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**This is the author's manuscript**

*Original Citation:*

*Availability:*

This version is available <http://hdl.handle.net/2318/56296> since

*Published version:*

DOI:10.1007/s11587-009-0050-4

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***This is an author version of the contribution published on:***

*Questa è la versione dell'autore dell'opera:*

*Ricerche mat. (2009) 58:103–127, DOI 10.1007/s11587-009-0050-4*

***The definitive version is available at:***

*La versione definitiva è disponibile alla URL:*

*<http://link.springer.com/article/10.1007/s11587-009-0050-4#page-1>*

# On the asymptotic behavior of the parameter estimators for some diffusion processes. Application to neuronal models

Maria Teresa Giraudo<sup>(a)</sup>, Rosa Maria Mininni<sup>(b)</sup> <sup>1</sup> and Laura Sacerdote<sup>(a)</sup>

<sup>(a)</sup> Department of Mathematics, University of Torino,  
Via Carlo Alberto 10, 10123 Torino, Italy

<sup>(b)</sup> Department of Mathematics, University of Bari,  
Via Orabona 4, 70125 Bari, Italy

`mariateresa.giraudo@unito.it`, `mininni@dm.uniba.it`,  
`laura.sacerdote@unito.it`

## Abstract

We consider a sample  $\{T_n\}_{1 \leq n \leq N}$  of i.i.d. times and we interpret each item as the first passage time (FPT) of a diffusion process through a constant boundary. The problem is to estimate the parameters characterizing the underlying diffusion process through the experimentally observable FPT's. Recently in [8] and [9] closed form estimators have been proposed for neurobiological applications. Here we study the asymptotic properties (consistency and asymptotic normality) of the class of moment type estimators for parameters of diffusion processes like those in [8] and [9]. Further, to make our results useful for application instances we establish upper bounds for the rate of convergence of the empirical distribution of each estimator to the normal density. Applications are also considered by means of simulated experiments in a neurobiological context.

**Keywords:** Diffusion processes; First-passage time; Moment type estimators; Asymptotic properties; Rate of convergence; Neuronal models.

**AMS keywords:** Primary: 62M05; 62F12. Secondary: 60J60; 62P10.

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<sup>1</sup>Author to whom correspondence should be sent.

# 1 Introduction

In a variety of different fields in applied mathematics like biology, social sciences, reliability, survival analysis, mathematical finance, etc... one may think of a sequence  $\{T_n\}_{1 < n < N}$  of independent and identically distributed random variables as a sample of first passage times (FPT's) of a diffusion process through a given boundary (cfr. for instance [29] and references given therein). The underlying stochastic process of interest is then a one-dimensional diffusion process  $X = \{X(t); t \geq 0\}$ . Starting the process  $X$  at a non-random value  $X(0) = x_0$ , it describes a latent unobserved dynamics that leads to some observable event when  $X(t)$  reaches a constant boundary  $S$ , or threshold. The time of such event can be defined as the random variable

$$T = \inf \{t > 0 : X(t) \geq S; X(0) = x_0\}, \quad (1)$$

which denotes the FPT of the process  $X$  through the threshold  $S$ .

Then, the experimentally observable data are the FPT's of the underlying stochastic process. In many application instances the problem arises to identify the unknown parameters of the diffusion process from the FPT observations  $\{T_n\}_{0 < n < N}$ .

The main difficulty with many realistic diffusion processes is that despite their conceptual simplicity, the functional form of the FPT probability density function (pdf) is in general not known, except for some special cases. We consider here the examples of the Ornstein-Uhlenbeck and of the Feller processes, whose applications as underlying processes in FPT models are well known (see e.g. [26], [27], [32], [1], [20]). Their first-passage time pdf can be evaluated only by numerical or asymptotical methods and simulation techniques and hence standard statistical inference such as maximum likelihood or Bayes estimation cannot be applied. Recently, some attempts to solve the estimation problem for diffusion parameters from FPT data have been proposed in the neurobiological context (cf. [17], [23], [8], [9], [10]). Only for the estimators given in [8] and [9] closed expressions were evaluated but their qualitative and asymptotic behavior was illustrated only by means of simulation examples.

Our primary goal in the present paper is to study from an analytic point of view the asymptotic properties (consistency and asymptotic normality) of a class of moment type estimators for parameters of diffusion processes defined in analogy with those in [8] and [9]. Since our results are of asymptotic type the next step considered in this paper concerns upper bounds for the rate of convergence of the empirical distribution of each estimator to the normal density.

The paper is organized as follows. In Section 2, the problem is formulated by recalling the necessary background on diffusion processes and introducing the class of moment estimators that will be needed. In Section 3 the asymptotic properties of the moment type estimators introduced for the parameters of a diffusion process observed only at times corresponding to FPT's are proved. In Section 4 we determine the size of the samples that guarantees an acceptable error when one substitutes the empirical distribution of the estimators with the normal one. In Section 5 we illustrate the theorems of Section 4 by means of two examples: the Ornstein-Uhlenbeck and the Feller processes. There we apply our asymptotic results to the moment estimators introduced in [8] and [9]. In Section 6 the accuracy of the moment type estimators and the appropriateness of analytical approximations to the normal density are discussed within the framework of neurobiological applications.

## 2 Problem formulation

We are concerned with one-dimensional diffusion processes  $X = \{X(t), t \geq 0\}$  that satisfy a linear stochastic differential equation (SDE) of the type:

$$dX(t) = a(X(t); \bar{\Theta})dt + b(X(t); \bar{\Theta})dW(t); \quad X(0) = x_0, \quad (2)$$

where  $W = \{W(t), t \geq 0\}$  is the standard Wiener process and  $a(\cdot)$  and  $b(\cdot)$ , called respectively drift and infinitesimal variance of the process  $X$ , are real functions of their argument obeying to mild assumptions. Here  $\bar{\Theta}$  represents the vector of parameters  $\theta_i, i = 1, \dots, m$  characterizing the process  $X(t)$ . We indicate as  $I$  the diffusion interval of the process  $X$ .

Closed form expressions for the pdf of the random variable  $T$  defined in (1) for the process  $X(t)$  solution to (2) are known only for a few particular instances that are often of scarce interest for applications.

We are interested in the estimation of the parameters that characterize the diffusion process  $X$  and that appear in the drift  $a(\cdot)$  and in the infinitesimal variance  $b(\cdot)$ . The expressions for the first and the second order moments of the FPT distribution are usually either unknown or known only in a rather complicated form, making a direct application of the moment type estimation procedure hard in the cases of interest (cf. [29]). However under suitable hypothesis a method that generalizes that proposed in [8] and [9] to other diffusion processes, possibly using different types of functionals, can be introduced.

Consider a specific diffusion process  $X$  and let  $T$  be its FPT random variable. Let us suppose that two smooth functions  $f_1(T)$  and  $f_2(T)$  exist such that their first moments  $E[f_1(T)]$  and  $E[f_2(T)]$  can be evaluated in a closed form as functions of the parameters characterizing the process. Appropriate conditions must also be imposed to ensure that  $|E[f_1(T)]| < +\infty$  and  $|E[f_2(T)]| < +\infty$ .

Relying on the sample  $(T_1, T_2, \dots, T_n)$ , where  $T_i, i = 1, \dots, n$  are i.i.d. random variables distributed as the first passage time  $T$ , one can estimate  $E[f_1(T)]$  and  $E[f_2(T)]$  through

$$Z_{1,n} = \frac{1}{n} \sum_{i=1}^n f_1(T_i), \quad Z_{2,n} = \frac{1}{n} \sum_{i=1}^n f_2(T_i). \quad (3)$$

respectively.

Aim of this work is the estimation of the vector of parameters  $\bar{\Theta}$  in the case where  $m = 2$ , i.e. for  $\bar{\Theta} = (\theta_1, \theta_2)^T$  (here  $T$  denotes transposition). We assume that the threshold  $S$  and all the other parameters are known from different types of direct measurements. We use the closed expressions of  $E[f_1(T)]$  and of  $E[f_2(T)]$  to determine the moment type estimators  $\hat{\Theta}_{1,n}$  and  $\hat{\Theta}_{2,n}$  of  $\theta_1$  and  $\theta_2$  respectively.

**Remark 1** *Cases where the number of parameters to be estimated is greater than 2 could also be considered by introducing additional functions  $f_i(T), i > 2$ , and corresponding closed form expressions for the moments  $E[f_i(T)], i > 2$ . Since this generalizations are theoretically simple but may imply further computations and heavier notations we limit ourselves to the case of  $m = 2$ .*

### 3 The asymptotic behavior of the estimators

We consider a probability space on which a parameterized family of probability measures is given:

$$(\Omega, \mathcal{F}, \{\mathbb{P}_{\bar{\Theta}}, \bar{\Theta} \in \Psi\}), \quad \Psi \subseteq \mathbb{R}^2.$$

For our purposes, we consider the subset  $\Psi = \{\bar{\Theta} : |E[f_i(T)]| < +\infty, i = 1, 2\}$ .

Let  $(T_1, T_2, \dots, T_n)$  be a sample of FPT observations of a diffusion process  $X$  solution to (2) and defined on  $(\Omega, \mathcal{F}, \mathbb{P}_0)$ , where  $\mathbb{P}_0$  denotes the probability measure corresponding to the couple  $\bar{\Theta}_0 = (\theta_1^{(0)}, \theta_2^{(0)}) \in \Psi$ .

We suppose that there exist two real-valued continuous functions  $g(x)$  and  $h(x, y)$ , defined for any real numbers  $x, y$  for which  $g(x) < +\infty$  and  $h(x, y) < +\infty$ , such that

$$\theta_1 = g(E[f_1(T)]) \quad \text{and} \quad \theta_2 = h(E[f_1(T)], E[f_2(T)]), \quad (4)$$

for any  $\bar{\Theta} = (\theta_1, \theta_2)^T \in \Psi$ . We study the asymptotic properties for estimators of the following form:

$$\hat{\Theta}_{1,n} = g(Z_{1,n}) \quad \text{and} \quad \hat{\Theta}_{2,n} = h(Z_{1,n}, Z_{2,n}) \quad (5)$$

for any  $n \geq 1$ .

The sequences  $\{\hat{\Theta}_{1,n}\}_{n \geq 1}$  and  $\{\hat{\Theta}_{2,n}\}_{n \geq 1}$  verify the classical asymptotic properties of this class of moment estimators. We recall here the ones we use in the sequel.

When  $\bar{\Theta} = \bar{\Theta}_0$ :

1. As  $n \rightarrow \infty$ , the Weak Law of Large Numbers states that

$$Z_{1,n} \xrightarrow{\mathbb{P}_0} E[f_1(T)], \quad Z_{2,n} \xrightarrow{\mathbb{P}_0} E[f_2(T)]. \quad (6)$$

Here and later  $\xrightarrow{\mathbb{P}_0}$  denotes convergence in  $\mathbb{P}_0$ -probability.

2. From the Central Limit Theorem the sequences of random variables  $\{Z_{1,n}\}_{n \geq 1}$  and  $\{Z_{2,n}\}_{n \geq 1}$  satisfy

$$\begin{aligned} \sqrt{n}(Z_{1,n} - E[f_1(T)]) &\xrightarrow{\mathcal{D}} N(0, \text{Var}(f_1(T))), \\ \sqrt{n}(Z_{2,n} - E[f_2(T)]) &\xrightarrow{\mathcal{D}} N(0, \text{Var}(f_2(T))), \end{aligned} \quad (7)$$

as  $n \rightarrow \infty$ . Here and later  $\xrightarrow{\mathcal{D}}$  denotes convergence in distribution under  $\mathbb{P}_0$  while  $N(a, b)$  denotes the normal distribution with mean  $a$  and variance  $b$ .

In the following whenever necessary to prove the asymptotic properties of the estimators  $\hat{\Theta}_{1,n}$  and  $\hat{\Theta}_{2,n}$  we also hypothesize the existence of closed form expressions for higher moments of the functions  $f_1(T)$  and  $f_2(T)$ ,  $E[f_i^n(T)]$  with  $i = 1, 2$ ;  $n > 1$ . In each case the conditions of finiteness of the absolute value of the involved expectations is assumed to be fulfilled.

We introduce the notation

$$(\xi_1, \xi_2)^T = (E[f_1(T)], E[f_2(T)])^T \quad (8)$$

and

$$\Sigma = \begin{pmatrix} \text{Var}(f_1(T)) & \text{Cov}(f_1(T), f_2(T)) \\ \text{Cov}(f_1(T), f_2(T)) & \text{Var}(f_2(T)) \end{pmatrix}. \quad (9)$$

In the sequel we also need the following functions:

$$v(\theta_1, \theta_2) = (g'(E[f_1(T)]))^2 \text{Var}(f_1(T)) > 0, \quad (10)$$

where  $g'$  denotes differentiation of order 1 with respect to the argument and

$$\begin{aligned} q(\theta_1, \theta_2) &= \nabla h(\xi_1, \xi_2)' \Sigma \nabla h(\xi_1, \xi_2) \\ &= \left( \frac{\partial h}{\partial \xi_1} \right)^2 \text{Var}(f_1(T)) + \left( \frac{\partial h}{\partial \xi_2} \right)^2 \text{Var}(f_2(T)) + 2 \frac{\partial h}{\partial \xi_1} \frac{\partial h}{\partial \xi_2} \text{Cov}(f_1(T), f_2(T)), \end{aligned} \quad (11)$$

where  $\nabla h(\xi_1, \xi_2)$  is the gradient vector of  $h$  in  $(\xi_1, \xi_2)^T$ , defined in (8), with components  $\frac{\partial}{\partial \xi_1} h(\xi_1, \xi_2)$  and  $\frac{\partial}{\partial \xi_2} h(\xi_1, \xi_2)$ .

It holds:

**Lemma 1** *Let  $\bar{\Theta}_0 = (\theta_1^{(0)}, \theta_2^{(0)})^T \in \Psi$  denote the parameter values of the diffusion process  $X$  and consider the sequences  $\{\hat{\Theta}_{1,n}\}_{n \geq 1}$  and  $\{\hat{\Theta}_{2,n}\}_{n \geq 1}$  of their moment type estimators defined in (5).*

*Let the functions  $g(x)$  and  $h(x, y)$  defined in (4) be continuously differentiable and assume that  $g$  has first order derivative different from zero.*

*The sequences  $\{\hat{\Theta}_{1,n}\}_{n \geq 1}$  and  $\{\hat{\Theta}_{2,n}\}_{n \geq 1}$  satisfy the following properties:*

**Consistency:** as  $n \rightarrow \infty$

$$\hat{\Theta}_{1,n} \xrightarrow{\mathbb{P}_0} \theta_1^{(0)}, \quad \hat{\Theta}_{2,n} \xrightarrow{\mathbb{P}_0} \theta_2^{(0)}. \quad (12)$$

**Asymptotic normality:** as  $n \rightarrow \infty$ ,

$$\sqrt{n} (\hat{\Theta}_{1,n} - \theta_1^{(0)}) \xrightarrow{\mathcal{D}} N(0, v(\theta_1^{(0)}, \theta_2^{(0)})), \quad (13)$$

where  $v$  has been defined in (10), and

$$\sqrt{n} (\hat{\Theta}_{2,n} - \theta_2^{(0)}) \xrightarrow{\mathcal{D}} N(0, q(\theta_1^{(0)}, \theta_2^{(0)})), \quad (14)$$

where  $q$  has been defined in (11), provided  $q(\theta_1^{(0)}, \theta_2^{(0)}) > 0$ .

**Proof.** The consistency property immediately follows from (6) and classical properties of convergence in probability using (4) and (5).

As far as the asymptotic normality is concerned, we apply the Delta Method (see e.g. [4, Theorem 5.5.24]) to the sequence of random variables

$$\sqrt{n} (g(Z_{1,n}) - g(E[f_1(T)])) = \sqrt{n} (\hat{\Theta}_{1,n} - \theta_1^{(0)}), \quad n \geq 1, \quad (15)$$

and its multivariate version (cfr. [4, Theorem 5.5.28]) to the sequence of random variables

$$\sqrt{n} (h(Z_{1,n}, Z_{2,n}) - h(\xi_1, \xi_2)) = \sqrt{n} (\hat{\Theta}_{2,n} - \theta_2^{(0)}), \quad n \geq 1. \quad (16)$$

Due to the convergence result (7) we can apply the univariate Delta Method to the sequence (15) since  $g$  is a differentiable function and its first-order derivative is different from zero. Expression (13) immediately follows from the use of Delta Method with asymptotic variance given by (10).

Since under the hypothesis (5) the estimator  $\widehat{\Theta}_{2,n}$  is expressed as a function  $h$  of the random vector  $(Z_{1,n}, Z_{2,n})^T$ , application of the Multivariate Delta Method to the sequence of random variables (16) leads to (14) with asymptotic variance given by (11) provided  $q(\theta_1^{(0)}, \theta_2^{(0)}) > 0$ .  $\square$

## 4 Upper bounds for the rate of convergence

Let us firstly consider the estimator  $\widehat{\Theta}_{1,n}$ . We define the random variables

$$S_n := \frac{\sqrt{n}(\widehat{\Theta}_{1,n} - \theta_1^{(0)})}{\sqrt{v(\theta_1^{(0)}, \theta_2^{(0)})}}, \quad n \geq 1. \quad (17)$$

Furthermore let  $G_n$  be the distribution function of  $S_n$ .

In the following we denote as  $\Phi$  the standard normal distribution function. It holds:

**Theorem 1** *Suppose the hypothesis of Lemma 1 hold. Assume moreover that the function  $g$  has continuous second-order derivative with respect to its argument. Then, for any  $\epsilon_n > 0$*

$$\sup_x |G_n(x) - \Phi(x)| \leq \epsilon_n + \frac{c E[|f_1(T) - E[f_1(T)]|^3]}{\text{Var}(f_1(T))^{\frac{3}{2}} \sqrt{n}} + \frac{\text{Var}(f_1(T))^{\frac{1}{2}} E[|B_n|]}{2 |g'(E(f_1(T)))| \epsilon_n \sqrt{n}} \quad (18)$$

with  $\{B_n\}_{n \geq 1}$  a sequence of random variables such that

$$B_n := g''(\zeta_n) \left( \frac{\sqrt{n}(Z_{1,n} - E[f_1(T)])}{\sqrt{\text{Var}(f_1(T))}} \right)^2, \quad n \geq 1 \quad (19)$$

where  $\zeta_n$  is a random point inside the interval  $(Z_{1,n}, E(f_1(T)))$ .

Furthermore

$$\lim_n E[|B_n|] = |g''(E(f_1(T)))|.$$

**Proof.** Consider the Taylor expansion of  $g(Z_{1,n})$  around  $\xi_1 = E[f_1(T)]$  up to the second-order term. From Taylor's formula with Lagrange remainder, we obtain

$$g(Z_{1,n}) = g(\xi_1) + g'(\xi_1)(Z_{1,n} - \xi_1) + \frac{g''(\zeta_n)}{2}(Z_{1,n} - \xi_1)^2.$$

Multiplying both sides by  $\frac{\sqrt{n}}{\sqrt{v(\theta_1^{(0)}, \theta_2^{(0)})}}$  we obtain

$$\frac{\sqrt{n}(g(Z_{1,n}) - g(\xi_1))}{\sqrt{v(\theta_1^{(0)}, \theta_2^{(0)})}} = \frac{g'(\xi_1) \sqrt{n}(Z_{1,n} - \xi_1)}{\sqrt{v(\theta_1^{(0)}, \theta_2^{(0)})}} + \frac{g''(\zeta_n) \sqrt{n}(Z_{1,n} - \xi_1)^2}{2 \sqrt{v(\theta_1^{(0)}, \theta_2^{(0)})}},$$



which can be rewritten as

$$S_n = T_n + R_n$$

where from (10)

$$T_n := \frac{g'(\xi_1) \sqrt{n} (Z_{1,n} - \xi_1)}{\sqrt{v(\theta_1^{(0)}, \theta_2^{(0)})}} = \frac{\sqrt{n} (Z_{1,n} - \xi_1)}{\sqrt{\text{Var}(f_1(T))}}$$

and

$$R_n := \frac{g''(\zeta_n) \sqrt{n} (Z_{1,n} - \xi_1)^2}{2 \sqrt{v(\theta_1^{(0)}, \theta_2^{(0)})}}.$$

From Lemma 1 of [22], for any sequence  $\epsilon_n > 0$  and  $x \in \mathbb{R}$  we have

$$|G_n(x) - \Phi(x)| \leq \epsilon_n + \sup_x |\mathbb{P}(T_n \leq x) - \Phi(x)| + \mathbb{P}(|R_n| \geq \epsilon_n). \quad (20)$$

Due to the convergence property (7) the classical Berry-Esseen bound (see e.g. [30, Theorem, Ch.3, §11.]) can be employed for  $T_n$ , so for the second term on the r.h.s. of (20) we have

$$\sup_x |\mathbb{P}(T_n \leq x) - \Phi(x)| \leq \frac{c E[|f_1(T) - \xi_1|^3]}{\text{Var}(f_1(T))^{\frac{3}{2}} \sqrt{n}}. \quad (21)$$

Here  $c$  is an absolute constant (the current best estimate is  $c = 0.7975$ ).

Moreover, for the third term on the r.h.s. of (20) by Markov inequality and by (10) we get:

$$\mathbb{P}(|R_n| \geq \epsilon_n) \leq \frac{E[|R_n|]}{\epsilon_n} = \frac{\text{Var}(f_1(T))^{\frac{1}{2}} E \left[ |g''(\zeta_n)| \left( \frac{\sqrt{n} (Z_{1,n} - \xi_1)}{\sqrt{\text{Var}(f_1(T))}} \right)^2 \right]}{2 |g'(E(f_1(T)))| \epsilon_n \sqrt{n}} \quad (22)$$

where the last equality comes from (10).

Taking into account (19), (22) can be rewritten as

$$\mathbb{P}(|R_n| \geq \epsilon_n) \leq \frac{\text{Var}(f_1(T))^{\frac{1}{2}} E[|B_n|]}{2 |g'(E(f_1(T)))| \epsilon_n \sqrt{n}}. \quad (23)$$

To determine the asymptotic value of  $E[|B_n|]$  we apply the Slutsky theorem (cfr. for instance [4, Th. 5.5.17]) to the terms in the product on the r.h.s. of (19). As far as the first term is concerned the convergence property (6) implies that

$$g''(\zeta) \xrightarrow{\mathbb{P}_0}_{n \rightarrow \infty} g''(\xi_1).$$

Furthermore, for the second term from the convergence property (7) it follows

$$\left( \frac{\sqrt{n} (Z_{1,n} - \xi_1)}{\sqrt{\text{Var}(f_1(T))}} \right)^2 \xrightarrow{\mathcal{D}}_{n \rightarrow \infty} \chi^2(1).$$

Hence

$$B_n \xrightarrow{\mathcal{D}}_{n \rightarrow \infty} g''(\xi_1) \chi^2(1)$$

and then

$$\lim_n E[|B_n|] = |g''(E(f_1(T)))|. \quad \square$$

A similar argument can now be used to establish a bound for the rate of convergence of the finite sample distribution function of the estimator  $\widehat{\Theta}_{2,n}$  to the normal one. We define the random variables

$$V_n = \frac{\sqrt{n}(\widehat{\Theta}_{2,n} - \theta_2)}{\sqrt{q(\theta_1^{(0)}, \theta_2^{(0)})}}, \quad n \geq 1, \quad (24)$$

and denote as  $Q_n$  the distribution function of  $V_n$ .

We further introduce the random variables

$$Y_i = \frac{\partial}{\partial \xi_1} h(\xi_1, \xi_2) (f_1(T_i) - \xi_1) + \frac{\partial}{\partial \xi_2} h(\xi_1, \xi_2) (f_2(T_i) - \xi_2), \quad i = 1, \dots, n, \quad (25)$$

where  $h$  and  $(\xi_1, \xi_2)^T$  have been defined in (4) and (8) respectively. They are i.i.d. random variables with zero mean and variance equal to  $q(\theta_1^{(0)}, \theta_2^{(0)})$ .

We can now state the following

**Theorem 2** *Suppose the hypothesis of Lemma 1 hold. Assume moreover that the function  $h$  has continuous second-order derivatives with respect to its arguments. Then, for any  $\epsilon_n > 0$*

$$\sup_x |Q_n(x) - \Phi(x)| \leq \epsilon_n + \frac{c E[|Y_1|^3]}{q(\theta_1^{(0)}, \theta_2^{(0)})^{\frac{3}{2}} \sqrt{n}} + \frac{E[|D_n|]}{2 \sqrt{q(\theta_1^{(0)}, \theta_2^{(0)})} \epsilon_n \sqrt{n}}, \quad (26)$$

where the random variable  $Y_1$  has been defined in (25) and  $\{D_n\}_{n \geq 1}$  is a sequence of random variables such that

$$D_n := n (Z_n - \xi)^T Hh(\zeta_{1,n}, \zeta_{2,n}) (Z_n - \xi), \quad n \geq 1 \quad (27)$$

where  $Hh(\zeta_{1,n}, \zeta_{2,n})$  denotes the Hessian matrix of  $h$  computed in  $(\zeta_{1,n}, \zeta_{2,n})^T$  with  $\zeta_{1,n}$  and  $\zeta_{2,n}$  random points inside the intervals  $(Z_{1,n}, \xi_1)$  and  $(Z_{2,n}, \xi_2)$ , respectively.

Moreover, as  $n \rightarrow \infty$

$$\begin{aligned} E[|D_n|] &\leq \left| \frac{\partial^2}{\partial^2 \xi_1} h(\xi_1, \xi_2) \right| \text{Var}(f_1(T)) + \\ &+ 2 \left| \frac{\partial^2}{\partial \xi_1 \partial \xi_2} h(\xi_1, \xi_2) \right| \sqrt{\text{Var}(f_1(T)) \text{Var}(f_2(T))} + \left| \frac{\partial^2}{\partial^2 \xi_2} h(\xi_1, \xi_2) \right| \text{Var}(f_2(T)). \end{aligned}$$

**Proof.** Consider the Taylor expansion of  $h(Z_{1,n}, Z_{2,n})$  around the vector  $(\xi_1, \xi_2)^T$  defined in (8) up to the second-order term. From Taylor's formula with Lagrange remainder, we obtain

$$h(Z_{1,n}, Z_{2,n}) = h(\xi_1, \xi_2) + \nabla h(\xi_1, \xi_2)^T (Z_n - \xi) + \frac{1}{2} (Z_n - \xi)^T Hh(\zeta_{1,n}, \zeta_{2,n}) (Z_n - \xi),$$

where  $Hh(\zeta_{1,n}, \zeta_2)$  denotes the Hessian matrix of  $h$  computed in  $(\zeta_{1,n}, \zeta_{2,n})^T$  and  $(Z_n - \xi) = (Z_{1,n} - \xi_1, Z_{2,n} - \xi_2)^T$ . By rearranging the terms we can write

$$\begin{aligned} \frac{\sqrt{n}(h(Z_{1,n}, Z_{2,n}) - h(\xi_1, \xi_2))}{\sqrt{q(\theta_1^{(0)}, \theta_2^{(0)})}} &= \frac{\sqrt{n} \nabla h(\xi_1, \xi_2)^T (Z_n - \xi)}{\sqrt{q(\theta_1^{(0)}, \theta_2^{(0)})}} \\ &\quad + \frac{\sqrt{n} (Z_n - \xi)^T Hh(\zeta_{1,n}, \zeta_{2,n}) (Z_n - \xi)}{2 \sqrt{q(\theta_1^{(0)}, \theta_2^{(0)})}} \end{aligned}$$

or, equivalently, from (16)

$$V_n = T_n + R_n,$$

where, using (25),

$$T_n := \frac{\sqrt{n} \nabla h(\xi_1, \xi_2)^T (Z_n - \xi)}{\sqrt{q(\theta_1^{(0)}, \theta_2^{(0)})}} = \frac{\sqrt{n}}{\sqrt{q(\theta_1^{(0)}, \theta_2^{(0)})}} \frac{1}{n} \sum_{i=1}^n Y_i,$$

and

$$R_n := \frac{\sqrt{n} (Z_n - \xi)^T Hh(\zeta_{1,n}, \zeta_{2,n}) (Z_n - \xi)}{2 \sqrt{q(\theta_1^{(0)}, \theta_2^{(0)})}}$$

Applying the classical Berry-Esseen bound to  $T_n = \frac{1}{\sqrt{n q(\theta_1^{(0)}, \theta_2^{(0)})}} \sum_{i=1}^n Y_i$  it follows that

$$\sup_x |\mathbb{P}(T_n \leq x) - \Phi(x)| \leq \frac{c E[|Y_1|^3]}{q(\theta_1^{(0)}, \theta_2^{(0)})^{\frac{3}{2}} \sqrt{n}}. \quad (28)$$

Furthermore, by Markov inequality

$$\mathbb{P}(|R_n| \geq \epsilon_n) \leq \frac{E[|R_n|]}{\epsilon_n} = \frac{E[n |(Z_n - \xi)^T Hh(\zeta_{1,n}, \zeta_{2,n}) (Z_n - \xi)|]}{2 \sqrt{q(\theta_1^{(0)}, \theta_2^{(0)})} \epsilon_n \sqrt{n}}. \quad (29)$$

Taking into account (27), (29) can be rewritten as

$$\mathbb{P}(|R_n| \geq \epsilon_n) \leq \frac{E[|D_n|]}{2 \sqrt{q(\theta_1^{(0)}, \theta_2^{(0)})} \epsilon_n \sqrt{n}}. \quad (30)$$

Then (20), (28) and (30) lead to the uniform upper bound for  $|Q_n(x) - \Phi(x)|$  given in (26).

Now we can apply a procedure similar to that used in Theorem 2 to prove that  $E[|B_n|]$  in (18) is bounded when  $n \rightarrow \infty$  to show that

$$\begin{aligned} E[|D_n|] &\leq \left| \frac{\partial^2}{\partial^2 \xi_1} h(\xi_1, \xi_2) \right| \text{Var}(f_1(T)) + \\ &\quad + 2 \left| \frac{\partial^2}{\partial \xi_1 \partial \xi_2} h(\xi_1, \xi_2) \right| \sqrt{\text{Var}(f_1(T)) \text{Var}(f_2(T))} + \left| \frac{\partial^2}{\partial^2 \xi_2} h(\xi_1, \xi_2) \right| \text{Var}(f_2(T)) \end{aligned}$$

as  $n \rightarrow \infty$ .  $\square$

**Remark 2** *Theorems 1 and 2 give a uniform error bound of order*

$$\epsilon_n + n^{-1/2} + (\epsilon_n \sqrt{n})^{-1},$$

*as  $n \rightarrow \infty$ , no matter how we choose the sequence  $\{\epsilon_n\}$  in (18) and (26), respectively.*

## 5 Examples

We consider here in particular the problem of parameter estimation for the Ornstein-Uhlenbeck and the Feller processes, whose applications as underlying processes in first-passage time models are well known: in biology as models for neuronal activity (see e.g. [26], [27], [21], [32]), in survival analysis (see [1]), in different areas of mathematical finance (see [20] and the references therein, [19], [25]). As we shall see in the following, both of them are fully described by five parameters:  $\mu, \sigma, b, S, x_0$ .

Their first-passage time pdf can be evaluated only by numerical or asymptotic methods ([2], [13], [14], [24], [29]) and simulation techniques (cfr. [15], [16]). As far as the problem of parameter estimation is concerned, Inoue et al. [17] proposed to evaluate the parameters  $(\mu, \sigma)$  of the Ornstein-Uhlenbeck process in terms of 1<sup>st</sup> and 2<sup>nd</sup> moments of the FPT distribution, but this method involves heavy computational efforts due to the complexity of the expressions for these moments. Muldowney and Iyengar [23] implemented a numerical method for inverting the Laplace transform of the Ornstein-Uhlenbeck process FPT pdf and numerically computed the maximum likelihood estimates for three parameters expressed as functions of the five model parameters. In Ditlevsen and Ditlevsen [7] (see also Ditlevsen and Lánský [10]) an integral equation estimation method (applicable to all one-dimensional diffusions with known transition density) is proposed to numerically estimate the parameters  $(\mu, \sigma)$  when samples of the first passage times through a given threshold are available. In the works of Ditlevsen and Lánský [8, 9], moment type estimators of  $(\mu, \sigma)$  are derived in the supra-threshold regime.

The Theorems in Section 4 can be employed to determine the properties of the estimators proposed in [8] and [9].

### 5.1 The Ornstein-Uhlenbeck process

The diffusion process  $X = \{X(t), t \geq 0\}$  that satisfies the following linear stochastic differential equation (SDE):

$$dX(t) = (\mu - bX(t))dt + \sigma dW(t); \quad X(0) = x_0, \quad (31)$$

where  $(\mu, b, \sigma) \in \mathbb{R} \times \mathbb{R}_+ \times \mathbb{R}_+$  are constants, and  $W = \{W(t), t \geq 0\}$  is the standard Wiener process is referred to as the Ornstein-Uhlenbeck (OU) process, also known in mathematical finance as the Vasicek model (see e.g., [31, Section 4.4]). The diffusion interval is  $I \equiv \mathbb{R}$  and the conditional density of  $X$  given the initial value  $X(0) = x_0$  is normal (see e.g., [26, Ch.4]) with mean and variance given by

$$E[X(t)|X(0) = x_0] = \frac{\mu}{b} + \left(x_0 - \frac{\mu}{b}\right) e^{-bt},$$

$$Var[X(t)|X(0) = x_0] = \frac{\sigma^2}{2b} (1 - e^{-2bt}).$$

Note that in (31) the diffusion term is constant.

We limit ourselves to the estimation problem for the parameters  $\mu$  and  $\sigma$  since in the application context the parameters  $S$  and  $b$  can often be determined in a direct way independently from the sample while one can fix  $x_0 = 0$  without affecting the generality of the model.

Let us consider the first-passage time of the OU process through a constant boundary  $S$ . No closed form for the pdf  $g_T(t)$  of  $T$  for the OU process is known for an arbitrary value of  $S$ . An explicit expression exists only in the specific case where  $S = \mu/b$  (cfr. [28],[3]):

$$g_T(t) = \frac{2b^{\frac{3}{2}}(S - x_0)e^{2bt}}{\sqrt{\pi\sigma^2}(e^{2bt} - 1)^{\frac{3}{2}}} \exp\left(\frac{-b(S - x_0)^2}{\sigma^2(e^{2bt} - 1)}\right).$$

The Laplace transform of  $T$  is explicitly known and its expression, when  $S, x_0 > 0$ , is given by (cfr. [28, formula (1a),(1b)])

$$E[e^{-\alpha T}] = \begin{cases} \frac{e^{\frac{b(x_0 - \mu/b)^2}{2\sigma^2}}}{e^{\frac{b(S - \mu/b)^2}{2\sigma^2}}} \cdot \frac{D_{-\alpha/b}(-(x_0 - \mu/b)\sqrt{2b/\sigma^2})}{D_{-\alpha/b}(-(S - \mu/b)\sqrt{2b/\sigma^2})}, & S > x_0; \\ \frac{e^{\frac{b(x_0 - \mu/b)^2}{2\sigma^2}}}{e^{\frac{b(S - \mu/b)^2}{2\sigma^2}}} \cdot \frac{D_{-\alpha/b}((x_0 - \mu/b)\sqrt{2b/\sigma^2})}{D_{-\alpha/b}((S - \mu/b)\sqrt{2b/\sigma^2})}, & S < x_0, \end{cases} \quad (32)$$

for any  $\alpha > 0$ , where  $D_\lambda(\cdot)$  is the parabolic cylinder function (cf. [11]). Due to the presence of a ratio of parabolic cylinder functions, the inverse Laplace transform can not be obtained in closed form. Hence the pdf of  $T$  is known only through numerical methods or asymptotically ([2], [14], [24], [29]) and simulation techniques (cfr. [15], [16]). This prevents from a direct use of the maximum likelihood method to obtain estimators of the parameters considered. Choosing as functionals  $f_1(T) = e^{-T}$  and  $f_2(T) = e^{-2T}$  respectively use of Theorems 1 and 2 could be done. However the heavy constraints required for the finiteness of the moments (32) with  $\alpha = 1, 2$  discourage this approach.

Ditlevsen in [6, Theorem 1] proved that the result (32) can be extended to the case where  $\alpha < 0$ . In particular, moments of the type  $E[e^{b\lambda T}]$  with  $\lambda > 0$  can be explicitly computed by using Doob optional stopping theorem on a suitably defined martingale when  $\lambda$  is a positive integer  $k \geq 1$ . This requests the fulfillment of specific conditions on the asymptotic mean and the asymptotic variance of the OU process to ensure that  $E[e^{b\lambda T}] < +\infty$ . The first four moments of  $e^{bT}$  have been computed in [6]. The first moment

$$E[e^{bT}] = \frac{\mu/b}{\mu/b - S}, \quad (33)$$

exists finite provided

$$\frac{\mu}{b} > S, \quad (34)$$

while the second one

$$E[e^{2bT}] = \frac{2(\mu/b)^2 - \sigma^2/b}{2(\mu/b - S)^2 - \sigma^2/b}, \quad (35)$$

exists finite provided

$$\frac{\mu}{b} > S; \quad \frac{\sigma^2}{2b} < (\mu/b - S)^2. \quad (36)$$

Furthermore

$$E[e^{3bT}] = \frac{2(\mu/b)^2 - 3\sigma^2/b}{2(\mu/b - S)^2 - 3\sigma^2/b} E[e^{bT}], \quad (37)$$

exists finite provided

$$\frac{\mu}{b} > S; \quad \frac{\sigma^2}{2b} < \frac{(\mu/b - S)^2}{3}, \quad (38)$$

while

$$E[e^{4bT}] = \frac{(2(\mu/b)^2 - 3\sigma^2/b)^2 - 6(\sigma^2/b)^2}{(2(\mu/b - S)^2 - 3\sigma^2/b)^2 - 6(\sigma^2/b)^2}, \quad (39)$$

exists finite provided

$$\frac{\mu}{b} > S; \quad \frac{\sigma^2}{2b} < \frac{(\mu/b - S)^2}{3 + \sqrt{6}}. \quad (40)$$

By identifying the functions  $f_1(T)$  and  $f_2(T)$  introduced in Section 2 respectively with  $e^{bT}$  and  $e^{2bT}$  and the parameter vector  $\bar{\Theta} = (\theta_1, \theta_2)^T$  with  $(\mu, \sigma)^T \in \Psi = \{\bar{\Theta} : \text{condition (36) holds}\}$ ,  $\Psi \subseteq \mathbb{R} \times \mathbb{R}_+$ , moment type estimators  $\hat{\mu}_n$  and  $\hat{\sigma}_n^2$  can be computed making use of the expressions (33) and (35) and of the sample estimators

$$Z_{1,n} = \frac{1}{n} \sum_{i=1}^n e^{bT_i}, \quad Z_{2,n} = \frac{1}{n} \sum_{i=1}^n e^{2bT_i}, \quad n \geq 1. \quad (41)$$

In this way one gets (cf. [8]):

$$\Theta_{1,n} = \hat{\mu}_n = bS \cdot \frac{Z_{1,n}}{Z_{1,n} - 1}, \quad \Theta_{2,n} = \hat{\sigma}_n^2 = 2bS^2 \cdot \frac{Z_{2,n} - Z_{1,n}^2}{(Z_{2,n} - 1)(Z_{1,n} - 1)^2}, \quad (42)$$

for any  $n \geq 1$ .

Let  $\bar{\Theta}_0 = (\mu_0, \sigma_0)^T \in \Psi$  denotes the parameter value of the OU process.

### Consistency and asymptotic normality

The consistency of the estimators (42) follows from Lemma 1 in Section 3 by choosing

$$g(x) = bS \cdot \frac{x}{x - 1}, \quad h(x, y) = 2bS^2 \cdot \frac{y - x^2}{(y - 1)(x - 1)^2}. \quad (43)$$

Furthermore the conditions in Lemma 1 for the asymptotic normality of the sequence  $\{\hat{\mu}_n\}_{n \geq 1}$  are satisfied since  $g$  in (43) is continuously differentiable with

$$g'(E[e^{bT}]) = -\frac{(\mu/b - S)^2}{S/b} \neq 0,$$

and

$$v(\mu_0, \sigma_0) = (g'(E[e^{bT}]))^2 \text{Var}(e^{bT}) > 0.$$

As far as the sequence  $\{\hat{\sigma}_n^2\}_{n \geq 1}$  of estimators for the parameter  $\sigma_0^2$  is concerned, Lemma 1 can be applied since the function  $h$  in (43) is continuously differentiable.

The asymptotic normality thus holds with asymptotic variance

$$\begin{aligned}
q(\mu_0, \sigma_0) &= \nabla h(\xi_1, \xi_2)^T \Sigma \nabla h(\xi_1, \xi_2) \\
&= \left( \frac{\partial h}{\partial \xi_1} \right)^2 \text{Var}(e^{bT}) + \left( \frac{\partial h}{\partial \xi_2} \right)^2 \text{Var}(e^{2bT}) + 2 \frac{\partial h}{\partial \xi_1} \frac{\partial h}{\partial \xi_2} \text{Cov}(e^{bT}, e^{2bT})
\end{aligned} \tag{44}$$

provided  $q(\mu_0, \sigma_0) > 0$  and (40) holds. Here

$$\Sigma = \begin{pmatrix} \text{Var}(e^{bT}) & \text{Cov}(e^{bT}, e^{2bT}) \\ \text{Cov}(e^{bT}, e^{2bT}) & \text{Var}(e^{2bT}) \end{pmatrix} \tag{45}$$

is the covariance matrix of the random vector  $(\xi_1, \xi_2)^T = (e^{bT}, e^{2bT})^T$  while the components of the gradient vector of  $h$  in  $(\xi_1, \xi_2)^T$  are

$$\begin{aligned}
\frac{\partial}{\partial \xi_1} h(\xi_1, \xi_2) &= 4bS^2 \cdot \frac{\xi_1 - \xi_2}{(\xi_2 - 1)(\xi_1 - 1)^3}; \\
\frac{\partial}{\partial \xi_2} h(\xi_1, \xi_2) &= 2bS^2 \cdot \frac{\xi_1 + 1}{(\xi_2 - 1)^2(\xi_1 - 1)}.
\end{aligned} \tag{46}$$

### Upper bounds for the rate of convergence

Let us consider the sequence  $\{\hat{\mu}_n\}_{n \geq 1}$ . Inequality (18) of Theorem 1 in Section 4 in the case of the OU process becomes:

$$\sup_x |G_n(x) - \Phi(x)| \leq \epsilon_n + \frac{c E[|e^{bT} - \mu_0|^3]}{\text{Var}(e^{bT})^{\frac{3}{2}} \sqrt{n}} + \frac{\text{Var}(e^{bT})^{\frac{1}{2}} E[|B_n|]}{2 |g'(E(e^{bT}))| \epsilon_n \sqrt{n}} \tag{47}$$

where the sequence of random variables  $B_n$  is defined as in (19).

Let us now consider the sequence  $\{\hat{\sigma}_n^2\}_{n \geq 1}$ . Inequality (26) in Theorem 2 for the case of the OU process becomes:

$$\sup_x |Q_n(x) - \Phi(x)| \leq \epsilon_n + \frac{c E[|Y_1|^3]}{q(\mu_0, \sigma_0^2)^{\frac{3}{2}} \sqrt{n}} + \frac{E[|D_n|]}{2 \sqrt{q(\mu_0, \sigma_0^2)} \epsilon_n \sqrt{n}} \tag{48}$$

where the sequence of random variables  $D_n$  has been defined in (27) of Theorem 3. The expressions of the partial derivatives  $\frac{\partial^2}{\partial^2 \xi_1} h(\xi_1, \xi_2)$ ,  $\frac{\partial^2}{\partial^2 \xi_2} h(\xi_1, \xi_2)$  and  $\frac{\partial^2}{\partial \xi_1 \partial \xi_2} h(\xi_1, \xi_2)$  follow immediately from (46).

## 5.2 The Feller process

The second diffusion process we will be concerned is the so-called Feller process  $X = \{X(t), t \geq 0\}$ , solution of the following SDE:

$$dX(t) = (\mu - bX(t))dt + \sigma \sqrt{X(t)} dW(t); \quad X(0) = x_0, \tag{49}$$

where  $(\mu, b, \sigma) \in \mathbb{R} \times \mathbb{R}_+ \times \mathbb{R}_+$  are constants. It has been proposed by Feller in [12] as a model for population growth, and is well known in stochastic finance as

the Cox-Ingersoll-Ross (CIR) model (see [5], [31]). The diffusion interval is now  $I = [0, \infty)$ . The nature of the lower boundary 0 depends on the relationship between the parameters  $\mu$  and  $\sigma^2$ . We will assume throughout the paper that the condition  $2\mu \geq \sigma^2$  holds. Under this condition, following Feller's classification of boundaries (see [18, Section 15.6]), the boundary 0 is entrance. In this case the boundary can be reached from any other level, but once attained the process can no longer evolve inside its interval of definition. The transition density of  $X$  given the initial value is a non-central Chi-square distribution with mean and variance (see e.g., [31, Section 4.4] or [13])

$$\begin{aligned} E[X(t)|X(0) = x_0] &= x_0 e^{-bt} + \frac{\mu}{b}(1 - e^{-bt}), \\ \text{Var}[X(t)|X(0) = x_0] &= \frac{y_0 \sigma^2}{b} (e^{-bt} - e^{-2bt}) + \frac{\mu \sigma^2}{2b^2} (1 - e^{-bt})^2. \end{aligned} \quad (50)$$

The stationary density of  $X$ , as  $t \rightarrow \infty$ , is the Gamma distribution with asymptotic mean  $\mu/b$  and variance  $\mu\sigma^2/2b^2$ .

The analytical form of the distribution of the first-passage time variable  $T$  defined in (1) is not available, thus only numerical and simulation techniques ([29], [16]) or approximation methods (cfr. [14], [24]) can be used.

Closed expressions of the first two moments of  $e^{bT}$  have been computed in [9]. By using suitable martingales from the conditional moments (50) and applying Doob's Optional Stopping Theorem (cfr. [9, Appendix]) one gets:

$$E[e^{bT}] = \frac{\mu/b - x_0}{\mu/b - S}, \quad (51)$$

which exists finite provided

$$\frac{\mu}{b} > S; \quad (52)$$

$$E[e^{2bT}] = \frac{(\mu/b - x_0)^2 + \sigma^2/b(\mu/2b - x_0)}{(\mu/b - S)^2 + \sigma^2/b(\mu/2b - S)}, \quad (53)$$

which exists finite provided

$$\frac{\mu}{b} > S; \quad \frac{\sigma^2}{2b} < \frac{(\mu/b - S)}{(\sqrt{1 + \frac{2\mu}{\sigma^2}} - 1)}. \quad (54)$$

Here again suitable conditions on the asymptotic mean and variance of the Feller process must be imposed to ensure that  $E[e^{b\lambda T}] < +\infty$ , when  $\lambda$  is a positive integer.

Following the same procedure used in [9] it is possible to compute the third and fourth conditional moments of  $e^{bT}$  for the Feller process. In particular we obtained

$$E[e^{3bT}] = \frac{(\mu/b - x_0)[2(\mu/b - x_0)^2 + 6\sigma^2/b(\mu/b - x_0) - 3\mu\sigma^2/b^2] + 3\sigma^4/b^3(\mu/3b - x_0)}{(\mu/b - S)[2(\mu/b - S)^2 + 6\sigma^2/b(\mu/b - S) - 3\mu\sigma^2/b^2] + 3\sigma^4/b^3(\mu/3b - S)}, \quad (55)$$

which exists finite provided  $\frac{\mu}{b} > S$  and the denominator is  $> 0$ , and

$$E[e^{4bT}] = \frac{[(\mu/b - x_0)^2 + 3\sigma^2/b(\mu/b - x_0) - 3\mu\sigma^2/2b^2]^2 + \sigma^4/b^3(2\mu + 3\sigma^2)(\mu/4b - x_0)}{[(\mu/b - S)^2 + 3\sigma^2/b(\mu/b - S) - 3\mu\sigma^2/2b^2]^2 + \sigma^4/b^3(2\mu + 3\sigma^2)(\mu/4b - S)}, \quad (56)$$



which exists finite provided  $\frac{\mu}{b} > S$  and the denominator is  $> 0$ .

We identify the functions  $f_1(T) \equiv e^{bT}$  and  $f_2(T) \equiv e^{2bT}$  and the parameter vector  $\bar{\Theta} = (\theta_1, \theta_2)^T$  with  $(\mu, \sigma)^T \in \Psi = \{\bar{\Theta} : \text{condition (54) holds}\}$ ,  $\Psi \subseteq \mathbb{R} \times \mathbb{R}_+$ . We hence employ the sample estimators (41). In this way we get the following moment type estimators for  $\mu$  and  $\sigma^2$ :

$$\widehat{\Theta}_{1,n} = \hat{\mu}_n = \frac{b(SZ_{1,n} - x_0)}{Z_{1,n} - 1}, \quad (57)$$

$$\widehat{\Theta}_{2,n} = \hat{\sigma}_n^2 = \frac{2b(S - x_0)^2(Z_{2,n} - Z_{1,n}^2)}{(Z_{1,n} - 1)[2(Z_{1,n} - 1)(SZ_{2,n} - x_0) - (SZ_{1,n} - x_0)(Z_{2,n} - 1)]}, \quad (58)$$

for any  $n \geq 1$ . Note that the denominator of (58) corrects a misprint in expression (25) of [9] introducing a factor  $(Z_{1,n} - 1)$  in the denominator.

Let now  $\bar{\Theta}_0 = (\mu_0, \sigma_0)^T \in \Psi$  denote the parameter values of the Feller process and consider the sequences  $\{\hat{\mu}_n\}_{n \geq 1}$  and  $\{\hat{\sigma}_n^2\}_{n \geq 1}$  of the moment type estimators (57) and (58).

### Consistency and asymptotic normality

The consistency of the estimators (57) and (58) immediately follows from Lemma 1 in Section 3 by choosing respectively

$$g(x) = \frac{b(Sx - x_0)}{x - 1},$$

$$h(x, y) = \frac{2b(S - x_0)^2(y - x^2)}{(x - 1)[2(x - 1)(Sy - x_0) - (Sx - x_0)(y - 1)]}. \quad (59)$$

As far as the asymptotic normality is concerned, let us firstly consider the sequence  $\{\hat{\mu}_n\}_{n \geq 1}$ . The conditions in Lemma 1 for the asymptotic normality of the estimator are satisfied since the function  $g$  in (59) is continuously differentiable with

$$g'(E[e^{bT}]) = -\frac{b(\mu/b - S)^2}{S - x_0} \neq 0$$

and

$$v(\mu_0, \sigma_0) = (g'(E[e^{bT}]))^2 \text{Var}(e^{bT}) > 0.$$

Lemma 1 can be applied also to the sequence  $\{\hat{\sigma}_n^2\}_{n \geq 1}$  since the function  $h$  in (59) is continuously differentiable.

The asymptotic normality thus holds with asymptotic variance

$$q(\mu_0, \sigma_0) = \nabla h(\xi_1, \xi_2)^T \Sigma \nabla h(\xi_1, \xi_2)$$

$$= \left(\frac{\partial h}{\partial \xi_1}\right)^2 \text{Var}(e^{bT}) + \left(\frac{\partial h}{\partial \xi_2}\right)^2 \text{Var}(e^{2bT}) + 2 \frac{\partial h}{\partial \xi_1} \frac{\partial h}{\partial \xi_2} \text{Cov}(e^{bT}, e^{2bT}), \quad (60)$$

provided  $q(\mu_0, \sigma_0) > 0$ , and the denominators in (55) and (56) are both  $> 0$ . Here  $\Sigma$  is the covariance matrix defined in (45). The partial derivatives of the function  $h$

computed in  $(\xi_1, \xi_2)^T = (e^{bT}, e^{2bT})^T$  are given by

$$\begin{aligned} \frac{\partial}{\partial \xi_1} h(\xi_1, \xi_2) &= -2b(S - x_0)^2 \left\{ \frac{\xi_1^2 - 2\xi_1 + \xi_2}{(\xi_1 - 1)^2 [2(\xi_1 - 1)(S\xi_2 - x_0) - (S\xi_1 - x_0)(\xi_2 - 1)]} \right. \\ &\quad \left. + \frac{(\xi_2 - \xi_1^2)[2(S\xi_2 - x_0) - S(\xi_2 - 1)]}{(\xi_1 - 1)[2(\xi_1 - 1)(S\xi_2 - x_0) - (S\xi_1 - x_0)(\xi_2 - 1)]^2} \right\}, \\ \frac{\partial}{\partial \xi_2} h(\xi_1, \xi_2) &= \frac{2b(S - x_0)^2(\xi_1 - 1)(S\xi_1 + x_0)}{[2(\xi_1 - 1)(S\xi_2 - x_0) - (S\xi_1 - x_0)(\xi_2 - 1)]^2}. \end{aligned} \tag{61}$$

### Upper bounds for the rate of convergence

As far as the sequence  $\{\hat{\mu}_n\}_{n \geq 1}$  is concerned, from Theorem 1 of Section 4 we obtain the same uniform upper bound for  $|G_n(x) - \Phi(x)|$  as in (47).

Analogously, for the sequence  $\{\hat{\sigma}_n^2\}_{n \geq 1}$  one gets from Theorem 2 of Section 4 the same bound as in (48), where the required second order partial derivatives of  $h(\xi_1, \xi_2)$  can be computed from (61).

## 6 Applications to neuronal models

One-dimensional diffusion processes  $X = \{X(t), t \geq 0\}$  are often employed in neurobiological modeling literature to describe the time evolution of the membrane potential between two consecutive firings (or spikes) of a neuron. The values assumed by the process  $X$  correspond to the differences between the physical value of the membrane potential and a reference value  $x_0$  denoted as reference level. A spike or action potential is elicited whenever  $X$  reaches for the first time a given threshold value  $S$ . After a spike the potential is reset to its initial value, considered to coincide with the resting level  $x_0$ . The mathematical counterpart of the time between successive spikes or interspike interval (ISI) is then the random variable first passage time  $T$  of the process  $X$  defined in (1).

Different models can be considered depending on the assumptions about the processing of incoming inputs to the neuron (cf. for instance [26], [32]). In particular the OU process, known in this framework as the stochastic leaky integrate-and-fire model, and the Feller process appear as good compromises between the computational tractability and the realism of the neuronal models.

We should remark that within the framework of neurobiological applications the parameter  $b$  appearing in the SDE's (31) and (49) is identified with  $1/\tau$ , where  $\tau > 0$  is the membrane time constant and reflects spontaneous voltage decay in the absence of neuronal input.

Note also that the five parameters on which the OU and the Feller process depend can be divided in two groups: the intrinsic parameters  $\tau$ ,  $x_0$  and  $S$ , and the parameters characterizing the net input,  $\mu$ , and the variability around the mean,  $\sigma^2$ . The first ones pertain to the neuron irrespectively of the incoming input while the second group depends on the signal impinging on the neuron and deeply influences its firing behavior. Two firing regimes can be then distinguished for the model neuron. If the

mean level  $\mu\tau$  that the depolarization attains for  $t \rightarrow \infty$  exceeds  $S$  the neuron is in the suprathreshold regime where the firing is rather regular. On the other hand if  $\mu\tau < S$  the cell is in the underthreshold regime where it could not fire in the absence of the noise contribution. Due to the conditions required by (33) and (51) we will be concerned here with the parameter estimation in the suprathreshold regime.

## 6.1 The OU process

To apply the results obtained in the previous Sections to the OU neuronal model samples of FPT's for the OU process were simulated by means of the methodology proposed in ([15]). Following the most common lines in neuromodelling literature we always chose  $S = 10$  mV and  $\tau = 10$  ms, while the necessity to satisfy the constraints of the existence of moments (33)-(39) and of the positivity of term (44) restricted the choice for possible values of the other parameters. We considered the following three sets of values for  $\mu$  and  $\sigma^2$ :

1.  $\mu_0 = 1.5$  mVms<sup>-1</sup>;  $\sigma_0^2 = 0.8$  mV<sup>2</sup>ms<sup>-1</sup>;
2.  $\mu_0 = 1.25$  mVms<sup>-1</sup>;  $\sigma_0^2 = 0.1$  mV<sup>2</sup>ms<sup>-1</sup>;
3.  $\mu_0 = 2$  mVms<sup>-1</sup>;  $\sigma_0^2 = 2.5$  mV<sup>2</sup>ms<sup>-1</sup>.

We executed a series of  $M = 1000$  simulations for each sample size chosen in correspondence with each one of the three parameter sets:  $n = 100, 500, 1000, 4000$ . For each simulation batch  $N = 10000$  realizations of the FPT were obtained. In Table 1 we show the mean values of the estimators obtained:

$$\widehat{\mu}_n = \frac{1}{M} \sum_{i=1}^M \widehat{\mu}_{n,i}; \quad \widehat{\sigma}_n^2 = \frac{1}{M} \sum_{i=1}^M \widehat{\sigma}_{n,i}^2 \quad (62)$$

together with the standard errors  $\sigma_{\widehat{\mu}_n}$ ,  $\sigma_{\widehat{\sigma}_n^2}$  and the asymptotic standard errors  $\sigma_{\widehat{\mu}_n}^{as} = \sqrt{\frac{v(\mu_0, \sigma_0)}{n}}$  and  $\sigma_{\widehat{\sigma}_n^2}^{as} = \sqrt{\frac{q(\mu_0, \sigma_0)}{n}}$ .

The estimates for the parameter  $\mu$  always appear to be unbiased and with small variance while the behavior of the estimator for the parameter  $\sigma^2$  is worse.

The small oscillations in the values of  $\widehat{\mu}_n$  as  $n$  increases are due to the computational imprecisions caused by the huge number of simulations run to obtain the required samples of FPT's.

To get a better insight into the goodness of the approximation of the distribution of the estimators with the normal one as a function of the sample size employed we show in Table 2 the upper bounds obtained by means of a suitable implementation of formulae (47) and (48) respectively for  $n = 100$  and  $n = 4000$ . Here Term 2 and Term 3 refer to the terms of order  $n^{-1/2}$  and  $(\epsilon_n \sqrt{n})^{-1}$  in such formulae respectively (we chose  $\epsilon_n = n^{-1/4}$ ).

Though the distribution of  $\widehat{\mu}_n$  appears to be better approximated by the normal one for every sample size with respect to the distribution of  $\widehat{\sigma}_n^2$ , it is however possible to employ such approximation for the estimator of  $\sigma^2$  for sample sizes that do not exceed some thousands. This is important in the field of neurobiological modeling since available sample sizes of recorded ISIs cannot be greater. Moreover one can also

remark that the lack of normality in the distribution of  $\widehat{\sigma}_n^2$  reported in [8] was due to the fact that the parameters chosen did not satisfy all the constraints quoted above.

To confirm these results we show in Fig. 1 the normal quantile plots corresponding to the distribution of the estimators  $\widehat{\mu}_n$  and  $\widehat{\sigma}_n^2$  in case 2. for  $n = 100$  and  $n = 4000$ .

## 6.2 The Feller process

The model which is known in the theoretical neurobiological literature as Feller model is characterized by the additional parameter  $V_I < 0$ , which represents the inhibitory reversal potential, with respect to the process described by means of (49). The corresponding SDE is the following:

$$dX(t) = (\mu - bX(t))dt + \sigma\sqrt{X(t) - V_I}dW(t); \quad X(0) = x_0, \quad (63)$$

and the diffusion interval is  $[V_I, \infty]$ . While the value of the parameter  $V_I$  can be obtained by means of neurophysiological measurements, a simple linear transformation changes the process  $X(t)$  defined in (63) into the process  $X(t)$  solution to (49). Using the same simulation methodology for the simulation of FPT's of diffusion processes as for the OU model we obtained samples of ISI values for the Feller neuronal model described by means of eq. (49). We chose here  $S = 20$  mV,  $x_0 = 10$  mV and  $\tau = 10$  ms, while to satisfy the constraints required for the existence of (51)-(56) and of (60) we selected the following three sets of values for  $\mu$  and  $\sigma^2$ :

1.  $\mu_0 = 4.0$  mVms<sup>-1</sup>;  $\sigma_0^2 = 0.5$  mVms<sup>-1</sup>;
2.  $\mu_0 = 5.0$  mVms<sup>-1</sup>;  $\sigma_0^2 = 1.0$  mVms<sup>-1</sup>;
3.  $\mu_0 = 4.5$  mVms<sup>-1</sup>;  $\sigma_0^2 = 1.0$  mVms<sup>-1</sup>.

The simulations were executed with the same criteria as for the OU model. The mean values of the estimators:

$$\bar{\mu}_n = \frac{1}{M} \sum_{i=1}^M \widehat{\mu}_{n,i}; \quad \bar{\sigma}_n^2 = \frac{1}{M} \sum_{i=1}^M \widehat{\sigma}_{n,i}^2 \quad (64)$$

together with the corresponding standard errors and the asymptotic standard errors are shown in Table 3.

Here again the estimates for the parameter  $\mu$  appear always better than those for  $\sigma^2$ .

In Table 4 we show the results obtained by estimating (47) and (48) on the basis of the simulated sample data respectively for  $n = 100$  and  $n = 4000$ .

Also in the case of the Feller model the normal approximation for the distribution of  $\widehat{\mu}_n$  appears to hold already for small sample sizes and such approximation holds better for every sample size with respect to the analogous one for the distribution of  $\widehat{\sigma}_n^2$ . In this last case larger sample sizes have to be employed to get a good approximation, however some proximity within the real distribution of the estimator and the asymptotic normal one can be achieved already for samples of some thousands of data.

A graphical confirmation of such behavior is given in Fig. 2 where normal quantile plots corresponding respectively to the distribution of the estimator  $\widehat{\mu}_n$  and  $\widehat{\sigma}_n^2$  in case 3. for  $n = 100$  and  $n = 4000$  are shown.

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| Case | n    | $\widehat{\mu}_n$ | $\sigma_{\widehat{\mu}_n}$ | $\sigma_{\widehat{\mu}_n}^{as}$ | $\widehat{\sigma}_n^2$ | $\sigma_{\widehat{\sigma}_n^2}$ | $\sigma_{\widehat{\sigma}_n^2}^{as}$ |
|------|------|-------------------|----------------------------|---------------------------------|------------------------|---------------------------------|--------------------------------------|
| 1    | 100  | 1.498             | 0.0295                     | 0.0309                          | 0.724                  | 0.2095                          | 0.7848                               |
| 1    | 500  | 1.497             | 0.0137                     | 0.0138                          | 0.769                  | 0.1423                          | 0.3510                               |
| 1    | 1000 | 1.495             | 0.0099                     | 0.0098                          | 0.778                  | 0.1181                          | 0.2482                               |
| 1    | 4000 | 1.496             | 0.0048                     | 0.0049                          | 0.782                  | 0.0639                          | 0.1241                               |
| 2    | 100  | 1.249             | 0.0086                     | 0.0090                          | 0.096                  | 0.0232                          | 0.0295                               |
| 2    | 500  | 1.248             | 0.0039                     | 0.0040                          | 0.098                  | 0.0122                          | 0.0132                               |
| 2    | 1000 | 1.248             | 0.0028                     | 0.0029                          | 0.098                  | 0.0087                          | 0.0093                               |
| 2    | 4000 | 1.248             | 0.0015                     | 0.0014                          | 0.099                  | 0.0043                          | 0.0047                               |
| 3    | 100  | 1.993             | 0.0644                     | 0.0655                          | 2.299                  | 0.7056                          | 1.3591                               |
| 3    | 500  | 1.991             | 0.0282                     | 0.0293                          | 2.407                  | 0.4377                          | 0.6078                               |
| 3    | 1000 | 1.989             | 0.0208                     | 0.0207                          | 2.426                  | 0.2901                          | 0.4298                               |
| 3    | 4000 | 1.989             | 0.0108                     | 0.0104                          | 2.443                  | 0.1825                          | 0.2149                               |

Table 1: Estimates for the OU process

| Case/n | Bounds for $\widehat{\mu}_n$ |        |        | Bounds for $\widehat{\sigma}_n^2$ |        |        |
|--------|------------------------------|--------|--------|-----------------------------------|--------|--------|
|        | Term 2                       | Term 3 | Total  | Term 2                            | Term 3 | Total  |
| 1/100  | 0.3817                       | 0.1952 | 0.8931 | 0.6828                            | 0.3207 | 1.3197 |
| 1/4000 | 0.0604                       | 0.0776 | 0.2637 | 0.1206                            | 0.1740 | 0.4203 |
| 2/100  | 0.2235                       | 0.1142 | 0.6539 | 0.6215                            | 0.3835 | 1.3212 |
| 2/4000 | 0.0353                       | 0.0454 | 0.2065 | 0.1193                            | 0.2216 | 0.4666 |
| 3/100  | 0.3169                       | 0.2070 | 0.8401 | 0.5752                            | 0.3596 | 1.2510 |
| 3/4000 | 0.0501                       | 0.0823 | 0.2582 | 0.0909                            | 0.2377 | 0.4543 |

Table 2: Upper bounds for the estimators of  $\mu$  and  $\sigma^2$

| Case | n    | $\widehat{\mu}_n$ | $\sigma_{\widehat{\mu}_N}$ | $\sigma_{\widehat{\mu}_n}^{as}$ | $\widehat{\sigma}_n^2$ | $\sigma_{\widehat{\sigma}_n^2}$ | $\sigma_{\widehat{\sigma}_n^2}^{as}$ |
|------|------|-------------------|----------------------------|---------------------------------|------------------------|---------------------------------|--------------------------------------|
| 1    | 100  | 3.981             | 0.1354                     | 0.1414                          | 0.467                  | 0.1571                          | 0.2244                               |
| 1    | 500  | 3.976             | 0.0614                     | 0.0632                          | 0.481                  | 0.0820                          | 0.1003                               |
| 1    | 1000 | 3.975             | 0.0453                     | 0.0447                          | 0.489                  | 0.0667                          | 0.0710                               |
| 1    | 4000 | 3.975             | 0.0218                     | 0.0224                          | 0.487                  | 0.0339                          | 0.0355                               |
| 2    | 100  | 4.955             | 0.2210                     | 0.2283                          | 0.926                  | 0.2898                          | 0.4047                               |
| 2    | 500  | 4.943             | 0.1005                     | 0.1021                          | 0.944                  | 0.1512                          | 0.1810                               |
| 2    | 1000 | 4.941             | 0.0697                     | 0.0722                          | 0.954                  | 0.1194                          | 0.1280                               |
| 2    | 4000 | 4.940             | 0.0354                     | 0.0104                          | 0.953                  | 0.0576                          | 0.0640                               |
| 3    | 100  | 4.461             | 0.2133                     | 0.2137                          | 0.903                  | 0.3174                          | 0.5726                               |
| 3    | 500  | 4.443             | 0.0928                     | 0.0956                          | 0.953                  | 0.2082                          | 0.2561                               |
| 3    | 1000 | 4.446             | 0.0675                     | 0.0676                          | 0.952                  | 0.1524                          | 0.1811                               |
| 3    | 4000 | 4.444             | 0.0328                     | 0.0338                          | 0.957                  | 0.0728                          | 0.0905                               |

Table 3: Estimates for the Feller process

| Case/n | Bounds for $\widehat{\mu}_n$ |        |        | Bounds for $\widehat{\sigma}_n^2$ |        |        |
|--------|------------------------------|--------|--------|-----------------------------------|--------|--------|
|        | Term 2                       | Term 3 | Total  | Term 2                            | Term 3 | Total  |
| 1/100  | 0.3098                       | 0.2236 | 0.8497 | 0.5312                            | 0.4217 | 1.2691 |
| 1/4000 | 0.0490                       | 0.0889 | 0.2636 | 0.0840                            | 0.2886 | 0.4983 |
| 2/100  | 0.2869                       | 0.2406 | 0.8438 | 0.6836                            | 0.5529 | 1.5527 |
| 2/4000 | 0.0454                       | 0.0957 | 0.2668 | 0.1051                            | 0.4181 | 0.6489 |
| 3/100  | 0.3493                       | 0.2703 | 0.9358 | 0.3214                            | 0.5019 | 1.1395 |
| 3/4000 | 0.0552                       | 0.1075 | 0.2885 | 0.0508                            | 0.3407 | 0.5172 |

Table 4: Upper bounds for the estimators of  $\mu$  and  $\sigma^2$



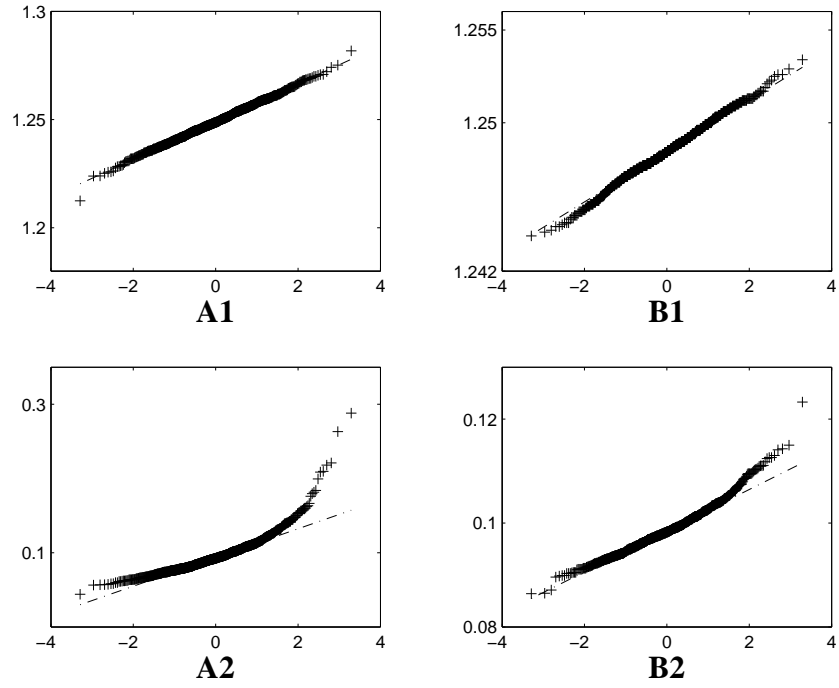


Figure 1: Normal quantile plots for  $\hat{\mu}_n$  and  $\hat{\sigma}_n^2$ , case 2.,  $n = 100$  (**A1-A2**) and  $n = 4000$  (**B1-B2**)

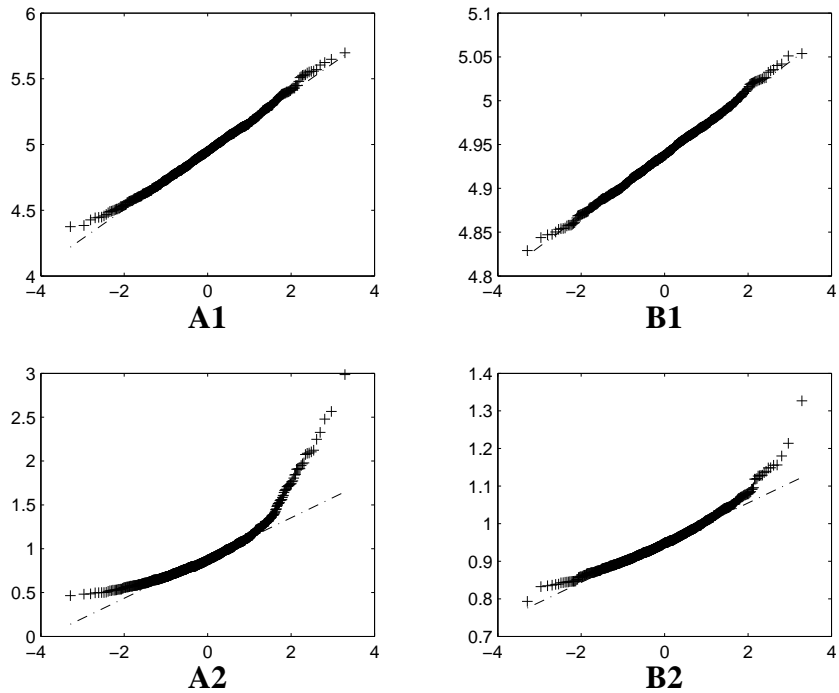


Figure 2: Normal quantile plots for  $\hat{\mu}_n$  and  $\hat{\sigma}_n^2$ , case 3.,  $n = 100$  (**A1-A2**) and  $n = 4000$  (**B1-B2**)