

The Spike Response Model: A Framework to Predict Neuronal Spike Trains

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

1 Introduction

The successful mathematical description of action potentials by Hodgkin and Huxley 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]).

In this paper, we make use of the Spike Response Model (SRM), a generic threshold model of the IF type. Similar to earlier work [2], we map the SRM to a detailed mathematical model of neuronal activity. But, in contrast of what has been done in [2], we go beyond the classic Hodgkin-Huxley neuron model of the squid axon and use instead a model of a cortical interneuron. Moreover, we use a different mapping technique that could also be applied to real neurons. We show that such a simple technique allows reliable prediction of the spike train of

a fast-spiking interneuron. Prediction of up to 80% of spikes with correct timing is achieved. The model also quantitatively reproduces the subthreshold behavior of the membrane voltage (see Fig. 1) as well as other characteristics of neuronal activity including mean rate and coefficient of variation (C_V).

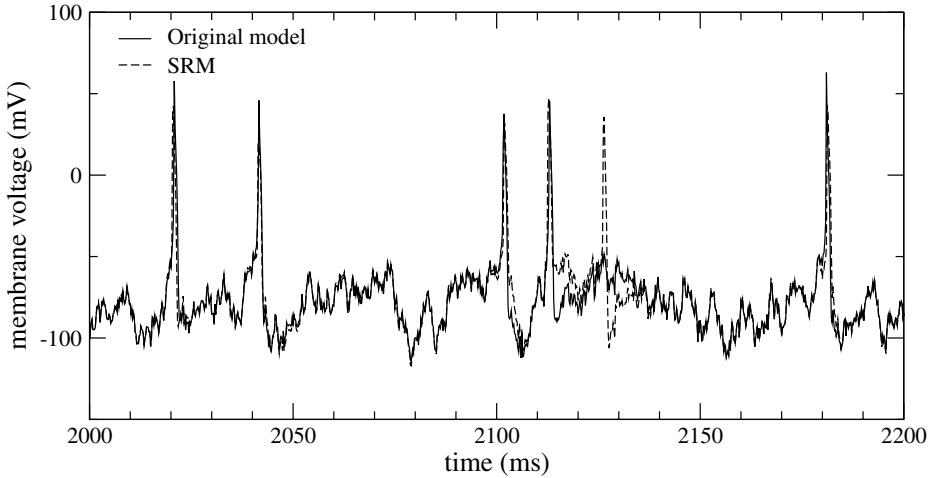


Fig. 1. The prediction of the SRM (dotted line) is compared to the target data (solid line). The model achieves very good prediction of the subthreshold behavior of the membrane voltage. The timing of all the spikes is predicted correctly, except that one extra spike is added at around 2125ms.

2 Model

In this section, we describe the SRM in detail. The state of a 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:

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

The last term accounts for the effect of an external current $I(t)$. The integration process is characterized by the kernel κ (additional external current). The kernel η includes the form of the spike itself as well as the after-hyperpolarization potential (AHP), if needed. As always, we have a threshold condition to account for spike generation:

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

Note that spiking occurs only if the membrane voltage crosses the threshold from below. The threshold itself can be taken either as constant or as time-dependent. We choose:

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

where γ_{ref} is a fixed absolute refractory period. θ_0 , θ_1 and τ_θ are parameters that will be chosen to yield the best fit to a test dataset (target spike train).

The SRM is more general than the classic leaky IF model. In particular, the choice of the kernel κ is not restricted. Moreover, κ is time-dependent since it depends on the time elapsed since the last spike $t - \hat{t}$. Finally, the AHP is described in a more realistic manner than in the leaky IF model where the time constant of the AHP is equal to the membrane time constant.

3 Methods

In this section, we begin by generating a test dataset using a conductance-based neuron model stimulated by *in-vivo*-like time-dependent current. Then, we explain the mapping of the SRM to the data, and finally, define how we quantify the predictive power of the model.

3.1 Generation of the Test Dataset

The test dataset is generated with a Hodgkin-Huxley-like model. The model was originally designed for fast-spiking interneurons [3] and was slightly modified for the present study. Note that an analytical reduction from this detailed model to the SRM is possible [1]. The model is integrated with a time step of 10^{-2} ms. 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 20 time steps ($= 0.2$ ms). The sampling frequency of our dataset is 5kHz. This highly variable temporal input is thought to approximate well *in-vivo* conditions [4]. For each spike train, we record the membrane voltage and the driving current. Both are needed later on.

3.2 Mapping of the Model

To realize the mapping of the SRM to the conductance-based neuron model, 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 the dataset generated with the detailed model 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 at times t_j and t_{j+1} . Therefore, we can rewrite equation (1) as follows:

$$u(t) - \eta(t - \hat{t}_j) = \int_{-\infty}^{+\infty} \kappa(t - \hat{t}_j, s) I(t - s) ds. \tag{4}$$

The right-hand side of equation (4) 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 for each timing by the Wiener-Hopf optimal filtering technique [5]. Let us consider each non-zero term of κ as a free parameter and try to minimize the squared distance between data $d(t) = u(t) - \eta(t - \hat{t}_j)$ and prediction $p(t) = \sum_s \kappa(t - \hat{t}_j, s) I(t - s)$ in a time window centered on $t - \hat{t}_j$. Then, the optimal filter for that window is the solution of the following linear system:

$$\begin{pmatrix} C(I, I)_0 & \cdots & C(I, I)_{M+N} \\ \cdots & \cdots & \cdots \\ C(I, I)_{-(M+N)} & \cdots & C(I, I)_0 \end{pmatrix} \begin{pmatrix} \kappa_{-N} \\ \cdots \\ \kappa_{+M} \end{pmatrix} = \begin{pmatrix} C(d, I)_{-N} \\ \cdots \\ C(d, I)_{+M} \end{pmatrix}. \tag{5}$$

$C(f, g)_i$ is the numerical cross-correlation of vector f with vector g at lag i . M (respectively N) is the maximum positive lag (respectively negative lag) for which κ is non-zero. It is obvious that this filter should be causal and therefore, $N = 0$. 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 . The result is 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, and only for time lags between 0 and about 30ms (for our dataset). The kernels are plotted in Fig. 2.

The final step is to choose and optimize the threshold. The absolute refractory period γ_{ref} is set to 2ms. All the other parameters: θ_0 , θ_1 and τ_θ (see equation (3)) are fitted in order to optimize the coincidence factor Γ using the *downhill simplex method* (see subsection 3.3 for definition of this quantity).

For some technical reasons, we use three spike trains of 10s each to do the mapping of the SRM to the detailed model. However, it is possible to do it with only one spike train.

3.3 Evaluation of Predictions

Once we are done with the mapping, we simulate the conductance-based model and the SRM with the same driving currents. These driving currents are new

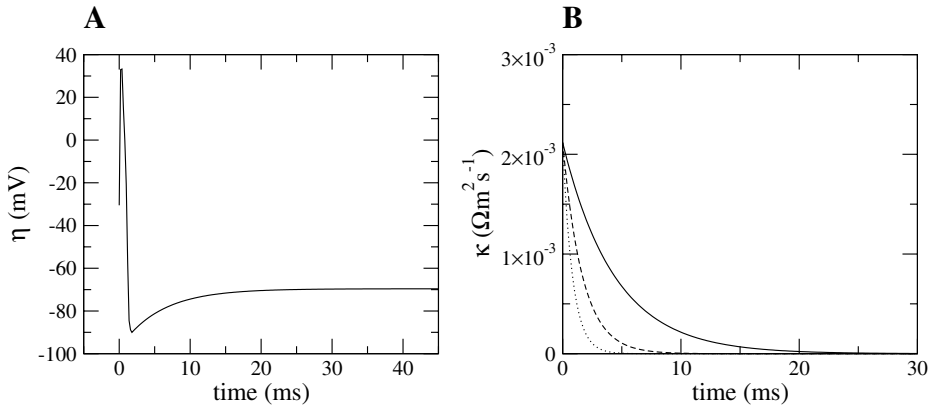


Fig. 2. Kernels extracted by the method described in text. **A.** Kernel η . **B.** Kernel κ at different timings: $t - \hat{t} = 0\text{ms}$ (dotted line), $t - \hat{t} = 10\text{ms}$ (dash-dotted line) and $t - \hat{t} = 100\text{ms}$ (solid line).

and have not been used during optimization. Then, we count the number of spikes in coincidence between both trains within a small time window $\pm\Delta$. As a measure of the quality of the prediction, we use the coincidence factor Γ [2]:

$$\Gamma = \frac{N_{coinc} - \langle N_{coinc} \rangle}{\frac{1}{2}(N_{SRM} + N_{data})} \frac{1}{\mathcal{N}}, \quad (6)$$

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 (it can be calculated exactly), N_{SRM} (respectively N_{data}) is the number of spikes elicited by the SRM (respectively by the conductance-based model) and \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). The denominator of the first term ensures that the mean frequency of both spike trains is roughly the same.

4 Results

In this section, we show the predictions obtained from the SRM and quantitatively compare the results to the test dataset (target spike trains) generated using the conductance-based model for fast-spiking interneurons. Unless specified, we used a dynamic threshold with $\theta_0 = -49.1\text{mV}$, $\theta_1 = 14.9\text{mV}$ and $\tau_\theta = 20.9\text{ms}$.

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 the effects of changing

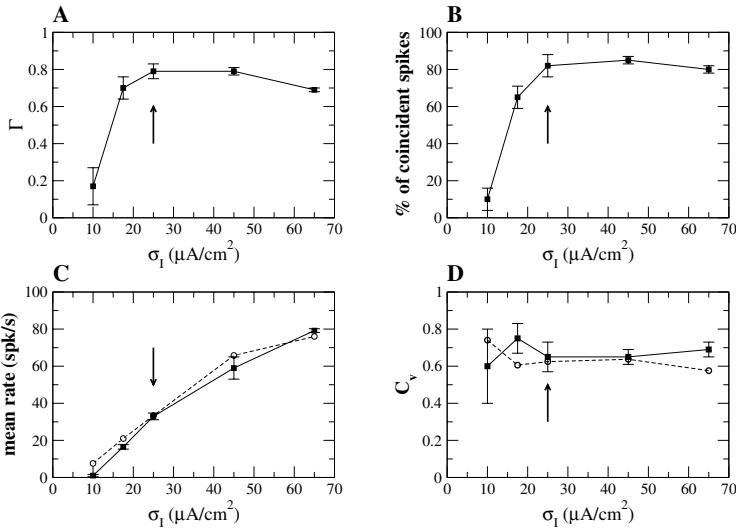


Fig. 3. The neuron is driven with zero mean Gaussian current. Panels A-D show results of the SRM (solid line with squares). In addition, panels C and D show the target values for mean rate and C_V (dotted line with circles). The arrows denote the point for which parameters of the threshold have been optimized (same in the four panels). Mean of five trials is plotted with two standard deviations for each point. **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.

variance with fixed mean, and Fig. 6 shows effects of changing mean with fixed variance. In both cases, $\Delta = 2\text{ms}$ and tested spike trains are 10s long.

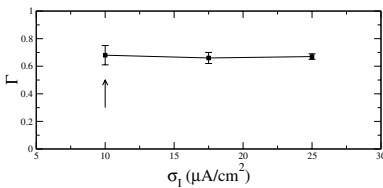


Fig. 4. SRM mapped to data at low rates (here, between 7 – 35spk/s). Γ is plotted versus the current's standard deviation σ_I ($\mu_I = 0$). The arrow denotes the point for which parameters of the threshold were optimized. The corresponding rates are, from left to right, 7.6, 21.0 and 33.3spk/s. Here, parameters of the threshold are: $\theta_0 = -52.5\text{mV}$, $\theta_1 = 37.5\text{mV}$ and $\tau_\theta = 5.2\text{ms}$.

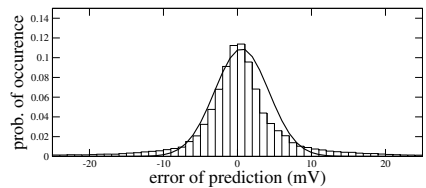


Fig. 5. Normalized histogram of the error of prediction of the membrane voltage. For each time step of one spike train, we report the predicted voltage minus the target voltage. The solid line is a fitted Gaussian distribution centered on mean $\mu = 0.6\text{mV}$ and with standard deviation $\sigma = 3.7\text{mV}$. Effects at the tails are due to missed and added spikes.

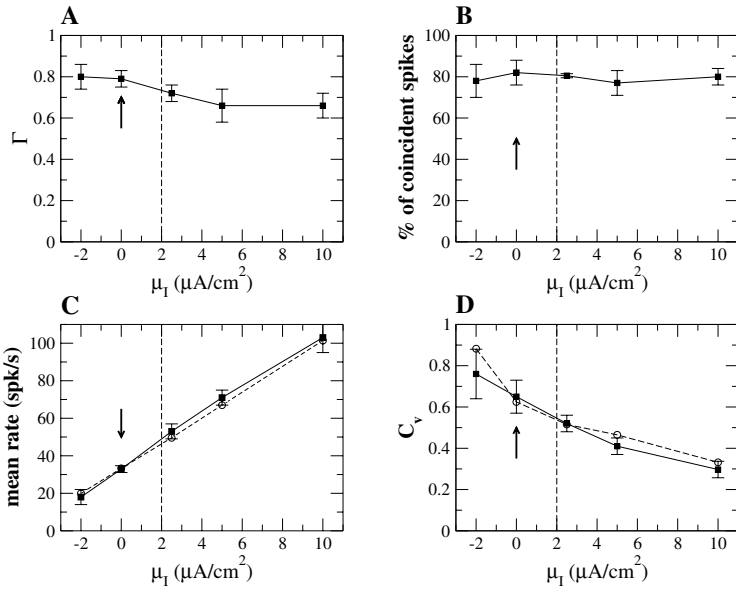


Fig. 6. The neuron is driven with varying mean Gaussian current. The current's standard deviation is held constant at $25\mu\text{A}/\text{cm}^2$. Panels A-D show results of the SRM (solid line with squares). In addition, panels C and D show the target values for mean rate and C_V (dotted line with circles). Mean of five trials is plotted with two standard deviations for each point. The vertical dotted line is the limit of the subthreshold constant current. The threshold's parameters are the same as in Fig. 3. **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.

The SRM produces very good predictions of the target spike trains over a broad range of means and standard deviations of the injected current. The model tuned using data at about 30Hz is still good for spike trains at 80Hz (Fig. 3, panel A). If optimized for low rates, the SRM can also achieve good performance of about $\Gamma = 0.7$ for $\sigma_I = 10\mu\text{A}/\text{cm}^2$ (Fig. 4). Predictions hold in the range 0-35Hz, which is roughly the range of interest for cortical pyramidal cells. The subthreshold behavior of the membrane voltage is also very nicely reproduced (see Fig. 1 and 5). Other standard quantities like the mean rate or the C_V of the interspike interval (ISI) distribution are predicted in the correct range, particularly the mean rate. This indicates that spikes that are missed or added do not modify crucially the pattern of the spike train (Fig. 3, 5 and 6).

The SRM is very robust against some modifications. Predictive power is still very good ($\Gamma > 0.7$) when using a shorter time window for coincidence detection ($\Delta = 1\text{ms}$) and using a constant threshold instead of a time-dependent threshold reduces only slightly the range of validity of the model. On the other hand, trying to simplify one of the kernel (η or κ) reduces significantly the quality of predictions (data not shown).

5 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 [6]. 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 reproduce the mean rate of neocortical pyramidal cells with the same kind of *in-vivo*-like input current [7].

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. A posteriori, we may interpret the kernel κ as the response kernel of an IF model with time-dependent time-“constant” [1]. The main advantage of this purely numerical approach (compared to an analytical or semi-analytical approach) is that it could, in principle, be extended to experimental data. Therefore, not only do 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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