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THRESHOLD SHAPE CORRESPONDING TO A GAMMA FIRING DISTRIBUTION IN AN ORNSTEIN-UHLENBECK NEURONAL MODEL

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ABSTRACT. We introduce two numerical methods to determine the shape of a time dependent boundary for the Ornstein-Uhlenbeck process that corresponds to an assigned first passage time probability density function. The application of these methods to the stochastic leaky integrate and fire neuronal model allows to check the reliability of specified densities as approximation of the interspike interval distribution. The cases of the Gamma and of the inverse Gaussian densities are discussed.

1 Introduction Firing time distribution plays a key role in the neuronal description and models devoted to mimic its behavior are of interest for coding comprehension. Its mathematical counterpart, i.e. the first passage time (FPT) of a stochastic process through a boundary, is the subject of investigations from analytical and numerical viewpoints (cf. Ricciardi et al., 1999 and papers cited therein). However this distribution is not available in closed form even for a simple model such as the stochastic leaky-integrate and fire one which describes the underthreshold membrane potential evolution of a neuron via an Ornstein-Uhlenbeck (OU) diffusion process. In this model a spike is generated when the membrane potential attains a threshold S, eventually time-depending. After each spike a new process starts making the interspike interval (ISI) a renewal process. The FPT distribution becomes the quantity that describes the probabilistic properties of the code. When the interest on the model focuses on single neuron behavior, the impossibility to determine closed form expressions for the FPT distribution can be partially avoided. Indeed one can use numerical methods or simulations (cf. Ricciardi and Sacerdote, 1979; Ricciardi et al., 1983; Buonocore et al., 1987; Ricciardi and Sato, 1990) to study the statistical properties of the ISI.

However, experimental techniques allow the simultaneous observation of the spikes generated from an increasingly high number of neurons. Hence, the necessity arises to model neuronal networks in order to interpret the spatio-temporal patterns of the observed spike trains. The numerical methods or the simulation techniques considered for the ISI studies, in the case of single neurons, become of difficult application and time consuming when one deals with networks. In this context one wish to determine the analytical expression of distributions that can approximate the FPT distribution in order to facilitate the description of the activity of single neurons of the network. This paper is motivated by this objective. In fact, we compare the FPT distribution of an OU process through a constant boundary with possible approximating distributions. These distributions are interpreted as FPT densities for an OU process, but each one corresponds to a different boundary shape. Hence we attribute the difference between the distributions to different shapes of the boundaries and we recognize the reliability of the approximating distribution by means of the distance between the boundaries. The main features of the OU model are briefly sketched in Section

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2 to introduce the notations, while we refer to Ricciardi and Sacerdote (1979) for a more detailed description of the model.

In Section 3 we propose two numerical methods that allow to understand the effect on the boundary shape of the use of a candidate distribution to approximate the FPT distribution. Indeed we generalize to the OU process recent results on the so called "inverse FPT problem" for the Wiener process (cf. Zucca et al., 2002). The methods allow to determine the boundary shape for which the FPT distribution of the OU process assumes a particular analytical expression. The first method, based on a probabilistic approach, can be viewed as a generalization of the Durbin work (cf. Durbin, 1971) for the direct problem to the inverse FPT problem. Indeed, we determine a stepwise linear approximation of the boundary making use of the results in Durbin for the FPT distribution of a Wiener process constrained by a piecewise linear boundary. The second method uses the numerical integration of a Volterra integral equation obtained from the Fortet equation (cf. Peskir, 2001). The comparison of the resulting boundary shape and a constant one allows to interpret the considered approximation in the modeling perspective.

Various distributions could be candidate to approximate the firing times probability density function (p.d.f.) when an OU model describes the membrane potential behavior, but their biological interpretation is unclear in the modeling context or it is limited to asymptotic arguments. The Gamma distribution is of interest because it verifies analytical and asymptotic properties observed on experimental histograms and therefore it has been considered in Giorno et al. (1997). A contribution towards the interpretation of this distribution in the neuronal models as a FPT p.d.f. can help to understand advantages and limits of its use.

In Section 4 the Gamma and the inverse Gaussian distribution are considered as possible candidates to approximate the unknown FPT of an OU process through a constant boundary. We measure the reliability of these approximations by means of the distance between the constant and the obtained boundary. Note that the methods presented in this paper could also be employed to check the reliability of other distribution candidates such as the generalized inverse Gaussian (cf. Iyengar and Liao, 1997).

2 The Ornstein-Uhlenbeck model The classical stochastic leaky integrate and fire model proposed to describe the membrane potential originally considered discontinuous trajectories (cf. Stein, 1965), but its mathematical analysis was difficult. Diffusion approximations have then been employed to simplify the study (cf. Capocelli and Ricciardi, 1971; Ricciardi and Sacerdote, 1979; Tuckwell and Cope, 1980; Lánský, 1984; Lánský and Sacerdote, 2001). In this limit the membrane potential evolution is described via an OU process obeying to the stochastic differential equation

$$dX(t) = \left(-\frac{X}{\vartheta} + \mu\right) dt + \sigma dW(t), \qquad X(0) = x_0, \tag{1}$$

where $\vartheta > 0$ is the constant of spontaneous decay of the membrane potential to the resting level, assumed to be zero, μ and $\sigma > 0$ are two constants accounting for the input signal and its variability respectively. Here $W(t)$ indicates a standard Wiener process. As is well known (cf. Ricciardi, 1977) the transition p.d.f. of this process

$$f(x,t \mid y,\tau) = \frac{\partial}{\partial x} \mathbb{P}(X(t) \leq x \mid X(\tau) = y) \tag{2}$$

verifies the Kolmogorov equation

$$\frac{\partial f}{\partial \tau} + \left(-\frac{y}{\vartheta} + \mu\right) \frac{\partial f}{\partial y} + \frac{\sigma^2}{2} \frac{\partial^2 f}{\partial y^2} = 0. \tag{3}$$

With the initial condition

$$\lim_{t\to t_0} f(x,t \mid x_0,t_0) = \delta(x-x_0), \tag{4}$$

equation (3) admits a unique solution that is a normal density function with mean

$$E[X(t) \mid x_0,t_0] = \mu\vartheta - (\mu\vartheta - x_0)\, e^{-\frac{t-t_0}{\vartheta}} \tag{5}$$

and variance

$$Var[X(t) \mid x_0,t_0] = \frac{\sigma^2\vartheta}{2}\left(1-e^{-2\frac{t-t_0}{\vartheta}}\right). \tag{6}$$

When the membrane potential $X(t)$ attains an assigned value $S > x_0$, eventually $S(t)$, a spike is generated and the process starts again from x_0. The FPT

$$T_{S,x_0} = \inf\{t : X(t) > S(t); \quad X(t_0) = x_0,\ S(t) > x_0\} \tag{7}$$

is the random variable modeling the ISI. When the passage through S is a sure event (i.e. when the boundary is bounded by a constant) one is interested in determining the probability density function

$$g(t \mid x_0,t_0) = \frac{\partial}{\partial t}\mathbb{P}\left(T_{S,x_0} < t\right). \tag{8}$$

In the sequel we will use the simplest notation $g(t)$ for $g(t \mid x_0,t_0)$ when it does not generate misunderstanding on the initial time and the starting point.

The function (8) is solution of the Fortet equation

$$f(S(t),t \mid x_0,t_0) = \int_{t_0}^{t} g(\tau \mid x_0,t_0)\, f(S(t),t \mid S(\tau),\tau)\, d\tau, \tag{9}$$

that is a Volterra integral equation of the first type when $g(\tau \mid x_0,t_0)$ is unknown. An analytical solution of this equation can be achieved only in very special instances of scarce interest for the model and various numerical methods have been employed in literature to solve this equation or other equivalent but more manageable equations. Alternatively simulations can be used to generate the random value of T_{S,x_0} (cf. Giraudo et al., 2001). Furthermore, the analytical expression of the moments of T_{S,x_0} is available when the boundary is constant (cf. Cerbone et al., 1981).

Other results on FPT distribution concern asymptotic instances for large times or boundaries (cf. Nobile et al., 1985; Giorno et al., 1997). When the time constant ϑ is large, the OU process tends to a Wiener one and the FPT distribution tends to the inverse Gaussian distribution. Finally, we recall that an OU process can be transformed into a standard Wiener process via a spatio-temporal transformation. The transformation

$$\begin{cases} x^* = xe^{\frac{t}{\vartheta}} - \beta\vartheta\left(e^{\frac{t}{\vartheta}}-1\right) \\ t^* = \frac{\sigma^2\vartheta}{2}\left(e^{2\frac{t}{\vartheta}}-1\right) \\ f^*(x^*,t^* \mid x_0^*,t_0^*) = e^{-\frac{t}{\vartheta}} f(x,t \mid x_0,t_0) \end{cases} \tag{10}$$

changes the Kolmogorov equation (3) into the Kolmogorov equation for a standard Wiener process. Furthermore, the FPT p.d.f. (8) of the OU process through a boundary $S(t)$ is related to the FPT $g^*(t^*)$ of a standard Wiener process through the transformed boundary

$$S^*(t^*) = S(t)\exp\left(\frac{t}{\vartheta}\right) - \beta\vartheta\left(\exp\left(\frac{t}{\vartheta}\right)-1\right)\Bigg|_{t=\varphi^{-1}(t^*)}. \tag{11}$$

Indeed one has

$$g^*(t^*) = g(t)\left.\frac{\exp\left(-2\frac{t}{\vartheta}\right)}{\sigma^2}\right|_{t=\varphi^{-1}(t^*)}. \tag{12}$$

Since the FPT p.d.f. of a Wiener process with diffusion coefficient σ^2, originated in x_0 at time t_0 through the linear boundary $l = \alpha + \beta t,\ \alpha > x_0$ is (cf. Ricciardi, 1977)

$$g_{(\alpha,\beta)}(t \mid x_0, t_0) = \frac{\alpha - x_0}{\sqrt{2\pi\sigma^2 (t-t_0)^3}} \exp\left[-\frac{(\alpha + \beta(t-t_0) - x_0)^2}{2\sigma^2 (t-t_0)}\right], \tag{13}$$

via (10) one can obtain the FPT for the OU process through the transformed boundary $S^*(t^*)$.

3 Numerical methods for the inverse FPT problem Motivated by neurobiological modeling problems, Capocelli and Ricciardi (1972) considered the problem of determining under which conditions a p.d.f. is a FPT for a diffusion process through a constant boundary. They proved that only a particular class of distributions plays the role of a FPT probability density. However, one can enlarge this class by admitting time varying boundaries. In this case the inverse FPT problem focuses on determining the boundary shape that makes an assigned p.d.f. a FPT p.d.f. for a specified diffusion process.

Two constructive methods to determine such shape have been proposed for the Wiener process in Zucca et al. (2002). The use of the transformation (10) allows the application of the first of these methods to the OU process, while the second one can be easily extended to the OU process.

Here we briefly sketch the two resulting algorithms to determine the shape of the boundary $S(t),\ t \in [0, T]$.

Let $g(t)$ be the assigned FPT p.d.f. of the process through the unknown boundary $S(t)$ and let $x_0 = 0$.

Method 1: Our objective is to determine a stepwise approximation $\tilde{S}(t)$ of $S(t)$ by means of an algorithm that allows to compute a stepwise approximation $\tilde{S}^*(t^*)$ of $S^*(t^*)$ for the corresponding transformed Wiener process.

Applying transformations (10) to $g(t)$ we obtain $g^*(t^*)$, the FPT p.d.f. of the transformed Wiener process through the transformed boundary $S^*(t^*)$.

When $S(0) = \alpha_0$ is known, we can schematize the algorithm through four main steps:

1. one transforms the OU time T into a time T^* for the corresponding Wiener process, making use of (10) and one considers a partition

$$t_i^* = ih, \qquad i = 0, ..., \frac{T^*}{h}, \qquad h > 0. \tag{14}$$

2. on the interval $[t_0^*, t_1^*]$ one solves, with respect to the unknown β_0, the equation

$$\int_{t_0^*}^{t_1^*} g^*(\tau)\, d\tau = \int_{t_0^*}^{t_1^*} g^*_{(\alpha_0,\beta_0)}(\tau \mid x_0^*, t_0^*)\, d\tau \tag{15}$$

where $g^*_{(\alpha_0,\beta_0)}(\tau \mid x_0^*, t_0^*)$ is the FPT p.d.f. (13) of a Wiener process originated in x_0^* at time t_0^* through the linear boundary $l = \alpha_0 + \beta_0 t^*$.

Note that, since (12) implies the conservation of the FPT probability mass for the transformed process, one has

$$\int_{t_i}^{t_{i+1}} g(\tau)\, d\tau = \int_{t_i^*}^{t_{i+1}^*} g^*(\tau)\, d\tau, \tag{16}$$

where t_i and t_{i+1} are obtained making use of (10).

3. for $i = 1, ..., \frac{T^*}{h} - 1$, making use of (16), one solves with respect to β_i successively the equations

$$\int_{t_i^*}^{t_{i+1}^*} g^*(\tau)\, d\tau = \int_{t_i^*}^{t_{i+1}^*} \int_{-\infty}^{c_i} g_{(\alpha_i,\beta_i)}(\tau \mid x, t_i^*)\, f_a(x, t_i^* \mid x_0^*, t_0^*)\, d\tau dx \tag{17}$$

where

$$\begin{aligned} c_i &= \alpha_{i-1} + \beta_{i-1} t_i^* \\ \alpha_i &= \alpha_{i-1} + (\beta_{i-1} - \beta_i)\, t_{i-1}^* \end{aligned} \tag{18}$$

and $f_a(x, t_i^* \mid x_0^*, t_0^*)$ indicates (cf. Durbin, 1971) the transition p.d.f. of a Wiener process originated at time t_0^* in x_0^* and constrained by the stepwise linear boundary

$$\tilde{S}_i^*(t^*) = \alpha_k + \beta_k t^*, \qquad t^* \in \left[t_k^*, t_{k+1}^*\right], \qquad k = 0, ..., i. \tag{19}$$

The analytical expression of the transition p.d.f. $f_a(x, t_i^* \mid x_0^*, t_0^*)$ is known to be

$$\begin{aligned} f_a(x, t_i^* \mid x_0^*, t_0^*) &= \frac{\partial}{\partial x} \mathbb{P}\left(W_{t_i^*} \leq x \mid W_0 = x_0; \quad W_s < \tilde{S}_i^*(s) \quad \forall s < t_i^*\right) \\ &= \prod_{i=1}^{k-1} \left(1 - e^{-2\frac{(c_{i-1} - x_{i-1})(c_i - x_i)}{\tau_i - \tau_{i-1}}}\right) \varphi\left(x, t_i^* - t_{i-1}^*\right), \end{aligned} \tag{20}$$

where $\varphi(x, u)$ is the probability density function of a random variable $N(0, u)$.

The computation of the multiple integral on the r.h.s. of (17) can be performed with a Monte Carlo method.

4. Using the inverse of transformation (10) one determines the values of the boundary $\tilde{S}(t)$ in the knots t_i of the OU process corresponding to (19). A linear interpolation on these values determines the shape of $\tilde{S}(t)$ that approximates $S(t)$.

Remark 1 Equations (15) and (17) express the equality between the crossing probabilities of the approximating distribution and the exact one. Indeed, on each time interval we determine the straight line for which the crossing probability of the Wiener process equals the probability of the original process on the corresponding interval.

Remark 2 When $S(t_0)$ is not known one can apply this algorithm making use of an arbitrary value for $S(t_0)$. Indeed the first value seriously influences only the first steps of the computation, since the approximated boundary oscillates around $S(t)$ (cf. Zucca et al., 2002).

Method 2: In analogy with the method used in Zucca et al. (2002) for the Wiener process we integrate the Fortet equation for the OU process through $S(t)$ on $(-\infty, S(T))$.

We obtain

$$1-\Phi\left(\frac{S(T)-\mu\vartheta+\mu\vartheta e^{-\frac{T}{\vartheta}}}{\sqrt{\frac{\vartheta\sigma^2}{2}\left(1-e^{-\frac{2T}{\vartheta}}\right)}}\right)= \tag{21}$$

$$=\int_0^T g(\tau)\left\{1-\Phi\left(\frac{S(T)-\mu\vartheta+(\mu\vartheta-S(\tau))e^{-\frac{T-\tau}{\vartheta}}}{\sqrt{\frac{\vartheta\sigma^2}{2}\left(1-e^{-\frac{2(T-\tau)}{\vartheta}}\right)}}\right)\right\}d\tau,$$

where $\Phi(\cdot)$ is the standard normal distribution.

Equation (21) is a nonlinear homogeneous Volterra integral equation of the second type with regular kernel with respect to the boundary $S(t)$ when g is an assigned distribution. A numerical procedure based on the Euler method can then be used to solve this equation in analogy with Zucca et al. (2002). Indeed, discretizing $t\in[0,T]$ with the partition

$$t_i = ih, \qquad i=0,\dots,\frac{T}{h}, \tag{22}$$

with $h>0$, one obtains

$$1-\Phi\left(\frac{S(t_i)-\mu\vartheta+\mu\vartheta e^{-\frac{t_i}{\vartheta}}}{\sqrt{\frac{\vartheta\sigma^2}{2}\left(1-e^{-\frac{2t_i}{\vartheta}}\right)}}\right)= \tag{23}$$

$$\begin{aligned}&= \sum_{j=1}^{i} g(t_j)\left\{1-\Phi\left(\frac{S(t_i)-\mu\vartheta+(\mu\vartheta-S(t_j))e^{-\frac{t_i-t_j}{\vartheta}}}{\sqrt{\frac{\vartheta\sigma^2}{2}\left(1-e^{-\frac{2(t_i-t_j)}{\vartheta}}\right)}}\right)\right\}h\\ i &= 1,\dots,n\end{aligned}$$

that is a triangular non linear system of n equations in the n unknowns $S(t_1),\dots,S(t_n)$, that can be solved by means of an iterative method.

Note that the initial value $S(t_0)$ is not assigned in this method. This implies a scarce reliability of our results only on the first steps when the involved integrals are computed with a rough approximation due to the use of Euler method.

4 Examples Two natural candidates to approximate the OU FPT p.d.f. through a constant boundary are the inverse Gaussian and the Gamma distribution. We consider these two distributions by means of some numerical examples and we use the methods of Section 3 to check the implications of these approximations on the boundary shape. The OU FPT p.d.f. values are obtained with the numerical algorithm of Buonocore et al. (1987).

a. Inverse Gaussian p.d.f.

Let us approximate the FPT p.d.f. of an OU process with $\vartheta = 10$ ms, $\sigma^2 = 20$ mV^2 ms^{-1}, $\mu = 0$ mV ms^{-1} through $S = 10$ mV with an inverse Gaussian p.d.f. (13). Hence, in this case we have $\alpha_{IG} = 10$ mV and, to determine the values of $\beta_{IG}, \sigma^2_{IG} > 0$ in (13), we equate the abscissae and the ordinates of the mode of the two p.d.f.s. We then determine the boundary shape of an OU process with $\vartheta = 10$ ms, $\sigma^2 = 20$ mV^2 ms^{-1}, $\mu = 0$ mV ms^{-1}, producing the considered inverse Gaussian as FPT p.d.f.

In Figure 1a we plot the resulting p.d.f.s. In Figure 1b we compare the boundary corresponding to the FPT p.d.f. (13), obtained by means of the methods of Section 3, with the constant boundary $S = 10$ mV. The agreement of the results obtained by means of both the methods of Section 3 guarantees the reliability of our results. Figure 1 confirms the well known fact that the inverse Gaussian approximation is reliable only in correspondence of small times. The use of our algorithms allows to interpret this increasing discrepancy of the p.d.f.s as caused by different boundary shapes. Indeed, the difference between the boundaries increases with the time. The use of the inverse Gaussian distribution in spite of the exact FPT distribution seems to imply the introduction of a sort of a refractory phenomenon that blocks the firing as the time increases. However, there are not experimental evidences that could validate a similar result. Hence, the use of the inverse Gaussian results acceptable only when one is interested in the spiking activity happening in very short times.

b. Gamma p.d.f.

In Giorno et al. (1997) this p.d.f. was considered as a good approximation for large times. With the aid of our methods we want to understand the effect of this approximation on the boundary values on the entire range of the times. To determine the values of the two parameters in the Gamma p.d.f

$$g(t) = \frac{\beta^\alpha}{\Gamma(\alpha)} t^{\alpha-1} e^{-t\beta}, \qquad t \geq 0, \tag{24}$$

following Giorno et al. (1997), we apply the moments method, making use of the tables in Cerbone et al. (1981), and we equate the mean and the variance of the two distributions.

As first example we consider the OU process with $\vartheta = 10$ ms, $\sigma^2 = 5$ mV^2 ms^{-1}, $\mu = 0$ mV ms^{-1}. When $S = 10$ mV one has $E(T_{s,x_0}) = 104.28$ ms and $V(T_{s,x_0}) = 10527.52$ ms^2. We determine the boundary corresponding to a Gamma density for this process. Figure 2 compares the FPT p.d.f.s (2a) and the corresponding boundaries (2b). As it is evident in Figure 2b the boundary corresponding to the Gamma p.d.f. can be interpreted as generated by an OU process crossing a boundary that converges very fast to a constant value. This result is confirmed in Figure 3 where the same example is considered for $t \in [0, 170]$ ms. Note that this last control is suggested by the large value of the mean firing time.

The approximating boundaries tend to the corresponding constants for $t \geq 8$ ms but the probability $P(T_{s,x_0} \leq 8) = 0.05$. Hence, in this case, the use of the Gamma p.d.f. in spite of the OU FPT p.d.f. through a constant boundary, results reliable since the only times that give rise to a different behavior are characterized by very low occurrence probability.

As a second example we consider the OU process with $\vartheta = 10$ ms, $\sigma^2 = 20$ mV^2 ms^{-1}, $\mu = 0$ mV ms^{-1} and we determine the boundary corresponding to a Gamma density for this process. When $S = 10$ mV one has $E(T_{s,x_0}) = 20.93$ ms and $V(T_{s,x_0}) = 584.2$ ms^2. Figure 4 compares the FPT p.d.f.s (4a) and the corresponding boundaries (4b). Also in this case, after a first interval, the use of the Gamma p.d.f. in spite of the OU FPT p.d.f. through a constant boundary, results reliable.

For short times the Gamma p.d.f. corresponds to a boundary which is lower of the assumed constant, hence the use of the approximation implies a firing facilitation immediately after a spike that has not a biological motivation. However, since the approximated boundary value converges rapidly to the constant, the use of the approximated FPT p.d.f. cannot have important consequences when one wish to simulate neuronal networks.

5 Conclusions A new constructive approach to the inverse FPT problem is applied to check the possibility to approximate a FPT p.d.f. with an assigned one. We show that the Gamma p.d.f. is a good approximation of the firing distribution in a leaky integrate and fire stochastic model when the parameters of the Gamma distribution are fixed with the moment method equating the mean and the variance of the considered distributions. However, this approximation generates very short ISI with a probability higher than the exact distribution. This fact has not important consequences since these ISI have still low occurrence probability. Hence, the use of this distribution can be a reliable shortcut for the description of the activity of single neurons in networks. The proposed numerical methods can find applications in more general instances such as the search of approximated FPTs p.d.f. of an OU process through time varying boundaries.

Furthermore, the introduction of suitable corrections into the first method of Section 3 allows its use for histograms obtained via experimental data and this will be the subject of a future report.

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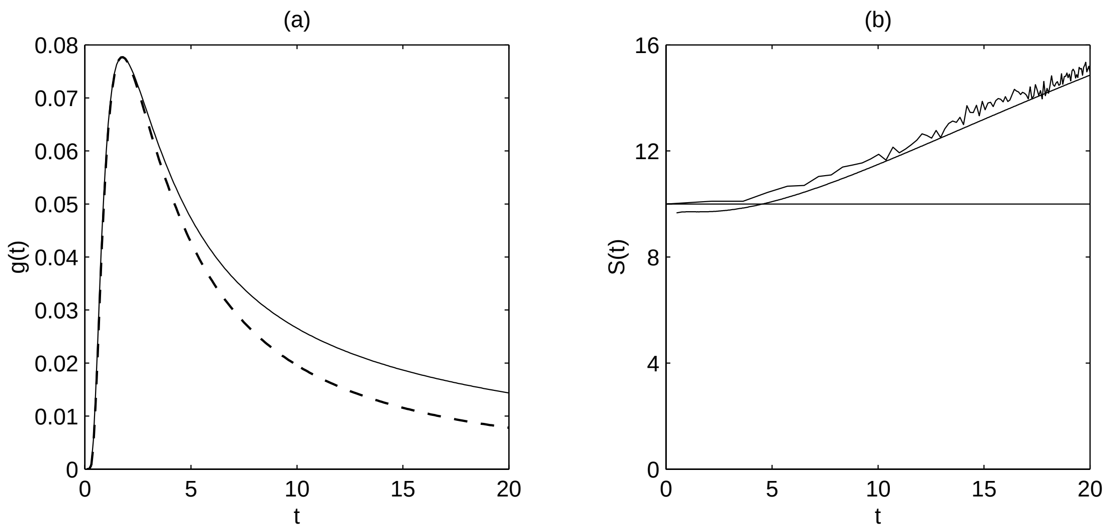

Figure 1. *(a) Comparison between the FPT p.d.f. of an OU process with* $\vartheta = 10$ *ms,* $\sigma^2 = 20$ mV^2 ms^{-1}, $\mu = 0$ mV ms^{-1} *with boundary value* $S = 10$ mV *(solid line) and the approximated inverse Gaussian p.d.f. (13) (dashed line) with parameters* $\alpha_{IG} = 10$ mV, $\beta_{IG} = 0.219$ mV *and* $\sigma^2_{IG} = 1.828$ mV^2 ms^{-1}. *(b) Comparison between the corresponding constant boundary and the approximated boundaries obtained by the method 1 (oscillating boundary) and method 2 (smooth boundary).*

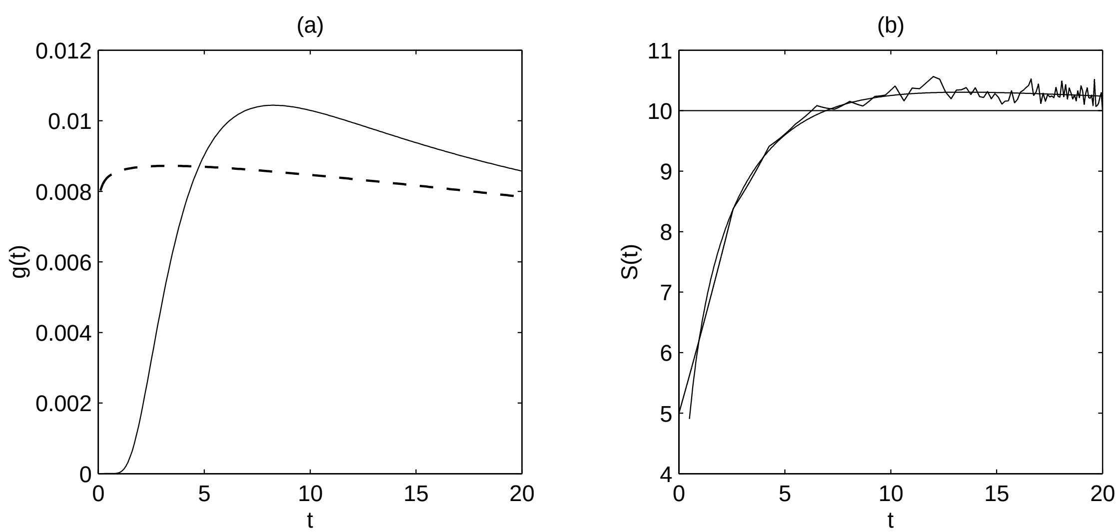

Figure 2. *(a) Comparison between the FPT p.d.f. of an OU process with* $\vartheta = 10$ *ms,* $\sigma^2 = 5$ mV^2 ms^{-1}, $\mu = 0$ mV ms^{-1} *with boundary value* $S = 10$ mV *(solid line) and the approximated Gamma p.d.f. with parameters* $\alpha = 1.033$, $\beta = 0.099$ ms^{-1} *(dashed line). (b) Comparison between the corresponding constant boundary and the approximated boundaries obtained by the method 1 (oscillating boundary) and method 2 (smooth boundary).*

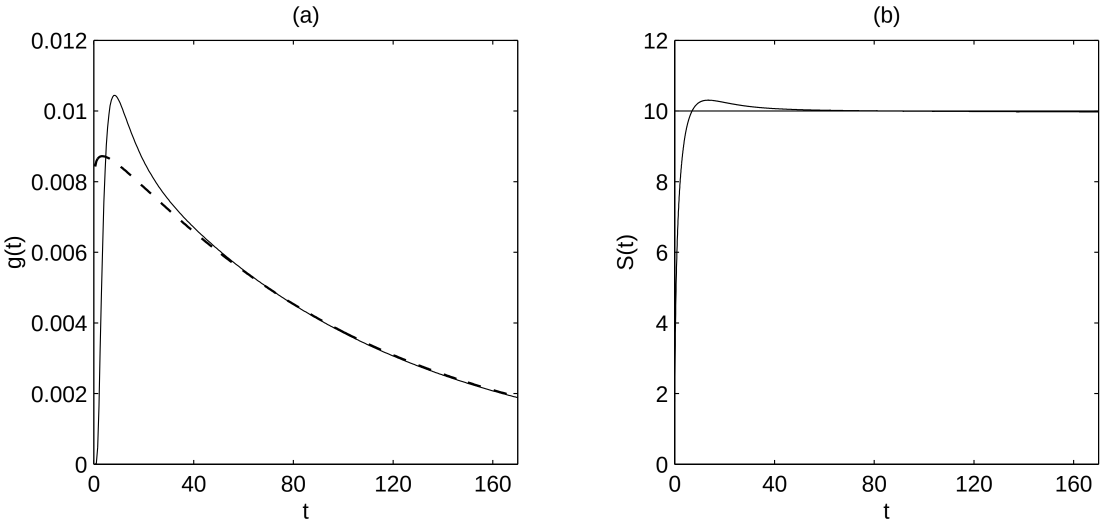

Figure 3. *(a) Comparison between the FPT p.d.f. of an OU process with* $\vartheta = 10$ *ms,* $\sigma^2 = 20$ *mV^2 ms^{-1},* $\mu = 0$ *mV ms^{-1} with boundary value* $S = 10$ *mV (solid line) and the approximated Gamma p.d.f.* $\alpha = 1.033$, $\beta = 0.099$ *ms^{-1} (dashed line) in the time interval* $[0, 170]$. *(b) Comparison between the corresponding constant boundary and the approximated boundaries obtained by the method 2.*

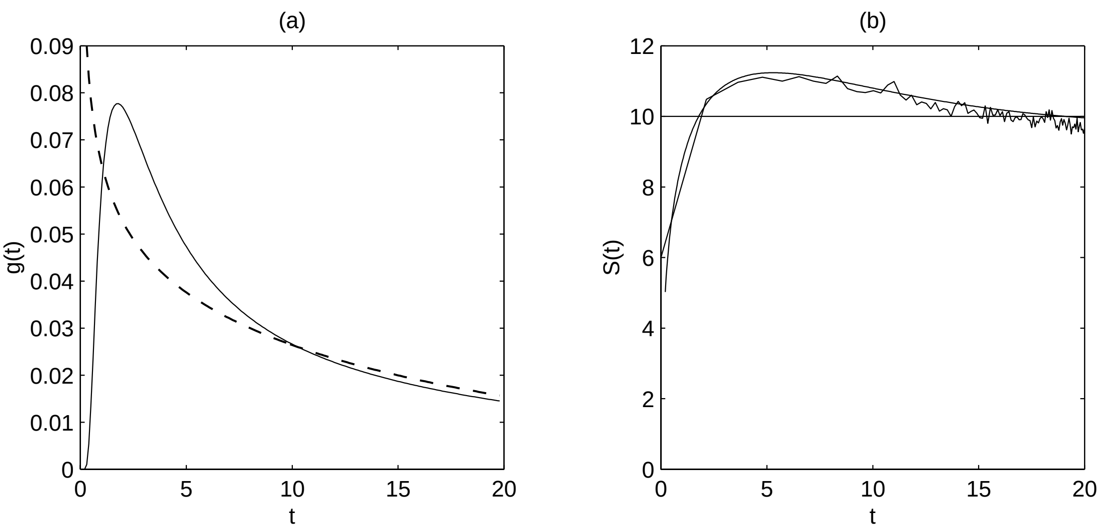

Figure 4. *(a) Comparison between the FPT p.d.f. of an OU process with* $\vartheta = 10$ *ms,* $\sigma^2 = 20$ *mV^2 ms^{-1},* $\mu = 0$ *mV ms^{-1} with boundary value* $S = 10$ *mV (solid line) and the approximated Gamma p.d.f.* $\alpha = 0.750$, $\beta = 0.358$ *ms^{-1} (dashed line). (b) Comparison between the corresponding constant boundary and the approximated boundaries obtained by the method 1 (oscillating boundary) and method 2 (smooth boundary).*