Reduced models of neuronal activity have spike timing predictive power

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Abstract

We demonstrate that a single-variable generalized integrate-and-fire model can quantitatively capture the dynamics of real cortical neurons. Contrary to classic integrate-and-fire models, here, parameters depend on the time elapsed since the last spike (Spike Response Model). We present a technique for systematically and numerically optimizing parameters in the Spike Response Model (SRM) based on intracellular recordings of the target neuron. To quantitatively test the predictive power of the SRM, we compare predicted spike trains to those in the target neuron when they are driven by identical randomly fluctuating input. This technique is tested on data simulated with a single-compartment Hodgkin-Huxley model first and then applied to intracellular in-vitro recordings of rat pyramidal cells. For random current input, the SRM reproduces $70\% - 80\%$ of the spikes of the target neuron (with temporal precision of ± 2ms) over a wide range of firing frequencies. For random conductance injection, up to 75% of spikes are coincident. This method is suitable both for systematic numerical model reduction and for construction of equivalent simple phenomological models of real neurons.

Keywords: Integrate-and-fire; *in-vitro* recordings; prediction of spike times; stochastic spike arrival.

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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 and the effect of the dendritic architecture. 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 model is certainly the Integrate-and-Fire model (for a review, see [1]). However, it is not clear yet if such a simplified model is at a sufficient enough level of description or not.

Here, we present a numerical technique which allows a systematic mapping of a simplified phenomological model, namely the Spike Response Model (SRM), to any target neuron. This technique makes use of intracellular recordings (i.e. both input signal and instantaneous membrane voltage recordings) to evaluate the response properties of the target neuron. The reduced model built in this way is quantitatively compared to both simulated data and *in-vitro* recordings and prediction of up to 80% of spikes with correct timing is achieved (see Fig. 1). In addition, many other aspects of neuronal activity are reliably predicted.

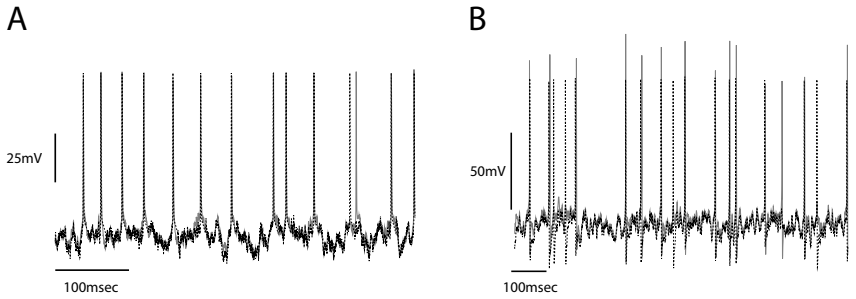

Fig. 1. The prediction of the Spike Response Model (SRM) is compared with the membrane voltage recording of the target neuron. **A.** The spike train of a real cortical neuron driven by gaussian noise current injected at the soma [2] (grey solid line) and the spike train predicted by the corresponding reduced SRM (dotted line). **B.** Same as in A except that the target neuron is a simulated Hodgkin-Huxley-type model driven by synaptic conductances resulting of massive stochastic presynaptic arrival. In both cases (A and B), predicted membrane voltage is almost indistinguishable from the target voltage.

2 Methods and results

We consider an isolated neuron stimulated by direct 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-hyper-polarization 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 is taken to be time-dependent $\theta(t - \hat{t}) =$

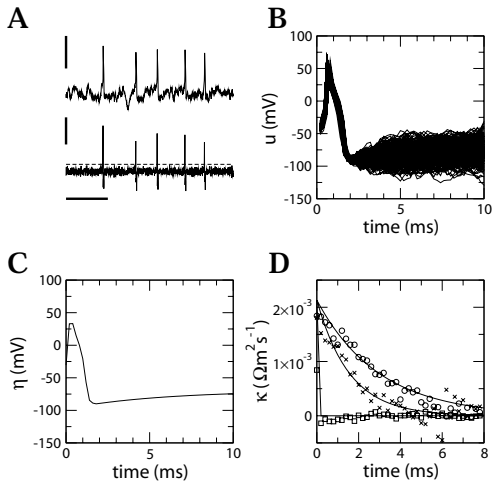

Fig. 2. Numerical reduction technique illustrated. Here, the target neuron is a simulated Hodkgin-Huxley-type neuron model. **A.** A sample of the spike train used for the reduction (top line) and the corresponding time derivative (bottom line). The dashed line indicates the threshold used to detect and align spikes (80mV/ms). Horizontal bar is 50ms. Vertical bars are 100mV (top) and 300mV/ms (bottom). **B.** About 300 spikes aligned with the same criterion as in A. **C.** The kernel η resulting from averaging the membrane voltage time course of spikes shown in B. **D.** The kernel $\kappa(\delta t, s)$ as a function of time s extracted by the method described in text for different time delays $\delta t = t - \hat{t}$. $\delta t = 0$ms (squares), $\delta t = 6$ms (crosses) and $\delta t = 10$ms (circles). Solid lines are exponential fits with $\kappa(\delta t, s) = \kappa_0 \exp(-s/\tau_\kappa(\delta t))$.

$\theta_0+\theta_1 \exp(-(t-\hat{t})/\tau_\theta)$ if $t-\hat{t} > \gamma_{ref}$ and $+\infty$ else, where γ_{ref} is a fixed absolute refractory period avoiding continuous firing. θ_0, θ_1 and τ_θ are parameters that will be chosen to yield the best fit to a given target spike train.

To evaluate the predictive power of the SRM, we drive both the target neuron and the SRM 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 [3]:

$$\Gamma = \frac{N_{coinc} - \langle N_{coinc} \rangle}{\frac{1}{2}(N_{SRM} + N_{data})} \frac{1}{\mathcal{N}}, \tag{3}$$

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 target neuron). $\mathcal{N}$ is a normalization factor ensuring that $\max(\Gamma) = 1$. Note that 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).

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. 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. The shape of spikes is usually highly stereotyped and presents only little variability. Given a sample spike train, we align all spikes and 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 from the very same spike train. Let us limit ourselves to the interval between two consecutive spikes $\hat{t}_j$ and $\hat{t}_{j+1}$. We can subtract η on both sides of equation (1). The right-hand side of the resulting equation is the convolution product between the driving current and a family of kernels κ parameterized by the variable $t-\hat{t}_j$. It is therefore possible to find the optimal kernel κ for each timing $t - \hat{t}$ by a method derived from the Wiener-Hopf optimal filtering technique [4]. Finally, we fit the resulting vector κ with a suitable function. 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_θ are fitted in order to optimize the coincidence factor Γ on the same sample spike train. Thus, only one spike train is used for the mapping. Fig. 2 illustrates this reduction technique with an Hodgkin-Huxley-type neuron model as the target neuron. It's obvious that the SRM can only predict neuronal activity of the neuron it has been mapped to.

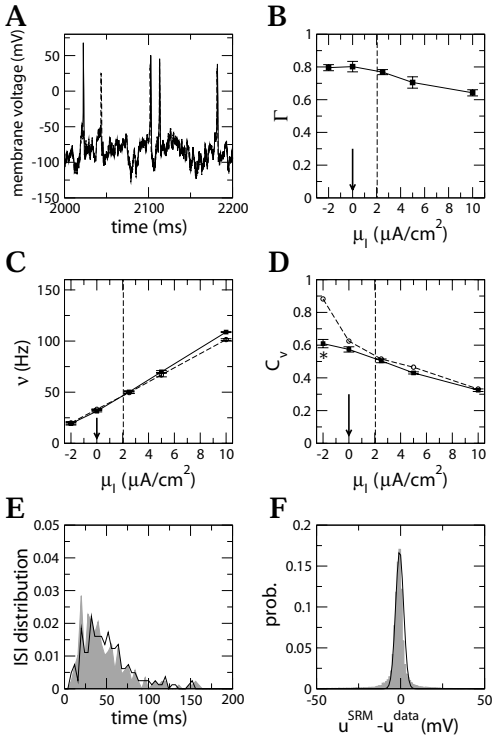

Fig. 3. Predictions of the numerically optimized Spike Response Model (SRM) compared to that of an Hodgkin-Huxley-type conductance-based model for random input with variable mean. **A.** The spike train of the SRM model (dashed line) is compared to that of the full neuron model (solid line, $\mu_I = -2.0\mu\mathrm{A/cm}^2$, $\sigma_I = 25.0\mu\mathrm{A/cm}^2$). **B.** Coincidence factor Γ. The standard deviation of the driving current is held constant to $\sigma_I = 25\mu\mathrm{A/cm}^2$ while we change its mean in the range $-2 \leq \mu_I \leq 10\mu\mathrm{A/cm}^2$. **C.** Mean rate of the SRM (solid line with squares) compared to that of the full model (dashed line with circles). **D.** $\mathrm{C_V}$ of the interspike interval distribution (ISI) of the SRM (solid line with squares) compared to that of the full model (dashed line with circles). The star indicates the point at which we chose the spike train used for panels E and F. **E.** The ISI distribution predicted by the SRM for one specific spike train (solid line) is compared to that predicted by the full model (light gray area). **F.** Normalized histogram of the error in prediction of the membrane voltage bin after bin for the same spike train as in E (light gray area). Fitted gaussian distribution (solid line; $\chi^2 = 4.1 \times 10^{-3}$; mean= -0.6mV; s.d.= 2.4mV). For panels B and C, each plotted point is the mean computed over five spike trains of 10s each (symbols) with one standard deviation (error bars). The arrows highlight the stimulation paradigm used for parameter optimization. The vertical dotted line indicates the approximative rheobase current.

This methodology and how to extend it to the case of stochastic spike arrival is extensively described elsewhere [5] and we refer interested readers to that paper as space is limited here.

Fig. 1 shows two samples of two distinct cases (real neuron driven by random current and simulated Hodgkin-Huxley-type model neuron driven by stochas-

tic spike arrival). Note that in both cases, most of the spikes are predicted with the correct timing but also that the subthreshold fluctuations of the membrane voltage are correctly predicted by the SRM (see also Fig. 3F). Fig. 3 shows extended analysis of results obtained with an Hodgkin-Huxley-type neuron model driven by random current. Panel A shows sample traces. The coincidence factor Γ is > 0.7 in a broad range of inputs (panel B) indicating that most of the spikes are predicted with the correct timing. The predicted mean rate is very close from the actual mean rate (panel C) as well as the interspike interval distribution and its C_V (panels D and E).

3 Conclusion

Prediction of neuronal activity using simplified models has benefited from many developments recently. Here, we propose a simple and general method to map a threshold model to any target neuron. 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 reasonable amount of intracellular recordings and can be used both for systematic numerical model reduction and for construction of equivalent simple phenomological models of real neurons. 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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