



Typical frequency-current curves of neurons obtained from a model based on cellular automaton



T.G. Correale^a, L.H.A. Monteiro^{a,b,*}

^aDepartamento de Engenharia de Telecomunicações e Controle, Universidade de São Paulo, Av. Prof. Luciano Gualberto, travessa 3, n.380, São Paulo, 05508-900, SP, Brazil

^bEscola de Engenharia, Universidade Presbiteriana Mackenzie, Rua da Consolação, n.896, São Paulo, 01302-907, SP, Brazil

ARTICLE INFO

Keywords:

Bifurcation
Cellular automaton
Frequency-current curve
Ion channel
Neurodynamics

ABSTRACT

Usually, neurons stimulated by constant current exhibit one of two types of behavior: for type-1 neurons, the curve representing “firing frequency versus input current” is continuous; for type-2 neurons, there is a discontinuity in such a curve. Here, we reproduce these typical behaviors from a discrete-time model based on the dynamics of ion channels. In this model, the axonal membrane is considered as a lattice and each patch of this lattice contains a set of ion channels. The state transitions of the voltage-gated ion channels are governed by deterministic rules. We show that the frequency-current relationship obtained from this model is similar to the one derived from the Hodgkin–Huxley equations, which are commonly used to describe type-2 neurons. We also show that our approach can be convenient to model type-1 neurons.

© 2017 Elsevier Inc. All rights reserved.

1. Introduction

Consider a neuron stimulated by a constant electric current. The frequency-current curve expresses the relationship between the current per unit area I applied to this neuron and the frequency f of its spikes. It is experimentally observed that, above a threshold current, the neuron fires periodically. Thus, there occurs a transition from a quiescent mode (with $f = 0$) to an oscillatory behavior (with $f > 0$). For type-1 neurons, this transition is smooth, continuous; for type-2 neurons, there is a jump, a discontinuity in the $f - I$ curve [1–6]. The classical equations proposed by Hodgkin and Huxley in 1952 [7] are usually employed to model type-2 neurons [2,8,9].

From the point of view of the Dynamical Systems Theory, qualitative changes on the asymptotical behavior caused by the variation of parameter values of a dynamical system are known as bifurcations. The transition from steady state to periodic solution found in neurons under current clamp can be a consequence of Hopf bifurcation, saddle-node-onto-limit-cycle bifurcation, or saddle-node-off-limit-cycle bifurcation [4–6,10,11]. In this case, the parameter value to be varied is the intensity of the input current.

Here, we show that our neuron model [12] can reproduce both types of $f - I$ curves. This discrete-time model for computing the time evolution of the electric potential of axonal membrane is based on cellular automaton (CA) [13], in which each cell represents a membrane patch. Each patch of the CA lattice contains a set of leak and voltage-gated ion channels and the state transitions occurring in the voltage-gated channels are driven by deterministic rules.

* Corresponding author.

E-mail addresses: luizm@mackenzie.br, luizm@usp.br (L.H.A. Monteiro).

This manuscript is organized as follows. In Section 2, our model is succinctly described. In Section 3, $f - I$ curves for both types of neurons are presented. For type-2 neurons, a comparison with the curve derived from the Hodgkin–Huxley equations is performed. In Section 4, the main conclusions are summarized.

2. The model

Here, we briefly review our model [12]. In this model, the axonal membrane is divided into small patches. In each patch, the membrane electric potential $E[t]$ at the time step t is due to two phenomena: the ionic diffusion below the membrane (which corresponds to the exchange of ions among neighbor patches) and the proportion of ion channels in the open state. The ions considered in this model are sodium and potassium. There are voltage-gated and leak ion channels.

Each voltage-gated ion channel is modeled as a finite-state machine. The transition from a state to another depends on $E[t]$ and local “timers”. A timer specifies the time interval that a voltage-gated channel remains in a particular state, forcing a transition when a time limit is reached; then, the timer is reset. Inspired by the Hodgkin–Huxley model [7], five timers are considered: two for the potassium channels, denoted by the time variables $t_{openingK}$ and t_{openK} , and three for the sodium channels, denoted by $t_{openingNa}$, t_{openNa} , and $t_{inactivatedNa}$. The corresponding time limits of these timers are $\tau_{openingK}$, τ_{openK} , $\tau_{openingNa}$, τ_{openNa} , and $\tau_{inactivatedNa}$. For potassium channels, the sequence of states is: opening \rightarrow open \rightarrow closed; for sodium channels, the sequence is: opening \rightarrow open \rightarrow inactivated \rightarrow closed. For all voltage-gated channels, the default state is closed, in which the channel does not allow the exchange of ions between inside and outside the axon. There is no timer associated to the closed state. Note that the opening state is intermediary between closed and open. In this state, the channel behaves as closed, but after a fixed time interval (given by $\tau_{openingK}$ or $\tau_{openingNa}$), it changes to open. The intention is to take into account the time that a voltage-gated channel spends to alter its physical conformation, when a tension threshold is exceeded. The number of voltage-gated sodium channels per patch and the number of voltage-gated potassium channels per patch are denoted by d_{Na} and d_K , respectively.

Let $s_K[t]$ be the state of a voltage-gated potassium channel at the time step t . The state-transition function $s_K[t + 1] = F(s_K[t])$ is written as:

$$s_K(t + 1) = \begin{cases} \text{opening,} & \text{if } (E[t] \geq E_{openLimK} \wedge s_K[t] = \text{closed}) \\ & \vee (t_{openingK} < \tau_{openingK} \wedge s_K[t] = \text{opening}) \\ \text{open,} & \text{if } (t_{openK} < \tau_{openK} \wedge s_K[t] = \text{open}) \\ & \vee (t_{openingK} = \tau_{openingK} \wedge s_K[t] = \text{opening}) \\ \text{closed,} & \text{if } (E[t] < E_{openLimK} \wedge s_K[t] = \text{closed}) \\ & \vee (t_{openK} = \tau_{openK} \wedge s_K[t] = \text{open}) \end{cases} \quad (1)$$

The symbols \wedge and \vee denote the “logical and” and the “logical or”, respectively. The parameter $E_{openLimK}$ is the tension threshold at which the potassium channels open. Note that a potassium channel will be in the opening state at $t + 1$, when at t either the membrane potential is equal to or greater than $E_{openLimK}$ and the previous state is closed, or if it is already in the opening state in t but $\tau_{openingK}$ was not reached yet. When $t_{openingK} = \tau_{openingK}$, the channel opens and it remains in this state for $t_{openK} < \tau_{openK}$. At $t_{openK} = \tau_{openK}$, the channel closes. It stays closed if the membrane potential of the patch in which the canal is embedded is less than $E_{openLimK}$.

Let $s_{Na}[t]$ be the state of a voltage-gated sodium channel at the time step t . The state-transition function $s_{Na}[t + 1] = F(s_{Na}[t])$ is given by:

$$s_{Na}(t + 1) = \begin{cases} \text{opening,} & \text{if } (E[t] \geq E_{openLimNa} \wedge s_{Na}[t] = \text{closed}) \\ & \vee (t_{openingNa} < \tau_{openingNa} \wedge s_{Na}[t] = \text{opening}) \\ \text{open,} & \text{if } (t_{openNa} < \tau_{openNa} \wedge s_{Na}[t] = \text{open}) \\ & \vee (t_{openingNa} = \tau_{openingNa} \wedge s_{Na}[t] = \text{opening}) \\ \text{inactivated,} & \text{if } (t_{inactivatedNa} < \tau_{inactivatedNa} \wedge s_{Na}[t] = \text{inactivated}) \\ & \vee (t_{openNa} = \tau_{openNa} \wedge s_{Na}[t] = \text{open}) \\ \text{closed,} & \text{if } (E[t] < E_{openLimNa} \wedge s_{Na}[t] = \text{closed}) \\ & \vee (t_{inactivatedNa} = \tau_{inactivatedNa} \wedge s_{Na}[t] = \text{inactivated}) \end{cases} \quad (2)$$

in which $E_{openLimNa}$ is the tension threshold at which the sodium channels open. Observe that after the open state, the sodium channels remain inactivated while $t_{inactivatedNa} < \tau_{inactivatedNa}$. When $t_{inactivatedNa} = \tau_{inactivatedNa}$, it closes. The other rules are similar to the rules governing the dynamics of the voltage-gated potassium channels.

The membrane electrical potential in a patch at the time t is determined from:

$$E[t] = propOpenNa[t] \times E_{Na} + propOpenK[t] \times E_K + propNotOpen[t] \times E_{local}[t] \quad (3)$$

if $E[t] - E[t - 1] \leq \frac{dE}{dt}|_{max} \times \Delta t$. When $E[t] - E[t - 1] > \frac{dE}{dt}|_{max} \times \Delta t$, then:

Download English Version:

<https://daneshyari.com/en/article/5775839>

Download Persian Version:

<https://daneshyari.com/article/5775839>

[Daneshyari.com](https://daneshyari.com)