Predicting the spike train of cortical neurons with high reliability

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Abstract

We propose a simple technique to map a generic threshold model, namely the Spike Response Model (SRM), to data of neuronal activity using a minimal amount of a priori information. The neuron is driven with *in-vivo*-like injected current, and we test to which extent it is possible to predict the real spike train. In particular, we look at the number of spikes correctly predicted within a desired temporal precision. We find that our model achieves prediction of up to 80% of the spikes with correct timing (±2ms). Other characteristics of activity, such as mean rate and coefficient of variation of spike trains, are predicted in the correct range as well.

Keywords: Spike Response Model; Integrate-and-Fire model; Neuronal activity prediction; Timing precision

1 Introduction

The seminal work by Hodgkin and Huxley, yielding a mathematical description of action potentials, has led to a whole series of papers that try to describe in detail the dynamics of various ionic currents. However, precise description of neuronal activity involves an extensive number of variables, which often prevents a clear understanding of the underlying dynamics. Hence, a simplified description is desirable and has been subject to numerous works. The most popular simplified models include the Integrate-and-Fire (IF) model, the FitzHugh-Nagumo model and the Morris-Lecar model (for a review, see [1]). On the other hand, it is not clear yet if simplified models are at a sufficient enough level of description or not.

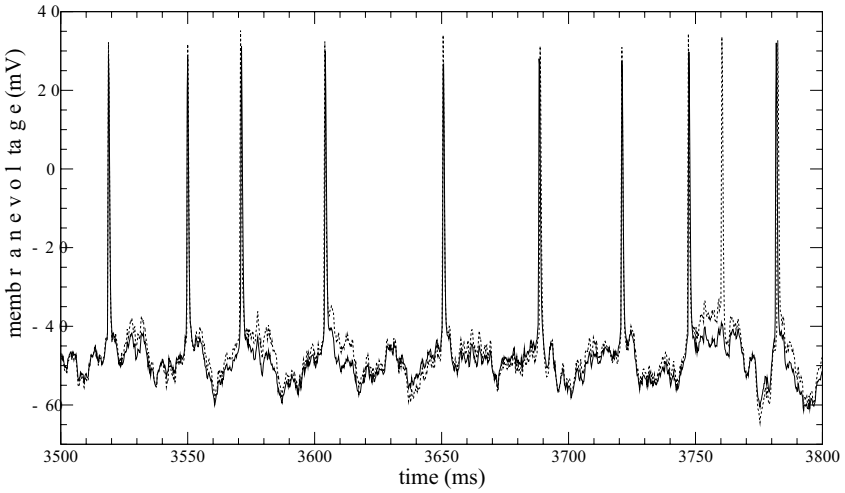

Fig. 1. The prediction of the SRM (dotted line) is compared to experimental data (solid line). A layer 5 pyramidal neuron of rat somatosensory cortex is driven by gaussian noise current, injected at the soma (mean $\mu_I = 600$pA, standard deviation $\sigma_I = 400$pA). The model achieves good prediction of the subthreshold behavior of the membrane voltage. The timing of all the nine spikes is predicted correctly, except that one extra spike is added at around 3760ms.

Here, similar to earlier work [2], we map a generic threshold model of the IF type (the SRM) to a conductance-based model of neuronal activity but also to experimental data. We show that a simple mapping technique allows reliable prediction of the spike train of a neuron. The SRM is quantitatively compared to a conductance-based model and prediction of up to 80% of spikes with correct timing is achieved. The SRM predicts the mean rate and the coefficient of variation (C_V) in the correct range as well. In addition, the subthreshold behavior of the membrane voltage is qualitatively compared to experimental data and reliable prediction is achieved (see Fig. 1).

2 Model and methods

We consider an isolated neuron stimulated by current injection. The state of the neuron is characterized by a single variable u, the membrane voltage of the cell. Let us suppose that the neuron has fired its last spike at time $\hat{t}$. At each time $t > \hat{t}$, the state of the cell is written:

$$u(t) = \eta(t - \hat{t}) + \int_0^{+\infty} \kappa(t - \hat{t}, s) I(t - s) ds. \tag{1}$$

The last term accounts for the external driving current $I(t)$. The input integration process is characterized by the kernel κ. The kernel η includes the form

of the spike itself as well as the after-hyperpolarization potential, if needed. A spike is elicited if the following threshold condition is satisfied:

$$\text{if } u(t) \geq \theta(t) \text{ and } \dot{u}(t) > 0 \text{ then, } \hat{t} = t. \tag{2}$$

Note that spiking occurs only if the membrane voltage crosses the threshold θ from below. The threshold itself can be taken either as a constant or as time-dependent. In this paper, we use a dynamic threshold with the form:

$$\theta(t - \hat{t}) = \begin{cases} +\infty & \text{if } t - \hat{t} \leq \gamma_{ref} \\ \theta_0 + \theta_1 \exp(-(t - \hat{t})/\tau) & \text{else} \end{cases}, \tag{3}$$

where γ_{ref} is a fixed absolute refractory period avoiding continuous firing. θ_0, θ_1 and τ are parameters that will be chosen to yield the best fit to a target spike train.

To evaluate the predictive power of the SRM, we stimulate the conductance-based model (or the real neuron) and the SRM both with the same driving current. Then, we count the number of spikes in coincidence between both spike trains within a small time window $\pm\Delta$. As a measure of the quality of the prediction, we use the coincidence factor Γ [2]:

$$\Gamma = \frac{N_{coinc} - \langle N_{coinc} \rangle}{\frac{1}{2}(N_{SRM} + N_{data})} \frac{1}{\mathcal{N}}, \tag{4}$$

where N_{coinc} is the number of coincident spikes, $\langle N_{coinc} \rangle$ is the mean number of spikes that would be predicted correctly by a homogeneous Poisson neuron firing at the same rate as the SRM, N_{SRM} (respectively N_{data}) is the number of spikes elicited by the SRM (respectively by the conductance-based model or the real neuron). $\mathcal{N}$ is a normalization factor ensuring that $\max(\Gamma) = 1$. Γ equals 1 if the spike train is predicted exactly and 0 if the prediction is not better than a Poisson neuron (Γ can be lower than 0).

Two datasets are used concurrently. One is generated with a conductance-based model (Hodgkin-Huxley-type model). This model was originally designed for fast-spiking interneurons [3] and slightly modified for the present study. The driving current is a random gaussian noise with constant mean μ_I and standard deviation σ_I. During integration, the value of the current is changed every 0.2ms. This highly variable temporal input is thought to approximate well *in-vivo* conditions [4]. The other dataset is composed of *in-vitro* recordings of layer 5 pyramidal neuron of rat somatosensory cortex [5]. Cells are driven with the same kind of input. For each spike train, we record the membrane voltage and the driving current. Both are needed later on.

To realize the mapping of the SRM to the data, we proceed in two steps. First, we extract the two kernels characterizing the model (κ and η) and second, we choose a specific threshold (θ) and optimize it in terms of quality of predictions. Let's start with the kernels. For the sake of simplicity, we assume that the mean driving current is zero but the method can easily be generalized. We start by extraction of the kernel η. It is well known that the shape of spikes is highly stereotyped and presents only little variability. We therefore select one spike train from a dataset and align all spikes. The mean shape of the spikes yields η. Detection and alignment of spikes is realized using a threshold condition on the first derivative of the membrane voltage. Once we are done with η, we extract the kernel κ. Let us limit ourselves to the interval between two consecutive spikes of the same spike train $\hat{t}_j$ and $\hat{t}_{j+1}$. Therefore, we can rewrite equation (1) as follows:

$$u(t) - \eta(t - \hat{t}_j) = \int_0^{+\infty} \kappa(t - \hat{t}_j, s) I(t - s) ds. \tag{5}$$

The right-hand side of equation (5) is the convolution product between the driving current and a family of kernels κ parameterized by the variable $t - \hat{t}_j$. It is then possible to find an approximation of the optimal kernel κ for each timing $t - \hat{t}$ by the Wiener-Hopf optimal filtering technique [6]. Finally, we fit the resulting vector κ with a suitable function (usually an exponential decay). The Wiener-Hopf method requires a window as large as the support of κ. It results that the dependency on $t - \hat{t}$ cannot be reproduced exactly. However, it is not a crucial point for correct prediction of the timing of the spikes but only for correct prediction of the membrane voltage just after emission of a spike. The kernels obtained for the conductance-based model are plotted in Fig. 2. The final step is to choose and optimize the threshold. The absolute refractory period γ_{ref} is set at 2ms. All the other parameters: θ_0, θ_1 and τ (see equation (3)) are fitted in order to optimize the coincidence factor Γ on the same spike train. Only one spike train is used for the mapping. It's obvious that the SRM can only predict neuronal activity of the neuron it has been mapped to (here, the conductance-based model or one particular cell of the experimental dataset).

3 Results

We test the predictive power of the SRM by comparing the responses of the conductance-based model neuron and the SRM to gaussian noise current with constant mean μ_I and standard deviation σ_I. Fig. 3 shows effects of changing mean with fixed variance. Each tested spike train is 10s long and the coincidence window $\Delta = 2$ms. The SRM produces very good predictions of the

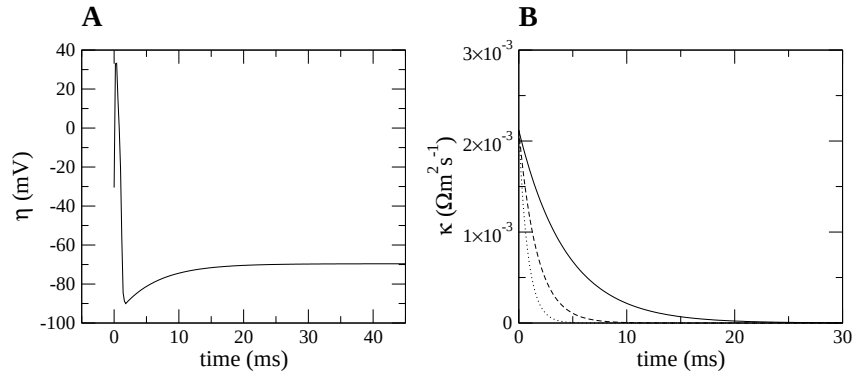

Fig. 2. Kernels extracted by the method described in text. **A.** Kernel η. **B.** Kernel κ at different timings: $t - \hat{t} = 0$ms (dotted line), $t - \hat{t} = 10$ms (dashed line) and $t - \hat{t} = 100$ms (solid line).

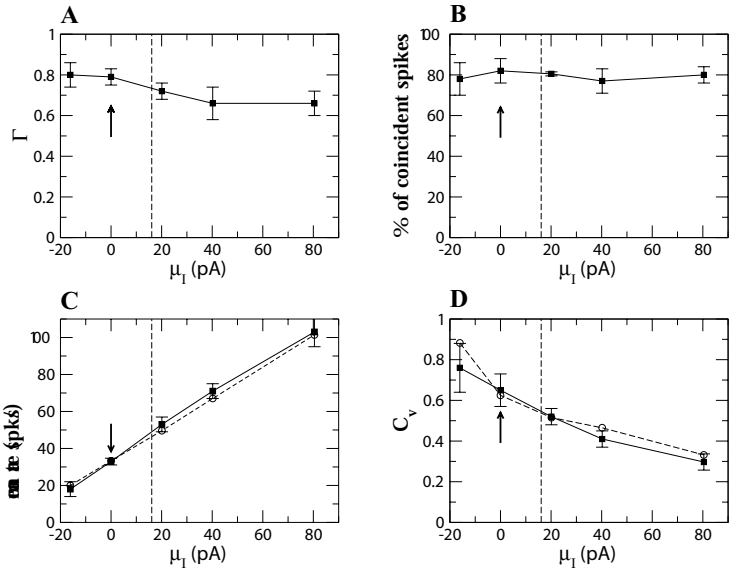

Fig. 3. The neuron is driven with varying mean gaussian current. The current's standard deviation is held constant at 200pA. Panels A-D show results of the SRM (solid line with squares). In addition, panels C and D show the target values for mean rate and C_V (dotted line with circles). Mean of five trials is plotted with two standard deviations for each point. The vertical dotted line is the rheobase current. The arrows denote the point for which parameters of the threshold were optimized. **A.** Coincidence factor Γ. **B.** Percentage of coincident spikes. **C.** Mean rate compared to target. **D.** C_V of the interspike interval distribution compared to target.

target spike trains over a broad range of means and standard deviations of the injected current. Other standard quantities like the mean rate or the C_V of the interspike interval distribution are predicted in the correct range, particularly the mean rate. This indicates that spikes that are missed or added by the SRM do not modify crucially the pattern of the spike train (Fig. 3, panel D). The subthreshold behavior of the membrane voltage is also predicted with good accuracy for real cortical cells (see Fig. 1).

4 Conclusion

Prediction of the activity of neurons was attempted in the past. Keat, Reinagel, Reid and Meister show that it is possible to predict the activity of neurons of the early visual system [7]. However, these neurons produce very stereotyped spike trains with short periods of intense activity followed by long periods of silence. More recently, Rauch, La Camera, Lüscher, Senn and Fusi observed that an IF model can predict the mean rate of cortical pyramidal cells with the same kind of *in-vivo*-like input current [5].

Here, we go one step further and propose a simple and general method to map a threshold model to data of neuronal activity. Once the mapping is realized, the model allows very reliable prediction of many aspects of neuronal activity, such as timing of the spikes, membrane voltage, mean rate and C_V of the ISI distribution. The method requires only a minimal amount of experimental information about the cell and can be used both with conductance-based models of neuronal activity and with experimental recordings. These results provide a basis for theoretical network studies on threshold models. They also offer an approach toward studying the integration of inputs in real neurons.

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