Neuronal Models with Current Inputs

Jianfeng Feng

COGS, Sussex University, Brighton BN1 9QH, UK
`http://www.cogs.susx.ac.uk/users/jianfeng`

Abstract. We propose a novel approach based upon a superposition of 'colored' and 'white' noise to approximate current inputs in neural models. Numerical results show that the novel approach substantially improves the approximation within widely, physiologically reasonable regions of the rising time of α-wave inputs.

1 Introduction

Although single neurone model with random inputs has been widely studied *in computo*, most of such studies are done under the assumption that inputs are instantaneous [1,2,3,4,5,13]. 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 [10] at page 184). Theoretically in [14] the authors have found the interesting impact of EPSP rising time courses in synchronising 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 it has been investigated for decades to use the Ornstein-Uhlenbeck process to approximate neuronal models with Poisson inputs.

We take into account 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.

$$dx_t = b(x_t, t)dt + \sigma(x_t, t)dB_t$$

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

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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 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 [6] 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 satisfying 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 'color' 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 has 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, thus documenting more thoroughly the restrictions and potential of the models. In [5] we have considered the behaviour of the integrate-and-fire model subjected to independent inputs with different distribution tails; in [6] we have taken into account the behaviour of the integrate-and-fire model with correlated inputs. On the other hand we have generalised these considerations to biophysical models and some intriguing properties have been found[2,7].

Due to space limit, we only summarize results here and refere the reader to [8] for details.

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

$$dV_t = -\frac{1}{\gamma}(V_t - V_{rest})dt + I_{syn}(t)dt \tag{1}$$

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 as the integrate-and-fire model. Synaptic input $I_{syn}(t)$ is modelled by

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

where $T_k^E = \sum_{i=1}^k t_i^E$ ($T_k^I = \sum_{i=1}^k t_i^I$) for i.i.d. random sequences $t_i^E, t_i^I, i = 1, 2, \cdots$, $a > 0, b > 0$ 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 cell's synaptic inputs. It assumes that the responds to the input instantaneously. There are some other optimal properties such as optimising the mutual information etc. for Poisson inputs[12].

Example 2 When

$$f(t - T_k^E) = \alpha^2(t - T_k^E)\exp(-\alpha(t - T_k^E)) \quad t > T_k^E$$

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 [13] 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 α-wave synapse. Here we emphasise that for the same neurone 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 hundreds milliseconds (see [10] at page 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 [11,15] defined by

$$dZ_t = -\frac{1}{\gamma}(Z_t - V_{rest})dt + \bar{I}_{syn}(t)dt \tag{2}$$

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

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

$\bar{a}, \bar{b}$ are the magnitude of a single EPSP and IPSP respectively, 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 hyperpolarise it. By choosing different reversal potentials and characteristic times of f, $\bar{I}_{syn}(t)$ corresponds to different kind of synapses such as NMDA, AMPA GABA$_A$ and GABA$_B$.

3 A Novel Approach

The method presented in the previous subsection, i.e. the usual approximation, are 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 that what we have missed in the usual approximation.

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

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

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

$$\begin{cases} d\xi^\alpha(t) = -\frac{\alpha}{2}\xi^\alpha(t)dt + dB_t \\ \xi^\alpha(0) = 0 \end{cases} \quad (4)$$

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

$$\langle (B_t - \eta^\alpha(t))^2 \rangle = t + c^2 \int_0^t \exp(-\alpha(t-s))ds - c\int_0^t \exp(-\frac{\alpha}{2}(t-s))ds \quad (5)$$

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

$$\begin{aligned} d\tilde{i}_{syn}(t) &= (ap\lambda_E - bq\lambda_I)dt + \sqrt{a^2p\lambda_E + b^2q\lambda_I}dB_t \\ &\quad -\sqrt{a^2p\lambda_E + b^2q\lambda_I}\frac{4-\sqrt{5}}{2}d\xi^\alpha(t) \end{aligned} \quad (6)$$

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

$$\begin{cases} dv_t = -\frac{1}{\gamma}(v_t - V_{rest})dt + (ap\lambda_E - bq\lambda_I)dt \\ \qquad\qquad + \sqrt{a^2 p\lambda_E + b^2 q\lambda_I}[dB_t - \frac{4-\sqrt{5}}{2} d\xi^\alpha(t)] \\ d\xi^\alpha(t) = -\frac{\alpha}{2}\xi^\alpha(t)dt + dB_t \\ \xi^\alpha(0) = 0 \end{cases} \tag{7}$$

In [8] numerical simulations are shown with $\alpha = 1$ and $\alpha = 0.01$. We see that a substantial improvement is achieved with the new scheme defined by Eq. (7).

We mention 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 'white' and 'color' 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 $I_{syn}(t)$ which is

$$\begin{aligned} &\langle (I_{syn}(t) - \langle I_{syn}(t)\rangle)(I_{syn}(s) - \langle I_{syn}(s)\rangle)\rangle \\ &= -\frac{2\lambda g^2}{\alpha} + \lambda g^2 s + \frac{2\lambda g^2}{\alpha}\exp(-\alpha s) + \lambda g^2 s\exp(-\alpha s) + \lambda g^2 \exp(-\alpha(t-s))[\\ &\quad -\frac{3}{4\alpha} - \frac{1}{4}(t-s) + \frac{2}{\alpha}\exp(-\alpha s) + s\exp(-\alpha s) + (t-s)\exp(-\alpha s) \\ &\quad -\frac{5}{4\alpha}\exp(-2\alpha s) - \frac{3s}{2}\exp(-2\alpha s) - \frac{3}{4}(t-s)\exp(-2\alpha s) \\ &\quad -\frac{\alpha s}{2}(t-s)\exp(-2\alpha s) - \frac{\alpha s^2}{2}\exp(-2\alpha s)] \end{aligned} \tag{8}$$

for $t \geq s$. When $t = s$ Eq. (8) is Eq. (3). Nevertheless, it is a hard problem due to terms taking the form of $t\exp(-t)$ in the auto-correlation of $I_{syn}(t)$. We then simply approximate the first order term $t - 11/(4\alpha)$ and omit all terms containing $\exp(-t)$ (see Eq. (3)). Numerical simulations show that the approximation scheme presented here improves considerably the usual approximation. Furthermore it is valid for $0 < \alpha \leq \infty$, i.e. when $\alpha = \infty$ Eq. (7) gives exactly the usual approximation.

The first exit time of a linear dynamic system with a 'color' 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 Eq. (5).

4 Biophysical Models

We apply results in the previous section to biophysical models. In fact the generalisation 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[2].

$$CdV = -g_{Na}m^3h(V - V_{Na})dt - g_kn^4(V - V_k)dt - g_L(V - V_L)dt + I_{syn}(t)dt \quad (9)$$

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

$$\begin{aligned} n_\infty &= \frac{\alpha_n}{\alpha_n + \beta_n}, & m_\infty &= \frac{\alpha_m}{\alpha_m + \beta_m}, & h_\infty &= \frac{\alpha_h}{\alpha_h + \beta_h} \\ \tau_n &= \frac{1}{\alpha_n + \beta_n}, & \tau_m &= \frac{1}{\alpha_m + \beta_m}, & \tau_h &= \frac{1}{\alpha_h + \beta_h} \end{aligned}$$

with

$$\begin{aligned} \alpha_n &= \frac{0.01(V + 55)}{\exp(-\frac{V + 55}{10}) - 1} & \beta_n &= 0.125\exp(-\frac{V + 65}{80}) \\ \alpha_m &= \frac{0.1(V + 40)}{1 - \exp(-\frac{V + 40}{10})} & \beta_m &= 4\exp(-\frac{V + 65}{18}) \\ \alpha_h &= 0.07\exp(-\frac{V + 65}{20}) & \beta_h &= \frac{1}{-\exp(\frac{V + 35}{10}) + 1} \end{aligned}$$

The parameters used in Eq. (9) are $C = 1, g_{Na} = 120, g_K = 36, g_L = 0.3, V_k = -77, V_{Na} = 50, V_L = -54.4$. 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. Fig. 1 in [2]). The initial values for m, n, h and the membrane potential are $0.0529, 0.317, 0.5961$ and -65 respectively.

Figures in [8] plot 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 words, the noninstantaneous input has more impact on the biophysical model than that on the integrate-and-fire model, which is basically a linear model.

From figures in [8] we might conclude that with current inputs, the efferent spike trains of the Hodgkin-Huxley model is quite regular with a CV less than .5. However, when standard deviation, s, of output interspike interval is plotted against mean firing time, m, we obtain approximately straight lines

$$s = km - r \quad (10)$$

This suggests an effective refractory period of about $m = r/k$. We note that for inputs of the usual approximation, it is about 10.46msec and for α-wave inputs is 11.25 msec. This implies that, once the effective refractory period is subtracted from each interspike interval, 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 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 Hodgkin-Huxley model is numerically solved using an algorithm for stiff equations from 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 threshould used in the simulations for the Hodgkin-Huxley model is 0 mV, as we employed before[2].

5 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, and any noninstantaneous inputs, analytical and numerical results are obtained for the 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 approximate scheme based upon a superposition of 'white' and 'color' noise to approximate neuronal models with current inputs. Numerical simulations show that the new scheme considerably improves the approximation. Since α-wave inputs are much more close 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

$$\begin{cases} \tilde{i}_{syn}(t) = [ap\lambda_E - bq\lambda_I]t \\ \qquad\qquad + \sqrt{a^2 p\lambda_E + b^2 q\lambda_I}\,[B_t - \frac{4-\sqrt{5}}{2}\xi^\alpha(t)] \\ d\xi^\alpha(t) = -\frac{\alpha}{2}\xi^\alpha(t)dt + dB_t \\ \xi^\alpha(0) = 0 \end{cases} \tag{11}$$

This also opens up new theoretical problems such as to estimate the first exit time of neuronal models subjected to a superposition of 'white' and 'color' noise inputs as defined by Eq. (11). A few issues we are going to further explore are

- It worths further studying 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 a small α.
- 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 intergrate-and-fire neuron, but for most parameter

values in the case of the Hodgkin-Huxley neuron. In fact, how the correlation in inputs (the color noise term) affects the output of a nonlinear system is extensively studied in the past few years, see for example [9]. 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.

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References

1. Brown D., and Feng J. (1999) Is there a problem matching model and real CV(ISI)? *Neurocomputing* **26-27** 117-122.
2. 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** 4731-4734.
3. Feng, J.(1997), Behaviours of spike output jitter in the integrate-and-fire model. *Phys. Rev. Lett.* **79** 4505-4508.
4. Feng J., and Brown D.(1998). Spike output jitter, mean firing time and coefficient of variation, *J. of Phys. A: Math. Gend.*, **31** 1239-1252.
5. 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** 369-376.
6. Feng J., and Brown D.(2000). Impact of correlated inputs onthe output of the integrate-and-fire mdoels *Neural Computation* **12** 711-732.
7. Feng J., and Brown D.(1999). Integrate-and-fire model and Hodgkin-Huxley model with correlated inputs *Phys. Rev. Lett.* (submitted).
8. Feng J., Li, G.B. (2001) Integrate-and-fire and Hodgkin-Huxley models with current inputs *J. Phys. A.* **34** 1649-1664.
9. Garcia-Ojalvao J., and, Sancho J.M. (1999) *Noise in Spatially Extended Systems* Springer-Verlag: New York.
10. Kandel E.R., Schwartz J.H., and Jessell T.M.(1991) *Principles Of Neural Science*, 3ed edition, Prentice-Hall International Inc.
11. 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**, 225-232.
12. Rieke, F., Warland, D., de Ruyter van Steveninck, R., and Bialek W. (1997) Spikes. The MIT Press.
13. Tuckwell H. C. (1988), *Stochastic Processes in the Neurosciences.* Society for industrial and applied mathematics: Philadelphia, Pennsylvania.
14. Van Vereeswijk C., Abbott L.F., and Ermentrout G.B. (1994), *Jour. Computat. Neurosci.* **1** 313-321.
15. 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** 345-368.