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Diffusion Approximation of the Neuronal Model with Synaptic Reversal Potentials

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Abstract. The stochastic neuronal model with reversal potentials is approximated. For the model with constant postsynaptic potential amplitudes a deterministic approximation is the only one which can be applied. The diffusion approximations are performed under the conditions of random postsynaptic potential amplitudes. New diffusion models of nerve membrane potential are devised in this way. These new models are more convenient for an analytical treatment than the original model with discontinuous trajectories.

1 Introduction

In the last two decades diffusion models for nerve membrane potential have been proposed and studied by a number of authors. These models have been usually derived applying a diffusion approximation on the model presented by Stein (1965). Not only the approximation itself but also mathematical properties of the substituted diffusion processes can be found in the following papers (Gluss 1967; Johannesma 1968; Roy and Smith 1969; Capocelli and Ricciardi 1971; Ricciardi 1976; Ricciardi and Sacerdote 1979; Tuckwell and Cope 1980; Sato 1982; Ricciardi et al. 1983). The precise relationship between Stein's model and the related diffusion processes together with the necessary and sufficient conditions on the approximation have been derived by Kallianpur (1983) and by Lánský (1984a).

It is well known fact that the changes in the depolarization of a nerve cell are state-dependent. (For examples see Schmidt 1978.) On the other side in the original Stein's model and also in its approximations the synaptic transmission is state-independent. Therefore a modification of the Stein's model which incorporates a more complete characterization of the process of synaptic transmission by inclusion of reversal potentials has been proposed by Tuckwell (1979). This model together with the original one has discontinuous trajectories. For that reason any mathematical treatment of them is complicated and it holds mainly for the Tuckwell's model for which the analytical results are exceptionally rare (Wilbur and Rinzel 1983; Smith and Smith 1984). Thus the diffusion approximation scheme has been used once again by Hanson and Tuckwell (1983). It should be noted here that some diffusion analogy of the model with reversal potentials had been also declared before Hanson's and Tuckwell's paper (Johannesma 1968; Wan and Tuckwell 1979) but without any formal argumentation.

The aim of this paper is an exact formulation of the diffusion approximation of the stochastic neuronal model with spontaneous decay and synaptic reversal potentials. In this way the paper represents a continuation of the previous work on this topic (Lánský 1984a). Moreover, new models of neuronal activity following from the diffusion approximation are devised. Their basic feature should be a link between biologically interpretable characteristics on one side and relatively simply tractable diffusion processes on the other side.

Approximation of the model is the only purpose of this article and we do not intend to present here a mathematical analysis of the proposed models. Namely, the formal descriptiön of neuronal firing in the terms of the first passage time problem and the parametrical inference of the models remain untouched. We hope to investigate both of them in our later work.

2 The Model and its Basic Modifications

Under the assumptions of the model with synaptic reversal potentials (Tuckwell 1979), the membrane potential is specified by one-dimensional stochastic process $X=\{X(t); t\geqq 0\}$ given by the stochastic differential equation

$$dX = -\frac{1}{\tau} X dt + a(V_E - X)\, dN^+(t) + i(X - V_I)\, dN^-(t)\,,$$

$$X(0) = x_0\,, \qquad (2.1)$$

where $\tau>0$, $-1<i<0<a<1$, $V_I<0<V_E$, $V_I<x_0<V_E$ are constants and $N^+(t)$, $N^-(t)$ are two independent homogeneous Poisson processes, $N^+(0)=N^-(0)=0$. This model postulates that each event of the excitatory process $N^+(t)$ depolarizes the membrane potential by $a(V_E-X(t))$ and analogously the inhibition process $N^-(t)$ produces a hyperpolarization of size $i(X(t)-V_I)$. The values $a(V_E-X(t))$ and $i(X(t)-V_I)$ are the values of excitatory, resp. inhibitory, postsynaptic potentials (EPSP, IPSP) under the condition that the membrane potential is equal to $X(t)$ at the instant of their generation. It is apparent that EPSP amplitudes decrease with the membrane potential X getting closer to excitatory reversal potential V_E and vice versa. The same statement holds symetrically for IPSP and inhibitory reversal potential V_I.

Between events of input processes $N^+(t)$ and $N^-(t)$, X decays exponentially to zero with time constant τ. This formulation of the model implies that instead of the membrane potential, its distance from the resting potential is described. This detail has to be kept in mind whenever any statistical inference for the models with spontaneous decay are studied (Lánský 1983a, 1984b). So aV_E, resp. $-iV_I$, is EPSP, resp. IPSP, amplitude in the moment when the membrane potential equals to the resting potential. In the same way fixing the initial voltage $X_0=0$ stands for the reset of the membrane potential to the resting level. For the simplicity of notation let all the stochastic processes considered in this paper have initial value equal to zero.

For X defined by Eq. (2.1), the first and second infinitesimal moments are

$$M_1(x) = \lim_{\Delta t\to 0} E(\Delta X(t)\,|\,X(t)=x)/(\Delta t)$$

$$= -x/\tau + \lambda a\,(V_E - x) + \omega i(x - V_I)\,, \qquad (2.2)$$

$$M_2(x) = \lim_{\Delta t\to 0} E(\Delta X(t)^2\,|X(t)=x)/(\Delta t) = \lambda a^2$$

$$\times\,(V_E - x)^2 + \omega i^2(x - V_I)^2\,, \qquad (2.3)$$

where λ and ω are intensities of the processes $N^+(t)$ and $N^-(t)$.

The result of diffusion approximation leads us to a diffusion process as a model of the membrane potential. Let $W=\{W(t); t\geqq 0\}$ be a standard Wiener process and let us suppose that $\mu(\cdot)$ and $\sigma(\cdot)\geqq 0$ are two continuous functions. Then the membrane potential $Y=\{Y(t); t\geqq 0\}$ is defined as the solution of the stochastic differential equation

$$dY = \mu(Y)dt + \sigma(Y)dW(t)\,. \qquad (2.4)$$

One method how to obtain the diffusion approximation Y to some discontinuous model X is to let Y have the same first two infinitesimal moments as X. Walsh (1981) calls this arrangement the usual approximation and he proposes it for the discontinuous models with relatively small jumps and states being far from the boundaries. Hanson and Tuckwell (1983) applied this method defining $\mu(y)$ and $\sigma(y)$ in Eq. (2.4) by M_1 and M_2 given by (2.2) and (2.3), so it means

$$\mu(y) = -y/\tau + \lambda a(V_E - y) + \omega i(y - V_I)\,, \qquad (2.5)$$

$$\sigma^2(y) = \lambda a^2(V_E - y)^2 + \omega i^2(y - V_I)^2\,. \qquad (2.6)$$

While the reversal potentials V_E and V_I are inaccessible boundaries between which the process (2.1) is confined, for the diffusion process with the drift (2.5) and infinitesimal variance (2.6) these boundaries are regular. Hanson and Tuckwell (1983) defeat this fact, which is one of the main objections against the diffusion analog of Stein's model, imposing some additional boundary conditions at V_I and V_E.

We should also bring to readers attention the diffusion model of Wan and Tuckwell (1979) with coefficients

$$\mu(y) = (-1/\tau + a)y + b,\ \sigma^2(y) = c^2y^2 \qquad (2.7)$$

which they declare to be the diffusion approximation of (2.1). The properties of the model are not discussed in their paper. It is obvious that for (2.4) specified by (2.7) there is a boundary point at zero. The parameters a, b, and c appearing in (2.7) are not explained in the cited paper, however, we can be sure that the model is in a form after some state space transformation.

A different approach to the diffusion approximation is based on the simultaneous decreasing of jump sizes, increasing of input processes intensities and considering the limits of infinitesimal moments of discontinuous process. This method has been applied in neuronal modelling mainly by Ricciardi and his coworkers, several times (Capocelli and Ricciardi 1971; Ricciardi 1976; Ricciardi and Sacerdote 1979) and it is a base for the weak convergence which is studied in neuronal context by Kallianpur (1983) and Lánský (1984a). Let us recall the procedure for Stein's model which is described by equation

$$dX = -\frac{1}{\tau} X dt + a dN^+(t) + i dN^-(t) \qquad (2.8)$$

with analogous interpretation as Eq. (2.1). The difference between (2.1) and (2.8) is obvious as for (2.8)

PSP are not state-dependent and the state space is $(-\infty, \infty)$. Now, for a sequence of models X_n specified by (2.8) we assume

$$a_n \to 0+, \; i_n \to 0-, \tag{2.9}$$

$$\lambda_n \to +\infty, \; \omega_n \to +\infty. \tag{2.10}$$

in such a way that the sequences of infinitesimal moments $\{M_i(x)\}_n$ converge the following way

$$\{M_1(x)\}_n \to -x/\tau + \mu, \; \{M_2(x)\}_n \to \sigma^2. \tag{2.11}$$

The limits (2.11) as well as all the others studied throughout this paper are the limits for $n \to \infty$. The limiting diffusion process is the Ornstein-Uhlenbeck process with the parameters

$$\mu(y) = -y/\tau + \mu, \; \sigma^2(y) = \sigma^2. \tag{2.12}$$

The state space of the process (2.4), (2.12) is $(-\infty, \infty)$.

Equation (2.1) can be generalized to handle nondeterministic EPSP and IPSP amplitudes. Such a model has been also introduced by Tuckwell (1979). Let $\{t_i^+\}_{i=1}^{\infty}$, resp. $\{t_i^-\}_{i=1}^{\infty}$, denote the moments of events of the process $N^+(t)$, resp. $N^-(t)$. Then the generalization of (2.1) takes the form

$$X(t) = -\frac{1}{\tau}\int_0^t X(s)ds + \sum_{j=1}^{N^+(t)} A_j(V_E - X(t_j^+)) + \sum_{j=1}^{N^-(t)} I_j(X(t_j^-) - V_I), \tag{2.13}$$

where A_j and B_j, $j = 1, \ldots$, are two sequences of independent identically distributed random variables. For the reason of correspondence to the model (2.1) we impose some additional conditions on EPSP and IPSP, especially, for $j = 1, \ldots$

$$P(A_j \in (0, 1)) = P(I_j \in (-1, 0)) = 1 \tag{2.14}$$

which ensures that the state space of $X(t)$ is (V_I, V_E) and

$$E(A_j) = a, \; E(I_j) = 1. \tag{2.15}$$

Another modification of the model (2.1) can be based on the assumption of neglected inhibition. It is quite common approach in the original Stein's model as it decreases the complexity of arising mathematical problems (Tuckwell 1975, 1976; Tsurui and Osaki 1976; Tuckwell and Richter 1978; Vasudevan et al. 1981; Wilbur and Rinzel 1982). Moreover, the modification is not only a formal one because the character of inhibition is different relatively to excitation. This fact is also utilized in our paper in such way that for some variants non-symmetrical excitation and inhibition is considered. Some attempt to study a state dependent inhibition had been done by Matsuyama (1976), with numerical results only.

The above summarized models attempt to characterize a stochastic variability of interspike intervals. It is achieved proposing that the neuron fires at the moment when the membrane potential exceeds a fixed threshold $S > 0$ for the first time. From this point of view the most important quantity is the random variable $T_S(X)$ defined as the first passage time of X across the threshold S, $T_S = \inf\{t \geqq 0;\ X(t) \geqq S\}$. It is worth to note that the relation $S < V_E$ can be fairly assumed and thus the behavior of X resp. Y above S is of no interest to us.

3 Approximation of the Model

For approximation of the model (2.1) by a diffusion process Y we need a sequence of processes X_n defined by (2.1) weakly converging to Y. The approach used in the approximation of Stein's model (2.8) by the Ornstein-Uhlenbeck process (2.4) with the coefficients (2.12) cannot be employed now. It follows immediately from the next arguments. Let a sequence of X_n is defined by (2.1) in such way that the intensities of input processes tend to infinity, (2.10) and simultaneously corresponding EPSP and IPSP amplitudes tend to zero, (2.9). Then the conditions on the infinitesimal means $\{M_1(x)\}_n \to \mu(x)$, $|\mu(x)| < \infty$ and $\mu(x) \neq 0$ imply $\{M_2(x)\}_n \to \sigma^2(x) \equiv 0$. Therefore the only approximation of (2.1) is the deterministic model $y(t)$ given by the equation

$$\mathrm{dy(t)} = \left[-\frac{1}{\tau}y(t) + \alpha(V_E - y(t)) + \beta(y(t) - V_I)\right]dt, \tag{3.1}$$

where we used the notation

$$\lambda_n a_n \to \alpha > 0, \tag{3.2}$$

$$\omega_n i_n \to \beta < 0. \tag{3.3}$$

The Eq. (3.1) can be formally identified as the deterministic leaky integrator commonly used in modelling of an inhibitory feedback or a phase-locking phenomenon (Knight 1972; Poppele and Chen 1972; Fohlmeister 1973; Ascoli et al. 1977; Scharstein 1979; Angelini et al. 1984). We can rewrite (3.1) in the form

$$dy(t) = [-\gamma y(t) + s]dt, \tag{3.4}$$

where

$$\gamma = 1/\tau + \alpha - \beta > 0, \tag{3.5}$$

$$s = \alpha V_E - \beta V_I, \tag{3.6}$$

which is the standard form of the deterministic leaky integrator with constant input s. Generally accepted procedure applied on Eq. (3.4) starts declearing s to be a time-variable input. It can be easily included in our version (3.1) approximating (2.1) under the condition of non-homogeneous Poisson processes $N^+(t)$ and $N^-(t)$ on the neuron input (Lánský 1984a). In that way we derive the deterministic leaky integrator

$$dy(t)=[(-1/\tau-\alpha(t)+\beta(t))\;y(t)+\alpha(t)\;V_E-\beta(t)\,V_I]dt \tag{3.7}$$

which could have some advantages over the standard version. Namely, there is excitation and inhibition separated and their influence appears also in the "leakage" term (3.5).

The impossibility to approximate the model (2.1) by a diffusion process can be overcome taking into account the model with random EPSP and IPSP described by Eq. (2.13). Let us define the sequence of models X_n analogously to (2.13) in the form

$$X_n(t)=-\frac{1}{\tau}\int_0^t X_n(s)ds+\sum_{j=1}^{N_n^+(t)} A_{nj}(V_E-X_n(t_{nj}^+)) + \sum_{j=1}^{N_n^-(t)} I_{nj}(X_n(t_{nj}^-)-V_I)\,, \tag{3.8}$$

where for each $n=1,\ldots,\{A_{nj}\}_{j=1}^{\infty}$ and $\{I_{nj}\}_{j=1}^{\infty}$ are two sequences of independent identically distributed random variables $\{t_{nj}^+\}_{j=1}^{\infty}$ and $\{t_{nj}^-\}_{j=1}^{\infty}$ are time moments of events in processes $N_n^+(t)$ and $N_n^-(t)$. We presume the existence of moments up to the fourth order for $\{A_{nj}\}_{j=1}^{\infty}$ and $\{I_{nj}\}_{j=1}^{\infty}$ and under above assumptions the subscript j can be dropped out whenever only the probability distributions are in question. For increasing input intensities (2.10) we assume that

$$\lambda_n E(A_n)\to\alpha>0\,, \tag{3.9}$$

$$\omega_n E(I_n)\to\beta<0\,, \tag{3.10}$$

what are conditions parallel to (3.2) and (3.3) for PSP with random amplitudes and

$$\lambda_n E(A_n^2)\to\sigma_E^2\,, \tag{3.11}$$

$$\omega_n E(I_n^2)\to\sigma_I^2\,. \tag{3.12}$$

Under the conditions (3.9)–(3.12) imposed on X_n the limits of first two infinitesimal moments can be computed

$$\{M_1(x)\}_n\to -x/\tau+\alpha(V_E-x)+\beta(x-V_I)\,, \tag{3.13}$$

$$\{M_2(x)\}_n\to\sigma_E^2(V_E-x)^2+\sigma_I^2(x-V_I)^2\,, \tag{3.14}$$

At this point it should be noted that almost nothing is assumed about $\{A_n\}$ and $\{I_n\}$ distributions and we may ask what are the consequences of conditions (3.9)–(3.12). They could be illustrated on the example where we propose for

$$\lambda_n=\lambda n\,,\;\omega_n=\omega n\,, \tag{3.15}$$

$$E(A_n)=an^{-1},\;E(I_n)=in^{-1}\,, \tag{3.16}$$

$$E(A_n^2)=\sigma_E^2 n^{-1},\;E(I_n^2)=\sigma_I^2 n^{-1}\,. \tag{3.17}$$

We can see that the condition (3.16) is an analog of (2.15), however, the requirement (2.14) cannot be accomplished simultaneously with (3.16) and (3.17). So we have to omit (2.14) and consequently X_n can reach or exceed the boundaries V_E, V_I, so the discontinuous models have state space $(-\infty,+\infty)$. On the other side we can made the probability of such excursion not only negligible small but adding the natural assumptions

$$E(A_n^4)=O(E^2(A_n^2)),\;E(I_n^4)=O(E^2(I_n^2)) \tag{3.18}$$

we can prove that the probability of X_n being confined in the interval $[V_I, V_E]$ tends to one with $n\to\infty$. Let $\Delta>0$, then for the probability of the excursion above V_E we obtain using Chebychev inequality

$$\begin{aligned} P(X_n(t+\Delta)\geqq V_E\,|\,X_n(t)=x\in(V_I, V_E)) &= P(A_n(V_E-x)\geqq V_E-x)\lambda_n\Delta+P(I_n(x-V_I) \\ &\geqq(V_E-x))\omega_n\Delta+o(\Delta) \\ &\leqq E(A_n^4)\lambda_n\Delta+((x-V_I)/(V_E-x))^4 \\ &\quad\times E(I_n^4)\omega_n\Delta\to 0. \end{aligned}$$

The existence of the limit is ensured by (3.11), (3.12), and (3.18) under the condition that the intensities tend to infinity, (2.10). The procedure for the boundary V_I is identical. For these reasons substituting the conditions (3.11), (3.12), and (3.18) instead of (2.14) makes no substantial difference between the models (3.8) and the model (2.1). Along these lines we may restrict ourselves to the diffusion approximation of (3.8) on $[V_I, V_E]$ only.

Theorem 1. *The sequence of processes* X_n *defined by* (3.8) *under the conditions* (2.10), (3.9)–(3.12), *and* (3.18) *converges weakly on* $[V_I, V_E]$ *to the diffusion process* (2.4) *specified by*

$$\mu(y)=-y/\tau+\alpha(V_E-y)+\beta(y-V_I)\,, \tag{3.19}$$

$$\sigma^2(y)=\sigma_E^2(V_E-y)^2+\sigma_I^2(y-V_I)^2\,, \tag{3.20}$$

$y\in[V_I, V_E],\; n\to\infty$.

Proof (Appendix). The diffusion process established in the Theorem 1 practically coincides with that proposed by Hanson and Tuckwell (1983) specified by (2.5) and (2.6). The role of this process in neuronal modelling seems to be limited as no analytical results except the stationary distribution is known. Therefore, the only application lies in simulation and numerical procedures. The main deffect of this process as a neuronal model is that both boundaries V_I and V_E are regular boundaries for the diffusion Y.

4 Diffusion Neuronal Models with Restricted State Space

For the reasons given in the end of the previous section we try to achieve some different limiting processes. Obviously the basic model has to be also at least slightly changed. Let us rewrite the model (2.13) into the form where deterministic and stochastic parts of EPSP and IPSP are separated,

$$X(t) = -\frac{1}{\tau}\int_0^t X(s)ds + a\int_0^t (V_E - X(s))dN^+(s)$$
$$+ i\int_0^t (X(s) - V_I)dN^-(s) + \sum_{j=1}^{N^+(t)} A'_j(V_E - X(t_j^+))$$
$$+ \sum_{j=1}^{N^-(t)} I'_j(X(t_j^-) - V_I)\,, \tag{4.1}$$

where $A'_j = A_j - a$, $I'_j = I_j - i$, and thus $E(A'_j) = E(I'_j) = 0$ which is ensured by the condition (2.15). We see once again from the formulation (4.1) that probabilities of A'_j, resp. I'_j, being not equal to zero can be made negligible small and so these two terms need not play any substantial role in the model behaviour. Keeping it in mind we may modify (4.1) to get a model with more convenient diffusion approximation than that derived in the previous section.

Let us assume the dependency of the random parts of EPSP and IPSP simultaneously on both reversal potentials in the following way

$$X(t) = -\frac{1}{\tau}\int_0^t X(s)ds + a\int_0^t (V_E - X(s))dN^+(s)$$
$$+ i\int_0^t (X(s) - V_I)dN^-(s) + \sum_{j=1}^{N^+(t)} A'_j(V_E - X(t_j^+))^{1/2}$$
$$\times (X(t_j^+) - V_I)^{1/2}$$
$$+ \sum_{j=1}^{N^-(t)} I'_j(V_E - X(t_j^-))^{1/2}(X(t_j^-) - V_I)^{1/2}\,. \tag{4.2}$$

The only difference between (2.1) and (4.2) is that in (4.2) EPSP and IPSP have additionally a random part which decreases near both boundaries while their deterministic part is the same as in (2.1). For the model (4.2) a sequence of X_n can be defined analogously as it is done by (3.8) with respect to (2.11),

$$X_n(t) = -\frac{1}{\tau}\int_0^t X_n(s)ds + a_n\int_0^t (V_E - X_n(s))dN_n^+(s)$$
$$+ i_n\int_0^t (X_n(s) - V_I)dN_n^-(s)$$
$$+ \sum_{j=1}^{N_n^+(t)} A'_{nj}(V_E - X_n(t_{nj}^+))^{1/2}(X_n(t_{nj}^+) - V_I)^{1/2}$$
$$+ \sum_{j=1}^{N_n^-(t)} I'_{nj}(V_E - X_n(t_{nj}^-))^{1/2}(X_n(t_{nj}^-) - V_I)^{1/2}\,, \tag{4.3}$$

where $A'_{nj} = A_{nj} - a_n$, $I'_{nj} = I_{nj} - i_n$, $E(A'_{nj}) = E(I'_{nj}) = 0$.

This model, together with the others defined in this section, is also asymptotically confined in $[V_I, V_E]$. It can be proved using Chebychev inequality in the same way as for (3.8). Under the same conditions as in Theorem 1 the infinitesimal means of X_n fulfill (3.13). The limit of the second moments is $(\sigma_E^2 + \sigma_I^2)(V_E - x)(x - V_I)$ and the following theorem can be proved.

Theorem 2. *The sequence of processes X_n given by* (4.3) *under the conditions* (2.10), (3.2), (3.3), (3.11), (3.12), *and* (3.18) *converges weakly in $[V_I, V_E]$ to the diffusion process* (2.4) *specified by* (3.19) *and*

$$\sigma^2(y) = (\sigma_E^2 + \sigma_I^2)(V_E - y)(y - V_I),\ y \in [V_I, V_E]\,. \tag{4.4}$$

Proof (Appendix). Both models established in Theorems 1 and 2 differ only in the variances $\sigma^2(y)$ while their drifts are identical. Let us demonstrate what is the consequence of this change. We transform the state space $[V_I, V_E]$ on the interval $[0, 1]$ in such a way that Y describes instead of the difference of the membrane potential from the resting level its difference from inhibitory reversal potential V_I. We put

$$y' = (y - V_I)/(V_E - V_I) \tag{4.5}$$

and we obtain instead of (3.19) and (4.4) the coefficients

$$\mu(y') = -V_I/(\tau(V_E - V_I)) + \alpha + (\beta - 1/\tau - \alpha)y'$$
$$= a' - \gamma y' \tag{4.6}$$
$$\sigma^2(y') = (\sigma_I^2 + \sigma_E^2)(1 - y')y' = \sigma^2 y'(1 - y')\,, \tag{4.7}$$

where for a' and γ defined in (3.5) and by (4.6) hold $a' > 0$, $\gamma > 0$ as it follows from (2.2) and (2.3). The diffusion process with the parameters (4.6) and (4.7) is well known in genetical applications and its behaviour at zero depends on the quantity $2a'/\sigma^2$ (Goel and Richter-Dyn 1974). Particularly, in our model for

$$2\alpha(V_E - V_I)\tau + 2V_I < \tau(\sigma_E^2 + \sigma_I^2)(V_E - V_I) \tag{4.8}$$

the boundary zero is regular and in the opposite case it is an entrance boundary.

As we pointed in the Introduction, the model with different types of excitation and inhibition plays a significant role in neuronal modelling not only for formal reasons. Let excitation in (2.13) be restricted on its deterministic part. The required sequence for the diffusion approximation can be written analogously to (3.8) and (4.3)

$$X_n(t) = -\frac{1}{\tau}\int_0^t X_n(s)ds + a_n\int_0^t (V_E - X_n(s))dN_n^+(s)$$
$$+ \sum_{j=1}^{N_n^-(t)} I_{nj}(X_n(t_{nj}^-) - V_I) \quad \text{for} \quad n = 1, \ldots \tag{4.9}$$

and in the same way as in the previous cases the theorem follows.

Theorem 3. *The sequence of processes X_n specified by* (4.9) *under the conditions* (2.10), (3.2), (3.12), *and* (3.18) *converges weakly on $[V_I, V_E]$ to the diffusion process* (2.4) *with coefficients* (3.19) *and*

$$\sigma^2(y) = \sigma_I^2(y - V_I)^2 \quad \text{for} \quad y \in [V_I, V_E],\ n \to \infty\,. \tag{4.10}$$

Proof (Appendix). A more convenient form of the resulting diffusion process is obtained by the transformation (4.5) achieving the drift (4.6) and

$$\sigma^2(y') = \sigma_I^2 y'^2 . \tag{4.11}$$

So, after a tedious derivation and argumentation we reach the model with coefficients (2.7) announced by Wan and Tuckwell (1979). To show the compatibility of this model with (2.1) we have to prove that zero is an inaccessible boundary. Using the notation of Ricciardi (1977) we have for $x' > 0$,

$$\begin{aligned} f(x) &= \exp\left(- \int_{x'}^{x} (a' - \gamma z)\sigma_I^{-2} z^{-2} dz \right) \\ &= K(x') \exp (a'\sigma_I^{-2} x^{-1} + \gamma\sigma_I^{-2} \ln x) \notin \mathscr{L}(0, x') , \\ g(x) &= (\sigma_I^2 x^2 f(x))^{-1} \\ &= \sigma_I^{-2} x^{-2} K(x') \\ &\quad \times \exp(-a'\sigma_I^{-2} x^{-1} - \gamma\sigma_I^{-2} \ln x) \in \mathscr{L}(0, x') , \end{aligned}$$

where $K(x')$ does not depend on x and a' and γ are defined by (4.6). By reason of integrability of $f(x)$ and $g(x)$ we deduce that for our parameters a' and γ the boundary zero is inaccessible.

The last model we would like to propose in this paper is a combination of those derived in Theorems 2 and 3. Let us assume that model (4.2) is brought closer to the basic one (2.1) and the sequence of X_n is defined in this manner

$$\begin{aligned} X_n(t) = &- \frac{1}{\tau} \int_0^t X_n(s) ds + a_n \int_0^t (V_E - X_n(s)) dN_n^+(s) \\ &+ i_n \int_0^t (X_n(s) - V_I) dN_n^-(s) \\ &+ \sum_{j=1}^{N_n^-(t)} I'_{nj} (X_n(t_{nj}^-) - V_I)^{1/2} \end{aligned} \tag{4.12}$$

with notations retained from (4.3). With exactly the same argumentation as in the previous cases, the last theorem can be stated.

Theorem 4. *The sequence of processes* (4.12) *under the conditions* (2.10), (3.2), (3.3), (3.12), *and* (3.18) *converges weakly in* $[V_I, V_E]$ *with* $n \to \infty$ *to the diffusion process* (2.4) *specified by* (3.19) *and*

$$\sigma^2(y) = \sigma_I^2 (y - V_I), \; y \in [V_I, V_E] . \tag{4.13}$$

Proof (Appendix). Applying the transformation (4.5), the drift is given by (4.6) and

$$\sigma^2(y') = \sigma_I^2 y' (V_E - V_I)^{-1} = \sigma_I'^2 y' . \tag{4.14}$$

The diffusion process with coefficients (4.6) and (4.14) was first studied by Feller (1951). The nature of the boundary zero for it is the same as for the process established in the Theorem 2 (Goel and Richter-Dyn 1974).

Not only varying PSP amplitudes but also nonconstant input rates can be included into the models $X(t)$ (Lánský 1984a). Considering non-homogeneous Poisson processes with rates $\lambda_n(t)$ and $\omega_n(t)$ then simple additional conditions ensure that Theorems 1–4 hold with nonstationary limiting diffusion processes. These processes can be valuable mainly in description of adaptation phenomena in spike generation, (Gestri et al. 1980; Lánský 1983b; Bruckstein et al. 1983; Bruckstein and Zeevi 1985). Non-stationary diffusion process as the limit of Stein's models was also suggested for the description of "burst like" neuron's stimulation by Ricciardi (1982).

Appendix

Before proving the Theorems we shortly indicate the meaning of the weak convergence. [For detailed explanation see Billingsley (1968).]

Let $D[0, \infty)$ be the space of all real-valued right continuous functions defined on $[0, \infty)$. Then a stochastic process $X = \{X(t); t \geqq 0\}$ can be defined as a function $X: \Omega \to D[0, \infty)$, where $(\Omega, \mathscr{F}, P)$ is a probability space. $D[0, \infty)$ with the Skorochod metric becomes a complete, separable metric space. The distribution of X is a measure on the Borel sets $\mathscr{B}(D)$,

$$\mu_X(A) = P(\omega : X(\cdot, \omega) \in A), \; A \in \mathscr{B}(D) .$$

The weak convergence of a sequence of stochastic processes X_n to a stochastic process Y with sample paths in $D[0, \infty)$ is a statement about the distributions μ_{X_n} and μ_Y. The meaning of it can be understood as follows: The sequence of distributions μ_{X_n} converges weakly to μ_Y if

$$\int_{D[0, \infty)} f d\mu_{X_n} \to \int_{D[0, \infty)} f d\mu_Y$$

for any real continuous bounded function $f \in D[0, \infty)$. The processes X_n and Y need not be defined on the same sample space.

To prove the weak convergence of the considered models we apply the martingale approach. We bring several definitions for that purpose at the beginning.

Let $\mathscr{F}' = \{\mathscr{F}_t, t \geqq 0\}$ be a nondecreasing family of σ-algebras, and $\mathscr{M}^2$ be a family of quadratically integrable martingales with respect to $\mathscr{F}'$. For $M \in \mathscr{M}^2$ we define

$$M^\varepsilon(t) = \sum_{s \leqq t} (M(s) - M(s-))^2 \chi\{|M(s) - M(s-)| > \varepsilon\} .$$

by $\overline{M^\varepsilon(t)}$ we denote the compensator of $M^\varepsilon(t)$. In our case $\overline{M^\varepsilon(t)}$ is a continuous increasing process such that $M^\varepsilon(t) - \overline{M^\varepsilon(t)}$ is a martingale. We say that a sequence of M_n, $M_n \in \mathscr{M}^2$, fulfils a condition of "asymptotic small jumps" (ASJ) if for any $\varepsilon > 0$ $M_n^\varepsilon(t)$ converges to zero in probability, as $n \to \infty$. Two sequences of stochastic processes $\{X_n(t), t \geqq 0\}$ and $\{Z_n(t), t \geqq 0\}$ are "C-contiguous" (C–C) if for any $T \sup\{t \in [0, T] | X_n(t) - Z_n(t)|\}$ tends to zero in probability, as $n \to \infty$. A stochastic process X is called a semi-martingale if there exists $M \in \mathscr{M}^2$ and an integrable, non-decreasing process $V = \{V(t), t \geqq 0\}$ such that $X(t) = X(0) + M(t) + V(t), t \geqq 0$. Let the symbol $\{<M(t)>, t \geqq 0\}$ denotes the quadratic variation of a martingale $\{M(t), t \geqq 0\}$. For $\mu(\cdot)$,

$\sigma^2(\cdot) > 0$ real, continuous and bounded we define

$$A(f, t) = \int_0^t \sigma^2(f(s))\,ds\,, \tag{A.1}$$

$$V(f, t) = \int_0^t \mu(f(s))\,ds\,, \tag{A.2}$$

where $(f, t) \in D[0, T]xR_+$.

For the proof of our Theorems we use the Theorem due to Rebolledo (1979).

Theorem. *Let X_n be a sequence of semi-martingales, $X_n(0) = x_n \in R$ and let the following conditions hold.*

(i) *For M_n the condition "ASJ" hold.*
(ii) *The couples of sequences $\langle M_n \rangle$ and $A(X_n, \cdot)$, and V_n and $V(X_n, \cdot)$ are "C–C".*
(iii) $x_n \to x_0 \in R$.

Then the probability distributions of X_n converge weakly to the probability distribution of X, as $n \to \infty$, where X is given by stochastic differential equation

$$dX(t) = \mu(X(t))dt + \sigma(X(t))dW(t),\ X(0) = x_0 .$$

To verify the assumptions (i)–(iii) for our sequences of stochastic processes X_n means to prove our Theorems. Moreover, due to the convention introduced in the second part of this paper the condition (iii) is always fulfilled as $x_n = x_0 = 0$ for all the models.

Let us start with the proof of Theorem 1 defining $M_n(t)$,

$$\begin{aligned} M_n(t) = X_n(t) - \frac{1}{\tau}\int_0^t X_n(s)ds - \int_0^t [&E(A_n)\lambda_n(V_E - X_n(s)) \\ &+ E(I_n)\omega_n(X_n(s) - V_I)]ds\,. \end{aligned} \tag{A.3}$$

Then $M_n(t)$ are quadratically integrable martingales and their quadratic variations are

$$\langle M_n(t) \rangle = \sum_{j=1}^{N_n^+(t)} A_{nj}^2(V_E - X_n(t_{nj}^+))^2 + \sum_{j=1}^{N_n^-(t)} I_{nj}^2(X_n(t_{nj}^-) - V_I)^2 \,. \tag{A.4}$$

Now $\mu(y)$ and $\sigma(y)$ are given by (3.19) and (3.20) for $y \in [V_I, V_E]$ and let $\mu(y) = \mu_1$, $\sigma(y) = \sigma_1$ for $y \leqq V_I$, $\mu(y) = \mu_2$, $\sigma(y) = \sigma_2$, for $y \geqq V_E$, μ_1, μ_2, σ_1, σ_2 are constants such that $\mu(y)$ and $\sigma(y)$ are continuous on R, $(\mu_1 = \mu(V_I)$, $\sigma_2 = \sigma(V_E)$, $\sigma_1 = \sigma(V_I)$, $\sigma_2 = \sigma(V_E)$. For the condition of the Rebolledo's theorem we have

$$\begin{aligned} M_n^\varepsilon(t) &= \sum_{s \leqq t} (X_n(s) - X_n(s-))^2 \chi\{|X_n(s) - X_n(s-)| > \varepsilon\} \\ &= \sum_{j=1}^{N_n^+(t)} A_{nj}^2(V_E - X(t_{nj}^+))^2 \chi\{|A_{nj}(V_E - X_n(t_{nj}^+)| > \varepsilon\} \\ &\quad + \sum_{j=1}^{N_n^-(t)} I_{nj}^2(X_n(t_{nj}^-) - V_I)^2 \chi\{|I_{nj}(X_n(t_{nj}^-) - V_I)| > \varepsilon\} \end{aligned} \tag{A.5}$$

and the compensator of $M_n^\varepsilon(t)$ is

$$\overline{M_n^\varepsilon(t)} = \lambda_n \int_0^t w_n^+(X_n(s))ds + \omega_n \int_0^t w_n^-(X_n(s))ds\,,$$

where

$$w_n^+(x) = \int (V_E - x)^2 y^2 \chi\{|y(V_E - x)| > \varepsilon\} dF_n^+(y)\,,$$
$$w_n^-(x) = \int (x - V_I)^2 y^2 \chi\{|y(x - V_I)| > \varepsilon\} dF_n^-(y)\,,$$

$F_n^+(y)$, resp. $F_n^-(y)$, stands for the distribution function of A_n, resp. I_n. So applying conditions (3.18) the preposition (i) is proved.

For (ii) we have $A(X_n, t)$ and $V(X_n, t)$ defined by (A.1) and (A.2) and therefore the proof of (ii) is identical with the assertion that for $n \to \infty$

$$\sup\left\{t \in [0, T];\ \left|\int_0^t \sigma^2(X_n(s))\,ds - \sum_{j=1}^{N_n^+(t)} A_{nj}^2(V_E - X_n(t_{nj}^+))^2 - \sum_{j=1}^{N_n^-(t)} I_{nj}^2(X_n(t_{nj}^-) - V_I)^2\right|\right\} \to 0\,,$$

which is obvious, as we realize that the term inside the absolute value is a martingale with quadratic variation approaching 0, as $n \to \infty$. The second part of (ii) follows immediately from the fact

$$\begin{aligned} V_n(t) = -\frac{1}{\tau}\int_0^t X_n(s)ds - \int_0^t [&\lambda_n E(A_n)\,(V_E - X_n(s)) \\ &+ \omega_n E(I_n)\,(X_n(s) - V_I)]\,ds\,. \end{aligned}$$

For the Theorem 2 (resp. 3., 4) the martingale has the same form (A.3) as for the proof of Theorem 1. There X_n are replaced by (4.3) [resp. (4.9), (4.12)] with only formal changes for deterministic and random PSP amplitudes. The proofs are for these Theorems identical and we bring here only the relationships of the corresponding quadrate variations (A.4). For Theorem 2.

$$\begin{aligned} \langle M_n(t) \rangle = &\sum_{j=1}^{N_n^+(t)} A_{nj}'^2[(V_E - X_n(t_{nj}^+))\,(X_n(t_{nj}^+) - V_I)] \\ &+ \sum_{j=1}^{N_n^-(t)} I_{nj}'^2[(V_E - X_n(t_{nj}^-))\,(X_n(t_{nj}^-) - V_I)] \\ &+ \int_0^t a_n^2(V_E - X_n(s))^2 dN_n^+(s) + \int_0^t i_n^2(X_n(s) - V_I)^2 dN_n^-(s)\,. \end{aligned}$$

In the case of Theorem 3 the quadratic variation is

$$\langle M_n(t) \rangle = \int_0^t a_n^2(V_E - X_n(s))^2 dN_n^+(s) + \sum_{j=1}^{N_n^-(t)} I_{nj}'^2(X_n(t_{nj}^-) - V_I)^2$$

and finally for Theorem 4

$$\begin{aligned} \langle M_n(t) \rangle = &\int_0^t a_n^2(V_E - X_n(s))^2 dN_n^+(s) + \int_0^t i_n^2(X_n(s) - V_I)^2 dN_n^-(s) \\ &+ \sum_{j=1}^{N_n^-(t)} I_{nj}'^2(X_n(t_{nj}^-) - V_I)\,. \end{aligned}$$

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