A qualitative comparison of some diffusion models for neural activity via stochastic ordering

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Abstract. A number of diffusion processes have been proposed as a continuous analog of Stein’s model for the subthreshold membrane potential of a neuron. Interspike intervals are then described as the first-passage-time of the corresponding diffusion model through a suitable threshold. Various biological considerations suggest the use of more sophisticated models in lieu of the Ornstein-Uhlenbeck model. However, the advantages of the additional complexity are not always clear. Comparisons among different models generally use numerical methods in specific examples without a general sensitivity analysis on the role of the model parameters. Here, we compare the distribution of interspike intervals from different models using the method of stochastic ordering. The qualitative comparison of the role of each parameter extends the results obtained from numerical simulations. One result on neurons with high positive net excitation is that the reversal potential models considered do not greatly differ from the Ornstein-Uhlenbeck model. For neurons with increased inhibition, the models give greater differences among the interspike interval distributions. In particular, when the mean trajectories are matched, the Feller model gives shorter times than the Ornstein-Uhlenbeck model but longer times than our double reversal potential model.

1 Introduction

Stochastic models of spike initiation in a single neuron have been developed and studied since the 1960s (for a general review, see Tuckwell 1988). In most of these models, the membrane potential is described by a one-dimensional stochastic process \( X = \{X(t), t \geq 0 \} \). This corresponds to a one-compartment or lumped model for the membrane voltage at the spike initiation site, i.e. a first-order differential equation with a noisy forcing function. Depending on the type of neuron being studied and the degree of biophysical realism desired, the differential equation may be linear, a simple R-C circuit, or include a dependence of the inputs on the membrane voltage. The input timings are often taken to be homogeneous Poisson processes. A spike is produced when the membrane voltage exceeds, for the first time, a voltage threshold \( \mathcal{S} \); then, the membrane potential resets to \( x_0 \), taken here to be the resting value, i.e. \( x_0 = 0 \). Mathematically, the interspike intervals (ISI) are modeled as first-passage-times (FPT) defined as \( T_{\mathcal{S}} = \inf\{t \geq 0; X(t) \geq \mathcal{S}, X(0) = x_0 \} \). Histograms of ISI and mean firing times have as a mathematical counterpart the FPT density function and mean FPT. This situation represents spontaneous discharge or the maintained response to a constant stimulus. The linear first-order Poisson-driven SDE is known as Stein’s model (Stein 1965) and serves as the starting point for many diffusion approximations and nonlinear extensions. Under the limit of many synaptic inputs, each producing a change in the membrane potential (post-synaptic potential or PSP), which is small, the resultant process \( X(t) \) becomes a diffusion process, which is mathematically more tractable. The diffusion analog of the Stein’s model is the Ornstein-Uhlenbeck (O.U.) process.

A more biologically realistic characterization of the effects of the synaptic inputs was developed by Tuckwell (1979). This extension is known as a reversal potential model and allows the PSPs to decrease in amplitude as they approach an equilibrium or reversal potential. The PSPs and corresponding reversal potentials may be positive (excitatory) or negative (inhibitory) depending upon the ions involved (Schmidt 1984).

The diffusion limits of Poisson-driven reversal potential models have been put in a general mathematical framework (Kallianpur and Wolpert 1987). We consider two particular reversal potential diffusion models. The first has a single, inhibitory, reversal potential and is known as the Feller model (e.g. Lánský et al. 1995). The second has both an excitatory and an inhibitory reversal potential and is denoted here as the LLS model (Lánská

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et al. 1994). We compare the FPTs of the O.U., Feller and LLS models as a function of the associated parameters. Many analytic or numerical FPT results are known for the O.U. process, fewer results are available for the Feller model and only moments are available for the LLS model (e.g. Ricciardi and Sato 1989; Lánský et al. 1994).

In Sect. 2, we describe the three models we will use and their basic properties. The criterion used for the choice of the parameters is discussed in Sect. 3. The aim of this paper is to complete the comparison study between Feller and O.U. models begun by Lánský et al. (1995) by means of computational examples. However, here we enlarge the comparison by considering the LLS model. Furthermore, we investigate differences and similarities among different models mainly from an intuitive viewpoint based on the form of the corresponding SDEs. To pursue this task, we use the method of stochastic ordering (Sacerdote and Smith 1999) and also the heuristic approach discussed by Smith (1992), distinguishing three different ranges for the parameters values corresponding to deterministic crossings, Poisson approximation crossings and an intermediate range. The theorem on stochastic ordering of FPTs, proved by Sacerdote and Smith (1999), allows comparisons in the intermediate range that are not otherwise available. A short review of the heuristic methods and of the ordering theorem are enunciated in Sect. 3. Finally, the theorem is used in Sects. 4 and 5 to compare the properties of the above mentioned models.

2 The models

Here, we introduce the main properties of the diffusion approximations of Stein’s model (Stein 1965) for the membrane potential behavior. The main features of Stein’s model are a linear summation of synaptic inputs and a spontaneous exponential decay of the membrane potential. While the latter property is transferred in the continuous approximations, the summation of synaptic inputs may become nonlinear. Diffusion approximations have been extensively discussed in the literature (Lánský and Sato and references therein) and we refer here directly to the continuous models. A common characteristic of the considered models is the assumption that the changes of the membrane potential $X(t)$ caused by the impinging PSPs can be described by means of a SDE

$$dX(t) = b(X(t)) \, dt + \sqrt{a(X(t))} \, dW(t), \quad X(0) = 0 .$$

(2.1)

Here, $W(t)$ is a standard Wiener process and the coefficients $b(x)$ and $a(x)$ are the conditional first and second moments, respectively, of the increments $\Delta X(t) = X(t + \Delta t) - X(t)$ in an infinitesimal time interval $\Delta t$:

$$b(x) = \lim_{\Delta t \to 0} E\{\Delta X(t)|X(t) = x\}/\Delta t ,$$

(2.2)

$$a(x) = \lim_{\Delta t \to 0} E\{(\Delta X(t))^2|X(t) = x\}/\Delta t ,$$

(2.3)

and are known as the drift and infinitesimal variance (diffusion coefficient), respectively. More detailed information on diffusion processes can be found in the book of Karlin and Taylor (1981). Here, $b(x)$ and $a(x)$ are assumed to be independent in time in order to consider the series of ISIs as a renewal process.

The three models being considered here differ in the choice for the diffusion coefficients $b(x)$ and $a(x)$, corresponding to different hypotheses about the effect of PSPs on the evolution of the membrane potential.

2.1 The Ornstein-Uhlenbeck model

This model arises as the continuous limit of the original Stein model. One further assumes that the effect of these PSPs is independent on the state of the membrane potential, and that in the absence of PSPs the membrane potential spontaneously decays to the resting level, assumed to be zero.

The drift and diffusion coefficients characterizing this model are:

$$b(x) = -\frac{x}{\theta} + \mu ,$$

(2.4)

$$a(x) = \sigma_{O.U.}^2 ,$$

(2.5)

where $\theta > 0$ reflects the spontaneous decay of the membrane potential, $\mu$ and $\sigma_{O.U.} > 0$ are two constants connected with the mean net excitation caused by PSPs and with the noise caused by the Poisson frequency of impinging PSPs, respectively (Lánský 1984 for more details). The mean trajectory of the modeled potential is:

$$EX(t) = \mu \theta \left(1 - e^{-t/\theta}\right) ,$$

(2.6)

and its variance is:

$$\text{Var} X(t) = \frac{\theta}{2} \sigma_{O.U.}^2 \left(1 - e^{-2t/\theta}\right) .$$

(2.7)

The mean FPT is

$$ET_S = \frac{\theta}{2} \left\{ \sum_{n=1}^{\infty} \frac{x_n^{2n}}{n(2n - 1)!!} - \sum_{n=1}^{\infty} \frac{x_n^{2n}}{n(2n - 1)!!} \right\} + \sqrt{\frac{\pi}{2}} \frac{x_1}{\theta} \phi \left( \frac{\frac{3}{2} - \frac{x_1^2}{2}}{2} \right) - x_S \phi \left( \frac{\frac{3}{2} - \frac{x_S^2}{2}}{2} \right) ,$$

(2.8)

where $x_1 = (-\mu \theta) \sqrt{2/\sigma_{O.U.}^2 \theta}$, $x_S = (S - \mu \theta) \sqrt{2/\sigma_{O.U.}^2 \theta}$, $(2n - 1)!!$ denotes the product of all the odd integers up to $2n - 1$ and $\phi(a,c;z)$ is the Kummer function (Ricciardi and Sato 1989). If $\mu \theta \ll S$ and $\sigma_{O.U.}$ is suitably small, the mean FPT can be approximated by

$$ET_S \approx \theta \ln \frac{S - \mu \theta}{\mu \theta} ,$$

(2.9)

while if $0 \ll S$, or equivalently if $\sigma_{O.U.}$ is sufficiently small and $\mu$ is suitably chosen in order to make the crossings a rare event, the approximation