Conductance-Based Integrate-and-Fire Models

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An alternative approach was to simplify the process of action potential generation by representing the neuron as an integrate-and-fire (IAF) device (see Arbib, 1995). In this case, the neuron produces a spike when its membrane potential crosses a given threshold value and the membrane is instantaneously reset to its resting level. Although this type of model has been extensively used for representing large-scale neuronal networks, an important drawback is that it neglects the variations of Na$^+$ and K$^+$ conductances, which may have important effects in spike generation (Mainen, 1995). Moreover, central neurons have been shown to contain a large spectrum of other intrinsic currents, which have a determinant effect on firing behavior (Llinás, 1988). In this case, the IAF paradigm is clearly inappropriate.

In this article, we propose a simplified model of action potentials based on HH equations. Besides its similarity with IAF models, this method is shown to capture the conductance changes due to action potentials, which has a determinant influence on electrophysiological behavior.

2 Pulse-Based Models for Voltage-Dependent Currents

We start from the equations of Hodgkin and Huxley (1952):

\[
\begin{align*}
C_m \dot{V} &= -g_{\text{leak}} (V - E_{\text{leak}}) - g_{\text{Na}} m^3 h (V - E_{\text{Na}}) - g_{\text{Kd}} n^4 (V - E_K) \\
\dot{m} &= \alpha_m(V) (1 - m) - \beta_m(V) m \\
\dot{h} &= \alpha_h(V) (1 - h) - \beta_h(V) h \\
\dot{n} &= \alpha_n(V) (1 - n) - \beta_n(V) n
\end{align*}
\]

(2.1)

where $V$ is the membrane potential, $C_m = 1 \mu F/cm^2$ is the membrane capacitance, and $g_{\text{leak}} = 0.1$ mS/cm$^2$ and $E_{\text{leak}} = -70$ mV are the leak conductance and reversal potential, respectively. $g_{\text{Na}} = 100$ mS/cm$^2$ and $g_{\text{Kd}} = 80$ mS/cm$^2$ are the maximal conductances of the sodium current and delayed rectifier with reversal potentials of $E_{\text{Na}} = 50$ mV and $E_K = -90$ mV. $m$, $h$, and $n$ are the activation variables, whose time evolution depends on the voltage-dependent rate constants $\alpha_m$, $\beta_m$, $\alpha_h$, $\beta_h$, $\alpha_n$, and $\beta_n$. The voltage-dependent expressions of the rate constants were as in the version described by Traub and Miles (1991).

The behavior of the HH model in a single compartment cell during a train of action potentials is shown in Figure 1 (left panel). As a consequence of the rapid changes in membrane voltage during action potentials, the time course of the rate constants exhibits sharp transitions. This is best illustrated by the behavior of $\alpha_m$: the function $\alpha_m(V)$ is approximately zero for the whole range of membrane potential below $\sim -50$ mV, then increases progressively with depolarization; consequently, before and after the action potential, $\alpha_m \sim 0$ and has positive values only during the spike (see Fig. 1).
Hodgkin-Huxley

Pulse-based

Figure 1: Comparison of action potential generation in Hodgkin-Huxley and pulse-based models. A train of spikes was generated by injecting a depolarizing current pulse (2 nA) in a single compartment model (area of 15,000 μm²; \( \bar{g}_{\text{Na}} = 30 \, \text{ms/cm}^2 \); other parameters as in section 2.1. The time course of...
given threshold. For example, \( \alpha_m \) will be assigned a positive value during the pulse and will be zero otherwise. Generalizing for other rate constants, before and after the pulse, we have:

\[
\begin{align*}
\alpha_m &= 0, & \beta_m &= \beta_M \\
\alpha_H &= \alpha_H, & \beta_H &= 0 \\
\alpha_n &= 0, & \beta_n &= \beta_N
\end{align*}
\]  
(2.2)

whereas during the pulse:

\[
\begin{align*}
\alpha_m &= \alpha_M, & \beta_m &= 0 \\
\alpha_H &= 0, & \beta_H &= \beta_H \\
\alpha_n &= \alpha_N, & \beta_n &= 0.
\end{align*}
\]  
(2.3)

Here, \( \alpha_M, \beta_M, \alpha_H, \beta_H, \alpha_N, \) and \( \beta_N \) are constant values. They are estimated from the value of the voltage-dependent expressions at hyperpolarized and depolarized potentials. Choosing \(-70 \text{ mV}\) and \(+20 \text{ mV}\) and using Traub and Miles’s formulation gives:

\[
\begin{align*}
\alpha_M &= \alpha_m(20) \simeq 22 \text{ ms}^{-1} \\
\beta_M &= \beta_m(-70) \simeq 13 \text{ ms}^{-1} \\
\alpha_H &= \alpha_H(-70) \simeq 0.5 \text{ ms}^{-1} \\
\beta_H &= \beta_H(20) \simeq 4 \text{ ms}^{-1} \\
\alpha_N &= \alpha_n(20) \simeq 2.2 \text{ ms}^{-1} \\
\beta_N &= \beta_n(-70) \simeq 0.76 \text{ ms}^{-1}.
\end{align*}
\]  
(2.4)

It is then straightforward to solve equations 2.1, leading to the following
Here, \( t_0 \) is the time at which the pulse began, and \( m_0, h_0, \) and \( n_0 \) are the values of \( m, h, \) and \( n \) at that time.

Using this procedure, the simplified model generated action potentials similar to the HH model (see Fig. 1, right panel). The time course of the activation variables \( m, h, \) and \( n \) was also comparable in both models. The optimal values of parameters were estimated by fitting expressions 2.5 and 2.6 directly to the original HH model. Using a simplex procedure (Press et al., 1986), and starting from different initial values of the parameters, the fitting led to a unique estimate of the pulse duration (0.6 ± 0.08 ms) and of the membrane threshold (−50.1 ± 0.3 mV; other parameters were as in Fig. 1).

The computational efficiency of the pulse-based mechanism is essentially due to the direct estimation of variables \( m,h,n \) from the membrane potential (see equations 2.5 and 2.6). Another factor providing further acceleration is that outside the pulse, an expression similar to equation 2.5 can be written for \( m^3 \) and \( n^4 \), which greatly reduces the number of multiplications since no exponentiation is calculated.

3 Comparison of Pulse-Based Models with Other Mechanisms

The important point of pulse-based (PB) models is that they provide a good approximation of dynamical properties of firing behavior described by the HH mechanism. These properties were tested in three ways: repetitive firing, random firing, and network behavior. First, the optimized PB model was compared to HH and IAF mechanisms following injection of current pulses of increasing amplitudes (see Fig. 2). Pulse-based models gave an excellent approximation of interspike intervals at different firing frequencies, the spike shape, and the rise and decay of the membrane potential. On the other hand, the IAF model taken in the same conditions gave a poor approximation (see Fig. 2). For IAF models, the threshold or the absolute refractory period affected the frequency of firing, but variations of these parameters failed to generate the correct firing frequencies.

Second, PB models were tested in the case of random synaptic bombardment in a single-compartment cell having AMPA and GABA\(_A\) postsynaptic receptors (see Fig. 3). The conductance of synaptic currents was chosen such that most postsynaptic potentials were subthreshold, occasionally leading to firing. This subthreshold dynamics is surprisingly irrelevant for spiking as PB and IAF mechanisms behaved very closely to the HH model (see Fig. 3), with spike timing differences of 1.1 ± 1.8 ms (average ± standard deviation) and rare occurrences of nonmatching spikes. The precision in spike timing was very sensitive to the value of the threshold and slightly better for PB models.

Third, PB models were tested in network simulations having both intrinsic and synaptic currents, besides \( I_{Na} \) and \( I_{Kd} \). The network considered was a model of spindle oscillations in interconnected thalamocortical (TC) and
Figure 2: Comparison of repetitive firing with three different models. A single compartment cell (same parameters as in equation 1) was simulated with injection of three depolarizing current pulses of increasing amplitudes (1 nA, 2 nA, and 4 nA). Top trace: Simulation using the original Hodgkin-Huxley model. Middle trace: Simulation using pulse-based equations (identical parameters as in Figure 1, right). Bottom trace: Simple integrate-and-fire model (the spike consisted of a sudden rise to 50 mV, immediately followed by a reset to $-90$ mV and an absolute refractory period of 1.5 ms; same threshold as the pulse-based mechanism). All models had identical passive properties.

thalamic reticular (RE) neurons (Destexhe, Bal, McCormick, & Sejnowski, 1996). These neurons have a set of intrinsic sodium, potassium, calcium, and
Figure 4: Comparison of simplified and original Hodgkin-Huxley models using simulations of circuits of neurons. Left panel: Model of spindle oscillations in a network of 16 thalamic neurons. Eight thalamocortical (TC) cells projected to 8 thalamic reticular (RE) neurons using AMPA-mediated contacts, whereas RE cells contacted themselves using GABA_A receptors and TC cells using a mixture of GABA_A and GABA_B receptors. Each neuron had Na^+, K^+, Ca^+, and cationic voltage-dependent currents described by Hodgkin-Huxley–type equations, whose parameters were obtained from voltage-clamp and current-clamp data (Destexhe et al., 1996). One cell of each type is represented during a spindle sequence. Middle panel: Same simulation using pulse-based mechanisms for action potentials. Right panel: Same simulation using integrate-and-fire models.

was not rigorously identical in the two models, but spindle oscillations had the correct frequency and phase relationships between cells. On the other hand, the high-frequency firing of TC and RE cells was not well captured by IAF mechanisms, which gave rise to different oscillation frequencies at
Table 1: Computational Performance of Different Methods for Generating Action Potentials.

<table>
<thead>
<tr>
<th>Method</th>
<th>NEURON (relative CPU time)</th>
<th>Minimal C Code (relative CPU time)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DE</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>DEo</td>
<td>0.32</td>
<td>0.45</td>
</tr>
<tr>
<td>PB</td>
<td>0.25</td>
<td>0.17</td>
</tr>
<tr>
<td>IAF</td>
<td>0.23&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.08</td>
</tr>
</tbody>
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Note: A single-compartment cell comprising passive currents, 1 nA injected current, and a model for action potentials was simulated. Different models for action potentials were: DE: Hodgkin-Huxley model described by differential equations; DEo: same equations solved using optimized algorithms; PB: pulse-based model; IAF: simple integrate-and-fire model. A backward Euler integration scheme was used with a time step of 0.025 ms over a total simulated time of 50 seconds. The equations were solved using either the NEURON simulator (Hines, 1993) or directly in C code (minimal code for solving the equations without graphic interface; the exact same algorithms and optimizations as in NEURON were used). Codes are available on request.

<sup>a</sup> IAF models could not be implemented optimally in NEURON.

4 Discussion

This article has presented a novel method to approximate the dynamics of action potentials. The model was based on the HH equations in which the time course of rate constants was approximated by a short pulse. In a previous article (Destexhe, Mainen, & Sejnowski, 1994a), similar PB mechanisms were introduced to model synaptic currents. The basis of the synaptic model was that artificially applied pulses of agonist gave rise to postsynaptic currents with a time course very similar to the intact synapse (e.g., Colquhoun, Jonas, & Sakmann, 1992). PB models of synaptic currents offered the advantages of being simple and fast, and they could be easily fit to experimental data.

In the case reported in this article, the pulse approximation of HH equations was based on the observation that rate constants undergo sharp transitions during action potentials (see Fig. 1), also leading to analytic resolution and therefore fast algorithms that can be fit easily to any template. In principle, the same approximation could be considered for other types of channels, under the important condition that rate constants display sharp transitions. A possible example would be Ca<sup>2+</sup>-dependent channels, assuming that an action potential triggers a short pulse of intracellular Ca<sup>2+</sup> concentration due to high-threshold Ca<sup>2+</sup> currents.

Are PB models different from conventional IAF mechanisms? Both methods share a fixed voltage threshold as well as a dead time following spikes to represent the absolute refractory period. PB models, however, significantly
differ from IAF models because they take into account the decay of variables $m$, $h$, and $n$ in between spikes, which has a determinant influence on repetitive firing at high frequencies. In IAF models, the membrane is reset instantaneously after a spike to a hyperpolarized level. In PB models, the reset occurs through the activation of the delayed-rectifier current, which has an effect over a longer period of time due to the relatively slow decay of the variable $n$. This is the main factor that affected the frequency of firing in Figure 2. However, we cannot exclude the possibility that more sophisticated IAF models (with relative refractory period or variable threshold) would
formance of IAF models (see Table 1). However, this increase of efficiency could be minimal in the case of network simulations where action potentials represent only a small fraction of the computation time. On the other hand, if PB models could be used in conjunction with pulse-based mechanisms applied to other types of currents, such as synaptic currents (Destexhe et al., 1994a; Lytton, 1996), then this approach could provide a considerable acceleration of computation time.

How can PB models be improved? An obvious improvement would be to apply the PB approximation to a simplified model of action potentials, such as that of Hindmarsh and Rose (1982), leading to PB models with fewer variables. Another improvement would be to add a relative refractory period or a variable threshold, for example, by making the threshold depend on the value of the inactivation variable \( h \). More optimal values of rate constants than equation 2.4 could also be obtained by fitting the model directly to HH equations using several templates, such as that of Figs. 2 and 3.

In conclusion, PB models capture important features of the firing behavior as described by HH mechanisms, but they do not apply to all cases. This approach is intermediate between simple IAF and more detailed biophysical models and may facilitate building large-scale network simulations that incorporate the intrinsic electrophysiological properties of single cells.

Acknowledgments

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References


