Computational Methods for the Evaluation of Neuron's Firing Densities*

Elvira Di Nardo[1], Amelia G. Nobile[2], Enrica Pirozzi[3], and Luigi M. Ricciardi[3]

[1] Università della Basilicata,
Dipartimento di Matematica,
Potenza, Italy
dinardo@unibas.it
[2] Università di Salerno,
Dipartimento di Matematica e Informatica,
Baronissi (SA), Italy
nobile@unisa.it
[3] Università di Napoli Federico II,
Dipartimento di Matematica e Applicazioni,
Napoli, Italy
{enrica.pirozzi,luigi.ricciardi}@unina.it

Abstract. Some analytical and computational methods are outlined, that are suitable to determine the upcrossing first passage time probability density for some Gauss-Markov processes that have been used to model the time course of neuron's membrane potential. In such a framework, the neuronal firing probability density is identified with that of the first passage time upcrossing of the considered process through a preassigned threshold function. In order to obtain reliable evaluations of these densities, ad hoc numerical and simulation algorithms are implemented.

1 Introduction

This contribution deals with the implementation of procedures and methods worked out in our group during the last few years in order to provide algorithmic solutions to the problem of determining the first passage time (FPT) probability density function (pdf) and its relevant statistics for continuous state-space and continuous parameter stochastic processes modeling single neuron's activity. In the neurobiological context, a classical approach to view neuronal activity as an FPT problem is to assume that a Markov process is responsible for the time course of the membrane potential under the assumption of numerous simultaneously and independently acting input processes (see also [16] and references therein). If one uses more realistic models based on correlated (non-Markov)

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Gaussian processes, serious difficulties arise because of lack of effective analytical methods for obtaining manageable closed-form expressions of the FPT pdf.

Here we shall focus on the FPT upcrossing problem that we define as an FPT problem to a boundary $S(t) \in C^1[0, +\infty)$ for the subset of sample paths of a one-dimensional non-singular Gaussian process $\{X(t), t \geq 0\}$ originating at time zero at a state X_0, that in turn is viewed as a random variable with pdf

$$\gamma_\varepsilon(x_0) \equiv \begin{cases} \dfrac{f(x_0)}{P\{X(0) < S(0) - \varepsilon\}}\,, & x_0 < S(0) - \varepsilon \\ \\ 0, & x_0 \geq S(0) - \varepsilon. \end{cases} \tag{1}$$

Here, $\varepsilon > 0$ is a fixed real number and $f(x_0)$ denotes the normal pdf of $X(0)$. Then,

$$T_{X_0}^{(\varepsilon)} = \inf_{t \geq 0}\{t : X(t) > S(t)\},$$

is the ε-upcrossing FPT of $X(t)$ through $S(t)$ and the related pdf is given by

$$g_u^{(\varepsilon)}(t) = \frac{\partial}{\partial t} P(T_{X_0}^{(\varepsilon)} < t) = \int_{-\infty}^{S(0)-\varepsilon} g(t|x_0)\, \gamma_\varepsilon(x_0)\, dx_0 \qquad (t \geq 0), \tag{2}$$

where

$$g(t|x_0) := \frac{\partial}{\partial t} P\left(\inf_{u \geq 0}\{u : X(u) > S(u)\} < t\right), \quad X(0) = x_0 < S(0), \tag{3}$$

denotes the FPT pdf of $X(t)$ through $S(t)$.

The specific nature of various numerical methods available to compute the ε-upcrossing pdf $g_u^{(\varepsilon)}(t)$ depends on the assumptions made on $X(t)$.

2 Upcrossing FPT Densities for Gauss-Markov Processes

We recall that a non singular Gaussian process $\{X(t), t \geq 0\}$ with mean $m(t)$ is Markov if and only if its covariance is of the form

$$c(s,t) = h_1(s)\, h_2(t), \qquad 0 \leq s \leq t < \infty, \tag{4}$$

where for $t > 0$

$$r(t) = \frac{h_1(t)}{h_2(t)} \tag{5}$$

is a monotonically increasing function and $h_1(t)\, h_2(t) > 0$ (cf. [8], [13]). Furthermore, any Gauss-Markov (GM) process with covariance as in (4) can be represented in terms of the standard Wiener process $\{W(t), t \geq 0\}$ as

$$X(t) = m(t) + h_2(t)\, W\big[r(t)\big]. \tag{6}$$

The class of all GM processes $\{X(t), t \in [0, \infty)\}$ with transition density function such that $f(x, t|y, \tau) \equiv f(x, t - \tau|y)$ is characterized by means and covariances of the following two forms:

$$m(t) = \beta_1 t + c, \quad c(s,t) = \sigma^2 s + c_1$$
$$(0 \le s \le t < \infty,\ \beta_1, c \in \mathbf{R},\ c_1 \ge 0,\ \sigma \ne 0)$$

or

$$m(t) = -\frac{\beta_1}{\beta_2} + c\, e^{\beta_2 t}, \quad c(s,t) = c_1\, e^{\beta_2 t}\left[c_2\, e^{\beta_2 s} - \frac{\sigma^2}{2c_1\beta_2}\, e^{-\beta_2 s}\right]$$
$$\left(0 \le s \le t < \infty,\ \beta_1, c, c_2 \in \mathbf{R},\ \sigma \ne 0,\ c_1 \ne 0, \beta_2 \ne 0,\ c_1 c_2 - \frac{\sigma^2}{2\beta_2} \ge 0\right).$$

The first type includes the Wiener process, while the second type includes the Ornstein–Uhlenbeck process.

For a non singular GM process with $m(t)$ and covariance $c(s,t) = h_1(s)\, h_2(t)$ for $s \le t$, the pdf (1) can be immediately evaluated. Indeed, $f(x_0)$ is a normal pdf with mean $m(0)$ and variance $h_1(0)h_2(0)$ and

$$P\{X(0) < S(0) - \varepsilon\} = \frac{1}{2}\left\{1 + \mathrm{Erf}\left[\frac{S(0) - \varepsilon - m(0)}{\sqrt{2h_1(0)h_2(0)}}\right]\right\}. \tag{7}$$

Furthermore, the ε-upcrossing FPT pdf is the unique solution of the second kind Volterra integral equation (cf. [6]):

$$g_u^{(\epsilon)}(t) = -2\, \psi_u^{(\epsilon)}[S(t), t] + 2\int_0^t \psi[S(t), t | S(\tau), \tau]\, g_u^{(\epsilon)}(t)\, d\tau \tag{8}$$

where

$$\Psi[S(t), t|y, \tau] = \left\{\frac{S'(t) - m'(t)}{2} - \frac{S(t) - m(t)}{2}\, \frac{h_1'(t)h_2(\tau) - h_2'(t)h_1(\tau)}{h_1(t)h_2(\tau) - h_2(t)h_1(\tau)}\right.$$
$$\left. - \frac{y - m(\tau)}{2}\, \frac{h_2'(t)h_1(t) - h_2(t)h_1'(t)}{h_1(t)h_2(\tau) - h_2(t)h_1(\tau)}\right\} f[S(t), t|y, \tau],$$
$$\psi_u^{(\epsilon)}[S(t), t] = \int_{-\infty}^{S(0)-\varepsilon} \psi[S(t), t|x_0]\, \gamma_\epsilon(x_0)\, dx_0.$$

A fast and accurate computational method is proposed in [6] to solve integral equation (8), that make use of the repeated Simpson rule. The proposed iteration procedure allows one to compute $\tilde{g}_u^{(\epsilon)}(kp)$, for $k = 2, 3, ...$, with time discretization step p in terms of computed values at the previous times $p, 2p, ..., (k-1)p$. The noteworth feature of this algorithm is its being implementable after simply specifying the parameter ϵ, functions $m(t), h_1(t), h_2(t)$ that characterize the process, boundary $S(t)$ and discretization step p. Furthermore, it does not involve any heavy computation, neither it requires use of any library subroutines, Monte Carlo methods or other special software packages to calculate high dimension multiple integrals.

3 Kostyukov Model

In the context of single neuron's activity modeling a completely different, apparently not well known, approach was proposed by Kostyukov *et al.* in [10] and

[11] in which a non-Markov process of a Gaussian type is assumed to describe the time course of the neural membrane potential.

Kostyukov model (K-model) makes use of the notion of correlation time. Namely, let $X(t)$ be a stationary Gaussian process with zero mean, unit variance and correlation function $R(t)$. Then,

$$\vartheta = \int_0^{+\infty} |R(\tau)|\, d\tau < +\infty$$

is defined as the correlation time of the process $X(t)$. Under the assumption that $\lim_{\varepsilon\to 0} P\{X(0) < S(0) - \varepsilon\} \simeq 1$, i.e. $\lim_{\varepsilon\to 0} \gamma_\varepsilon(x_0) \simeq f(x_0)$, Kostyukov works out an approximation $q(t)$ to the upcrossing FPT pdf. This approximation is obtained as solution of the integral equation

$$\int_0^t q(\tau)\, K(t,\tau)\, d\tau = 1 - \Phi[S(t)], \tag{9}$$

where

$$K(t,\tau) = \begin{cases} \frac{1}{2}, & t = \tau \\ 1 - \Phi\left\{ \frac{(t-\tau+\vartheta)\, S(t) - \vartheta\, S(\tau)}{\sqrt{(t-\tau+\vartheta)\,(t-\tau)}} \right\}, & t > \tau, \end{cases}$$

and where $\Phi(z)$ is the distribution function of a standard Gauss random variable. Note that equation (9) can be solved by routine methods. Furthermore, under the above approximation, in equation (9) the unique parameter ϑ characterizes the considered class of stationary standard Gaussian processes.

4 Upcrossing FPT Densities for Stationary Gaussian Processes

Let $X(t)$ be a stationary Gaussian process with mean $m(t) = 0$ and covariance $E[X(t)X(\tau)] = c(t,\tau) = c(t-\tau)$ such that $c(0) = 1, \dot{c}(0) = 0$ and $\ddot{c}(0) < 0$. By using a straightforward variant of a method proposed by Ricciardi and Sato ([14], [15]) for the determination of the conditional FPT density g, in [7] we have obtained the following series expansion for the upcrossing FPT pdf:

$$g_u^{(\varepsilon)}(t) = W_1^{(u)}(t) + \sum_{i=1}^{\infty} (-1)^i \int_0^t dt_1 \int_{t_1}^t dt_2 \cdots \int_{t_{i-1}}^t dt_i W_{i+1}^{(u)}(t_1,\ldots,t_i,t). \tag{10}$$

Here,

$$W_{i+1}^{(u)}(t_1,\ldots,t_i,t) = \left[\int_{-\infty}^{S(0)-\varepsilon} f(z)dz \right]^{-1} \int_{-\infty}^{S(0)-\varepsilon} W_{i+1}(t_1,\ldots,t_i,t|x_0) f(x_0) dx_0, \tag{11}$$

where $W_n(t_1,\ldots,t_n|x_0)dt_1\cdots dt_n$, $\forall n\in\mathbf{N}$ and $0<t_1<\ldots<t_n$, denotes the joint probability that $X(t)$ crosses $S(t)$ from below in the time intervals $(t_1,t_1+dt_1),\ldots,(t_n,t_n+dt_n)$ given that $X(0)=x_0$.

The evaluation of the partial sums of the above series expansion is made hardly possible because of the outrageous complexity of the functions $W_n^{(u)}$ and of their integrals. However, approximations of upcrossing FPT density can be carried out by evaluating first of all $W_1^{(u)}(t)$. The explicit expression of $W_1^{(u)}(t)$ is (cf. [4]):

$$
\begin{aligned}
W_1^{(u)}(t) = {} & \frac{\exp\Big\{-\dfrac{S^2(t)}{2}\Big\}}{2\pi\left[1+\mathrm{Erf}\left(\dfrac{S(0)-\varepsilon}{\sqrt{2}}\right)\right]}\Bigg\{[-\ddot{c}(0)]^{1/2}\exp\left(-\frac{[\dot{S}(t)]^2}{2[-\ddot{c}(0)]}\right)[1+\mathrm{Erf}(U_\varepsilon(t))] \\
& -\frac{\dot{c}(t)}{\sqrt{1-c^2(t)}}\exp\left(-\frac{[S(0)-\varepsilon-S(t)c(t)]^2}{2[1-c^2(t)]}\right)[1-\mathrm{Erf}(V_\varepsilon(t))] \qquad (12)\\
& -\frac{\dot{S}(t)}{\sqrt{1-c^2(t)}}\int_{-\infty}^{S(0)-\varepsilon}\exp\left(-\frac{[x_0-S(t)c(t)]^2}{2[1-c^2(t)]}\right)\left[1-\mathrm{Erf}\left(\frac{\sigma(t|x_0)}{\sqrt{2}}\right)\right]\,dx_0\Bigg\}
\end{aligned}
$$

where:

$$
\Lambda_3=\begin{pmatrix} 1 & c(t) & \dot{c}(t)\\ c(t) & 1 & 0\\ \dot{c}(t) & 0 & -\ddot{c}(0)\end{pmatrix}
$$

$$
\sigma(t|x_0)=\left(\frac{1-c^2(t)}{\|\Lambda_3\|}\right)^{1/2}\left\{\dot{S}(t)+\frac{\dot{c}(t)[c(t)S(t)-x_0]}{1-c^2(t)}\right\}
$$

$$
\begin{aligned}
\mathrm{Erf}(z) &:= \frac{2}{\sqrt{\pi}}\int_0^z e^{-y^2}dy\\
U_\varepsilon(t) &:= \frac{-\ddot{c}(0)[S(0)-\varepsilon-S(t)c(t)]-\dot{c}(t)\dot{S}(t)}{\sqrt{2\,\|\Lambda_3\|\,[-\ddot{c}(0)]}}\\
V_\varepsilon(t) &:= \frac{-\dot{c}(t)[S(0)-\varepsilon-S(t)c(t)]+\dot{S}(t)[1-c^2(t)]}{\sqrt{2\,\|\Lambda_3\|\,[1-c^2(t)]}}\,.
\end{aligned}
$$

A numerical approximation of (12) was proposed in [4] and evaluated by using NAG routines based on an adaptative procedure described in [1]. For each $t>0$, the function $W_1^{(u)}(t)$ provides an upper bound to the upcrossing FPT pdf. The numerical computations indicate that this can be taken as a good approximation of $\tilde{g}_u^{(\varepsilon)}(t)$ only for small values of t.

Equations (10) and (11) call for alternative procedures to gain more information on upcrossing FPT pdf. To this aim, we have updated an algorithm (cf. [2]) for the construction of sample paths of the specified stationary Gaussian process $X(t)$, with random initial point, under the assumption of rational spectral density such that the degree of the polynomial in its denominator is larger than that in the numerator. Since the sample paths of the simulated process are generated independently of each other, the simulation procedure is particularly suited to run on supercomputers. A parallel simulation procedure has been implemented on a IBM SP-Power4 machine to generate the sample paths of $X(t)$ and to record their upcrossing FPT times through the preassigned boundary in order to construct reliable histograms estimating the FPT pdf $\tilde{g}_u^{(\varepsilon)}(t)$. To evaluate the upcrossing FPT densities, we have chosen X_0 randomly according to the initial pdf $\gamma_\varepsilon(x_0)$. To this purpose, we have made use of the following acceptance-rejection method (cf. for instance [12]):

STEP 1 Generation of pseudo-random numbers U_1, U_2 uniformely distributed in $(0,1)$;
STEP 2 $Y \leftarrow \log U_2 + S(0) - \varepsilon$;
STEP 3 if $U_1 < \exp\left\{-\dfrac{(Y+1)^2}{2}\right\}$ then $X_0 \leftarrow Y$ else goto STEP 1;
STEP 4 STOP.

Let us observe that the random variable Y in STEP 2 is characterized by the pdf

$$h(y) = \begin{cases} e^{y-[S(0)-\varepsilon]}, & \text{if } y < S(0)-\varepsilon \\ 0, & \text{if } y \geq S(0)-\varepsilon. \end{cases} \tag{13}$$

We point out that our simulation algorithm stems directly out of Franklin's algorithm [9]. We have implemented it in both vector and parallel modalities (see [2], [5]) after suitably modifying it for our computational needs: Namely, to obtain reliable approximations of upcrossing densities (cf. [3], [4], [5]). Thus doing, reliable histograms of FPT densities of stationary Gaussian processes with rational spectral densities can be obtained in the presence of various types of boundaries.

5 Computational Results

In order to compare the results obtained via different methods for determining the upcrossing FPT pdf, we start considering the particular stationary standard Gaussian process $X(t)$ having correlation function

$$R(t) = e^{-\beta|t|}\cos(\alpha t), \tag{14}$$

where $\alpha = 10^{-5}$ and $\beta = \vartheta^{-1}$. The approximation $\tilde{g}_u(t)$ for the FPT density of this process in the presence of the threshold

$$S(t) = -t^2/2 - t + 5 \tag{15}$$

is estimated via 10^6 simulated paths with the following choices of correlation times:

(i) $\vartheta = 0.008, \quad 0.016, \quad 0.032, \quad 0.064, \quad 0.128, \quad 0.256, \quad 0.512, \quad 1.024,$

in Fig. 1(a) and with

(ii) $\vartheta = 2.048, \quad 4, \quad 8, \quad 16, \quad 32, \quad 64, \quad 100, \quad 200,$

in Fig. 1(b).

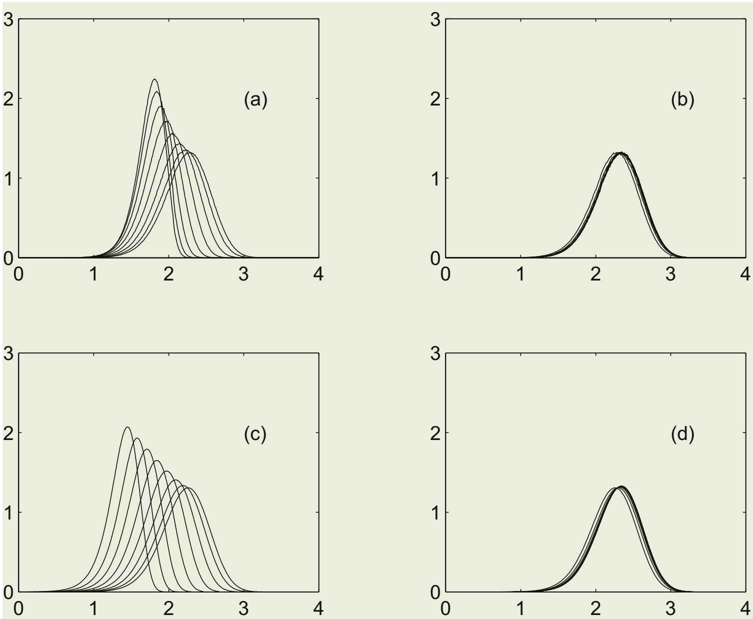

Fig. 1. Plot of the simulated $\tilde{g}_u(t)$ in Fig. 1(a) and in Fig. 1(b) and plot of $\tilde{g}_u(t)$ for the OU-model in Fig. 1(c) and in Fig. 1(d), with threshold $S(t) = -t^2/2 - t + 5$

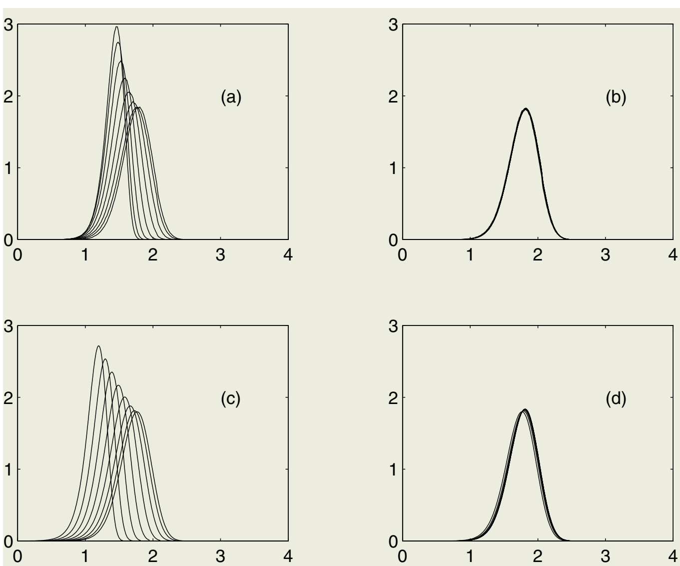

Fig. 2. Plot of the simulated $\tilde{g}_u(t)$ in Fig. 2(a) and in Fig. 2(b) and plot of $\tilde{g}_u(t)$ for the OU-model in Fig. 2(c) and in Fig. 2(d), with threshold $S(t) = -t^2 - t + 5$

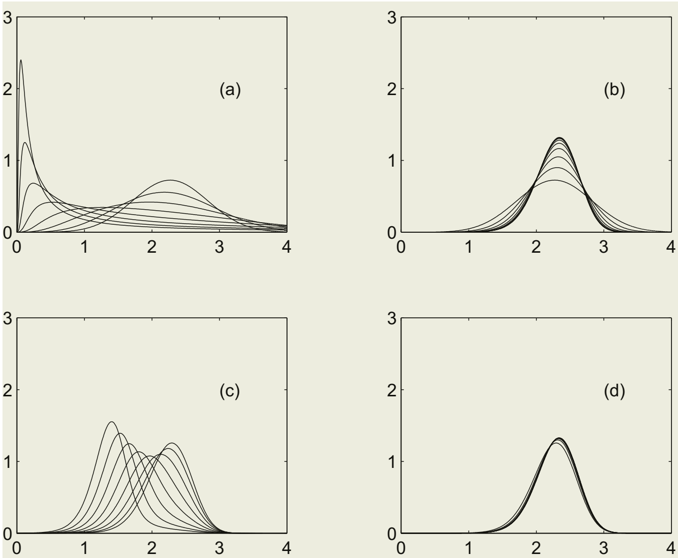

Fig. 3. Plot of $\tilde{g}_u(t)$ for the Wiener model in Fig. 3(a) and in Fig. 3(b) and plot of $q(t)$ for the Kostyukov-model in Fig. 3(c) and in Fig. 3(d), with threshold $S(t) = -t^2/2 - t + 5$

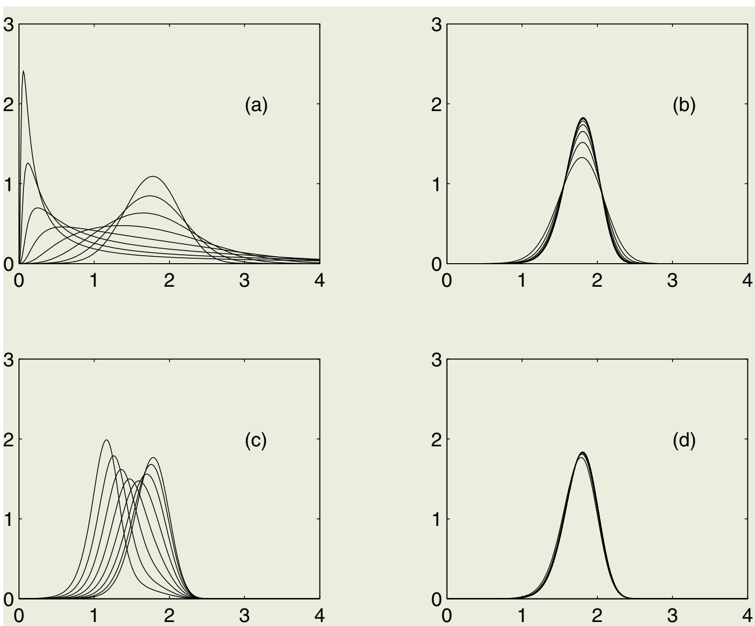

Fig. 4. Plot of $\tilde{g}_u(t)$ for the Wiener model in Fig. 4(a) and in Fig. 4(b) and plot of $q(t)$ for the Kostyukov-model in Fig. 4(c) and in Fig. 4(d),with threshold $S(t) = -t^2 - t + 5$

Furthemore, for the stationary GM process $X(t)$ with

$$m(t) = 0, \quad c(s,t) = e^{-(t-s)/\vartheta} \quad (s < t), \tag{16}$$

known as the Ornstein-Uhlenbeck (OU) model, the FPT density approximation $\tilde{g}_u(t)$ in the presence of threshold (15) is evaluated via (8) and is plotted in Fig. 1(c) and Fig. 1(d) for the values of ϑ respectively indicated in (i) and (ii). Note that for values of α close to zero, (14) is near the OU correlation function, given by

$$e^{-t/\vartheta} \quad (t \geq 0).$$

Figure 2 is the same of Fig. 1 for the threshold

$$S(t) = -t^2 - t + 5. \tag{17}$$

We notice that for large correlation times the firing densities in Fig. 1(b) exhibit features similar to those of the OU-model in Fig. 1(d). Similar considerations hold for the case of Fig. 2(b) and Fig. 2(d).

Let us now focus our attention on a non stationary GM process $X(t)$ (Wiener-model) with

$$m(t) = 0, \quad c(s,t) = s/\vartheta \quad (s < t). \tag{18}$$

The approximation $\tilde{g}_u(t)$ for this process in the presence of threshold (15) is estimated via (8) for the choices of the ϑ as (i) in Fig. 3(a) and as (ii) in Fig. 3(b). Finally, the function $q(t)$ of the K-model in the presence of threshold (15) is evaluated via (9) with ϑ as (i) in Fig. 3(c) and as (ii) in Fig. 3(d). Figure 4 is the same as Fig. 3 but for threshold (17).

We point out that again for large values of ϑ the firing densities in Fig. 3(b) exhibit features similar to those of the Wiener-model in Fig. 3(d). The same occurs in Fig. 4(b) and Fig. 4(d). Hence, the validity of approximations of the firing densities in the presence of memory effects by the FPT densities of Markov type is clearly related to the magnitude of the involved correlation time. Indeed, it could be shown that the asymptotic behavior of all these models becomes increasingly similar as ϑ grows larger.

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