|) & (\gamma \leqslant 0) \end{cases}$$

away from the boundary $x = 1$, where $C_2(z)$ and $C_3(z)$ are as given in (15) and (17) of Section 2, and the Taylor series representation

$$(35A) \qquad T_2(x) = D_2(\gamma)\left[t + \gamma t^2 + \frac{1 + 2\gamma^2}{3}t^3 + \ldots\right] - \left[\tfrac{2}{3}D_1(\gamma)t^3 + \ldots\right],$$

with

$$(35B) \qquad D_2(z) = 4e^{z^2}\int_z^\infty e^{-s^2}\left[\int_o^s D_1(t)dt\right]ds,$$

for $1 - x = 0(\varepsilon)$. With $\gamma = 0(1)$, $D_1(\gamma)$ can be obtained from a standard table for the error function while $D_2(\gamma)$ is easily calculated.

For $1 - x >> \varepsilon$, we have

$$(36) \qquad \mathrm{var}[\tau_\theta(x)] \sim \begin{cases} C_1^2(\gamma) + C_2(\gamma) & (\gamma \geqslant 0) \\ [C_1(|\gamma|) + g(|\gamma|)]^2 + C_3(|\gamma|) & (\gamma \leqslant 0) \end{cases}$$

Asymptotic results for coefficient of variation

The coefficient of variation of the interspike time is defined as

$$(37) \qquad \text{C.V.} = \frac{\text{standard deviation of interspike interval}}{\text{mean interval}},$$

and is employed as one means of quantifying the regularity of a train of spikes. For the model neuron initially at rest

$$(38) \qquad \text{C.V.} = \frac{\sqrt{T_2(0) - [T_1(0)]^2}}{T_1(0)}.$$

We will obtain a number of asymptotic results for this quantity for various ranges of dimensionless input mean α and standard deviation ε.

A. *Asymptotic behaviour for small input variability.*—For $0 < \varepsilon << 1$ and $\alpha > 1$, we find, from the regular perturbation solutions (7) and (8) when $\frac{\alpha - 1}{\varepsilon} >> 1$ and from the matched asymptotic solution (30) and (34) when $\alpha = 1 + \gamma\varepsilon > 1$,

$$(39)\quad \text{C.V.} \sim \begin{cases} \dfrac{\varepsilon}{\sqrt{2}}\left[\dfrac{1}{(\alpha-1)^2} - \dfrac{1}{\alpha^2}\right] \Big/ \left\{ ln\left(\dfrac{\alpha}{\alpha-1}\right) - \dfrac{\varepsilon^2}{4}\left[\dfrac{1}{(\alpha-1)^2} - \dfrac{1}{\alpha^2}\right]\right\} & (\alpha >> 1 + 0(\varepsilon)) \\[2ex] \dfrac{1}{ln\left(\dfrac{1}{\varepsilon}\right)} \sqrt{(K_b^2 + 2K_d) + [K_1^2(\gamma) - 2K_2(\gamma)]} & (\alpha = 1 + \gamma\varepsilon > 1). \end{cases}$$

It is seen from (39) that we have $0 < \text{C.V.} < 1$ for sufficiently small ε with $\text{C.V.} \to 0$ as $\varepsilon \to 0$, which is what we expect for $\alpha > 1$.

For $0 \leqslant \alpha < 1$, we obtain, from (19) and (23) when $\frac{1-\alpha}{\varepsilon} >> 1$ and from (32) and (34) when $\alpha = 1 - |\gamma|\varepsilon$ (with $\gamma = 0(1)$),

$$(40)\quad \text{C.V.} \sim \begin{cases} 1 - \dfrac{1}{C}\left[ln\left(\dfrac{\alpha}{\varepsilon}\right) + ln\left(\dfrac{1-\alpha}{\varepsilon}\right)\right] & \left(1 << \dfrac{1-\alpha}{\varepsilon} \leqslant \dfrac{1}{\varepsilon}\right) \\[2ex] \dfrac{1}{ln\left(\dfrac{1}{\varepsilon}\right)} \sqrt{(K_b^2 + 2K_d) + 3[g(|\gamma|) - K_1(|\gamma|)]^2} & (\alpha = 1 - |\gamma|\varepsilon). \end{cases}$$

Here we have $0 < \text{C.V.} < 1$ for $0 \leqslant \alpha < 1$ and $0 < \varepsilon << 1$ with

$$(41)\quad \text{C.V.} \to \frac{\sqrt{K_b^2 + 2K_d}}{ln(1/\varepsilon)},$$

as α approaches 1 from below. Note that deleting the underlined (small) term in (23) for $T_2(x)$ would have given a qualitatively incorrect result for the C.V.

For the remaining range, $-\infty < \alpha < 0$ we obtain from the asymptotic solutions (19) and (23) $\left(\text{with } 0 \leqslant \frac{x-\alpha}{\varepsilon}\right)$,

$$(42)\quad \text{C.V.} \sim \begin{cases} 1 + \dfrac{1-\alpha}{|\alpha|} e^{-(1-2\alpha)/\varepsilon^2}, & (-\alpha >> \varepsilon) \\[2ex] 1 - \dfrac{1}{C} ln\left(\dfrac{1-\alpha}{\varepsilon}\right), & (-\alpha << \varepsilon) \end{cases}$$

The behaviour of C.V. in the range given by (42) will be discussed in the next section.

B. *Structure of C.V. for negative α and small input variability.*—For inhibition dominant inputs, we find from (42) some interesting behaviour of the C.V. as a function of α. Whereas the C.V. is less than unity for small negative values of $\alpha\,(0 < -\alpha << \varepsilon)$, we find that for larger negative values of $\alpha\,(-\alpha >> \varepsilon > 0)$ the C.V. attains values greater than unity and

$$\lim_{\alpha \to -\infty} \text{C.V.} = 1 \qquad (0 < \varepsilon << 1). \tag{43}$$

We will show that there is exactly one finite value of α, depending on ε and denoted by $\bar{\alpha}$, at which C.V. attains the value unity. To obtain $\bar{\alpha}$, we begin by using the expression for the C.V. (valid for all values of α)

$$\text{C.V.} \sim 1 + \frac{1}{C}\left[\sqrt{\pi}g_o(t_o) + g_e(t_o) - \ln\left(\frac{1}{\varepsilon} + t_o\right)\right] + 0\left(\frac{1}{C^2}\right) \tag{44}$$

where $t_o = -\alpha/\varepsilon > 0$ and $C = g\left(\frac{1-\alpha}{\varepsilon}\right) = 0(\varepsilon e^{(1-\alpha)^2/\varepsilon^2})$ for $0 < \varepsilon << 1$. [Note that t_o may be 0(1) and hence the power series expressions for T_1 and T_2 have to be used in (44). These power series expressions are most useful for $|t| = o(1)$ but are valid for all t, $0 \leqslant |t| < \infty$.] From equation (44), we see that the C.V. for $0 < \varepsilon << 1$ is (up to exponentially small terms) unity at $t_o = \bar{t}_o$ determined bv

$$\ln\left(\frac{1}{\varepsilon} + \bar{t}_o\right) = \sqrt{\pi}g_o(\bar{t}_o) + g_e(\bar{t}_o). \tag{45}$$

This transcendental equation for $\bar{t}_o$ has exactly one real root which is positive and increases with decreasing ε, since $\ln\left(\frac{1}{\varepsilon} + \bar{t}_o\right)$ is monotone increasing and concave while $\sqrt{\pi}g_o(t_o) + g_e(t_o)$ is monotone increasing and convex. For a given $\bar{t}_o$ where C.V. is unity, we have $\alpha = \bar{\alpha} = -\varepsilon\bar{t}_o$ and we see, from (44) and the fact that the quantity in square brackets there changes sign, that C.V. < 1 for $\bar{\alpha} < \alpha < 0$ and C.V. > 1 for $\alpha < \bar{\alpha} < 0$. Furthermore, an analysis of (45) shows that we have

$$\bar{\alpha} \gtrsim -\varepsilon \tag{46A}$$

for ε around 0·01, whereas for larger values of ε (but not greater than around 0·7) we have

$$\bar{\alpha} \gtrsim -\tfrac{1}{2}\varepsilon\sqrt{\pi}\left[\sqrt{1 + \frac{4}{\pi}\ln\left(\frac{1}{\varepsilon}\right)} - 1\right]. \tag{46B}$$

It is clear from the above analysis that C.V. must attain a maximum value at some negative value of $\alpha = \alpha^*$, depending on ε. For a fixed ε, $0 < \varepsilon << 1$, the maximum point α^* is determined by the condition

$$\left.\frac{d[\text{C.V.}]}{dt_o}\right|_{t_o = t_o^*} = 0, \tag{47A}$$

which gives (with primes indicating differentiation with respect to the argument)

$$\text{(47B)} \quad \sqrt{\pi}g_o(t_o^*) + g_e(t_o^*) - \frac{\varepsilon}{2(1 + \varepsilon t_o^*)}[\sqrt{\pi}g_o'(t_o^*) + g_e'(t_o^*)] = ln\left(\frac{1}{\varepsilon} + t_o^*\right).$$

This transcendental equation has exactly one real root which is positive. An analysis of (47B) shows that the location of $\alpha^* = -\varepsilon t_o^*$ recedes toward $-\infty$ as ε decreases and is given approximately by the formula

$$\text{(48)} \qquad \alpha^* \cong \bar{\alpha} - \tfrac{1}{2}\varepsilon^2$$

The maximum value of the C.V. is given by

$$\text{(49)} \qquad [\text{C.V.}]_{\max} \sim 1 + \frac{\varepsilon[\sqrt{\pi}g_o'(t_o^*) + g_e'(t_o^*)]}{2C(1 + \varepsilon t_o^*)} + 0\left(\frac{1}{C^2}\right)$$

which tends to unity from above as $\varepsilon \to 0$, since the exponential growth of C in the denominator for small ε dominates the corresponding growth of the numerator.

C. *Limiting behavior of coefficient of variations for vanishing* ε.—In the limit as $\varepsilon \to 0$ the input becomes deterministic and crossings are only possible when $\alpha > 1$. Then, since the output is also deterministic, the C.V. is necessarily zero. This is consistent with formulas (39) and (41) when $\varepsilon \to 0$. When ε is very small and $\alpha < 1$, we see from (19) and (23) that the second moment of the interspike time is asymptotically twice the square of the mean; hence, for very small ε and $\alpha < 1$, the standard deviation and the mean of the output are approximately equal, i.e., C.V. $\to 1$ as $\varepsilon \to 0$ for $\alpha < 1$. This is consistent with the fact that there are no deterministic threshold crossings and only infrequent random ones; thus, we have effectively a waiting time problem for rare events (c.f. Poisson process where C.V. of waiting time for one event is unity). Therefore, the overall picture for the C.V. as $\varepsilon \downarrow 0$ is that of a step function $H(1 - \alpha)$.

D. *Asymptotic behavior for large input variability.*—When the standard deviation of the noise is large compared to its mean, we obtain the following asymptotic result for the coefficient of variation of the interspike time:

$$\text{(50)} \qquad \text{C.V.} \sim \sqrt{\frac{2\varepsilon ln(2)}{\sqrt{\pi}}}\left\{1 + \left(\frac{\pi}{4ln2} - 1\right)\frac{1 - 2\alpha}{\sqrt{\pi\varepsilon}} + 0\left(\frac{\alpha^2}{\varepsilon^2}\right)\right\}.$$

This result may be obtained from the exact series solution in (21) and (23) or from the equivalent series form of the solution given by Ricciardi and Sacerdote (1979). Thus we see that, for any fixed α, the C.V. increases as the square root of ε and exceeds unity for sufficiently large ε whatever α may be. Note, however, that unless α is much less than ε, higher order terms than those given explicitly in (50) must be retained to obtain an accurate estimate of the C.V. For $|\alpha| >> \varepsilon$, however, we will find in the next subsection a simple expression for the C.V.

E. *Asymptotic behavior for large mean input.*—When $\alpha >> 1$ we may rescale the boundary value problem for the first two moments so that the regular perturbation solution of (7) and (8) again applies. We then find

$$\text{(51)} \qquad \text{C.V.} \sim \frac{\varepsilon}{\sqrt{\alpha}}\left(1 - \frac{1}{4\alpha}\right), \qquad (\alpha >> 1,\ \alpha >> \varepsilon^2)$$

Similarly when $-|\alpha| >> \varepsilon^2$, we find after rescaling that the first part of (42) applies in the form

$$\text{(52)} \qquad \text{C.V.} \sim 1 + (1 + 1/|\alpha|)e^{-(2|\alpha|+1)/\varepsilon^2} \qquad (|\alpha| >> -\varepsilon^2)$$

We see therefore that for a fixed ε, we have C.V. $\to 0$ as $\alpha \to \infty$ and C.V. $\downarrow 1$ as $\alpha \to -\infty$.

F. *The overall dependence of the C.V. on α and ε.*—The asymptotic results given so far in this section provide a useful partial picture of the dependence of the coefficient of variation of the interspike time on the dimensionless mean α and standard deviation ε of the input to the model neuron. An alternate method of determining the C.V. is by direct numerical integration of the differential equations for $T_1(x)$ and $T_2(x)$. Fortunately the region in the (α, ε) half-space where this is not hampered by numerical difficulties due to excessively large numbers complements the regions in which the asymptotic expression we have obtained are valid. Thus it is now possible to obtain the complete qualitative picture of the dependence of the C.V. on α and ε. As a check on the accuracy of some of these results, the tables of Keilson and Ross (1975) have been employed where appropriate.

Figure 2 shows a set of C.V. versus α curves for various ε (with α-axis stretched four folds in the range $0 \leqslant \alpha \leqslant 2$). A description of this figure is as follows. In the limiting case $\varepsilon = 0$ the C.V. versus α curve is the step function $H(1 - \alpha)$ as discussed in part C of this section. The curves for $\varepsilon << 1$ depart slightly from the step function with maxima slightly greater than 1 at some negative value of α. They cross the step function at negative values of α as illustrated by the curve for $\varepsilon = 1/\sqrt{2}$. As ε increases, the value of the maximum increases and moves to the right as does the position at which the C.V. curve crosses the line C.V. $= 1$. At still larger values of ε the position α^* of the maximum of the C.V. recedes toward more negative α-values whereas the value of $\bar{\alpha}$ at which C.V. $= 1$ continues to increase as does maximum C.V.

At intermediate values of ε, represented by $\varepsilon = \sqrt{2}$ in Fig. 2, the value of the C.V. remains above unity for all negative and some positive values of α, with C.V. $\to 0$ as $\alpha \to \infty$. As ε increases further, the position α^* of the maximum C.V. is located approximately at $-\varepsilon\sqrt{2}$ and the maximum grows approximately in proportion to $\sqrt{\varepsilon}$ (equation (50)). A representative curve for larger ε is given by the curve for $\varepsilon = 10$ which shows the limits C.V. $\downarrow 1$ as $\alpha \to -\infty$ and C.V. $\to 0$ as $\alpha \to +\infty$.