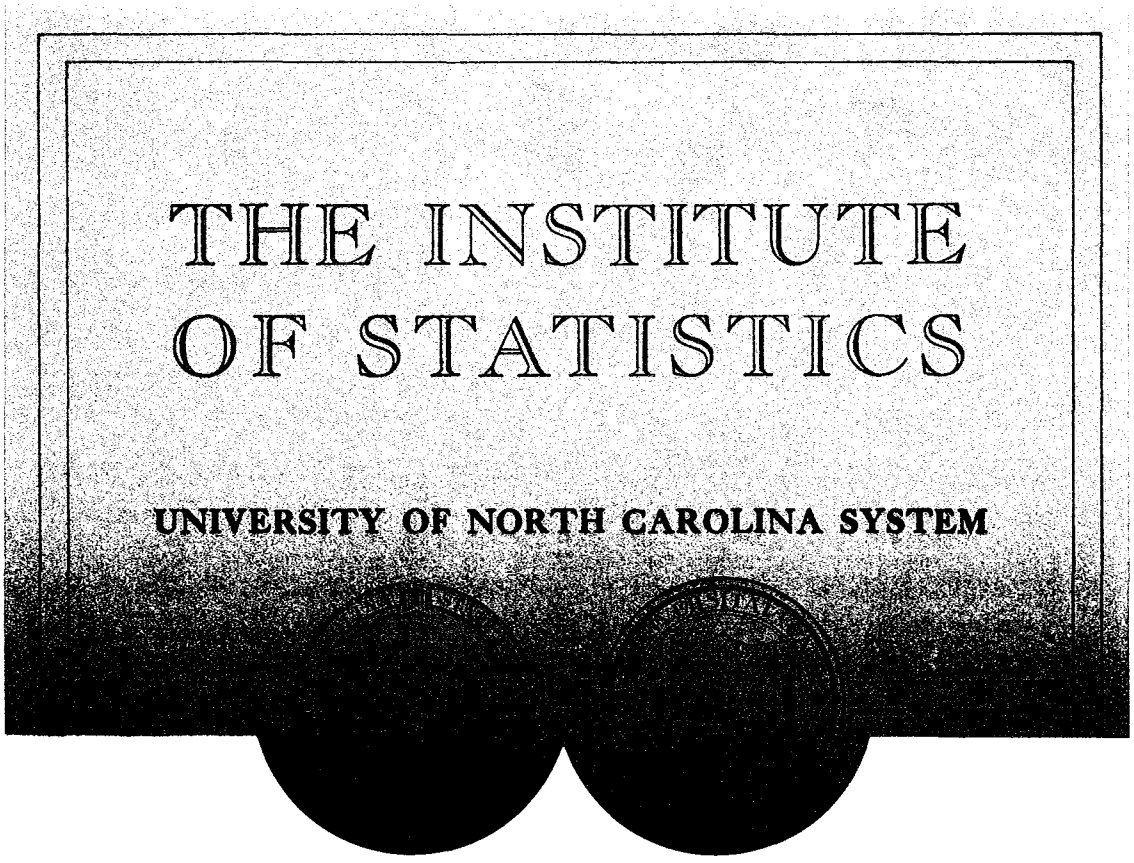

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ABSTRACT

This paper examines a one dimensional stochastic differential equation model for the membrane potential in a neuron with synaptic reversal potentials and random postsynaptic potentials. A diffusion approximation for the original process with discontinuous trajectories is derived and some of its properties are presented. Using the mean of the diffusion process, an approximation for the mean first passage time is obtained and compared with that resulting from Stein's original model.

1. Introduction

Neuronal models of single cells reflect the electrical properties of the membrane via electric circuit models that contain energy storage elements. Such circuit models can be written in terms of a differential equation for the membrane voltage. When the inputs to the cell are random, then the differential equation has a "noisy" input and its solution can often be approximated by a diffusion process. In other cases, such as in neurons with one or a few synaptic inputs near the trigger zone, a Poisson driven differential equation may be a biologically more appropriate model. An action potential (spike) is produced when the membrane voltage exceeds a voltage threshold and corresponds to the first passage time for the associated stochastic process (for a more detailed biological description see, e.g., Kandel and Schwartz, 1985). Several reviews on stochastic neuronal models are available (Fienberg, 1974; Holden, 1976; Sampath and Srinivasan, 1977; Yang and Chen, 1978; Tuckwell, 1988, 1989; Lánský et al., 1990). The spontaneous or resting activity of a neuron or the steady state response to a constant stimulus is mainly described in these studies.

The aim of the presented contribution is to study one of the more sophisticated neural models with Poisson driven inputs under the conditions that the intensities of these input processes are *sufficiently* high and the effect caused by them are *relatively* small. Then the original model is replaced by a more tractable diffusion process. The construction of the diffusion approximations examined here

can be found in the above reviews or in a number of other papers concerning this topic (Gluss, 1967; Roy and Smith, 1969; Capocelli and Ricciardi, 1971; Ricciardi, 1977; Hanson and Tuckwell, 1983; Kallianpur, 1983; Lánský, 1984; Kallianpur and Wolpert, 1987; Lánský and Lánská, 1987).

The scalar diffusion process $X = \{X(t);\ t \geq 0\}$ can be described by the stochastic differential equation

$$dX(t) = \mu(X(t),t)\,dt + \sigma(X(t),t)\,dW(t)\,,\ \ X(0) = x_0\ , \tag{1.1}$$

where $W = \{W(t); t \geq 0\}$ is a standard Wiener process and μ and σ are real-valued functions of their arguments satisfying certain regularity conditions (Karlin and Taylor, 1981). Here, the process X represents changes in the membrane potential between two consecutive neuronal firings (spikes) and t represents the time since the last spike. The reference level for the membrane potential is usually taken to be the resting potential. The initial voltage (the reset value following a spike) is denoted as x_0 , and is often assumed to be equal to the resting potential.

An action potential (spike) is produced when the membrane voltage X exceeds for the first time a voltage threshold, for simplicity assumed to be equal to a constant $S > x_0$. It corresponds to the first passage time problem for the associated stochastic process. Thus in studies on neuronal models we are mainly interested in the properties of the random variable T_{S,x_0}, which is defined by the relationship

$$T_{S,x_0} = \inf\{t \geq 0;\ X(t) \geq S,\ X(0) = x_0\}, \tag{1.2}$$

so T_{S,x_0} is the theoretical counterpart of the ISI.

The importance of interspike intervals follows as a consequence of the generally accepted

hypothesis that the information transferred within the nervous system is usually encoded by the timing of spikes. Therefore the reciprocal relationship between the frequency on one hand and the interspike interval on the other leads to the study of the distribution of T_{S,x_0}. When the distribution is too difficult to obtain, the analysis is usually restricted to its moments, primarily the mean and the variance.

2 Model

The stochastic model proposed by Stein (1965) is an integrate-and-fire model of neuronal firing. The main feature of the model is the passive decay of the membrane potential and linear summation of discrete excitatory and inhibitory synaptic inputs driven by time homogeneous Poisson processes.

The summation of synaptic inputs is state-independent in Stein's original model. From the experimental results it is well known that the changes in the depolarization of a nerve cell are state-dependent (see, e.g., Kandel and Schwartz 1985). Therefore a more complex characterization of the process of synaptic transmission has been proposed by Tuckwell (1979). There the transmitter action at the synaptic junction is controlled by a reversal potential, whose main effect is to bound the membrane potential fluctuations. This is done by decreasing the amplitudes of the postsynaptic potentials induced by the input signals, in accordance to how close the membrane potential gets to the reversal potential.

Stein's stochastic neuronal model with reversal potentials is given by a stochastic differential equation

$$dX = -\tfrac{1}{\tau}Xdt + a(V_E - X)dN^+(t) + i(X - V_I)dN^-(t), \quad X(0) = x_0, \tag{2.1}$$

where $\tau > 0$, $-1 < i < 0 < a < 1$ are constants; $N^+=\{N^+(t), t \geq 0\}$, $N^-=\{N^-(t), t \geq 0\}$ are

two independent homogeneous Poisson processes with $N^+(0) = N^-(0) = 0$ and intensities λ, ω resp.; $V_I < x_0$ is a constant representing the inhibitory reversal potential and $V_E > S$ stands for another constant, the excitatory reversal potential. In model (2.1) the jumps caused by the input are state-dependent in such a way that their magnitude decreases linearly as X approaches the boundaries V_I, V_E resp. Hence the process cannot go below the value of the inhibitory reversal potential V_I.

The processes N^+ and N^- imitate the input to the neuron and are an idealization of the stream of excitatory and inhibitory postsynaptic potentials, respectively. The fact that N^+ and N^- are homogeneous processes reflects a time invariant input; that is, the model is appropriate for spontaneous activity or for evoked activity related to a constant stimulus of long duration. The change in the depolarization of a nerve cell when it receives synaptic inputs depends on the difference between the prior voltage and the synaptic reversal potential characteristic of activated synapses. The amplitudes of the postsynaptic potentials at the resting level are equal to aV_E for the excitatory ones and to iV_I for the inhibitory ones. The membrane constant, τ, depicts the rate at which the membrane potential decays to the resting potential in the absence of any synaptic input.

Stein's model, as well as its modification using the reversal potentials, has discontinuous trajectories. It makes their mathematical treatment complicated and therefore diffusion approximations with similar statistical properties are often used instead. For that purpose (2.1) has to be partly modified, for example, by introducing random PSP's into the model (2.1). Then

$$dX = -\tfrac{1}{\tau}Xdt + (a + A)(V_E - X)dN^+(t) + (i + I)(X - V_I)dN^-(t), \quad X(0) = x_0, \qquad (2.2)$$

where the interpretation of the parameters is the same as for (2.1) and additionally A and I are r.v.'s, $E(A) = E(I) = 0$, defined on $(-a,1-a)$, resp., $(-1-i,-i)$. The model (2.2) reflects better the behavior of real neurons than (2.1) as it has been pointed out by Sampath and Srinivasan (1977,p. 88) that

constant jumps are one drawback of these models. However, the resultant diffusion approximation has properties not suitable for the description of the neuron (Lánský and Lánská, 1987). Capocelli and Ricciardi (1971) provided some plausible arguments for a different state dependency of PSP fluctuations. Here we consider a model with random PSP's in which variability decays with the distance from the reversal potentials

$$dX = -\frac{1}{\tau}Xdt + [a(V_E - X) + A\sqrt{(V_E - X)(X - V_I)}\,]dN^+(t) +$$

$$+ [i(X - V_I) + I\sqrt{(V_E - X)(X - V_I)}\,]\,dN^-(t), \quad X(0) = x_0, \tag{2.3}$$

It means that the variability of PSP amplitudes is negligible when the membrane potential takes values close to the reversal potential and increases with the distance from them. It is maximal for $x(t) = (V_E + V_I)/2$.

For the model (2.3) the first two infinitesimal moments are

$$M_1(x) = \lim_{\Delta t \to 0} E(\Delta X(t)|X(t)=x)/(\Delta t) = -x/\tau + \lambda a(V_E - x) + \omega i(x - V_I) \tag{2.4}$$

and

$$M_2(x) = \lim_{\Delta t \to 0} E(\Delta X(t)^2|X(t)=x)/(\Delta t)$$

$$= \lambda a^2(V_E - x)^2 + \omega i^2(x - V_I)^2 + \left(\lambda E(A^2) + \omega E(I^2)\right)(V_E - x)(x - V_I) \tag{2.5}$$

Now, for a sequence of models (2.3) we assume $a_n \to 0_+$, $i_n \to 0_-$, $\lambda_n \to \infty$, $\omega_n \to \infty$ in such a way

that $a_n\lambda_n \to \mu \geq 0$, $i_n\omega_n \to \nu \leq 0$ and simultaneously $E(A_n^2) \to 0_+$, $E(I_n^2) \to 0_+$, ensuring $(\lambda_n E(A_n^2) + \omega_n E(I_n^2)) \to \sigma_A^2 + \sigma_I^2 = \sigma^2 > 0$. In this way we may consider, as $M_j(x) \to 0$ for $j > 2$, a diffusion process (1.1) specified by infinitesimal mean

$$\mu(x) = -x/\tau + \mu(V_E - x) + \nu(x - V_I) = -\alpha x + \beta \tag{2.6}$$

where $\alpha = 1/\tau + \mu - \nu > 0$, $\beta = \mu V_E - \nu V_I$ and by infinitesimal variance

$$\sigma^2(x) = \left(\sigma_A^2 + \sigma_I^2\right)(V_E - x)(x - V_I) = \sigma^2(V_E - x)(x - V_I) \tag{2.7}$$

Of course, that all the models (2.1), (2.2), (2.3) and that specified by (2.6) and (2.7) are characterized by the same functional form for the mean trajectory

$$E(X(t)) = x_0 e^{-\alpha t} + \beta(1 - e^{-\alpha t})/\alpha \tag{2.8}$$

with β/α as the asymptotic level as $t \to +\infty$.

For the reason that the boundary $V_E > S$, and the threshold S will be an absorbing barrier for the first passage time problem, we limit ourselves to the question of what is the behavior of the membrane potential at V_I. For that purpose it is convenient to transform the process X(t) into a process Y(t) defined on the interval (0,1) using the transformation $y = (x - V_I)/(V_E - V_I)$. We get

$$\mu(y) = -\alpha y + (\beta - \alpha V_I)/(V_E - V_I) = -\alpha y - V_I/(\tau(V_E - V_I)) + \mu \tag{2.9}$$

$$\sigma^2(y) = \sigma^2(1 - y)y \tag{2.10}$$

Following the results presented by Goel and Richter-Dyn (1974) we may deduce the boundary behavior for the original model. For $\mu - V_I/(\tau(V_E - V_I)) < \sigma^2/2$ the boundary V_I is regular, otherwise it is an entrance boundary. Of course we have to take into consideration that also the threshold and initial depolarization are changed using the transformation. The transition probability density function for the process Y can be written as an infinite series of either hypergeometric functions (Goel and Richter-Dyn, 1974) or, if we linearly transform the process X to (−1, 1), Jacobi polynomials (Karlin and Taylor, 1981).

Some information about the character of the membrane potential can be deduced from its stationary distribution (Hanson and Tuckwell, 1983). Solving the corresponding differential equation we can derive

$$\phi(x) = \frac{(V_E - V_I)^{B-A-1}}{\sigma^2} \frac{\Gamma(B-A)}{\Gamma(B)\Gamma(-A)} (V_E - x)^{-A-1}(x - V_I)^{B-1} \qquad (2.11)$$

where $A = \frac{2(\beta - \alpha V_E)}{\sigma^2(V_E - V_I)}$ and $B = \frac{2(\beta - \alpha V_I)}{\sigma^2(V_E - V_I)}$.

Because both boundaries V_E and V_I are attainable for some values of parameters (here we do not take into account that crossing $S < V_E$ terminates the process) some extra (reflecting) conditions have to be specified. The shape of the distribution (2.11) is that of a Beta distribution.

For the solution of the first passage time problem there exist Siegert's equation for the Laplace transform $g_S(\lambda|x_0)$ of the first passage time density,

$$\frac{1}{2}\sigma^2(x_0) \frac{\partial^2 g_S(\lambda|x_0)}{\partial {x_0}^2} + \mu(x_0) \frac{\partial g_S(\lambda|x_0)}{\partial x_0} - \lambda g_S(\lambda|x_0) = 0 \qquad (2.12)$$

with initial condition $g_S(\lambda|S) = 1$ and $g_S(\lambda|x_0) < \infty$ for each x_0. Using the form of infinitesimal moments given by (2.9) and (2.10), the equation (2.12) can be identified with the Gaussian equation (Abramowitz and Stegun, 1964)

$$(x_0-1)x_0 \frac{\partial^2 g_S(\lambda|x_0)}{\partial x_0^2} + [\gamma - (\kappa + \theta + 1)x_0] \frac{\partial g_S(\lambda|x_0)}{\partial x_0} - \kappa\theta g_S(\lambda|x_0) = 0 \qquad (2.13)$$

which has a general solution

$$g_S(\lambda|x_0) = C_1 F(\kappa,\theta,\gamma,x_0) + C_2 x_0^{1-\gamma} F(\kappa + 1 - \gamma, \theta + 1 - \gamma, 2 - \gamma, x_0) \qquad (2.14)$$

where $F(\kappa,\theta,\gamma,x_0)$ is a hypergeometric series $F(\kappa,\theta,\gamma,x_0) = 1 + \frac{\kappa\theta}{1!\gamma}x_0 + \frac{\kappa(\kappa+1)\theta(\theta+1)}{2!\ \gamma(\gamma+1)}x_0^2 + \ldots$ For a specific solution we have to identify values for the parameters.

Without a knowledge of the distribution for the first passage time of the membrane trajectory through the threshold S, a recursion relation is available for the moments of the r.v. T_{S,x_0},

$$\frac{1}{2}\sigma^2(x_0) \frac{\partial^2 M_n(S|x_0)}{\partial x_0^2} + \mu(x_0) \frac{\partial M_n(S|x_0)}{\partial x_0} = - nM_{n-1}(S|x_0), \qquad (2.15)$$

for $n = 1, \ldots,$ and $M_0(S|x_0) = 1$, $M_n(S|S) = 0$.

Nevertheless some information can be obtained from the moments of X, namely the mean membrane potential trajectory (Smith and Smith, 1984). One way of approximating the mean interspike interval $E(T_{S,x_0})$ is to use the time t^*, taken for the mean voltage given by (2.8) to cross the threshold. The approximation t^* will be finite if the asymptotic mean membrane potential crosses the threshold, i.e. $\beta\alpha^{-1} > S$. Under this condition and setting $E(X(t)) = S$ then solving it for t, we

obtain

$$t^* = -\alpha^{-1}\ln\left(\frac{S\alpha - \beta}{x_0\alpha - \beta}\right) \tag{2.16}$$

The condition for application of (2.16) is modified if the spontaneous decay of the membrane potential is neglected, $\tau = \infty$. Then the ratio between the input intensities has to fulfil the condition

$$\frac{\mu}{\nu} < \frac{V_I - S}{V_E - S} \tag{2.17}$$

The reliability of the approximation (2.17) depends on the variance of the process X and it can be found in Smith and Smith (1984, eq. 7).

The approximation for the mean firing time gives an interesting comparison with Stein's original model when $x_0 = 0$

$$dX = -\tfrac{1}{\tau}Xdt + b_E\, dN^+(t) + b_I\, dN^-(t), \quad X(0) = 0, \tag{2.18}$$

where b_E (b_I) represents the excitatory (inhibitory) PSP sizes and the Poisson inputs are as before. If we set $\lambda b_E = \mu V_E$ and $\omega b_I = \nu V_I$, the approximation for the mean firing time, $\tilde{t}$, is given by

$$\tilde{t} = -\tau \ln\left(1 - \frac{S}{\tau(\mu V_E - \nu V_I)}\right) \tag{2.19}$$

Paralleling the arguments in Smith and Smith (1984), $\tilde{t}$ may be greater or smaller than the corresponding estimate, t^*, from the above reversal potential models. For a given τ, μ, v, V_E, V_I , if $\tilde{t} > t_c$, then $\tilde{t} < t^*$ and if $\tilde{t} < t_c$, then $\tilde{t} > t^*$ where t_c is the time at which the mean voltage

trajectories for the two models intersect. Of course, we have assumed that the asymptotic level of the mean voltage in the reversal potential model, β/α, is greater than S so that the approximation method is applicable.

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