Integrate-and-fire and Hodgkin-Huxley models with current inputs

Integrate-and-fire and Hodgkin–Huxley models with current inputs

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Abstract
For the integrate-and-fire model and the Hodgkin–Huxley model, we consider
how current inputs including α-wave and square-wave affect their outputs.
Firstly the usual approximation is employed to approximate the models with
current inputs which quantitatively reveals the difference between instantaneous
and noninstantaneous (current) inputs. When the rising time of α-wave
inputs is long or the ratio between the inhibitory and excitatory inputs is
close to one, the usual approximation fails to approximate the α-wave inputs
in the integrate-and-fire model. For the Hodgkin–Huxley model, the usual
approximation in general gives an unsatisfying approximation. A novel
approach based upon a superposition of 'coloured' and 'white' noise is then
proposed to replace the usual approximation. Numerical results show that
the novel approach substantially improves the approximation within widely
physiologically reasonable regions of the rising time of α-wave inputs.

PACS numbers: 0540J, 0250, 0590, 8435, 8719L

1. Introduction

Although the single neuron model with random inputs has been widely studied *in computo*, most
such studies are done under the assumption that inputs are instantaneous [1–5, 7, 8, 15, 19, 24].
This assumption is certainly an approximation to the physiological data: any physical
process takes time to accomplish. The rising time of excitatory postsynaptic potentials, for
example, ranges from a few milliseconds to a few hundred milliseconds (see [17, p 184]).
Theoretically in [25] the authors have found the interesting impact of EPSP rising time courses
in synchronizing neuronal activities.

In this paper we address the following two important issues: how the time courses of
EPSPs and IPSPs affect the output of a single neuron model—the integrate-and-fire model
and the Hodgkin–Huxley model—and how to employ the Ornstein–Uhlenbeck type process to
approximate the models with current inputs. The second issue is important since we all know
that theoretically it is very difficult to deal with a system with Poissonian form inputs. For
example using the Ornstein–Uhlenbeck process to approximate neuronal models with Poisson
inputs has been investigated for decades.

We take into account the two most commonly encountered noninstantaneous inputs: α-wave and square-wave inputs. We find that the mean and variance of α-wave and square-wave inputs are both weaker than that of Poisson inputs, as one might expect, and therefore the mean of interspike intervals (ISIs) of efferent spike trains of the integrate-and-fire model and the Hodgkin–Huxley model is greater than that of Poisson inputs. The classical approach, the usual approximation, is first applied to approximate the models with current inputs. By the usual approximation, we mean to approximate a stochastic process by a diffusion process, i.e.

$$\mathrm{d}x_\mathrm{t} = b(x_\mathrm{t}, t)\,\mathrm{d}t + \sigma(x_\mathrm{t}, t)\,\mathrm{d}B_\mathrm{t}$$

where B_t is the standard Brownian motion ('white' noise) and b, σ are appropriately defined functions. For the integrate-and-fire model, the approximation to the mean firing time of efferent ISIs is always valid when the ratio between inhibitory and excitatory inputs is low, but not for the CV. In other words, in the regions of a small ratio between inhibitory and excitatory inputs and in order to tell the difference between inputs from different sources, we have to consider the high order statistics of efferent spike trains. Combining our previous results [10] and the results in this paper, we further conclude that in the regions of high ratio between inhibitory and excitatory inputs, the mean firing time is very sensitive to small perturbations. For the Hodgkin–Huxley model we find that the usual approximation is not satisfied even at a very low ratio between inhibitory and excitatory inputs. This also reveals an essential difference between some simple, linear model such as the integrate-and-fire model and the biophysical, nonlinear model such as the Hodgkin–Huxley model. We then propose a novel scheme to approximate the models with current inputs: to replace the 'white' noise in the usual approximation by a superposition of 'coloured' and 'white' noise. Numerical results show that the novel scheme considerably improves the approximation, for both the integrate-and-fire and the Hodgkin–Huxley model, within widely physiologically reasonable regions of model parameters.

This is the third of our series of papers aiming to elucidate how more realistic inputs, in contrast to conventional i.i.d. Poisson inputs which have been intensively studied in the literature, affect the outputs of simple neuronal models and thus possibly to provide a full spectrum of the behaviour inherent in these models. This way we can document more thoroughly the restrictions and potential of the models. In [8] we have considered the behaviour of the integrate-and-fire model subjected to independent inputs with different distribution tails; in [10] we have taken into account the behaviour of the integrate-and-fire model with correlated inputs. On the other hand we have generalized these considerations to biophysical models and some intriguing properties have been found [3, 11].

2. Integrate-and-fire model with synaptic inputs

Suppose that, when the membrane potential V_t is between the resting potential V_rest and the threshold V_thre, it is given by

$$\mathrm{d}V_\mathrm{t} = -\frac{1}{\gamma}(V_\mathrm{t} - V_\mathrm{rest})\,\mathrm{d}t + I_\mathrm{syn}(t)\,\mathrm{d}t \tag{2.1}$$

where $1/\gamma$ is the decay rate. When V_t is greater than V_thre a spike is emitted and V_t is reset to V_rest. The model is termed the integrate-and-fire model. Synaptic input $I_\mathrm{syn}(t)$ is modelled by

$$I_\mathrm{syn}(t) = a\sum_{k=1}^{\infty} f(t - T_k^\mathrm{E})I_{\{t \geqslant T_k^\mathrm{E}\}} - b\sum_{k=1}^{\infty} f(t - T_k^\mathrm{I})I_{\{t \geqslant T_k^\mathrm{I}\}}$$

where $T_k^\mathrm{E} = \sum_{i=1}^{k} t_i^\mathrm{E}$ ($T_k^\mathrm{I} = \sum_{i=1}^{k} t_i^\mathrm{I}$) for i.i.d. random sequences $t_i^\mathrm{E}, t_i^\mathrm{I}, i = 1, 2, \ldots,$ $a > 0, b > 0$ the magnitude of single EPSP and IPSP and I is the indicator function. In

the remaining part of the paper we always assume that the distribution of t_i^E is identical to t_i^I and so, when we speak of a property of EPSP inputs we simply imply the same property is true for IPSP inputs. t_1^E is assumed to be exponentially distributed with intensity λ.

Example 1. When

$$f(t - T_k^E) = \delta_{(t - T_k^E)}(0)$$

then $N(t) = \int_0^t I_{syn}(s)\, ds$ (instantaneous inputs) is the Poisson process with intensity λ.

The Poisson process input is an approximation to a cell's synaptic inputs. It assumes that it responds to the input instantaneously. There are some other optimal properties such as optimizing the mutual information, etc., for Poisson inputs [20].

Example 2. When

$$f(t - T_k^E) = \alpha^2(t - T_k^E)\exp\left(-\alpha(t - T_k^E)\right) \qquad t > T_k^E$$

we have α-wave inputs or an α-synapse. α-wave input is, of course, again an approximation to actual current inputs. We refer the reader to [24] for a discussion on the choice of this function. In contrast to Poisson inputs now the inputs take time to rise and then decay.

The rising time is $1/\alpha$, which is the characteristic time of an α-wave synapse. Here we emphasize that for the same neuron the time course of input EPSPs might be very different: for example, the rising time for an increased-conductance EPSP due to the opening of a channel could be a few milliseconds, but the rising time for a decreased-conductance EPSP is a few hundred milliseconds (see [17, p 184]). When α is small, α-wave inputs can be thought of as an approximation to continuous current inputs; when α is large they approximate Poisson inputs.

Example 3. When

$$f(t - T_k^E) = \frac{1}{\delta} I_{\{T_k^E < t < T_K^E + \delta\}}$$

we have square wave inputs and its duration time is δ.

A slightly more general model than the integrate-and-fire model defined above is the integrate-and-fire model with reversal potentials [18, 26] defined by

$$dZ_t = -\frac{1}{\gamma}(Z_t - V_{rest})\, dt + \bar{I}_{syn}(t)\, dt \qquad (2.2)$$

where V_{rest} is the resting potential. Synaptic inputs are given by

$$\bar{I}_{syn}(t) = \bar{a}(V_E - Z_t)\sum_{k=1}^{\infty} f(t - T_k^E)I_{\{t \geqslant T_k^E\}} + \bar{b}(V_I - Z_t)\sum_{k=1}^{\infty} f(t - T_k^I)I_{\{t \geqslant T_k^I\}}$$

$\bar{a}, \bar{b}$ are the magnitude of a single EPSP and IPSP, respectively, and V_E and V_I are the reversal potentials. Z_t (membrane potential) is now a birth-and-death process with boundaries V_E and V_I. Once Z_t is below V_{rest} the decay term $Z_t - V_{rest}$ will push the membrane potential Z_t up, whereas when Z_t is above V_{rest} the decay term will hyperpolarize it. By choosing different reversal potentials and characteristic times of f, $\bar{I}_{syn}(t)$ corresponds to different kinds of synapses such as NMDA, AMPA GABA$_A$ and GABA$_B$.

3. Usual approximation

In order to assess the impact of input time courses on the models, in this section we first calculate the mean and variance of inputs, which in turn gives us the required estimations needed for the usual approximation.

Let $T_k = \sum_{i=1}^{k} t_i$ where $t_i, i = 1, \ldots,$ are negative exponentially distributed random variables with rate λ.

3.1. Analytical results

For carrying out the usual approximation, we only need to know the mean and variance. We can calculate the mean and variance of inputs either in current $I_{\text{syn}}(t)$ or in voltage $\int_0^t I_{\text{syn}}(s)\, ds$. An easy calculation on α-wave inputs tells us that, in order to recover the usual approximation for the Poisson process, i.e. when $\alpha \to \infty$ the usual approximation to the α-wave input is coincident with that to the Poisson input, we have to consider the mean and variance of inputs in voltage as we develop below.

Let us define

$$
\mu(t, \lambda) = E \int_0^t I_{\text{syn}}(s)\, ds
$$
$$
\sigma^2(t, \lambda) = E \left(\int_0^t I_{\text{syn}}(s)\, ds \right)^2 - \left(E \int_0^t I_{\text{syn}}(s)\, ds \right)^2
$$

(3.1)

the mean and variance of inputs in *voltage*. We then have the following lemma.

Lemma 1. *If $\int_0^\infty f(s)\, ds = 1$ and*

$$
I_{\text{syn}}(t) = \sum_{k=1}^{\infty} f(t - T_k) I_{\{t \geqslant T_k\}}
$$

we have

$$
\mu(t, \lambda) = \lambda t \left[1 - \int_t^\infty f(u)\, du \right] - \lambda \int_0^t u f(u)\, du
$$

(3.2)

$$
\sigma^2(t, \lambda) = \lambda t \left[1 - \int_t^\infty f(u)\, du \right]^2 - \lambda \int_0^t \int_0^t \max(u, v) f(u) f(v)\, du\, dv.
$$

(3.3)

Proof. Through some routine algebraic calculation, we can obtain

$$
f_{T_k}(x) = e^{-\lambda x} x^{k-1} \frac{\lambda^k}{(k-1)!} \qquad x \geqslant 0
$$
$$
f_{T_k, T_j}(x, y) = e^{-\lambda x} \frac{\lambda^k (x - y)^{k-j-1} y^{j-1}}{(j-1)!(k-j-1)!} \qquad 0 \leqslant y \leqslant x \quad 1 \leqslant j < k
$$

where $f_{T_k}(x)$ is the probability density function of T_k and $f_{T_k, T_j}(x, y)$ is the joint probability density function of (T_k, T_j).

Notice that

$$
\int_0^t I_{\text{syn}}(s)\, ds = \int_0^t \sum_{k=1}^{\infty} f(s - T_k) I_{\{s \geqslant T_k\}}\, ds\, I_{\{t \geqslant T_k\}}.
$$

We have

$$E \int_0^t I_{\text{syn}}(s)\,\mathrm{d}s = \int_0^t \int_0^t \sum_{k=1}^{\infty} f(s-x) I_{\{s \geqslant x\}} f_{T_k}(x)\,\mathrm{d}s\,\mathrm{d}x$$

$$= \lambda \int_0^t \int_0^t f(s-x) I_{\{s \geqslant x\}}\,\mathrm{d}s\,\mathrm{d}x$$

$$= \lambda \int_0^t (t-s) f(s)\,\mathrm{d}s$$

which gives us the desired expression for equation (3.2).

It is easy to see that

$$E \left(\int_0^t I_{\text{syn}}(s)\,\mathrm{d}s \right)^2 = M_t + D_t$$

where

$$M_t = E \sum_{k=1}^{\infty} \left(\int_0^{t-T_k} f(u)\,\mathrm{d}u \right)^2 I_{\{t \geqslant T_k\}}$$

$$D_t = 2E \sum_{k=2}^{\infty} \sum_{j=1}^{k-1} I_{\{t \geqslant T_k\}} I_{\{t \geqslant T_j\}} \int_0^{t-T_k} f(u)\,\mathrm{d}u \int_0^{t-T_j} f(v)\,\mathrm{d}v.$$

We calculate D_t first:

$$D_t = 2 \int_0^t \int_0^x \int_0^{t-x} \int_0^{t-y} f(u) f(v) \sum_{k=2}^{\infty} \sum_{j=1}^{k-1} f_{T_k, T_j}(x, y)\,\mathrm{d}u\,\mathrm{d}v\,\mathrm{d}y\,\mathrm{d}x$$

$$= 2\lambda^2 \int_0^t \int_0^x \int_0^{t-x} \int_0^{t-y} f(u) f(v)\,\mathrm{d}u\,\mathrm{d}v\,\mathrm{d}y\,\mathrm{d}x$$

$$= 2\lambda^2 \int_0^t \int_0^u f(u) f(v)(t-u)(t-v)\,\mathrm{d}u\,\mathrm{d}v$$

$$= \lambda^2 \int_0^t \int_0^t f(u) f(v)(t-u)(t-v)\,\mathrm{d}u\,\mathrm{d}v$$

$$= \left(E \int_0^t I_{\text{syn}}(s)\,\mathrm{d}s \right)^2.$$

Therefore we have

$$E \left(\int_0^t I_{\text{syn}}(s)\,\mathrm{d}s \right)^2 - \left(E \int_0^t I_{\text{syn}}(s)\,\mathrm{d}s \right)^2 = E \left(\int_0^t I_{\text{syn}}(s)\,\mathrm{d}s \right)^2 - \left(E \int_0^t I_{\text{syn}}(s)\,\mathrm{d}s \right)^2$$

$$= M_t = \lambda \int_0^t \left(\int_0^x f(u)\,\mathrm{d}u \right)^2 \mathrm{d}x$$

and so equation (3.3) follows. $\qquad\qquad\square$

A comparison with Poisson input is informative here. When $f(t) = \delta_t(0)$ we see that $\mu(t, \lambda) = \lambda t$ and $\sigma^2(\lambda, t) = \lambda t$. The lemma above tells us that the input mean (equation (3.2)) and variance (equation (3.3)) are both smaller than that of the Poisson process, no matter what the function f is.

Lemma 1 also tells that the usual approximation [24] for a current input without reversal potentials takes the form

$$I_{\text{syn}}(t)\,\mathrm{d}t = \mu'(t, \lambda)\,\mathrm{d}t + \sqrt{(\sigma^2(t, \lambda))'}\,\mathrm{d}B_t$$

$$= \lambda\mu(t)\,\mathrm{d}t + \sqrt{\lambda\mu(t)}\,\mathrm{d}B_t \qquad\qquad (3.4)$$

where $\mu(t) = 1 - \int_t^\infty f(u) \, du$ and $(\cdot)'$ is the derivative with respect to t. Note that when $f(t) = \delta_t(0)$ the formula above again gives us the familiar one in the literature [24].

The analogous conclusion is true for the model with reversal potentials. Equation (3.4) is a general and useful formula which tells us that, for any current input, by using equation (3.4) we could have its usual approximation. Another feature of equation (3.4) is that, compared to Poisson inputs, we only have one additional free parameter $\mu(t)$ which reflects the effect of current inputs. Hence for any given current inputs, by equation (3.2) we can calculate the exact form of $\mu(t)$. In terms of $\mu(t)$ we obtain an approximation to models with current inputs.

3.2. α-wave

In this section we consider the stochastic process

$$I_{\text{syn}}(t) = \sum_{k=1}^\infty \alpha^2 (t - T_k) \exp\left(-\alpha(t - T_k)\right) I_{\{t \geqslant T_k\}}.$$

Let us assume that the neuron connects with p excitatory synapses and q inhibitory synapses. Each excitatory synapses transmit EPSPs at a rate of λ_E Hz and each inhibitory synapses transmit IPSPs at a rate of λ_I Hz, i.e. $\lambda = \lambda_E p$.

As a corollary of lemma 1 we have the following conclusion.

Theorem 1. *For α-wave inputs we have the following usual approximation:*

$$\mathrm{d}V_t = -\frac{1}{\gamma}(V_t - V_{\text{rest}}) \, \mathrm{d}t + \mathrm{d}i_{\text{syn}}(t) \tag{3.5}$$

with

$$\mathrm{d}i_{\text{syn}}(t) = [ap\lambda_E - bq\lambda_I]\mu(t) \, \mathrm{d}t + \left[\sqrt{a^2 p\lambda_E + b^2 q\lambda_I}\right] \mu(t) \, \mathrm{d}B_t \tag{3.6}$$

and

$$\mu(t) = 1 - \exp(-\alpha t) - \alpha t \exp(-\alpha t). \tag{3.7}$$

As a consequence of theorem 1, we have the following theorem for the model with reversal potentials.

Theorem 2. *For α-synapse inputs we have the following usual approximation:*

$$\mathrm{d}Z_t = -\frac{1}{\gamma}(Z_t - V_{\text{rest}}) \, \mathrm{d}t + \mathrm{d}\bar{i}_{\text{syn}}(t) \tag{3.8}$$

with

$$\begin{aligned}
\mathrm{d}\bar{i}_{\text{syn}}(t) = {} & [\bar{a}\lambda_E p(Z_t - V_E) - \bar{b}\lambda_I q(Z_t - V_I)]\mu(t) \, \mathrm{d}t \\
& + \left[\sqrt{\bar{a}^2 p\lambda_E(Z_t - V_E)^2 + \bar{b}^2 q\lambda_I(Z_t - V_I)^2}\right] \mu(t) \, \mathrm{d}B_t.
\end{aligned} \tag{3.9}$$

All conclusions above indicate that, in terms of the usual approximation, noninstantaneous inputs are equivalent to instantaneous inputs by multiplying $\mu(t)$, which converge to one depending only on the characteristic time, α, of the input.

3.3. Square-wave

Square-wave input is another commonly used form of EPSP and IPSP defined by

$$I_{syn}(t) = \sum_{i=1}^{\infty} \frac{1}{\delta} I_{\{T_i \leqslant t < T_i + \delta\}}.$$

By an application of lemma 1, we have the following conclusions.

Theorem 3. *For square-wave inputs we have the following usual approximation:*

$$di_{syn}(t) = [ap\lambda_E - bq\lambda_I]\bar{\mu}(t)\,dt + \left[\sqrt{a^2 p\lambda_E + b^2 q\lambda_I}\right]\bar{\mu}(t)\,dB_t \qquad (3.10)$$

where

$$\bar{\mu}(t) = \begin{cases} \dfrac{t}{\delta} & \text{when} \quad t \leqslant \delta \\ 1 & \text{otherwise.} \end{cases} \qquad (3.11)$$

The conclusions above imply that the transition period for square-wave input is $t = \delta$: as soon as $t > \delta$ square-wave input is identical to that of Poisson input, provided that the usual approximation is used. It is also easily seen that, for square-wave input, its mean, variance and CV are all smaller than that of the Poisson process.

We have similar conclusions for the model with reversal potentials.

Theorem 4. *For square-wave inputs we have the following usual approximation:*

$$d\bar{i}_{syn}(t) = [\bar{a}p\lambda_E(V_E - Z_t) + \bar{b}q\lambda_I(V_I - Z_t)]\bar{\mu}(t)\,dt$$
$$+ \left[\sqrt{\bar{a}^2 p\lambda_E(Z_t - V_E)^2 + \bar{b}^2 q\lambda_I(Z_t - V_I)^2}\right]\bar{\mu}(t)\,dB_t. \qquad (3.12)$$

3.4. Numerical results

We employ the following parameters in our numerical simulations: $a = b = 0.5$ mV, $V_{rest} = -50$ mV, $V_{thre} = -30$ mV, $p = q = 100$, $\lambda_E = 100$ Hz and $\lambda_I = 0, 10, 20, \ldots, 100$ Hz, which is the set of parameters used elsewhere [2,4,6,7,9] and is thought to be in physiological regions of the visual cortex cells [22, 23]. As before [2, 4, 6, 7, 9] we numerically solve the membrane equations of V_t by an Euler scheme [12] with a step size of 0.01. Further small time steps are used and we conclude no significant improvements are obtained. In simulations, 1000 spikes are generated for each set of parameters with $V_0 = V_{rest}$ and $I_{syn}(0) = 0$. For minimizing the influence of nonstationarity (V_t is reset to V_{rest} after spiking, but $I_{syn}(t)$ is not reset to zero) the first five spikes are discarded in all subsequent analysis.

From simulation results we see that, when α is large (see figure 3) or δ is small (see figure 1), and when λ_I/λ_E is small, the difference between α-wave or square-wave input and Poisson inputs is small; but when λ_I/λ_E approaches one, the difference becomes obvious.

We further consider the breakdown of the usual approximation. In figure 4 we go to an extreme case by showing numerical results of $\alpha = 0.01$, that is an EPSP takes 100 ms to rise (see example 2). As one might expect, the CV of efferent spike trains is much smaller than that with the usual approximaiton inputs. However, and most interestingly, the mean of ISIs of efferent spike trains is still close to that of the usual approximation inputs. The mean of efferent ISIs predominantly depends on the mean of input EPSPs and IPSPs, as we have observed in the case of correlated inputs (see [10, figures 2–5]), but the variance is sensitive
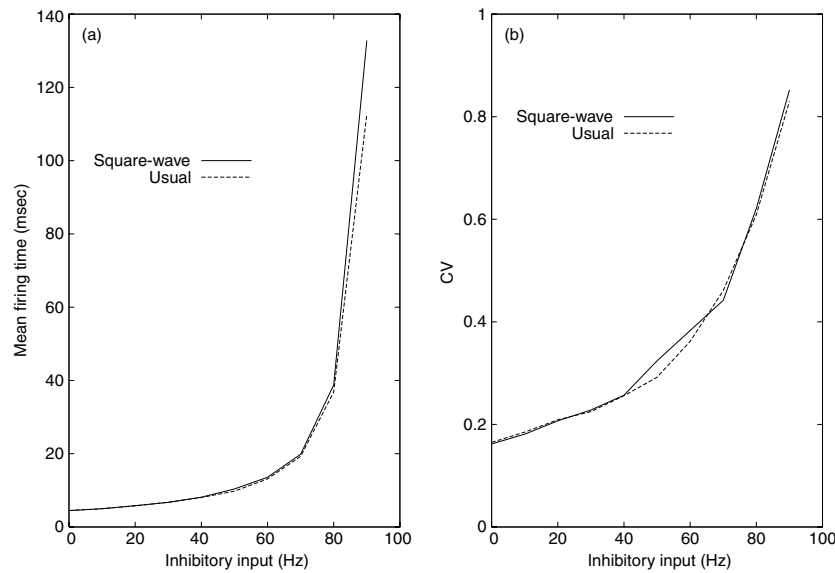
Figure 1. Mean and CV of square-wave inputs of the integrate-and-fire model with $\delta = 1$ ms and the usual approximation inputs (numerical results). When λ_I is smaller than 90 Hz, the discrepancy between the usual approximation inputs and square-wave inputs is small. In general the usual approximation gives an excellent approximation to the square-wave inputs.

to input variance. The results suggest simply that the output mean firing time depends on the deterministic part of the inputs. We consider the following equation:

$$dV_t = -\frac{V_t}{\gamma}\,dt + (ap\lambda_E - bq\lambda_I)\,dt \tag{3.13}$$

i.e. equation (3.5) with stochastic term being zero and $\mu(t) = 1$. Solving equation (3.13), we obtain

$$V_t = (ap\lambda_E - bq\lambda_I)\gamma\left(1 - \exp\left(-\frac{t}{\gamma}\right)\right).$$

Therefore the time at which V_t reaches V_{thre} is

$$T = \gamma \log(1 - V_{\text{th}}/(\gamma(ap\lambda_E - bq\lambda_I))). \tag{3.14}$$

We compare T with the mean firing time obtained in terms of the usual approximation inputs[1] in figure 2. A reasonable approximation is obtained when $\lambda_I < 80$ Hz. Note that this approximation is only valid in the regions of λ_I in which the attractor of the deterministic part is above the threshold (see [9] for details).

A neuron is supposed to distinguish inputs between different sources and so successfully interacts with its environment. If we assume that different rising times of afferent EPSPs— inputs from different sources—carry different information, then in terms of the mean firing time the integrate-and-fire model cannot tell the difference, comparing figure 3 with 4. Nevertheless, the second order statistics can do it (see figures 1–4). There are many authors who have suggested that higher order statistics are necessary for information processing. Here we provide a concrete example to show the importance of higher order statistics in neuronal

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[1] Since we only consider model behaviour when inputs become stationary, the mean firing time obtained in terms of the usual approximation for the integrate-and-fire model are almost identical, see figures 1, 3 and 4.
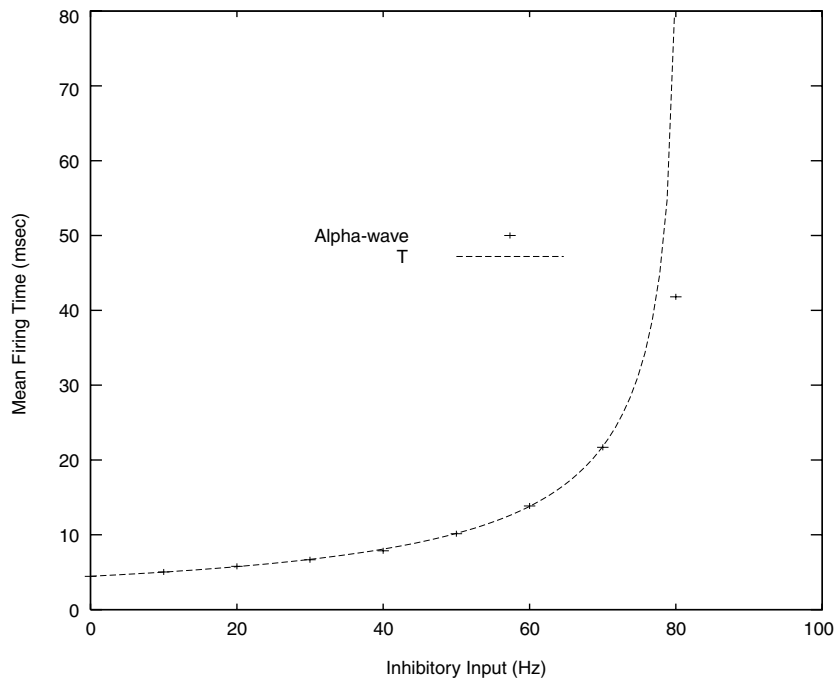
Figure 2. Mean of α-wave inputs with $\alpha = 1$ (numerical results) and T defined by equation (3.14) of the integrate-and-fire model. We see that, when the ratio between inhibitory and excitatory inputs is small ($\lambda_I < 80$ Hz), T gives rise to an excellent approximation. A comparison with figure 4 with $\alpha = 0.01$ tells us that the same conclusion is true, see also figure 1.
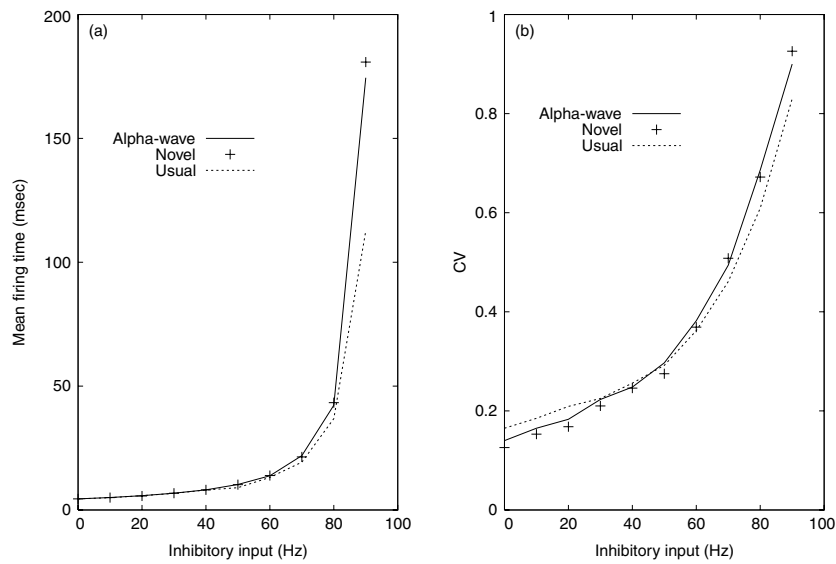

Figure 3. Output mean and CV of the integrate-and-fire model of α-wave inputs with $\alpha = 1$ and the usual approximaiton inputs (numerical results). When λ_I is smaller than 80 Hz, the discrepancy between the usual approximation inputs and α-wave inputs is small.
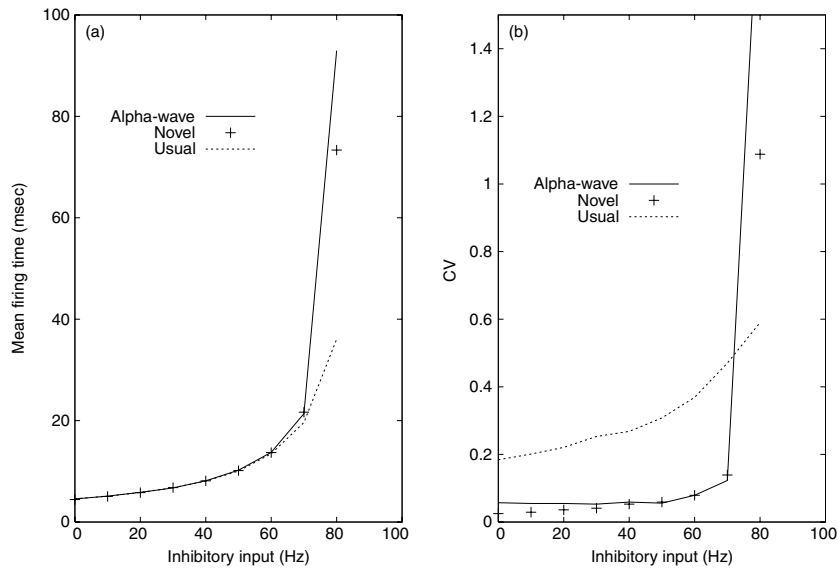
Figure 4. Mean and CV of the integrate-and-fire model of α-wave inputs with $\alpha = 0.01$, the usual approximaiton inputs and the novel scheme inputs (numerical results). We are only able to simulate for λ_I up to 70 Hz. We see that, when λ_I is smaller than 70 Hz, the discrepancy of mean between the usual approximation inputs and α-wave inputs is small, but not for CV.

model behaviour. In contrast, if we assume that the time course of inputs is irrelevant, and only the occurrence time of spikes carries information, then in the region where λ_I/λ_E is small, the integrate-and-fire device serves as an ideal unit for information processing: in terms of the mean firing time it is very robust with respect to different time courses of EPSPs and IPSPs, as shown in figures 1–4. But in the region where λ_I/λ_E approaches one, the integrate-and-fire device becomes very sensitive to the fluctuation of inputs.

In conclusion (figures 1–4), when the ratio between inhibitory and excitatory inputs is small (for discussions of this issue, see, e.g., [2–4,6–10,16,21,22]), in terms of the mean firing time, noninstantaneous inputs and the usual approximation inputs produce similar results. When the ratio approaches one, the discrepancy between two input patterns becomes obvious and thus the usual approximation breaks down. This conclusion simply indicates that if we suppose a neuron operates in the exact balance region, then using the usual approximation to replace the noninstantaneous inputs, which is mostly used in the literature, is not appropriate.

Can we develop a new approximation scheme to improve the approximation? This is the task of the next section.

4. A novel approach

The method presented in the previous section, i.e. the usual approximation, is well known in the literature. But as we have shown before, it fails to approximate the true behaviour of the model with current inputs when either the ratio between inhibitory and excitatory inputs approaches one or the rising time is slow. It is then a natural question to ask what we have missed in the usual approximation.

Looking at the variance $\sigma(t, \lambda)$ given by

$$\sigma(t, \lambda)^2 = \lambda \left[t - \frac{11}{4\alpha} + \frac{4}{\alpha} e^{-\alpha t} + 2t e^{-\alpha t} - \frac{5}{4\alpha} e^{-2\alpha t} - \frac{3t}{2} e^{-2\alpha t} - \frac{\alpha t^2}{2} e^{-2\alpha t} \right] \tag{4.1}$$

we see that the leading term we omit in the usual approximation is $11/4\alpha$. Since in the usual approximation only the derivative of $\sigma(t, \lambda)$ is used, the constant term disappears. We therefore want to find a process $\eta^\alpha(t)$ satisfying the property that

$$\langle (B_t - \eta^\alpha(t))^2 \rangle = t - \frac{11}{4\alpha} + O(t \exp(-\alpha t)).$$

We choose an Ornstein–Uhlenbeck process given by

$$\begin{aligned} d\xi^\alpha(t) &= -\frac{\alpha}{2} \xi^\alpha(t) \, dt + dB_t \\ \xi^\alpha(0) &= 0. \end{aligned} \tag{4.2}$$

Let $\eta^\alpha(t) = c\xi^\alpha(t)$, where c is a constant satisfying

$$\langle (B_t - \eta^\alpha(t))^2 \rangle = t + c^2 \int_0^t \exp(-\alpha(t-s)) \, ds - c \int_0^t \exp\left(-\frac{\alpha}{2}(t-s)\right) ds. \tag{4.3}$$

We find a new scheme $\tilde{i}_{\text{syn}}(t)$ to approximate $I_{\text{syn}}(t)$ defined by

$$d\tilde{i}_{\text{syn}}(t) = (ap\lambda_E - bq\lambda_I) \, dt + \sqrt{a^2 p \lambda_E + b^2 q \lambda_I} \, dB_t - \sqrt{a^2 p \lambda_E + b^2 q \lambda_I} \frac{4 - \sqrt{5}}{2} \, d\xi^\alpha(t). \tag{4.4}$$

For specification we write down the full integrate-and-fire model again here:

$$dv_t = -\frac{1}{\gamma}(v_t - V_{\text{rest}}) \, dt + (ap\lambda_E - bq\lambda_I) \, dt + \sqrt{a^2 p \lambda_E + b^2 q \lambda_I} \left[dB_t - \frac{4 - \sqrt{5}}{2} \, d\xi^\alpha(t) \right]$$

$$d\xi^\alpha(t) = -\frac{\alpha}{2} \xi^\alpha(t) \, dt + dB_t \qquad \xi^\alpha(0) = 0. \tag{4.5}$$

In figures 3 and 4 numerical simulations are shown with $\alpha = 1$ and 0.01. We see that a substantial improvement is achieved with the new scheme defined by equation (4.5).

We now give a few words on the novel approach presented here. Instead of the widely used Brownian motion approximation to the α wave, we have to used a superposition of the 'white' and 'coloured' noise approximation, i.e. the term $B_t - \eta^\alpha(t)$. The fact that this calibration improves the usual approximation is, however, not surprising at all. Due to the current input, we naturally expect that there are temporal correlations in inputs. We have tried different ways to approximate the auto-correlation of $I_{\text{syn}}(t)$ which is

$$\langle (I_{\text{syn}}(t) - \langle I_{\text{syn}}(t) \rangle)(I_{\text{syn}}(s) - \langle I_{\text{syn}}(s) \rangle) \rangle$$

$$\begin{aligned} &= -\frac{2\lambda g^2}{\alpha} + \lambda g^2 s + \frac{2\lambda g^2}{\alpha} \exp(-\alpha s) + \lambda g^2 s \exp(-\alpha s) + \lambda g^2 \exp(-\alpha(t-s)) \\ &\quad \times \left[-\frac{3}{4\alpha} - \frac{1}{4}(t-s) + \frac{2}{\alpha} \exp(-\alpha s) + s \exp(-\alpha s) + (t-s) \exp(-\alpha s) \right. \\ &\quad -\frac{5}{4\alpha} \exp(-2\alpha s) - \frac{3s}{2} \exp(-2\alpha s) - \frac{3}{4}(t-s) \exp(-2\alpha s) \\ &\quad \left. -\frac{\alpha s}{2}(t-s) \exp(-2\alpha s) - \frac{\alpha s^2}{2} \exp(-2\alpha s) \right] \end{aligned} \tag{4.6}$$

for $t \geqslant s$. When $t = s$ equation (4.6) is (4.1). Nevertheless, it is a hard problem due to terms taking the form of $t \exp(-t)$ in the auto-correlation of $I_{\mathrm{syn}}(t)$. We then simply approximate the first order term $t - 11/(4\alpha)$ and omit all terms containing $\exp(-t)$ (see equation (4.1)). Numerical simulations show that the approximation scheme presented here improves considerably the usual approximation. Furthermore it is valid for $0 < \alpha \leqslant \infty$, i.e. when $\alpha = \infty$ equation (4.5) gives exactly the usual approximation.

The first exit time of a linear dynamic system with a 'coloured' noise perturbation has been widely discussed in the literature and different analytical approaches to estimate it have been put forward. We will discuss it in a subsequent publication.

Finally we point out that, much as we confine ourselves to the α-wave inputs, the approach presented here is readily generalized to any form of current inputs by calculating the constant c in equation (4.3).

5. Biophysical models

We apply the results of the previous section to biophysical models. In fact the generalization is almost straightforward since essentially we have approximated synaptic inputs in the previous section.

We consider the following Hodgkin–Huxley model with parameters given in the literature [3]:

$$C \, dV = -g_{\mathrm{Na}} m^3 h (V - V_{\mathrm{Na}}) \, dt - g_k n^4 (V - V_k) \, dt - g_L (V - V_L) \, dt + I_{\mathrm{syn}}(t) \, dt \qquad (5.1)$$

where

$$\frac{dn}{dt} = \frac{n_\infty - n}{\tau_n} \qquad \frac{dm}{dt} = \frac{m_\infty - m}{\tau_m} \qquad \frac{dh}{dt} = \frac{h_\infty - h}{\tau_h}$$

and

$$n_\infty = \frac{\alpha_n}{\alpha_n + \beta_n} \qquad m_\infty = \frac{\alpha_m}{\alpha_m + \beta_m} \qquad h_\infty = \frac{\alpha_h}{\alpha_h + \beta_h}$$

$$\tau_n = \frac{1}{\alpha_n + \beta_n} \qquad \tau_m = \frac{1}{\alpha_m + \beta_m} \qquad \tau_h = \frac{1}{\alpha_h + \beta_h}$$

with

$$\alpha_n = \frac{0.01(V + 55)}{1 - \exp\left(-\frac{V+55}{10}\right)} \qquad \beta_n = 0.125 \exp\left(-\frac{V + 65}{80}\right)$$

$$\alpha_m = \frac{0.1(V + 40)}{1 - \exp\left(-\frac{V+40}{10}\right)} \qquad \beta_m = 4 \exp\left(-\frac{V + 65}{18}\right)$$

$$\alpha_h = 0.07 \exp\left(-\frac{V + 65}{20}\right) \qquad \beta_h = \frac{1}{\exp\left(-\frac{V+35}{10}\right) + 1}.$$

The parameters used in equation (5.1) are $C = 1$, $g_{\mathrm{Na}} = 120$, $g_K = 36$, $g_L = 0.3$, $V_k = -77$, $V_{\mathrm{Na}} = 50$ and $V_L = -54.4$. All parameters in synaptic inputs are the same as in the previous sections except that $a = b = 1.$, since when $a = b = 0.5$ the firing time is too long (cf [3], figure 1). The initial values for m, n, h and the membrane potential are 0.0529, 0.317, 0.5961 and -65, respectively.

Figure 5 plots a comparison with different inputs with $\alpha = 1$. Again it is evident to see that the novel approach of the previous section gives a much better approximation than the usual approximation. Comparing to the results obtained from the integrate-and-fire model, we see that both the usual approximation and the novel approach gives worse results. In other
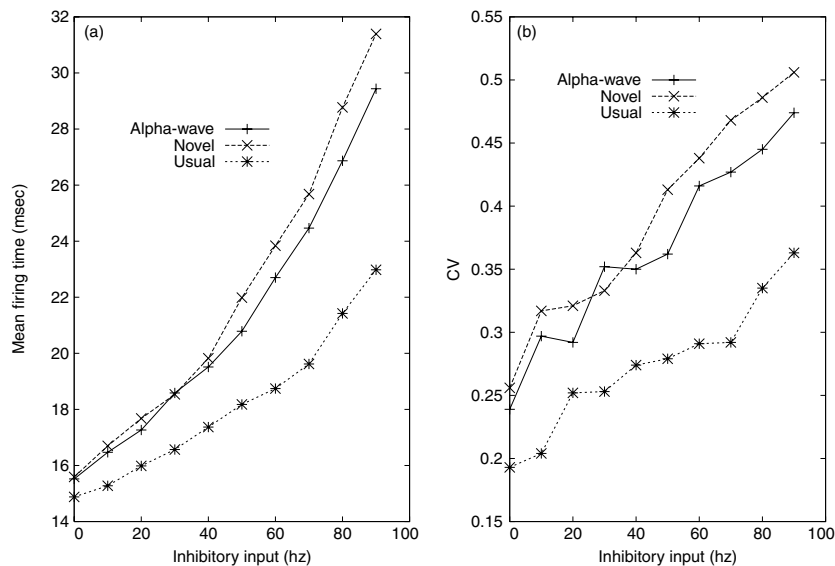
Figure 5. Mean and CV of α-wave inputs, the usual approximation and novel scheme inputs with $\alpha = 1$ for the Hodgkin–Huxley model (numerical results).

words, the noninstantaneous input has more impact on the biophysical model than on the integrate-and-fire model, which is basically a linear model.

From figure 5 we might conclude that, with current inputs, the efferent spike trains of the Hodgkin–Huxley model are quite regular with a CV less than 0.5. However, when standard deviation, s, of output ISI is plotted against mean firing time, m, we obtain approximately straight lines (cf figure 6):

$$s = km - r. \tag{5.2}$$

This suggests an effective refractory period of about $m = r/k$. We note that, for inputs of the usual approximation, it is about 10.46 ms and for α-wave inputs it is 11.25 ms. This implies that, once the effective refractory period is subtracted from each ISI, CV is about 0.65 for Poisson inputs and 0.8 for α-wave inputs. The CV and refractory period of the usual approximation are both smaller than that of the α wave. The conclusions above agrees with our basic belief, that all neurons fire irregularly when subjected to sufficient low intensity random input, and almost all neurons fire regularly if driven very hard.

The conclusions above are further tested in figures 7 and 8 with $\alpha = 0.5$. We see that all conclusions remain true.

The Hodgkin–Huxley model is numerically solved using an algorithm for stiff equations from the NAG library (D02NBF) with step size of 0.01. Further small step sizes are used and we conclude no significant improvements are observed. The spike detecting threshold used in the simulations for the Hodgkin–Huxley model is 0 mV, as we employed before [3].

6. Discussion

We have presented a theoretical and numerical approach for studying the impact of noninstantaneous inputs on the output of neuronal models. For α-wave and square-wave inputs, and any noninstantaneous inputs, analytical and numerical results are obtained for the
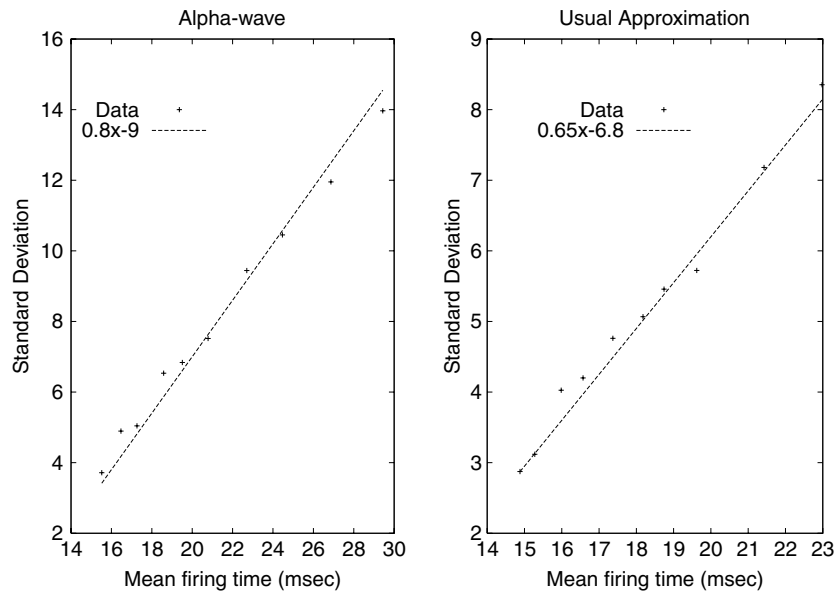
Figure 6. Standard deviation against mean firing time for the Hodgkin–Huxley model with α-wave inputs and the usual approximation inputs, $\alpha = 1$. Lines are obtained from linear regressions.
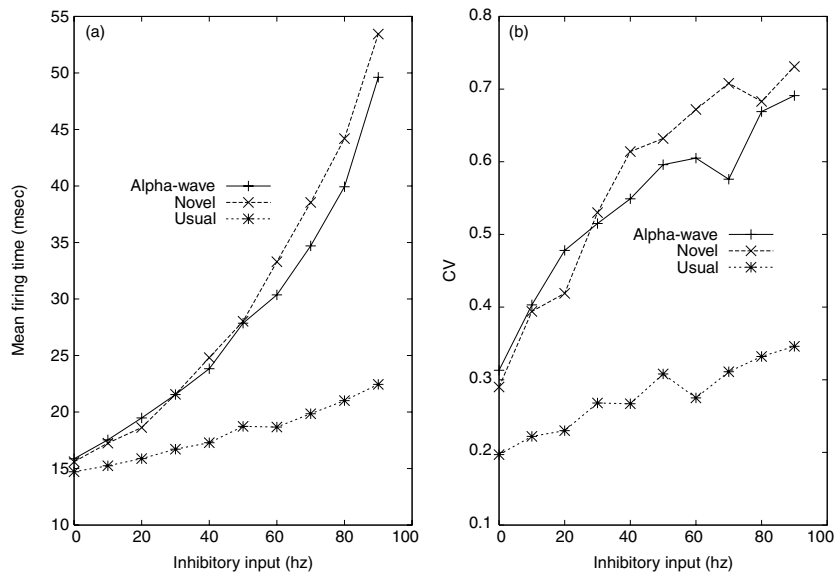

Figure 7. Mean and CV of α-wave inputs, the usual approximation and novel scheme inputs with $\alpha = 0.5$ for the Hodgkin–Huxley model (numerical results).

usual approximation which essentially reveals the difference between the instantaneous and noninstantaneous inputs. When the ratio between inhibitory and excitatory inputs is low and the rising time is short, the usual approximation produces satisfying results for the integrate-and-fire model, but not for the Hodgkin–Huxley model. We then proposed a new approximation scheme based upon a superposition of 'white' and 'coloured' noise to approximate neuronal
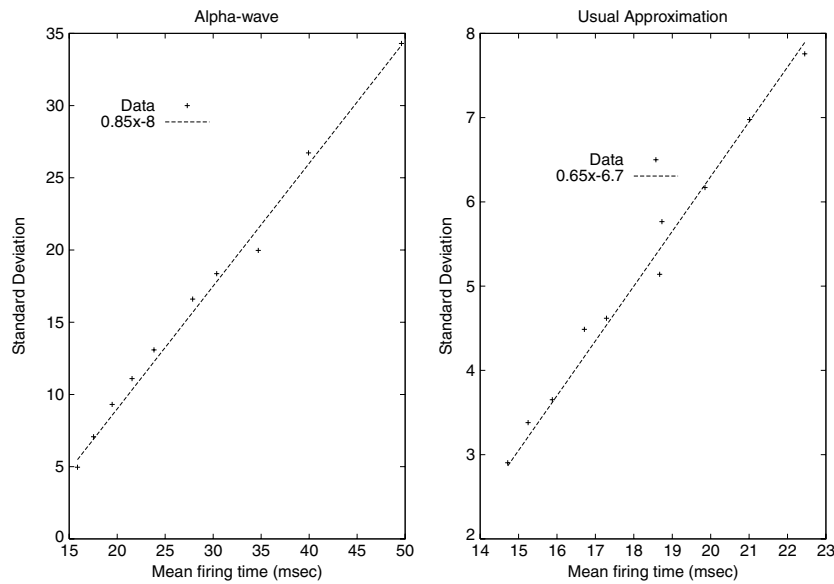
Figure 8. Standard deviation against mean firing time for the Hodgkin–Huxley model with α-wave inputs and the usual approximation inputs, $\alpha = 0.5$. Lines are obtained from linear regressions.

models with current inputs. Numerical simulations show that the new scheme considerably improves the approximation. Since α-wave inputs are much closer to actually biological reality than instantaneous inputs and are widely applied in modeling neural activities, we conclude that in studying neuronal activities subjected to synaptic inputs it is reasonable to replace the classical Ornstein–Uhlenbeck process by the following process:

$$\tilde{i}_{\text{syn}}(t) = [ap\lambda_{\text{E}} - bq\lambda_{\text{I}}]t + \sqrt{a^2 p\lambda_{\text{E}} + b^2 q\lambda_{\text{I}}} \left[B_t - \frac{4 - \sqrt{5}}{2} \xi^\alpha(t) \right]$$

$$\mathrm{d}\xi^\alpha(t) = -\frac{\alpha}{2} \xi^\alpha(t)\,\mathrm{d}t + \mathrm{d}B_t$$

$$\xi^\alpha(0) = 0.$$

$$(6.1)$$

This also opens up new theoretical problems such as how to estimate the first exit time of neuronal models subjected to a superposition of 'white' and 'coloured' noise inputs as defined by equation (6.1). A few issues we are going to explore further are:

- It is worth studying further the effect of more biologically realistic inputs such as AMPA, NMDA, GABA$_A$ and GABA$_B$ on the output of neuronal models. AMPA and GABA$_A$ are fast and equivalent to the case of a large α, while NMDA and BABA$_B$ are slow and equivalent to a small α. We refer the reader to [13], which is a direct application of our current results, for details.
- We have observed in the present paper that α plays a more important role in the nonlinear model (the Hodgkin–Huxley model) than the 'linear' model (the integrate-and-fire model). The usual diffusion approximation gives poor results in estimating the mean first exit time and CV for some parameter values in the case of the integrate-and-fire neuron, but for most parameter values in the case of the Hodgkin–Huxley neuron. In fact, how the correlation in inputs (the coloured noise term) affects the output of a nonlinear system has been extensively studied in the past few years, see, e.g., [14]. We expect that α could

play a role of a 'time switcher' in neuronal models: the input could be subthreshold or superthreshold, by controlling α alone.

Acknowledgments

References

[1] Abbott L F, Varela J A, Sen K and Nelson S B 1997 Synaptic depression and cortical gain control *Science* **275** 220–3
[2] Brown D and Feng J 1999 Is there a problem matching model and real CV(ISI)? *Neurocomputing* **26–7** 117–22
[3] Brown D, Feng J and Feerick S 1999 Variability of firing of Hodgkin–Huxley and FitzHugh-nagumo neurones with stochatic synaptic input *Phys. Rev. Lett.* **82** 4731–4
[4] Feng J 1997 Behaviours of spike output jitter in the integrate-and-fire model *Phys. Rev. Lett.* **79** 4505–8
[5] Feng J and Cassia-Moura R 1999 Output of a neuronal population code *Phys. Rev.* E **59** 7246–9
[6] Feng J 1999 Origin of firing varibility of the integrate-and-fire model *Neurocomputing* **26–7** 87–91
[7] Feng J and Brown D 1998 Spike output jitter, mean firing time and coefficient of variation *J. Phys. A: Math. Gen.* **31** 1239–52
[8] Feng J and Brown D 1998 Impact of temporal variation and the balance between excitation and inhibition on the output of the perfect integrate-and-fire model *Biol. Cybern.* **78** 369–76
[9] Feng J and Brown D 1999 Coefficient of variation greater than 0.5 How And When? *Biol. Cybern.* **80** 291–7
[10] Feng J and Brown D 2000 Impact of correlated inputs onthe output of the integrate-and-fire mdoels *Neural Comput.* **12** 711–32
[11] Feng J and Brown D 1999 Integrate-and-fire model and Hodgkin–Huxley model with correlated inputs *Phys. Rev.* E, at press
[12] Feng J, Lei G and Qian M 1992 Second-order algorithms for SDE *J. Comput. Math.* **10** 376–87
[13] Feng J, Li G B, Brown D and Buxton H 2000 Balance between four types of synaptic input for the integrate-and-fire model *Phys. Rev.* E at press
[14] Garcia-Ojalvao J and Sancho J M 1999 *Noise in Spatially Extended Systems* (Berlin: Springer)
[15] Harris C M and Wolpert D M 1998 signal-dependent noise determines motor planning *Nature* **394** 780–4
[16] Konig P, Engel A K and Singer W 1996 Integrator or coincidence detector? The role of the cortical neuron revisited *TINS* **19** 130–7
[17] Kandel E R, Schwartz J H and Jessell T M 1991 *Principles Of Neural Science* 3rd edn (Englewood Cliffs, NJ: Prentice-Hall)
[18] Musila M and Lánský P 1994 On the interspike intervals calculated from diffusion approximations for Stein's neuronal model with reversal potentials *J. Theor. Biol.* **171** 225–32
[19] Ricciardi L M and Sato S 1990 Diffusion process and first-passage-times problems *Lectures in Applied Mathematics and Informatics* ed L M Ricciardi (Manchester: Manchester University Press)
[20] Rieke F, Warland D, de Ruyter van Steveninck R and Bialek W 1997 *Spikes* (Cambridge, MA: MIT Press)
[21] Softky W and Koch C 1993 The highly irregular firing of cortical-cells is inconsistent with temporal integration of random EPSPs *J. Neurosci.* **13** 334–50
[22] Shadlen M N and Newsome W T 1994 Noise, neural codes and cortical organization *Curr. Opin. Neurobiol.* **4** 569–79
[23] Thomson A M 1997 Activity-dependent properties of synaptic transmission at two classes of connections made by rat neocortical pyramidal *J. Physiol.* **502** 131–47
[24] Tuckwell H C 1988 *Stochastic Processes in the Neurosciences* (Philadelphia, PA: Society for Industrial and Applied Mathematics)
[25] Van Vereeswijk C, Abbott L F and Ermentrout G B 1994 *J. Comput. Neurosci.* **1** 313–21
[26] Wilbur W J and Rinzel J 1983 A theoretical basis for large coefficient of variation and bimodality in neuronal interspike interval distributions *J. Theor. Biol.* **105** 345–68