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The transfer function of neuron spike

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ABSTRACT

The mathematical modeling of neuronal signals is a relevant problem in neuroscience. The complexity of the neuron behavior, however, makes this problem a particularly difficult task. Here, we propose a discrete-time linear time-invariant (LTI) model with a rational function in order to represent the neuronal spike detected by an electrode located in the surroundings of the nerve cell. The model is presented as a cascade association of two subsystems: one that generates an action potential from an input stimulus, and one that represents the medium between the cell and the electrode. The suggested approach employs system identification and signal processing concepts, and is dissociated from any considerations about the biophysical processes of the neuronal cell, providing a low-complexity alternative to model the neuronal spike. The model is validated by using *in vivo* experimental readings of intracellular and extracellular signals. A computational simulation of the model is presented in order to assess its proximity to the neuronal signal and to observe the variability of the estimated parameters. The implications of the results are discussed in the context of spike sorting.

1. Introduction

The mathematical modeling of neuronal signals is one of the most relevant problems in neuroscience. This question has been driven by technological advances that allowed the experimental acquisition of neuronal signal in several situations, establishing the basis for many quantitative models found in literature (Koch & Segev, 1998; Sterratt, Graham, Gillies, & Willshaw, 2011). Such models have been widely employed to solve computational tasks in a computer (Gao, Yang, Cai, & Liu, 2012; Menezes & Monteiro, 2011) and to understand the functioning of nervous systems (Monteiro, Bussab, & Chaui-Berlinck, 2002; Steuber & Jaeger, 2013). One of the first models was proposed by Huxley and Hodgkin in the 1950s, using a system of continuous-time equations based on experiments with giant squid cells (Hodgkin & Huxley, 1952). This model served as inspiration for subsequent proposals, mainly focused on the reproduction of the action potential dynamics, as in FitzHugh (1961). Discrete-time versions (Ibarz, Casado, & Sanjuán, 2011), as the McCulloch–Pitts model, can be considered simplifications to facilitate simulations in digital environments.

There are many biophysical and chemical factors involved in the generation of neuronal signals; hence, to model such signals is a particularly difficult task. Moreover, the neuron behavior is highly influenced by the connections with surrounding nerve cells, forming a network which itself poses a great challenge for mathematical representation (Dayan & Abbott, 2005). Most of the referred models are designed with the main intent of representing the neuronal dynamics and the interaction with external agents. However, in several situations, a parametrization associated solely with the signal waveform is of great interest.

Extra and intracellular action potential recordings have been used to tune the parameter values of continuous-time nonlinear models, which explicitly consider the physical properties of the neuronal membrane. This tuning is commonly performed by using parameter estimation techniques (Gold, Henze, Koch, & Buzsáki, 2006; Tabak, Murphey, & Moore, 2000; Toth, Kostuk, Meliza, Margoliash, & Abarbanel, 2011; Wang et al., 2014; Willms, Baro, Harris-Warrick, & Guckenheimer, 1999). However, the number of parameters to be matched can be as great as 100 (Gold, Henze, & Koch, 2007). In fact, the complexity of these models can impair computational simulations and analytical studies involving many neurons. There are also discrete-time nonlinear models that can generate a signal which is qualitatively similar to neuronal recordings (Aihara, Takabe, & Toyoda, 1990; Girardi-Schappo, Tragtenberg, & Kinouchi, 2013; Hsu, Gobovic, Zaghloul,

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& Szu, 1996; Mesbah, Moghtadaei, Golpayegani, & Towhidkhah, 2014). However, these models neither take into account details of the neurophysiological processes nor experimental data. Their parameter values are empirically set.

The parametrization of intracranial signals is of great interest in the context of the identification problem. The study of efficient techniques to isolate the firings of each active cell from an extracellular mixture containing sequences of spikes from several neurons is a problem extensively discussed in Neuroscience, formally known as *spike sorting*. Usually these techniques are implemented in three stages (Gibson, Judy, & Markovic, 2012; Lewicki, 1998; Quiroga, Nádasdy, & Ben-Shaul, 2004; Rutishauser, Schuman, & Mamelak, 2006): from raw electrical potentials recorded by using arrays of electrodes, spikes are detected, then parameterized, and finally sorted, attributing every single spike observed to a particular neuron. In this context, a relevant question is how the parameter sets describe effectively the neuronal activities over time. A simplified model of how the signal that arrives at the electrodes is formed from a stimulus and its evolution over time can possibly help to elucidate this question.

The main goal of this paper is to propose a discrete-time linear time-invariant (LTI) model with a rational function, to represent the neuronal spike observed by an electrode located in the surroundings of the nerve cell. This approach provides a low-complexity alternative to the neuronal spike model, employing system identification and signal processing concepts. It is dissociated from any considerations about the biophysical processes of the neuronal cell, and it is not directly derived from any traditional neuronal models. The model is validated by using *in vivo* experimental readings of intracellular and extracellular signals. Although the proposed model does not fully comprise the cellular dynamics, it allows a straightforward simulation of the neuronal activity by a pair of linear equations, once its parameters are obtained.

The remainder of this paper is organized into five sections. In Section 2, the experimental methods involved in the data acquisition of neuronal electrical signals are briefly described. The proposed model is introduced in Section 3, in the form of a cascade association of two subsystems: one that generates an action potential from an input stimulus, and one that represents the medium between the cell and the electrode. The parameters for these subsystems are estimated from experimental data in Section 4. In Section 5, a computational simulation of the model is presented in order to assess its proximity to the neuronal signal and the variability of the estimated parameters. The implications of the results are discussed in Section 6, considering the limitations of the proposed approach.

2. Experimental methods

The estimation of the proposed model parameters is performed by using *in vivo* experimental data recordings of neuronal signals generated by mice, provided by CRCNS (*Collaborative Research in Computational Neuroscience*) (Henze, Harris et al., 2000). For each experiment in the database, there are time series of action potentials obtained directly from the cell body through glass micropipettes, and of the electric potential observed simultaneously in the external environment, through electrodes placed in an area near the chosen cell. These external electrodes are mounted in arrays of four to six uniformly spaced elements, providing spatial diversity in the recordings of the electric potential outside the cell.

All the recordings were obtained from the region of the hippocampus; a great part of the pulses corresponds to the pyramidal cell activity observed in a layer known as CA1. The time series were digitized at 12 or 16 bits, and sampled at frequency

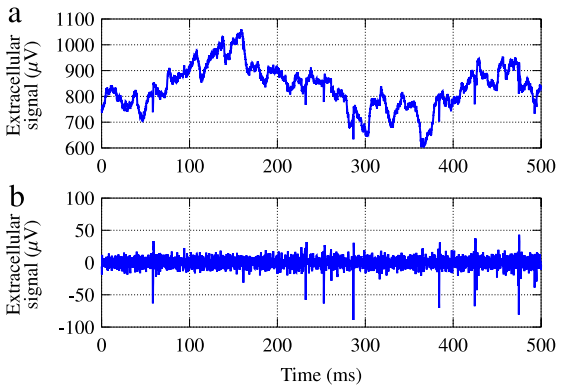

Fig. 1. (a) Segment of the original acquired extracellular signal; (b) the same segment after filtering to remove low frequency components.

of 10, 20, 25 or 50 kHz, depending on the experiment. The values were then recorded in binary files, and made publicly available by CRCNS at their website (Henze, Harris et al., 2000).

According to the coordinators of the experiment, the extracellular signal was first amplified 1000–8000 times, and filtered at the source by a low pass filter with cutoff frequency of 3 kHz (Henze, Borhegyi et al., 2000). Before using the digitalized data in the modeling process, however, we also employed a filtering process in each sequence. In the extracellular sequence, we applied an elliptical-type high-pass filter with cutoff frequency of 300 Hz. The purpose of this filtering is to remove low frequency components, mainly associated with the LFP (Local Field Potential). Although it also contains some information about the neuronal activity (Scherberger, Jarvis, & Andersen, 2005), this fact is not addressed in the proposed parametrization. Fig. 1 shows a fragment of the extracellular signal before and after this stage. The intracellular sequence, composed almost exclusively by the action potential of the neuron, is also passed through a high-pass filter, but with cutoff frequency of 50 Hz. This filtering only aims to remove low frequency components, especially in zero frequency, to ensure the level of the resting potential near zero.

After the filtering process, we selected a fixed interval of 25 s within one of the available recordings, containing 86 action potentials of the same neuron. We noted that the corresponding intracellular series contains solely these action potentials, as it is obtained directly in the membrane of a single neuron, while the extracellular series contains the spikes of all neurons in the region during the same time interval. Centered around the exact sample of the maximum value of each signal, we defined a window of 14 ms ($N = 140$ samples for a sampling rate of 10 kHz).

In the remainder of this paper, the intracellular and extracellular signals inside each time window are denoted as $\{s(\ell)\}$ and $\{y(\ell)\}$, respectively, and the estimate of these signals are denoted as $\{\hat{s}(\ell)\}$ and $\{\hat{y}(\ell)\}$ with $\ell = 0, \ldots, N-1$.

3. The proposed model

The main goal of parametric modeling is to build a mathematical model able to represent relevant characteristics of a given signal by a reduced set of parameters. Here we consider the specific case of modeling the discrete-time extracellular signal $y(n)$ whose sample set is obtained through direct observation inside a fixed time window.

Fig. 2 shows the simplified block diagram of the proposed model, in which $x(n)$ is the input and the output $\hat{y}(n)$ is the estimate of $y(n)$. We assume that this signal can be represented by a LTI