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UPWARD FIRST CROSSING PROBLEMS FOR NEURONAL MODELING'S PARADIGM

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1. Introduction

In this paper the instantaneous return process in the presence of refractoriness is investigated for diffusion models of single neuron's activity. Steady-state probability densities and asymptotic moments of the neuronal membrane potential will be obtained in a form that is suitable for quantitative evaluations.

It should be recalled that since the classical paper by Gerstein and Mandelbrot [2], numerous attempts have been made to formulate stochastic models for single neuron's activity that would reproduce the essential features of the behavior exhibited by living cells under spontaneous or stimulated conditions (cf. for instance, [6], [8], [9], [10] and the bibliography quoted therein). A quantitative description of the behavior of the membrane potential as an instantaneous return process has then been provided in [3], [4], [5] and [7], assuming that after each firing the neuron's membrane potential is either reset to a unique fixed value or that the reset value is characterized by an assigned probability density function (pdf).

The return process paradigm for the description of the time course evolution of the membrane potential is further exploited in the present paper in which the additional assumption of neuronal refractoriness is included. Specifically, given the regular time-homogeneous diffusion process $\{X(t), t \geq 0\}$ defined over the interval $I = (r_1, r_2)$, we construct the return process in the presence of refractoriness $\{Z(t), t \geq 0\}$ in (r_1, S), with $S \in I$, as follows. Starting at a point $x_0 \in (r_1, S)$ at time zero, when $X(t)$ for the first time attains the threshold S a firing takes place; after the firing, a period of refractoriness of random duration occurs, during which either the neuron is completely unable to respond, or only partially responds to the received stimulations. At the end of the period of refractoriness the process is instantaneously reset at some fixed value ϱ. The subsequent evolution of the process then goes on like as $X(t)$ until the boundary S is again reached. A new firing then occurs, followed by the period of refractoriness, and so on. It is reasonable to assume that during each period of refractoriness the firing threshold S acts as an elastic barrier, in the sense that it behaves as a reflecting boundary for a random duration after which the process is killed (i.e., the period of refractoriness ends). We assume that the degree of elasticity of the boundary depends on the choice of two parameters α (absorbing coefficient) and β (reflecting coefficient), with $\alpha > 0$ and $\beta \geq 0$. Hence, when $Z(t)$ reaches the elastic boundary S, it can be either reflected with probability $\beta/(\alpha + \beta)$ or killed with probability $\alpha/(\alpha + \beta)$.

Under the present paradigm, the process $\{Z(t), t \geq 0\}$, describing the time course of the membrane potential, consists of recurrent cycles of random duration $F_0, R_1, F_1, R_2, F_2, \ldots$, where the F_i $(i = 0, 1, \ldots)$ and the R_i $(i = 1, 2, \ldots)$ are independently distributed random variables. Here, F_0 denotes the first firing time, i.e. the first passage time (FPT) from x_0 to S, F_i $(i = 1, 2, \ldots)$ is the $(i+1)$-th first passage times from ϱ to S, and R_i $(i = 1, 2, \ldots)$ describes the i-th period of refractoriness, i.e. the first exit times (FET) from S through the elastic boundary S. We denote by $g(S, t|x_0)$ the pdf of F_0, by $g(S, t|\varrho)$ the pdf of F_i $(i = 1, 2, \ldots)$ and by $g_e(S, t|S)$ the pdf of R_i $(i = 1, 2, \ldots)$.

In order to be able to apply the specified paradigm to the description of neuronal models in the presence of refractoriness, on investigation of certain general features of diffusion processes in the presence of an elastic boundary is a prerequisite. Here, by elastic boundary we mean a boundary that is "partially transparent", in the sense that its behavior lies in between total absorption and total reflection. This task will be accomplished in the next Section, where we shall analyze the statistical features of the random variable modeling the number of neuronal firings and describe the time evolution of the membrane potential by means of the afore mentioned return process.

2. Effect of Refractoriness

Let $A_1(x)$ and $A_2(x)$ be drift and infinitesimal variance of $X(t)$, respectively. Throughout, we shall assume that Feller conditions are fulfilled [1]. Furthermore, let $h(x)$ and $k(x)$ denote scale function and speed density of $X(t)$:

$$h(x) = \exp\Big\{-2\int^x \frac{A_1(z)}{A_2(z)}\, dz\Big\}, \qquad k(x) = \frac{2}{A_2(x)\, h(x)}\cdot$$

and

$$H(r_1, x] = \int_{r_1}^x h(z)\, dz, \qquad K(r_1, x] = \int_{r_1}^x k(z)\, dz$$

scale and the speed measures, respectively. If *(i)* r_1 is a natural nonattracting boundary and $K(r_1, x] < \infty$, or *(ii)* r_1 is an entrance boundary, the first passage probability $P(S|x)$ from x to S is unity and the mean FPT can be evaluated in the following way:

$$t_1(S|x) := \int_0^\infty t\, g(S, t|x)\, dx = \int_x^S h(z)\, dz \int_{r_1}^z k(u)\, du \qquad (x \leq S). \tag{1}$$

Furthermore, under the same assumptions, if $\alpha > 0$ the first exit probability $\widehat{P}(S|x)$ is unity and the mean FET can be seen to be given by:

$$\widehat{t_1}(S|x) := \int_0^\infty t\, g_e(S, t|x)\, dx = t_1(S|x) + \frac{\beta}{\alpha} \int_{r_1}^S k(z)\, dz \qquad (x \leq S), \tag{2}$$

where α and β are the elasticity coefficients.

We shall first provide a description of the random process $\{M(t), t \geq 0\}$, representing the number of firings released by the neuron up to time t within the return process description $\{Z(t), t \geq 0\}$. To this purpose, for all $z \in (r_1, S)$, let

$$\begin{aligned} p_n(t|z) &= P\{M(t) = n, t \in F_n | Z(0) = z\} \qquad (n = 0, 1, \ldots) \\ \widehat{p}_n(t|z) &= P\{M(t) = n, t \in R_n | Z(0) = z\} \qquad (n = 1, 2, \ldots). \end{aligned} \tag{3}$$

Since $X(t)$ is time-homogeneous, the following relations hold:

$$
\begin{aligned}
p_0(t|x_0) &= 1 - \int_0^t g(S,\tau|x_0)\, d\tau \\
p_n(t|x_0) &= g(S,t|x_0) * g_e(S,t|S) * p_{n-1}(t|\varrho) \\
&= g(S,t|x_0) * g_e(S,t|S) * [g(S,t|\varrho) * g_e(S,t|S)]^{(n-1)} * \Big[1 - \int_0^t g(S,\tau|\varrho)\, d\tau\Big] \\
&\qquad\qquad (n = 1, 2, \ldots) \\
\widehat{p}_1(t|x_0) &= g(S,t|x_0) * \Big[1 - \int_0^t g_e(S,\tau|S)\, d\tau\Big] \\
\widehat{p}_n(t|x_0) &= g(S,t|x_0) * g_e(S,t|S) * \widehat{p}_{n-1}(t|\varrho) \\
&= g(S,t|x_0) * [g_e(S,t|S) * g(S,t|\varrho)]^{(n-1)} * \Big[1 - \int_0^t g_e(S,\tau|S)\, d\tau\Big] \\
&\qquad\qquad (n = 2, 3, \ldots),
\end{aligned}
$$

where $(*)$ means convolution, "$(n-1)$" exponent indicates $(n-1)$-fold convolution, g is the FPT pdf of $X(t)$ through S and g_e is the FET pdf of $X(t)$ through the elastic boundary S. The probabilities $p_n(t|x_0)$ and $\widehat{p}_n(t|x_0)$ can be used to arise to the statistical characteristics of the random variable that describes the number of firings.

We now consider the stochastic process $\{Z(t), t \geq 0\}$ and for all $z \in (r_1, S)$ we set:

$$
\begin{aligned}
\varphi_n(x,t|z) &= \frac{\partial}{\partial x} P\{Z(t) < x, t \in F_n | Z(0) = z\} \qquad (n = 0, 1, \ldots) \\
\widehat{\varphi}_n(x,t|z) &= \frac{\partial}{\partial x} P\{Z(t) < x, t \in R_n | Z(0) = z\} \qquad (n = 1, 2, \ldots).
\end{aligned} \tag{4}
$$

Again by virtue of the time-homogeneity of $X(t)$, one has:

$$
\begin{aligned}
\varphi_0(x,t|x_0) &= f_a(x,t|x_0) \\
\varphi_n(x,t|x_0) &= g(S,t|x_0) * g_e(S,t|S) * \varphi_{n-1}(x,t|\varrho) \\
&= g(S,t|x_0) * g_e(S,t|S) * [g(S,t|\varrho) * g_e(S,t|S)]^{(n-1)} * f_a(x,t|\varrho) \\
&\qquad\qquad (n = 1, 2, \ldots) \\
\widehat{\varphi}_1(x,t|x_0) &= g(S,t|x_0) * f_e(x,t|S) \\
\widehat{\varphi}_n(x,t|x_0) &= g(S,t|x_0) * g_e(S,t|S) * \widehat{\varphi}_{n-1}(x,t|\varrho) \\
&= g(S,t|x_0) * [g_e(S,t|S) * g(S,t|\varrho)]^{(n-1)} * f_e(x,t|S) \quad (n = 2, 3, \ldots),
\end{aligned} \tag{5}
$$

where f_a is the transition pdf of $X(t)$ in the presence of an absorbing boundary in S and f_e is the transition pdf of $X(t)$ in the presence of an elastic boundary in S. The transition pdf of $Z(t)$ can be expressed as

$$
\varphi(x,t|x_0) = \varphi_0(x,t|x_0) + \sum_{n=1}^{\infty} \Big[\varphi_n(x,t|x_0) + \widehat{\varphi}_n(x,t|x_0)\Big]
$$

The steady-state pdf

$$
\gamma(x) := \lim_{t \to \infty} \varphi(x,t|x_0) \tag{6}
$$

of $Z(t)$ can now be explicitly obtained as

$$\gamma(x) = \frac{k(x)}{\widehat{t}_1(S|\varrho)} \left\{ \int_{M(x,\varrho)}^{S} h(z)\, dz + \frac{\beta}{\alpha} \right\}, \qquad x, \varrho \in (r_1, S), \tag{7}$$

where $M(x, \varrho) = \max(x, \varrho)$. The asymptotic moments are then given by

$$\begin{aligned} E(Z^n) &= \int_{r_1}^{S} x^n\, \gamma(x)\, dx \\ &= \frac{1}{\widehat{t}_1(S|\varrho)} \left\{ \int_{\varrho}^{S} h(z)\, dz \int_{r_1}^{z} x^n\, k(x)\, dx + \frac{\beta}{\alpha} \int_{r_1}^{S} x^n\, k(x)\, dx \right\} \end{aligned} \tag{8}$$

Note that for $\beta = 0$, i.e. in the absence of refractoriness, (7) and (8) are in agreement with the corresponding results for the instantaneous return process in the absence of refractoriness (cf. [5]), being $\widehat{t}_1(S|\varrho) \equiv t_1(S|\varrho)$.

Use of the above analytical results now allows one to disclose the effects of refractoriness on any specified diffusion neuronal models. Some instances of particular relevance are presently under investigation and will be reported at the workshop.

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