

## Estimation of the input parameters in the Feller neuronal model

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The stochastic Feller neuronal model is studied, and estimators of the model input parameters, depending on the firing regime of the process, are derived. Closed expressions for the first two moments of functionals of the first-passage time (FTP) through a constant boundary in the suprathreshold regime are derived, which are used to calculate moment estimators. In the subthreshold regime, the exponentiality of the FTP is utilized to characterize the input parameters. The methods are illustrated on simulated data. Finally, approximations of the first-passage-time moments are suggested, and biological interpretations and comparisons of the parameters in the Feller and the Ornstein-Uhlenbeck models are discussed.

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### I. INTRODUCTION

The stochastic leaky integrate-and-fire (LIF) neuronal models are common theoretical tools for studying properties of real neuronal systems. They represent a compromise between a similarity to real neurons and mathematical tractability (see, e.g., [1–4]). In these models, a neuron is characterized by a single stochastic differential equation describing the evolution of neuronal membrane potential in dependency on time. Due to the simplicity of these models, some of their features are qualitatively questionable, the most critical ones being unlimited membrane potential fluctuations and state-independent changes of the voltage. Modifications of the basic LIF model have been introduced, in which these unfavorable properties are removed (e.g., [5–8]).

The deterministic LIF model is and has been very popular in theoretical neuroscience, with roots in the beginning of the previous century [9], and it has been compared to more elaborated models (e.g., [10,11]). The results suggest that despite drastic simplifications, the model is relatively reliable in mimicking the more complex ones. The simplest way to construct a stochastic LIF model is to take the deterministic LIF model and add a suitable type of noise, usually Gaussian white noise, but other forms are also possible. Adding Gaussian white noise converts the deterministic LIF model into the Ornstein-Uhlenbeck (OU) model. If Poissonian noise is added we end up with Stein's model or modifications of it [7,12]. In this paper we replace the additive Gaussian white noise by a multiplicative Gaussian white noise that makes neuronal response to input state dependent. This step ensures that membrane potential fluctuations are bounded.

Another way to construct a stochastic model with Gaussian white noise (either additive or multiplicative) is to apply a diffusion approximation method, starting from a model with Poissonian noise in which the input rates of synaptic

bombardment are assumed to be high and the contributions of individual postsynaptic potentials are assumed very small. Whereas the diffusion approximation of the basic LIF model results in the OU process, for the LIF model with state-dependent jumps, the range of limiting processes is large [6,8]. The OU process retains the criticizable unlimited membrane potential fluctuations, whereas the diffusion variants of the LIF models with variable synaptic conductance effects caused by introduction of reversal (also called equilibrium) potentials can have either a bounded or unbounded state space (for details see [6]). All these models have been deeply investigated in recent years [13–19].

Firing is not an intrinsic property of the LIF models or their modifications, and a firing threshold has to be imposed. An action potential (spike) is produced when the membrane voltage reaches the voltage threshold and corresponds to the FTP for the associated stochastic process describing the voltage. In the moment of spike generation, the voltage is instantaneously reset to its initial value. Time intervals between action potentials are identified with experimentally observable interspike intervals (ISIs). The importance of the ISIs follows from the generally accepted hypothesis that the information transferred within the nervous system is encoded by the timing of the action potentials. The diffusion variants of the LIF models are popular because the first-passage-time problem is easier to solve for the diffusion process than for its counterpart with discontinuous trajectories.

Studies devoted to the comparison of the leaky integrate-and-fire neuronal models with experimental data are rare. Some references are [20–26]. At present, we are not aware of any attempt to identify parameters of a diffusion model with restricted space to ISI data. The aim of the present contribution is to derive methods of parameter estimation based on ISI data in the diffusion variant of the LIF model with inhibitory reversal potential. This model is usually called the Feller model. The choice of considering only one reversal potential simplifies the treatment and it has been shown [27] that the inhibitory reversal potential probably plays a more important role than the excitatory one.

Similarly to the OU model, the parameters of the Feller model can be divided into two categories: the input param-

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eters depend on the activity of the neurons in the networks, and the intrinsic parameters characterize the neuron itself, independently of its activity. In fact, the input parameters are a combination of the input excitation and inhibition rates and the intrinsic parameters. This follows from the studies on diffusion models with reversal potentials [6,17,28,29] and it is explained in Sec. V of this paper. Only the estimation of the input parameters is considered, assuming the intrinsic parameters are known and fixed.

The Feller process has many applications apart from neuronal modeling. In 1951 Feller [30] proposed it as a model for population growth, from where the neuronal community adapted its name. Cox, Ingersoll, and Ross [31] proposed it in 1985 to model short term interest rates, and it has been and still is widely studied in the mathematical finance literature under the name of the CIR model. Pedersen [32] used it to model nitrous oxide emission from soil. In survival analysis, Aalen and Gjessing [33] applied the process as a model for the individual hazard rate. Recently Doering and co-workers studied numerical aspects of the process [34].

Closed expressions for the first two moments of functionals of the FTP through a constant boundary are derived and used to construct moment estimators, valid in a subset of the parameter space. The method is illustrated on simulated data. The first two moments of the FTP and approximations are given. Finally, it is shown that the way the diffusion model is derived from the LIF model with Poissonian noise influences the interpretation of its parameters. The paper represents a parallel study to that on the OU neuronal model [26].

## II. THE MODEL AND ITS PROPERTIES

The changes in the membrane potential between two consecutive neuronal firings are represented by a stochastic process  $Y_t$  indexed by the time  $t$ . The reference level for the membrane potential is taken to be the resting potential. The initial voltage (the reset value following a spike) is assumed to be equal to the resting potential, and set to zero,  $Y_0=y_0=0$ . An action potential is produced when the membrane voltage  $Y_t$  exceeds a voltage threshold for the first time, for simplicity assumed to be equal to a constant  $S_y > 0$ . Formally, the interspike interval (ISI) is identified with the FTP of the threshold,

$$T = \inf\{t > 0: Y_t \geq S_y\}. \quad (1)$$

It follows from the model assumptions that for time-homogeneous input containing either a Poissonian or white noise only, the interspike intervals form a renewal process and the initial time can always be identified with zero. Here we consider the white noise input and  $Y_t$  is a diffusion process.

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

$$dX_t = \mu(X_t, t)dt + \sigma(X_t, t)dW_t, \quad (2)$$

where  $W = \{W_t; t \geq 0\}$  is a standard Wiener process and  $\mu(\cdot)$  and  $\sigma(\cdot)$  are real-valued functions of their arguments called

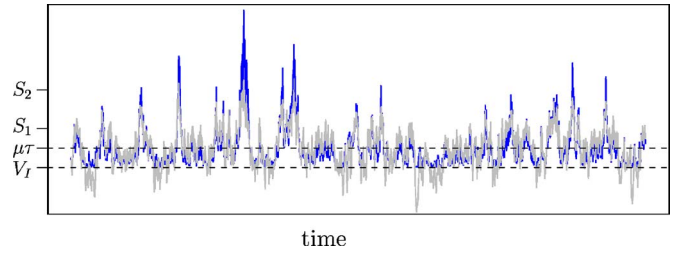


FIG. 1. (Color online) Realizations of  $X_t$  (membrane potential against time, arbitrary units) for the Feller process (dark line) and the OU process (gray line) in absence of a threshold. For comparison, the same realization of a white noise process was used in the two simulations. The dashed lines are the asymptotic depolarization  $\mu\tau$ , which is equal for the two simulations, and the reversal potential  $V_l$  for the Feller process, respectively. If the threshold value equals  $S_1$ , the interspike intervals would be nearly equal for the two processes, for  $S_2$  they would be different.

the infinitesimal mean and variance. The most common of these neuronal models is the OU model given by

$$dY_t = \left(-\frac{Y_t}{\tau} + \mu\right)dt + \sigma dW_t; \quad Y_0 = y_0 = 0, \quad (3)$$

see, e.g., [1–4]. The constant  $\mu$  characterizes the neuronal input,  $\tau > 0$  reflects spontaneous voltage decay (the membrane time constant) in the absence of input, and  $\sigma > 0$  is the second input parameter determining the amplitude of the noise. The diffusion term  $\sigma(\cdot)$  of model (3) is state independent. The process is unbounded, which is physiologically unrealistic. In this paper we investigate the more realistic Feller model [30] that introduces an inhibitory reversal potential that bounds the process from below, given by

$$dY_t = \left(-\frac{Y_t}{\tau_y} + \mu_y\right)dt + \sigma_y \sqrt{Y_t - V_l} dW_t; \quad Y_0 = y_0 = 0, \quad (4)$$

where  $V_l < 0$  is the inhibitory reversal potential. In Fig. 1 the two processes are simulated in the absence of a threshold, using the same realization of a white noise for comparison. Parameters are chosen such that they have the same asymptotic mean and variance, see below. The Feller process (dark line) is seen never to go below the value of the reversal potential, whereas the OU process (grey line) does. The Feller process attains larger values more often. From Fig. 1 it appears that if the threshold value equals  $S_1$ , the interspike intervals would be nearly equal for the two processes, whereas for the threshold equal to  $S_2$  they would be different, and the Feller model would spike more often. This observation is valid under the assumption that the reset does not influence the process behavior qualitatively.

Analogously to the OU model, the parameters appearing in (1) and (4) can be divided into two groups: parameters characterizing the input,  $\mu_y$  and  $\sigma_y$ , and intrinsic parameters,  $\tau_y$ ,  $y_0$ ,  $V_l$ , and  $S_y$ , which describe the neuron irrespectively of the incoming signal [35]. The process (4) defines a

diffusion process, which can be transformed to the standard form of the Feller process [30] by setting  $X_t = Y_t - V_I$ . We obtain

$$dX_t = \left( -\frac{X_t}{\tau} + \mu \right) dt + \sigma \sqrt{X_t} dW_t; \quad X_0 = x_0 = -V_I, \quad (5)$$

where  $\mu = \mu_y - V_I/\tau_y$ ,  $\tau = \tau_y$ , and  $\sigma = \sigma_y$ . The interspike interval  $T$  is now identified with the FTP of the threshold,  $S = S_y - V_I$  by process  $X_t$ . Note by the comparison of Eqs. (3) and (5) that  $\sigma$  in (5) has not only different units but also a different interpretation. Whereas in (3) it is the amplitude of noise, in (5) it is only a proportion of the noise.

Following Feller's classification of boundaries (see, e.g., [36]), the boundary 0 is entrance if  $2\mu \geq \sigma^2$ , which is a reasonable assumption in the neuronal context that we will assume in the rest of the paper. In this case  $X_t$  lives on the positive real axis and (5) admits a stationary distribution. In the original parametrization the condition corresponds to  $\mu_y - V_I/\tau_y \geq \sigma_y^2/2$ , and  $Y_t > V_I$  for all  $t$ .

The transition density of process (5) is a noncentral chi-square distribution with conditional mean and variance

$$E[X_t | X_0 = x_0] = \mu\tau + (x_0 - \mu\tau)e^{-t/\tau}, \quad (6)$$

$$\text{var}[X_t | X_0 = x_0] = \frac{\mu\tau^2\sigma^2}{2}(1 - e^{-t/\tau})^2 + x_0\tau\sigma^2(1 - e^{-t/\tau})e^{-t/\tau}, \quad (7)$$

see, e.g., [31]. The asymptotic stationary distribution in the absence of a threshold is a gamma distribution with a shape parameter  $2\mu/\sigma^2$  and scale parameter  $\tau\sigma^2/2$ . Thus, the asymptotic mean and variance is  $E[X_t] = \mu\tau$  and  $\text{var}[X_t] = \mu\tau^2\sigma^2/2$ .

Again analogously to the OU model, two distinct firing regimes, usually called sub- and suprathreshold, can be established for the Feller model. In the suprathreshold regime, the asymptotic mean depolarization  $\mu\tau$  given by (6) is above the firing threshold  $S$  and the ISIs are relatively regular (deterministic firing—which means that the neuron is active also in the absence of noise). In the subthreshold regime,  $\mu\tau \ll S$ , and firing is caused only by random fluctuations of the depolarization (stochastic or Poissonian firing). The term “Poissonian firing” indicates that when the threshold is far above the steady-state depolarization  $\mu\tau$  (relatively to  $\sigma$ ), the firing achieves characteristics of a Poisson point process [37,38].

The FPT problem for model (5) has not been solved and only numerical ([39], section VI), [40] or simulation [41] techniques are available.

#### A. Approximations of the ISI moments

Closed form expressions for the mean and variance of  $T$  were calculated in [27,42]:

$$E[T] = \frac{S - x_0}{\mu} + \sum_{n=1}^{\infty} \frac{\tau(S^{n+1} - x_0^{n+1})}{(n+1) \prod_{i=0}^n (\mu\tau + i\tau\sigma^2/2)}, \quad (8)$$

$$\text{var}[T] = \frac{2E[T]S}{\mu} + \sum_{n=1}^{\infty} \frac{2\tau E[T]S^{n+1}}{(n+1) \prod_{i=1}^n (\mu\tau + i\tau\sigma^2/2)} - 2\tau^2 \sum_{n=0}^{\infty} \frac{(S^{n+1} - x_0^{n+1}) \left( \sum_{j=1}^n \frac{1}{j} \right)}{(n+1) \prod_{i=0}^n (\mu\tau + i\tau\sigma^2/2)} \quad (9)$$

in the case  $2\mu \geq \sigma^2$ . Define  $k = 2\mu/\sigma^2$ , then the assumption that 0 is entrance boundary implies  $k \geq 1$ . Rewriting (8) and (9) by substituting  $k$  yields

$$\begin{aligned} E[T] &= \frac{S - x_0}{\mu} + \tau \sum_{n=2}^{\infty} \frac{k^n \Gamma(k)}{n \Gamma(k+n)} \frac{(S^n - x_0^n)}{(\mu\tau)^n} \\ &\approx \frac{S - x_0}{\mu} + \tau \sum_{n=2}^{\infty} \frac{\Gamma(k)}{\Gamma(k+n+1)} \left( \frac{kS}{\mu\tau} \right)^n \\ &= \frac{S - x_0}{\mu} - \frac{\tau}{k} - \frac{S}{(k+1)\mu} + \tau \left( \frac{\mu\tau}{kS} \right)^k \exp \left\{ \frac{kS}{\mu\tau} \right\} \Gamma \left( \frac{kS}{\mu\tau}; k \right) \end{aligned} \quad (10)$$

since  $S/x_0 > 1$ . Here  $\Gamma(x; p) = \int_0^x t^{p-1} e^{-t} dt$  is the incomplete gamma function. The first term in (10) corresponds to the mean FPT for the Wiener process with drift  $\mu$ , so that the mean FPT of the Feller process is always larger. For finite  $k$ , that is for  $\sigma^2 > 0$ , or in suprathreshold regime, that is for  $\mu\tau > S$ , the sums are convergent. This agrees with the deterministic model, where firing only occurs if  $\mu\tau > S$ . In suprathreshold regime the convergence will be fast. A cruder approximation yields

$$E[T] \approx \tau \left( \frac{\mu\tau}{kS} \right)^k \exp \left\{ \frac{kS}{\mu\tau} \right\} \Gamma \left( \frac{kS}{\mu\tau}; k \right) - \frac{\tau}{k}. \quad (11)$$

Moreover,

$$\begin{aligned} \text{var}[T] &= 2E[T] \left[ \frac{S}{\mu} + \tau \sum_{n=2}^{\infty} \frac{\Gamma(k)}{n \Gamma(k+n)} \left( \frac{kS}{\mu\tau} \right)^n \right] \\ &\quad - 2\tau^2 \sum_{n=2}^{\infty} \frac{k^n \Gamma(k) \left( \sum_{j=1}^{n-1} \frac{1}{j} \right) (S^n - x_0^n)}{n \Gamma(k+n) (\mu\tau)^n} \\ &\approx 2E[T] \left( E[T] + \frac{x_0}{\mu} \right) - 2\tau^2 \sum_{n=2}^{\infty} \frac{\Gamma(k) \frac{1}{n} \left( \sum_{j=1}^{n-1} \frac{1}{j} \right)}{\Gamma(k+n)} \left( \frac{kS}{\mu\tau} \right)^n \\ &\approx 2E[T] \left( E[T] + \frac{x_0}{\mu} \right) + \frac{\tau S}{\mu} \end{aligned}$$

$$-\tau^2 \left(\frac{\mu\tau}{kS}\right)^{k-1} \exp\left\{\frac{kS}{\mu\tau}\right\} \Gamma\left(\frac{kS}{\mu\tau}; k\right), \quad (12)$$

where we have used the crude approximation  $\frac{1}{n}(\sum_{j=1}^{n-1} j) \approx 1/2$ , which is exact for  $n=2$  and  $n=3$ .

For comparison with the approximations of the ISI moments in the OU model calculated in [26], we also approximate (8) and (9) using the simpler expressions (20) and (21) derived below when (22) is fulfilled. The Taylor expansion of  $\log(e^{T/\tau})$  to second order around  $E[e^{T/\tau}]$  and taking expectations yields

$$\begin{aligned} E[T] &= \tau E[\log e^{T/\tau}] \approx \tau \log(E[e^{T/\tau}]) - \frac{\tau \text{var}[e^{T/\tau}]}{2E[e^{T/\tau}]^2} \\ &= \tau \log\left(\frac{\mu\tau - x_0}{\mu\tau - S}\right) \\ &\quad - \frac{\tau^2 \sigma^2 (S - x_0)(\mu\tau(S + x_0)/2 - x_0 S)}{2(\mu\tau - x_0)^2 [(\mu\tau - S)^2 + \tau\sigma^2(\mu\tau/2 - S)]}. \end{aligned} \quad (13)$$

Notice that the first term corresponds to the passage time in the deterministic model when  $\sigma^2=0$ . The mean FPT decreases as  $\sigma^2$  increases. Repeating the calculation for  $[\log(e^{T/\tau})]^2$  yields

$$\begin{aligned} E[T^2] &= \tau^2 E[(\log e^{T/\tau})^2] \approx \tau^2 [\log(E[e^{T/\tau}])]^2 \\ &\quad - [\log(E[e^{T/\tau}]) - 1] \frac{\tau^2 \text{var}[e^{T/\tau}]}{E[e^{T/\tau}]^2} \end{aligned} \quad (14)$$

so that

$$\begin{aligned} \text{var}[T] &\approx \frac{\tau^2 \text{var}[e^{T/\tau}]}{E[e^{T/\tau}]^2} \\ &= \frac{\tau^3 \sigma^2 (S - x_0)[\mu\tau(S + x_0)/2 - x_0 S]}{(\mu\tau - x_0)^2 [(\mu\tau - S)^2 + \tau\sigma^2(\mu\tau/2 - S)]} \end{aligned} \quad (15)$$

ignoring higher order terms.

### III. ESTIMATION OF THE INPUT PARAMETERS

Estimators of the parameters of model (5) from ISI data could be derived if the FPT distribution was known. Unfortunately this is not the case, and we therefore propose estimators based on moments of functionals of the FPT and on approximations of the distribution.

In the subthreshold regime the ISIs are approximately exponentially distributed, which suggests the corresponding maximum likelihood estimators. In the suprathreshold regime, where an approximate distribution is not available, we propose a moment estimator. It is not obvious how to determine the regime since  $\mu$  is unknown, but one could, e.g., perform an exponential distribution test. If an exponential distribution of ISIs is rejected, the suprathreshold estimation procedure is applied.

The data are assumed to be  $n$  observations of  $T$ :  $t_i, i=1, \dots, n$ . The model implies that the neuronal output forms a renewal process, so that the observations will be independent and identically distributed.

#### A. Subthreshold regime

If  $\mu\tau \ll S$  relative to  $\sigma$  the first-passage-time density function can be approximated by an exponential distribution [27,37,38,43]

$$f(t) = \frac{1}{\lambda} \exp(-t/\lambda), \quad (16)$$

where  $\lambda$  is the mean, and can therefore be approximated using (11) for large  $S$ :

$$\lambda = \tau \Gamma\left(\frac{2\mu}{\sigma^2}\right) \left(\frac{\tau\sigma^2}{2S}\right)^{2\mu/\sigma^2} \exp\left(\frac{2S}{\tau\sigma^2}\right) - \frac{\tau\sigma^2}{2\mu}, \quad (17)$$

since  $\lim_{x \rightarrow \infty} \Gamma(x; p) = \Gamma(p)$ . From this distribution it is only possible to determine  $\mu$  and  $\sigma$  up to the parameter function  $\lambda$ . The maximum likelihood estimator is

$$\hat{\lambda} = \bar{t} = \frac{1}{n} \sum_{i=1}^n t_i. \quad (18)$$

The asymptotic variance of the estimator estimated from the inverted Fisher information evaluated at the optimum is given by

$$\text{var}[\hat{\lambda}] = \frac{\hat{\lambda}^2}{n}. \quad (19)$$

#### B. Suprathreshold regime

To derive the moment estimators, a closed expression for  $E[e^{T/\tau}]$  is deduced requiring  $\mu\tau > S$  (suprathreshold), and an additional condition on  $\sigma$  defined below provides a closed expression for  $E[e^{2T/\tau}]$ , by defining suitable martingales and applying Doob's Optional-Stopping Theorem, in a similar way as done in [26,44] for the OU neuronal model. In the Appendix it is shown that

$$E[e^{T/\tau}] = \frac{\mu\tau - x_0}{\mu\tau - S} \quad (20)$$

if  $\mu\tau > S$ , and

$$E[e^{2T/\tau}] = \frac{(\mu\tau - x_0)^2 + \tau\sigma^2(\mu\tau/2 - x_0)}{(\mu\tau - S)^2 + \tau\sigma^2(\mu\tau/2 - S)}, \quad (21)$$

if

$$\frac{\tau\sigma^2}{2} \left( \sqrt{1 + \frac{2\mu}{\sigma^2}} - 1 \right) < (\mu\tau - S). \quad (22)$$

The restrictions on the parameter space is illustrated in Fig. 2 as a function of  $k=2\mu/\sigma^2$ ,  $k \geq 1$ . If  $\mu\tau > g(k)S$  then (22) is fulfilled, where  $g(k)=k/(k+1-\sqrt{k+1})$  is a strictly decreasing function of  $k$ . If  $\sigma \rightarrow 0$  for fixed  $\mu$ , then  $k \rightarrow \infty$  and  $g(k) \rightarrow 1$  (see Fig. 2), and in this limit only the suprathreshold regime is required. If  $k=1$  the condition is  $\mu\tau > g(1)S=S/(2-\sqrt{2})$ .

Straightforward estimators of  $E[e^{T/\tau}]$  and  $E[e^{2T/\tau}]$  are obtained from the empirical moments:

$$Z_1 = \hat{E}[e^{T/\tau}] = \frac{1}{n} \sum_{i=1}^n e^{t_i/\tau}, \quad (23)$$



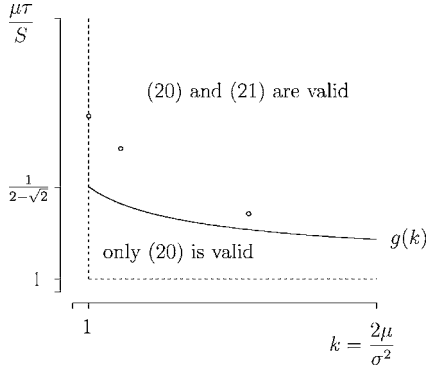


FIG. 2. Part of parameter space where (20) and (21) are valid, and thus where the estimators (25) and (26) are defined. The axes are nondimensionalized. The vertical axis indicates the ratio between asymptotic mean and threshold, the horizontal axis indicates the size of  $\sigma^2$  relative to  $\mu$ . The points are the different values used in the simulations.

$$Z_2 = \hat{E}[e^{2T/\tau}] = \frac{1}{n} \sum_{i=1}^n e^{2t_i/\tau}. \quad (24)$$

Moment estimators of the parameters, assuming that the data are in the allowed parameter region, are then obtained from Eqs. (20) and (21)

$$\hat{\mu} = \frac{SZ_1 - x_0}{\tau(Z_1 - 1)} \quad (25)$$

and

$$\hat{\sigma}^2 = \frac{(S - x_0)^2(Z_2 - Z_1^2)}{\tau[(Z_1 - 1)(SZ_2 - x_0) - (SZ_1 - x_0)(Z_2 - 1)/2]}. \quad (26)$$

Note that the asymptotic depolarization will always be estimated to be suprathreshold ( $\hat{\mu}\tau > S$ ). It follows from Eq. (25) that  $\hat{\mu} \approx S/\tau$  if  $Z_1 \approx Z_1 - 1$ . In other words, if  $t_i \gg \tau$  for some  $i$ , the data suggest that the model is not in the suprathreshold regime. This shows the importance of the time constant for determining the firing regimes.

#### IV. NUMERICAL RESULTS

Trajectories from the Feller process (5) in suprathreshold regime were simulated according to the Milstein scheme [41] with a stepsize of 0.01 msec for different input parameter values. In all simulations the values  $\tau=10$  msec,  $S=20$  mV,

and  $x_0=10$  mV were used, which corresponds to the values  $\tau_y=10$  msec,  $S_y=10$  mV,  $y_0=0$  mV, and  $V_I=-10$  mV in the untransformed process (4). The process was run until reaching a threshold  $S$  where the time was recorded. Three sets of parameter values for  $\mu$  and  $\sigma$  were considered. These parameter values are illustrated as points in Fig. 2. For each set of parameter values 1000 data sets of 100 ISIs were generated, and on each of them  $\mu$  and  $\sigma$  were estimated. In Table I the values used in the simulations and mean and standard deviation of the 1000 estimates obtained for each parameter and in each simulation are listed.

Normal quantile plots of the estimates are in Fig. 3. The estimator of  $\mu$  appears non-biased, with small variance and normally distributed, whereas the estimator of  $\sigma$  underestimates the correct value and is far from being normal, with a heavy tail to the right.

#### V. DIFFUSION APPROXIMATION APPROACH

In this section we will show that the interpretation of the parameters of the Feller process is not as straightforward as in the OU model. The diffusion model (4) can be obtained from the deterministic LIF model by adding a noise which restricts the state space from below. However, if we approach the problem from the LIF model with reversal potentials and discontinuous jumps, the conclusions are not as simple. The discrete model is given by equation

$$dX_t = -\frac{X_t}{\theta} + a(V_E - X_t)dP_t + i(X_t - V_I)dQ_t, \quad (27)$$

where  $1 > a > 0$  and  $-1 < i < 0$  are contributions of excitatory and inhibitory postsynaptic potentials driven by Poissonian inputs  $P$  and  $Q$  with intensities  $\lambda$  and  $\omega$ , respectively. The constant  $\theta > 0$  is the membrane time constant, and  $V_E > 0$  is the excitatory reversal potential. Under conditions suitable for the diffusion approximation, namely  $a \rightarrow 0$ ,  $i \rightarrow 0$ ,  $\lambda \rightarrow \infty$ ,  $\omega \rightarrow \infty$ , in such a way that  $\lambda a \rightarrow \alpha > 0$ ,  $\omega i \rightarrow \beta < 0$ ,  $\lambda a^2 \rightarrow 0$ , and  $\omega i^2 \rightarrow \sigma^2$ , the limiting diffusion process is

$$dY_t = \left[ \left( -\frac{1}{\theta} - \alpha + \beta \right) Y_t + \alpha V_E - \beta V_I \right] dt + \sigma \sqrt{Y_t - V_I} dW_t, \quad (28)$$

which can be written in the form

TABLE I. Parameter values for  $\mu$  and  $\sigma$  used in the simulations, and mean  $\pm$  standard deviation of the 1000 estimates  $\hat{\mu}$  and  $\hat{\sigma}$  obtained for each combination of parameter values.

$k$	$\mu \left( \frac{\text{mV}}{\text{msec}} \right)$	$\sigma \left( \frac{\text{mV}}{\text{msec}} \right)$	$\hat{\mu}$	$\hat{\sigma}$
1	4.5	3.0	4.34 $\pm$ 0.47	1.98 $\pm$ 0.45
2	4.0	2.0	3.92 $\pm$ 0.33	1.45 $\pm$ 0.27
6	3.0	1.0	2.98 $\pm$ 0.17	0.71 $\pm$ 0.10

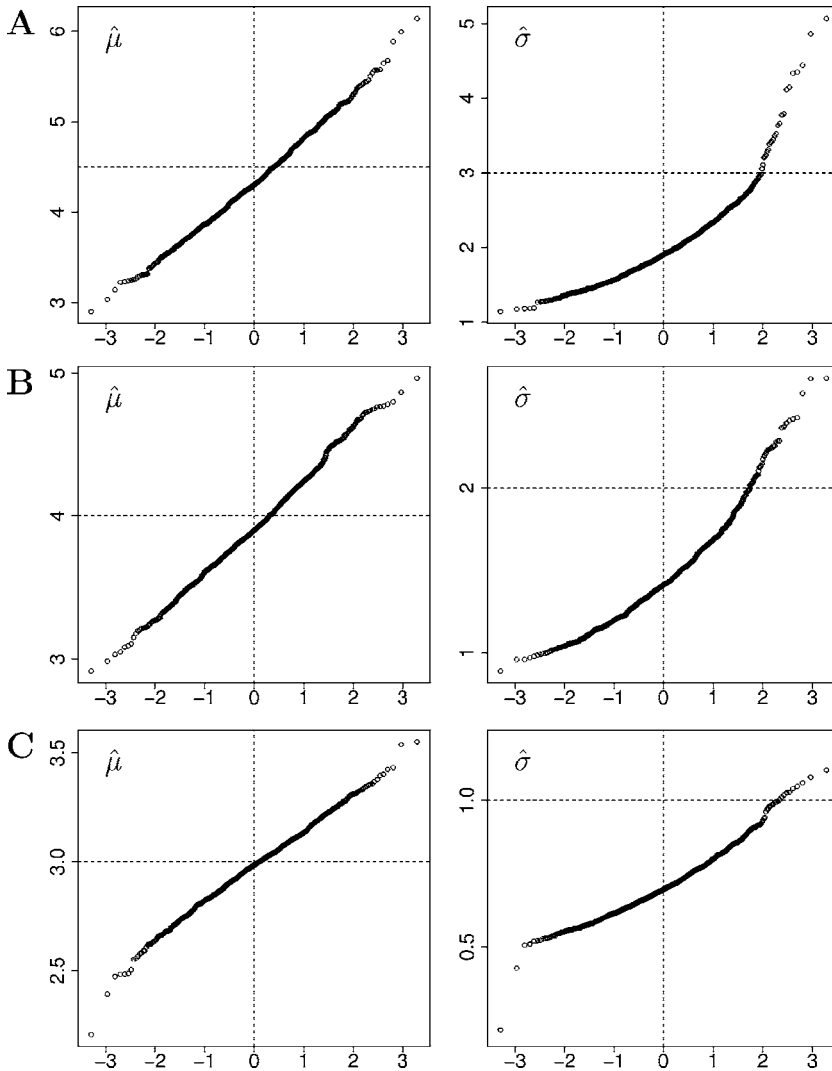


FIG. 3. Gaussian quantile plots (empirical versus theoretical quantiles) for the estimators (25) and (26) from the 1000 artificial data sets simulated with A:  $\mu = 4.5$  mV/msec and  $\sigma = 3$  mV/msec, B:  $\mu = 4$  mV/msec and  $\sigma = 2 \sqrt{\text{mV}/\sqrt{\text{msec}}}$ , and C:  $\mu = 3$  mV/msec and  $\sigma = 1$  mV/msec. In all simulations  $\tau = 10$  msec,  $S = 20$  mV, and  $x_0 = 10$  mV. The horizontal lines are set at the parameter values used in the simulations.

$$dY_t = \left( -\frac{1}{\tau} Y_t + \mu \right) dt + \sigma \sqrt{Y_t - V_t} dW_t, \quad (29)$$

where  $\tau = \theta / [1 + \theta(\alpha - \beta)]$  and  $\mu = \alpha V_E - \beta V_I$ . This makes the estimation procedure more complicated since  $\tau$  in Eq. (29) is no longer an intrinsic parameter as in the OU process given by Eq. (3).

This approach has some consequences for the results presented in the previous sections. It would be more appropriate to estimate not only  $\mu$  and  $\sigma$  in Eq. (5), but also the “membrane time constant”  $\tau$ , which now depends on the input. It follows from Eq. (29) that  $\tau < \theta$ , which may have a substantial effect on the model behavior. The smaller the value of  $\tau$ , the lower is the firing frequency. Thus, an increase in  $\mu$  is, at least partly, compensated by a decrease of “the membrane time constant.” This implies that the firing rate would increase less steeply with increasing excitation than in the OU model. Moreover, the OU model has been criticized for a too narrow coding range (range where firing frequency is above zero, but not below some physiologically acceptable level). From the above considerations follows that inclusion of the reversal potential not only has the desirable feature of restricting

the state-space, but also increases the coding range of the neuron.

## VI. DISCUSSION

The distribution of the FTP,  $T$ , through a constant boundary by a Feller process has been the subject of many studies, not only in neuronal modeling [45]. The distribution is probably unknown in analytical form. In this paper we propose moment estimators of the input parameters, in dependency on the sub- or suprathreshold conditions. Only the situation where the intrinsic parameters are assumed to be known is considered. The main contribution is the derivation of expressions for  $E[e^{T/\tau}]$  and  $E[e^{2T/\tau}]$ . This leads to simple and closed expressions for moment estimators of  $\mu$  and  $\sigma$  in the suprathreshold regime and when  $\sigma$  is small relative to the distance between the asymptotic depolarization and the threshold. The results obtained from the simulated data show that the proposed estimation procedure in the suprathreshold regime works well for  $\mu$ . The variance parameter  $\sigma$  is more difficult. This is in agreement with the results obtained for the OU model [26]. Moreover, approximations of  $E(T)$  and  $\text{var}(T)$  from exact formulas were presented.

Considering the stochastic diffusion models, the literature often makes reference to cortical neurons *in vivo* which are characterized by irregular spike sequences and many synaptic inputs with relatively small individual contributions to the membrane depolarization [15,18,19,46–49]. We have shown that having one or more ISIs in a studied sample which is several times longer than the membrane time constant,  $\tau$ , implies that the neuronal firing cannot be described by the Feller model in a suprathreshold regimen. The same conclusion was drawn for the OU model [26]. We therefore deduce that cortical neurons can be described by such a diffusion model in the suprathreshold regime only for short time periods.

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APPENDIX

Consider the Feller model for the membrane potential  $X$  at time  $t$

$$dX_t = \left( -\frac{X_t}{\tau} + \mu \right) dt + \sigma \sqrt{X_t} dW_t; \quad X_0 = x_0, \quad (A.1)$$

where  $\tau > 0$ ,  $2\mu \geq \sigma^2$ ,  $0 < x_0 < S$ , and  $S$  is the threshold value of the stopping time

$$T = \inf\{t > 0 : X_t \geq S\}. \quad (A.2)$$

We will now prove (20) and (21) using martingales, which will be defined using the conditional moments from the Feller process. In general, for a martingale  $M_t$  and a stopping time  $\mathcal{T}$ , we have  $E[M_{\mathcal{T} \wedge t}] = E[M_0]$ . For a subcase the stronger result holds (see [50], p. 221):

*Doob's Optional-Stopping Theorem.* Let  $\mathcal{T}$  be a stopping time and let  $M_t$  be a uniformly integrable martingale. Then  $E[M_{\mathcal{T}}] = E[M_0]$ .

For  $t > s$  the conditional moments are

$$E[\mu\tau - X_t | X_s] = (\mu\tau - X_s) e^{-(t-s)/\tau} \quad (A.3)$$

$$E[(\mu\tau - X_t)^2 | X_s] = (\mu\tau - X_s)^2 e^{-2(t-s)/\tau} + \frac{\mu\tau^2 \sigma^2}{2} (1 - e^{-(t-s)/\tau})^2 + \tau\sigma^2 X_s (1 - e^{-(t-s)/\tau}) e^{-(t-s)/\tau}. \quad (A.4)$$

Define the filtration  $\mathcal{F}_t = \sigma(X_s; 0 \leq s \leq t)$ , the sigma-algebra generated by  $X_s$  for  $0 \leq s \leq t$ . Then the process

$$M_t^{(1)} = (\mu\tau - X_t) e^{t/\tau}, \quad (A.5)$$

is a martingale with respect to  $\mathcal{F}_t$  by (A.3), and because  $E[M_t^{(1)}] < \infty$  since  $X_t$  follows a noncentral chi-square distribution. Therefore  $M_{T \wedge t}^{(1)}$ , the process  $M_t^{(1)}$  stopped at  $T$ , is also a martingale (see [50], p. 99). Moreover, if  $\mu\tau > S$

then  $M_{T \wedge t}^{(1)}$  is uniformly integrable. To show this it is enough to show that  $|M_{T \wedge t}^{(1)}| \leq Y$  for all  $t$ , for some non-negative variable  $Y$  with  $E[Y] < \infty$  (see [50], p. 128). We have  $E[M_0^{(1)}] = E[M_{T \wedge t}^{(1)}]$  so that

$$(\mu\tau - x_0) = E[(\mu\tau - X_{T \wedge t}) e^{T \wedge t / \tau}] \geq (\mu\tau - S) E[e^{T \wedge t / \tau}]. \quad (A.6)$$

When  $\mu\tau > S$  the coefficient to  $E[e^{T \wedge t / \tau}]$  is positive, and (A.6) can be rearranged to

$$\frac{\mu\tau - x_0}{\mu\tau - S} \geq E[e^{(T \wedge t) / \tau}]. \quad (A.7)$$

Taking limits on both sides we obtain

$$\frac{\mu\tau - x_0}{\mu\tau - S} \geq \lim_{t \rightarrow \infty} E[e^{T \wedge t / \tau}] = E[e^{T / \tau}] \quad (A.8)$$

by monotone convergence. The variable  $Y = \mu\tau e^{T/\tau}$  is thus a non-negative variable with  $E[Y] < \infty$ , and  $|M_{T \wedge t}^{(1)}| = (\mu\tau - X_{T \wedge t}) e^{T \wedge t / \tau} \leq \mu\tau e^{T / \tau} = Y$ . Doob's Optional-Stopping Theorem can therefore be applied to  $M_{T \wedge t}^{(1)}$  in suprathreshold regime yielding

$$\mu\tau = E[M_0^{(1)}] = E[M_T^{(1)}] = E[(\mu\tau - X_T) e^{T / \tau}] = (\mu\tau - S) E[e^{T / \tau}], \quad (A.9)$$

which finally yields (20). Now define

$$M_t^{(2)} = (\mu\tau - X_t)^2 e^{2t/\tau} + \tau\sigma^2 (\mu\tau - X_t) e^{2t/\tau} + \frac{\mu\tau^2 \sigma^2}{2} (1 - e^{2t/\tau}) \quad (A.10)$$

which is a martingale with respect to  $\mathcal{F}_t$ :

$$\begin{aligned}
 E[M_t^{(2)}|\mathcal{F}_s] &= E[M_t^{(2)}|X_s] = E\left[ (\mu\tau - X_t)^2 e^{2t/\tau} + \tau\sigma^2(\mu\tau - X_t)e^{2t/\tau} + \frac{\mu\tau^2\sigma^2}{2}(1 - e^{2t/\tau})|X_s \right] \\
 &= (\mu\tau - X_s)^2 e^{2s/\tau} + \frac{\mu\tau^2\sigma^2}{2}(e^{t/\tau} - e^{s/\tau})^2 + \tau\sigma^2 X_s(e^{t/\tau} - e^{s/\tau})e^{s/\tau} + \tau\sigma^2(\mu\tau - X_s)e^{(t+s)/\tau} + \frac{\mu\tau^2\sigma^2}{2}(1 - e^{2t/\tau}) \\
 &= (\mu\tau - X_s)^2 e^{2s/\tau} + \tau\sigma^2(\mu\tau - X_s)e^{2s/\tau} + \frac{\mu\tau^2\sigma^2}{2}(1 - e^{2s/\tau}) \\
 &= M_s^{(2)}
 \end{aligned}
 \tag{A.11}$$

using (A.4), and that all moments of the noncentral chi-square variable are finite, so that  $E[M_t^{(2)}] < \infty$ . Therefore

$$\begin{aligned}
 &(\mu\tau - x_0)^2 + \tau\sigma^2(\mu\tau - x_0) \\
 &= E[M_0^{(2)}] = E[M_{T\wedge t}^{(2)}] \\
 &= E[(\mu\tau - X_{T\wedge t})^2 e^{2T\wedge t/\tau} + \tau\sigma^2(\mu\tau/2 - X_{T\wedge t})e^{2T\wedge t/\tau} \\
 &\quad + \mu\tau^2\sigma^2/2] \\
 &\geq [(\mu\tau - S)^2 + \tau\sigma^2(\mu\tau/2 - S)]E[e^{2T\wedge t/\tau}] + \frac{\mu\tau^2\sigma^2}{2},
 \end{aligned}
 \tag{A.12}$$

where we have used that  $(\mu\tau - X_{T\wedge t})^2 > (\mu\tau - S)^2$  when  $\mu\tau > S$ . When

$$\frac{\tau\sigma^2}{2} \left( \sqrt{1 + \frac{2\mu}{\sigma^2}} - 1 \right) < (\mu\tau - S)
 \tag{A.13}$$

is fulfilled the coefficient to  $E[e^{2T\wedge t/\tau}]$  is positive, and (A.12) can be rearranged to

$$\frac{(\mu\tau - x_0)^2 + \tau\sigma^2(\mu\tau/2 - x_0)}{(\mu\tau - S)^2 + \tau\sigma^2(\mu\tau/2 - S)} \geq E[e^{2(T\wedge t)/\tau}].
 \tag{A.14}$$

Taking limits on both sides we obtain

$$\frac{(\mu\tau - x_0)^2 + \tau\sigma^2(\mu\tau/2 - x_0)}{(\mu\tau - S)^2 + \tau\sigma^2(\mu\tau/2 - S)} \geq \lim_{t \rightarrow \infty} E[e^{2(T\wedge t)/\tau}] = E[e^{2T/\tau}]
 \tag{A.15}$$

by monotone convergence. Taking  $Y = [(\mu\tau)^2 + \mu\tau^2\sigma^2/2]e^{2T/\tau} + \mu\tau^2\sigma^2/2$ , which is non-negative, we obtain the uniform integrability since  $|M_{T\wedge t}^{(2)}| \leq Y$  and  $E[Y] < \infty$  if condition (A.13) is fulfilled. Doob's Optional-Stopping Theorem can therefore be applied to  $M_{T\wedge t}^{(2)}$  which finally yields (21).

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