# New parameter relationships determined via stochastic ordering for spike activity in a reversal potential neural model

Laura Sacerdote[(1)], Charles, E. Smith[(2)]
[(1)]Dept. of Mathematics, University of Torino
[(2)]Dept. of Statistics; North Carolina State University

**Abstract.** The Feller diffusion process is a more general and realistic model for the subthreshold membrane potential of a neuron than the Ornstein-Uhlenbeck process. However a consequence of this increased realism is an increased difficulty in interpreting the dependence of the spike times on the parameter values. In a few instances, mainly for the case of deterministic crossings, the trajectory of the mean membrane potential provides intuition for the role of the parameters. We make use of a new approach to establish the dependence of spikes times on the model parameters, namely by ordering the first passage times. We discuss in detail four scenarios for the Feller model. These cases either confirm the intuition from the mean trajectory plots, or provide a method for the instances where the former approach cannot be used. The functional dependence among the model parameters, (e.g. membrane time constant, reversal potential, etc.) resulting from the ordering theorem, appears to be a new and useful way to analyze FPTs.

## 1 Introduction

The Feller process has been proposed as a model of the subthreshold membrane behavior by various authors (cf. [2], [3], [1], [5]). A realistic advantage of this model with respect to the Ornstein-Uhlenbeck process, is that the introduction of state-dependent changes in depolarization constrains the membrane potential values to a finite interval. No procedure exists to obtain closed form expressions for the firing distribution, so both the models

have been in many ways investigated. Numerical methods have been used to study the firing times corresponding to different choices of the parameters characterizing the model in ([6],[1]) while in ([4]) firing times obtained from this model are compared with that obtained from the Ornstein-Uhlenbeck model. However numerical methods are of little help if one is interested in determining the functional dependence of spikes times on the parameters in the model.

The simplicity of the Ornstein-Uhlenbeck model can help the intuition if one wish understand the effect of a parameter value on the spikes times while this approach cannot be employed in the case of the Feller model since the complexity of the used mathematical process used limits to a few instances the use of this method. Indeed, as we illustrate in Section 2 by means of some examples, the use of mean trajectory plots is useful in understanding the dependences from the parameters of the Feller model only if spikes correspond to the so called "deterministic crossings" (cf. [9]).

Here we propose a new approach to the study of parameter dependence of spikes times. We make use of a theorem proved in ([7]) to order first passage times corresponding to different processes. In Section 3 we re-state this theorem in the particular instance of the comparison of first passage times of two Feller processes characterized by two different set of values of the parameters.

In Section 4 we analyze, with the help of the aforementioned theorem, the dependence of spikes times on the values of the inhibitory reversal potential, the membrane spontaneous decay time constant, the noise characterizing the model and the net excitation impinging upon the neuron. Some figures corresponding to biologically significative choices for the parameters illustrate the results. Furthermore we determine, making use of stochastic ordering relationship, different sets of values for the parameters corresponding to the same spike distribution. For example we can prove in this way that a percent change of the coefficient describing the noise of the membrane can be balanced by a corresponding percent variation of the boundary, reversal potential and net excitation values.

## 2 The model

The classical Stein model ([10]) for the description of the membrane potential, adapted to consider inhibitory reversal potentials, is given by the

stochastic differential equation (SDE) (cf.[3]):

$$\begin{aligned} dY &= \tfrac{-Y}{\tau}dt + \alpha_E dN^+ + (\varepsilon(Y - V_I) + \xi\sqrt{Y - V_I})dN^-, \\ Y(0) &= y_0 > V_I \end{aligned} \tag{1}$$

where $\tau > 0, \alpha_E > 0, < -1 < \varepsilon < 0, V_I < 0$ are constants and $N^+ = \{N^+(t), t \geq 0\}, N^- = \{N^-(t), t \geq 0\}$ are two independent homogeneous Poisson processes with intensities $\lambda, \omega$ respectively. The constant $V_I$ represents the inhibitory reversal potential, $\alpha$ is the size of the excitatory postsynaptic potential (EPSP) and $\varepsilon$ characterizes the size of the inhibitory postsynaptic potential (IPSP).

$\xi$ is a random variable, independent of $N^+, N^-$, defined at an appropriate interval in order to avoid a jump to values below $V_I$, and for which $E(\xi) = 0$. The corresponding diffusion model, known as the Feller model (cf. [4]) is defined by the SDE:

$$\begin{aligned} dY_t &= (\tfrac{-Y_t}{\theta} + \mu)dt + \sigma\sqrt{Y_t - V_I}dW_t, \\ Y(0) &= y_0 > V_I \end{aligned} \tag{2}$$

where

$$\theta = \frac{\tau}{1 - \varepsilon\omega\tau} < \tau \tag{3a}$$

and $\mu, \sigma > 0$ are new constants which follow from a suitable limiting procedure performed on a sequence of models (1). The mean trajectory of the model is

$$E(Y_t \,|Y_0 = 0) = \mu\theta\left(1 - e^{-\frac{t}{\theta}}\right) \tag{4}$$

and the variance of the trajectories is

$$Var(Y_t \,|Y_0 = 0) = \frac{\sigma^2\theta V_I}{2}\left(1 - e^{-\frac{2t}{\theta}}\right) + \frac{\sigma^2\theta^2\mu}{2}\left(1 - e^{-\frac{t}{\theta}}\right)^2. \tag{5}$$

The distribution of spike times, that corresponds mathematically to the first passage times (FPT) of the process (2) through a boundary , cannot be written in closed form and the model is generally analyzed with the help of numerical procedures (cf. [1]). The first moments of the FPT can be written in closed form (cf. [1]) but the complexity of these expressions makes it difficult to understand any functional relationship between FPTs and parameters values. A first approach to determining the dependency of FPT on the individual parameters comes from considering mean trajectory

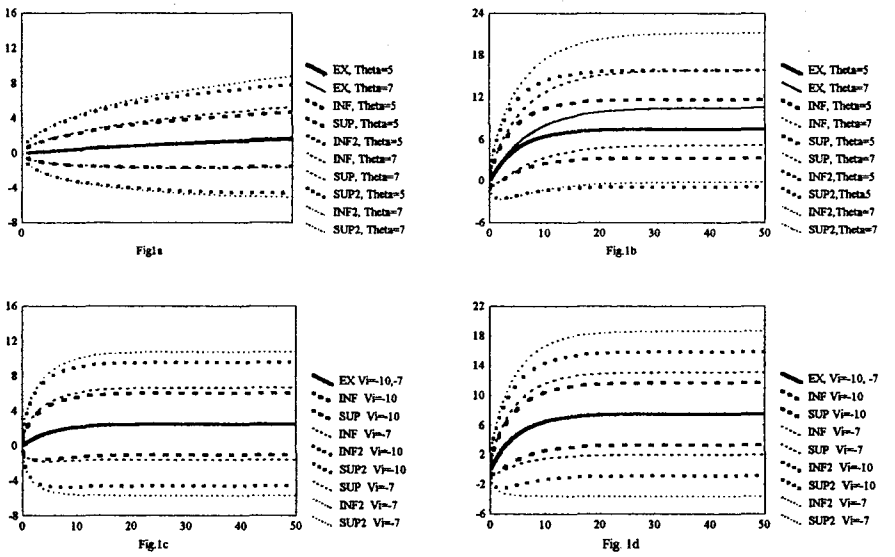


Figure 1:

plots, obtained by plotting (4) as a function of $t$ and consideringthe bands obtained adding $\pm\sqrt{Var(Y_t\,|Y_0=0)}$, or $\pm 2\sqrt{Var(Y_t\,|Y_0=0)}$, to its value. Figs. 1 a-d are examples of these plots obtained by varying the parameters $\theta, \mu$ and $V_I$ respectively. The values used for these parameters are in a biologically reasonable range (cf. [4] and references quoted therein). For the case considered in Fig. 1a, crossing of a boundary in $S = 10$ is due to the noise, while for the case of Fig 1b there are deterministic crossings when $\theta = 7$. In this last instance we can easily deduce from Fig. 1b that FPT corresponding to higher values of $\theta$ are faster. However an analogous approach cannot be used for the instances considered in Fig. 1a, since crossings are due to the noise and the shapes of the mean trajectory looks quite similar.

A similar problem arises when one attempts to understand the dependency of FPT's on $V_I$. Some authors propose a value of $-10$ mV ([4] and references cited therein) while others suggest a value of $-7$ mV, but it is not easy to understand the implications of these two choices on firing times. Indeed, as shown by the mean trajectory plots in Figs.1c and 1d, (when $\mu = 1.5$ mV, $\sigma^2 = 4$ mVms$^{-1}$, $\theta = 5$ ms or 7 ms respectively), for these in-

stances, the boundary crossings are caused by the noise. Furthermore use of analytical expressions of (4) and (5) becomes difficult as parameters values are changed simultaneously. Hence the use of an alternative approach to this analysis seems desiderable to improve the understanding of this model. In the next Section we consider a method to compare spikes times as the parameter values change.

# 3 Stochastic ordering of FPT

Theorems useful for ordering first passage times of diffusion processes through boundaries have been recently considered in ([7]). Here we rewrite a Theorem and a Corollary proved in that paper, with reference to the particular equations holding for the reversal potential model of the neural activity discussed in Section 2. We refer to the cited paper for the proof and additional comments.

**Theorem 1** *Consider two diffusions $Y_1, Y_2$ satisfying the SDE (2) and characterized by parameters $(\theta_1, \mu_1, \sigma_1, V_I^1, S, x_0)$ and $(\theta_2, \mu_2, \sigma_2, V_I^2, S, x_0)$ respectively. Let the parameters satisfy one of the three following cases:*

$$a. \begin{cases} \theta_1 \geq \theta_2 \\ \frac{2}{\sigma_1^2}\left(\mu_1 - \frac{V_I^1}{\theta_1}\right) \geq \frac{2}{\sigma_2^2}\left(\mu_2 - \frac{V_I^2}{\theta_2}\right) \end{cases} \tag{6}$$

*or*

$$b. \begin{cases} \theta_1 < \theta_2, \\ \frac{2}{\sigma_1^2}\left(\mu_1 - \frac{V_I^1}{\theta_1}\right) < \frac{2}{\sigma_2^2}\left(\mu_2 - \frac{V_I^2}{\theta_2}\right) \\ S \leq \min\left(\frac{\left(\mu_1 - \frac{V_I^1}{\theta_1}\right) - \frac{2\sigma_1^2}{\sigma_2^2}\left(\mu_2 - \frac{V_I^2}{\theta_2}\right)}{2\left(\frac{1}{2\theta_1} - \frac{1}{2\theta_2}\right)} + V_I^{(1)}, \frac{\frac{\sigma_2^2}{\sigma_1^2}\left(\mu_1 - \frac{V_I^1}{\theta_1}\right) - \left(\mu_2 - \frac{V_I^2}{\theta_2}\right)}{2\left(\frac{1}{2\theta_1} - \frac{1}{2\theta_2}\right)} + V_I^{(2)}\right) \end{cases} \tag{7}$$

*then the first passage times $T_{Y_1}(S\,|y_0)$ and $T_{Y_2}(S\,|y_0)$ of the processes $Y_1, Y_2$ originating at $Y_i = y_0, i = 1, 2$, satisfy the inequality:*

$$T_{Y_1}(S\,|y_0) \leq T_{Y_2}(S\,|y_0). \tag{8}$$

*with probability one. Furthermore the inequality (8) holds if*

$$c. \begin{cases} \theta_1 \geq \theta_2, \\ \frac{2}{\sigma_1^2}\left(\mu_1 - \frac{V_I^1}{\theta_1}\right) < \frac{2}{\sigma_2^2}\left(\mu_2 - \frac{V_I^2}{\theta_2}\right) \end{cases} \tag{9}$$

*and the process is constrained by a reflecting boundary in*

$$y = \max\left(\frac{\frac{2\sigma_1^2}{\sigma_2^2}\frac{\mu_2\theta_2 - V_I^2}{\theta_2} - \frac{\mu_1\theta_1 - V_I^1}{\theta_1}}{\left(\frac{1}{\theta_1} - \frac{1}{\theta_2}\right)} + V_I^{(1)}, \frac{\frac{\mu_2\theta_2 - V_I^2}{\theta_2} - \frac{\sigma_2^2}{\sigma_1^2}\frac{\mu_1\theta_1 - V_I^1}{\theta_1}}{\left(\frac{1}{\theta_1} - \frac{1}{\theta_2}\right)} + V_I^{(2)}\right) \quad (10)$$

We can use relationships (6), ( 7), (9) to study the effect of changes in the parameters values on the model features. In particular we can compare the distributions of spikes times since a relation that holds with probability one holds for the distributions (cf. [8]). Hence by means of this theorem we can determine ranges of parameters values that increase the spiking times.

Note that condition (10) changes the hypothesis of the model by introducing a boundary that cannot be justified from a biological point of view. However as we will see in next section, since the conditions of the theorem are only sufficient„ in some instances (8) holds on intervals larger than that determined by means of the theorem. In particular condition (10) can be removed in various instances and the result can be used for the models under consideration.

Another approach to the analysis of the dependence of spiking times consists of determining possible values for the parameters of the model that produce equal first passage times. This study can be carried out by means of a Corollary to Theorem 1 that we write here in the particular case of two Feller models characterized by parameters $\left(\theta_1, \mu_1, \sigma_1, V_I^1, S_1, y_0^{(1)}\right)$ and $\left(\theta_2, \mu_2, \sigma_2, V_I^2, S_2, y_0^{(2)}\right)$.

**Corollary 2** *Let*

$$\begin{aligned} g_i(y) &= \frac{2}{\sigma_i}\sqrt{y - V_I^{(i)}}, \qquad (11a) \\ i &= 1, 2 \end{aligned}$$

*if*

$$\begin{aligned} &a.\ \theta_1 = \theta_2 \\ &b.\ S_2 = \frac{\sigma_2^2}{\sigma_1^2}(S_1 - V_I^{(1)}) + V_I^{(2)} \\ &c.\ y_0^{(2)} = \frac{\sigma_2^2}{\sigma_1^2}(y_0^{(1)} - V_I^{(1)}) + V_I^{(2)} \qquad (12) \\ &d.\ \frac{2}{\sigma_1^2}\left(\mu_1 - \frac{V_I^{(1)}}{\theta_1}\right) = \frac{2}{\sigma_2^2}\left(\mu_2 - \frac{V_I^{(2)}}{\theta_2}\right) \end{aligned}$$

*then*

$$T_{Y_1}(S_1 \left| y_0^{(1)}\right.) = T_{Y_2}(S_2 \left| y_0^{(2)}\right.). \qquad (13)$$

## 4 Results and discussion

We consider here some particular choices of parameters values for which (6) and ( 7) or (9) hold. In all the instances we assume $S = 10$ mV, $y_0 = 0$ mV, if we do not explicitly state different values for the boundary and the initial value.

The first scenario we analyze is the dependence of spike times on $\theta$, a constant that is function of the membrane time constant $\tau$ and of the IPSPs via (3a). Consider two models characterized by equals values for all parameters except $\theta_1 > \theta_2$. In this case condition (9) is verified. Hence first passage times are inversely proportional to the value of $\theta$ for a model with a reflecting boundary at $y$. However, if the absorbing boundary $S$ is far enough from $V_I$ , the presence of the reflecting boundary (10) do not effect the order relationships between FPTs and can be disregarded. Hence (8) holds for the original model. In Fig. 2a we give an example of some instances where (8) holds. We plot the first passage times distribution for $\theta = 5, 7$ ms and $\sigma^2 = 0.4$ mVms$^{-1}$, $V_I = -10$ mV. Fig. 2b exemplifies a case where the effect of (10) cannot be disregarded. Indeed high depolarization values of the membrane potential become attainable because of the smaller value of $V_I = -7$ mV and of the larger noise coefficient $\sigma^2 = 1.6$ mVms$^{-1}$. In this instance the spikes times are not ordered, for example if $\theta = 3.5$ ms and $\theta = 8$ ms as shown in Fig. 2b.

The second scenario considers the effect of decreasing the value of $V_I$. Making use of (6) with all the parameters equal in the two models except $V_I^{(1)} < V_I^{(2)}$, the FPT for the first model is smaller than for the second. Note that this result cannot be easily explained with intuition. Indeed we have smaller firing times when we consider a larger diffusion interval for the membrane potential process. However we enphasize that the role of $V_I$ is more complex since it changes the IPSP effect on the membrane potential behavior. In Fig. 3 we illustrate by means of two different examples the theoretical results obtained from (6) regarding the role of $V_I$ . The two curves on the top compare FPT distribution of two models characterized by $V_I = -10$ mV or $-7$ mV, $\mu = 1$ mV, $\sigma^2 = 0.4$ mVms$^{-1}$, $\theta = 5$ ms while the two curves at the bottom consider the same choices of values except $\mu = 0$ mV. Note that both sets of the parameters the FPT can be ordered but when one introduces a net positive excitation the distance between the two curves decreases. Hence in this instance the model is less effected by reversal potential values.

The next situation considers the dependence on $\mu$. Use of (6) in this instance confirms our intuition. Indeed a larger net excitation implies smaller

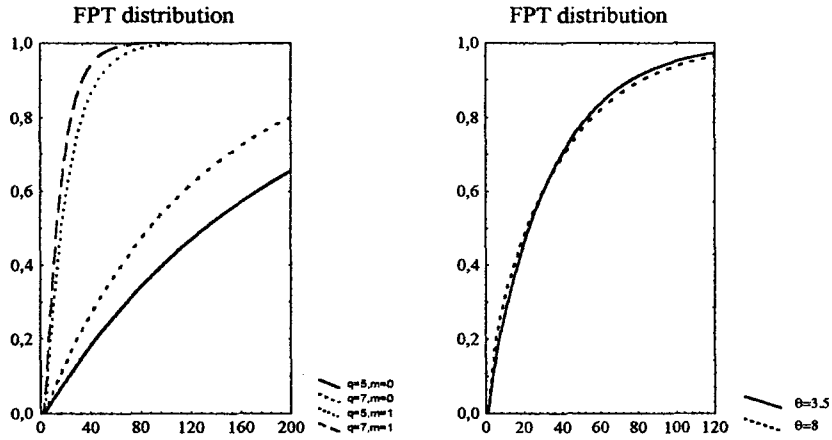


Fig. 2a

Fig. 2b

Figure 2:

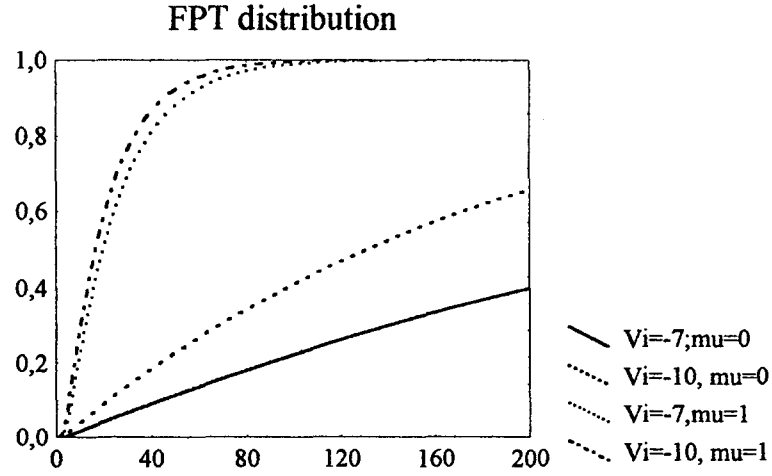


Figure 3:

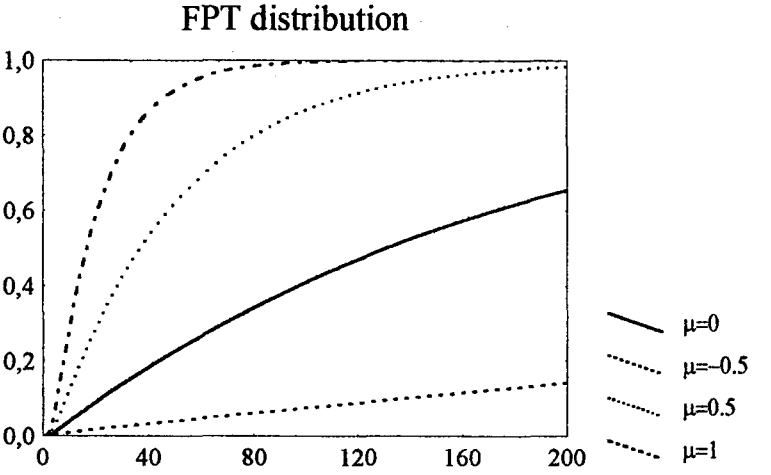


Figure 4:

spiking times if the other parameters are kept equal. Fig. 4 illustrates this result when $\theta = 5$ ms, $\sigma^2 = 0.4$ mVms$^{-1}$, $V_I = -10$ mV and $\mu = 1, 0, -1$ mV respectively.

Finally we consider the dependency of FPT on the noise parameter $\sigma^2$. Since following Feller's classification of boundaries, for $\mu - V_I/\theta \geq \sigma^2/2$ the inferior boundary is entrance, in order to keep the realism of the model, $\sigma^2$ must satisfy this inequality. In this instance if $\sigma_1^2 < \sigma_2^2$, the FPT of the first model is faster than the second. This confirms the intuition that the noise facilitates the crossings.

In these four scenarios we have tried to understand the effect of the changing an individual parameter. However the Theorem can be used in more complex circumstances when more than one parameter varies and the intuition from the mean trajectories can give misleading results.

Finally we analyze an application of the Corollary. We consider the following instance: assume we have determined the value of the infinitesimal variance with a possible error of 10%. We want understand if this error can be balanced by a variation in the values of the other parameters to obtain FPTs that are equal. Making use of the Corollary it is easy to see that if corresponding to an increased value of $\sigma^2$, we increase, by the same percentage, the coefficient $\mu$, the boundary value and decrease the reversal potential, the FPT distribution cannot change. The curve in Fig. 5 can be

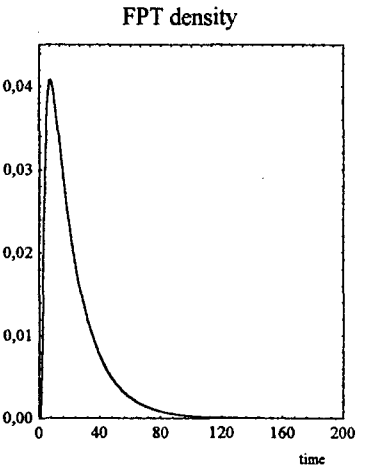


Fig. 5a

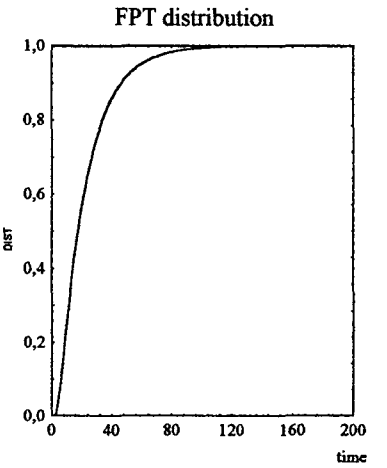


Fig. 5b

Figure 5:

drawn either with the choice for the parameters $\sigma^2 = 0.4$ mV, $\theta = 5$ ms, $\mu = 1$ mV, $V_I = -10$ mV, $S = 10$ mV and $y_0 = 0$ mV or with another choice $\sigma^2 = 0.44$ mV, $\theta = 5$ ms, $\mu = 1.1$ mV, $V_I = -11$ mV, $S = 11$ mV and $y_0 = 0$ mV. Making use of the Corollary we could determine many other instances that give rise to the same shape. Hence we cannot uniquely determine parameters values from measures of spike times.

# 5 Conclusion

The use of stochastic ordering between FPTs helps to understand the dependence of spike times on the parameters characterizing the phenomena when one consider complex models. Some of the results seems intuitive but in various instances a simple approach can give rise to misleading results. A different use of theorems in ([7]) permit the comparison, via stochastic order of different diffusion models proposed in literature, such as the Ornstein-Uhlenbeck and the Feller model, and this will be the content of a forthcoming paper where we plan to analyze the model with inhibitory and excitatory reversal potentials proposed in ([5]).

**Acknowledgement 3** *The work for this paper was done when the first*

*named author was visiting NCSU at Raleigh, NC. She would like to thank her colleagues at the Department of Statistics for their kind hospitality. Work supported by C.N.R. contract 97.00935.CT01 and by INDAM.*

## References

[1] Giorno, V., Lánský, P., Nobile, A.G. and Ricciardi, L.M. (1988). Diffusion approximation and first-passage-time problem for a model neuron. III. A birth-and-death approach, Biol. Cybern. **58**, 387-404.

[2] Hanson, F.B. and Tuckwell, H.C. (1983) Diffusion approximation for neuronal activity including synaptic reversal potentials.J. Theor. Neurobiol. **2**, 127-153.

[3] Lánský, P. and Lánská, V. (1987) Diffusion approximations of the neuronal model with synaptic reversal potentials. Biol. Cybern. **56**, 19-26.

[4] Lánský, P., Sacerdote, L. and Tomassetti, F. (1995) On the comparison of Feller and Ornstein-Uhlenbeck models for neural activity. Biol. Cybern. **73**, 457-465.

[5] Lánská, V., Lánský, P. and Smith, C.E. (1994) Synaptic transmission in a diffusion model for neural activity. J.Theor. Biol. **166**, 393-406.

[6] Ricciardi, L.M. and Sacerdote, L., (1979) The Ornstein-Uhlenbeck process as a model for neuronal activity, Biol. Cybern. **35**, 1-9.

[7] Sacerdote, L. and Smith, C.E. (1999) Stochastic ordering for first passage times of diffusion processes through boundaries. Mimeo Series 2515, Institute of Statistics, North Carolina State University, Raleigh, NC, USA.

[8] Shaked, M. and Shanthikumar, J., G.(1988) On the 1st passage times of pure jump-processes. J.Appl. Prob. **20** (2), 427-446.

[9] Smith, C.E. (1992) A Heuristic approach to stochastic models of single neurons. In: Neural Nets: Foundations and Applications. 561-587, Academic Press.

[10] Stein, R.B. (1965) A theoretical analysis of neuronal variability. Biophys. J. **5**, 173-195.