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Modeling of Bursting Neurons and Its Characteristic using Nonlinear Time Series Analysis

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Abstract

It is well known that burst patterns of neuronal networks may play an important role in information processing in the brain. We consider that it is advantageous to construct a model using mathematical neuronal models producing burst patterns, because it is such models are easier to study and more accessible as compared to real biological neuronal data. In this study, we use the Izhikevich neuron model to produce burst patterns and apply an attractor reconstruction to the Izhikevich neuron data.

1. Introduction

Burst patterns within neurons may play an important role in information processing in the brain. Therefore, burst detection and burst pattern analyzes methods are developed, which are used in various fields [1]. Although it is important to study burst patterns, as these can relate to network synchronicity and synaptic connectivity, unveiling the structure of the whole neuronal network is also required. Nonlinear time-series analysis is a useful tool for characterizing the dynamics behind observed time-series data [2]. Typically, neuronal data obtained from living neurons is high-dimensional and dynamic data, therefore nonlinear time-series analysis is suitable to characterize neuronal data. Previously, we proposed a visualization method for bursting patterns of whole neural networks using nonlinear time series analysis [3]. We applied nonlinear time-series analysis to three sets of time-series data from a neuronal culture measured at days in vitro (DIV) 15, 20 and 30, respectively. By using computer simulations, we confirmed that the characteristics of these neuronal networks change across different DIV and that the proposed visualization methods are suitable to capture the essence of these changes.

However, it is difficult to extract the ground-truth of the underlying network morphology for data obtained from real biological neuronal networks. To relate these time-series analysis results to the underlying network morphology, it is required to construct a model using mathematical neuron models producing such burst patterns. In this study, we propose a visualization method of network characteristics of burst patterns obtained from Izhikevich neuron model using nonlinear time-series analysis. From the simulation results, we confirm that the Izhikevich neuron model shows similar development stages as biological neurons, by controlling the parameters of the coupling probability and strength.

2. Attractor reconstruction of biological neuron data

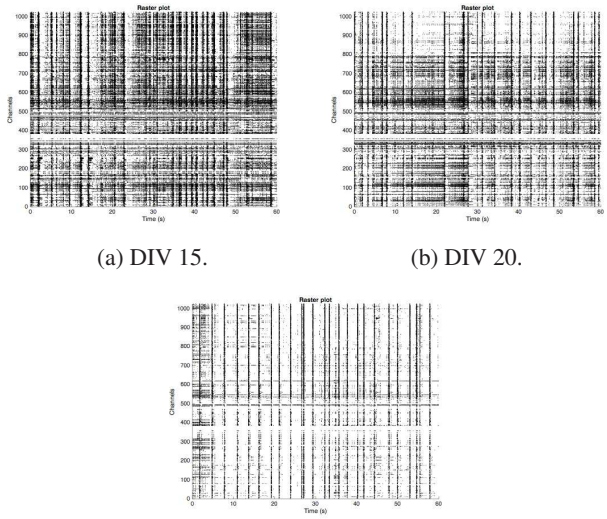
2.1 Neuron data set

We used a CMOS-based high-density microelectrode array (HD-MEA) system MaxOne (MaxWell Biosystems AG, Zurich, Switzerland) composed of 26,400 platinum electrodes in a regular grid format with 17.5 m electrode center-to-center distance (3,265 electrodes/mm^2)[4]. Up to 1,024 electrodes could be simultaneously recorded by routing the electrodes to low-noise read-out channels through a flexible switch-matrix approach [5]. On-chip circuitry was used to amplify (0-78 dB programmable gain), filter, and digitalize (10-bit, 20 kHz) the recorded signals. Online spike detection was performed by the MaxLab Live software (threshold: x5 RMS noise).

Primary cell cultures were prepared as described in Ref. [6], in accordance to Swiss Federal Laws on animal welfare. Briefly, cells from embryonic day 18 Wistar rat cortices were dissociated in 2 ml of trypsin with 0.25 % EDTA (Invitrogen, California, USA) with trituration. The MaxOne HD-MEA recording setup was placed in a recording incubator (65 % humidity) to ensure controlled environmental conditions (36°C and 5 % CO_2). During experiments, the MaxOne chips were transferred to the recording incubator and covered with sterilized lids to minimize media evaporation. Cultures were recorded at DIV 15, 20, and 30.

2.2 Attractor reconstruction

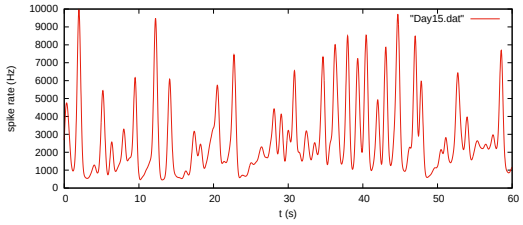
Figure 1 shows the raster plot obtained from the same neuronal culture across multiple days; DIV 15, 20 and 30, using 1,024 electrodes. Next, we calculate the spike rate at time bins, then time-series data is obtained as shown in Fig. 2.



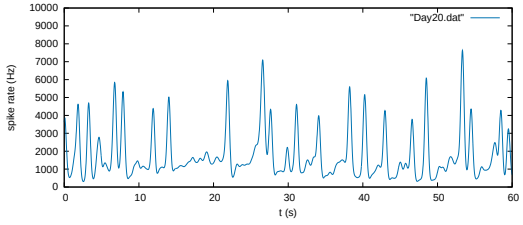
(a) DIV 15. (b) DIV 20.

(c) DIV 30.

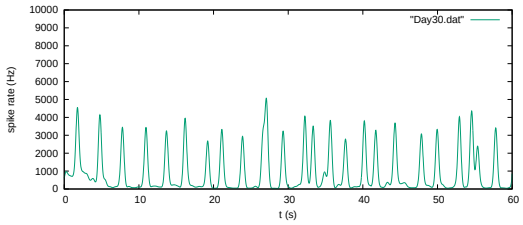
Figure 1: Raster plot of cultured neurons from 1,024 electrodes.



(a) DIV 15.



(b) DIV 20.



(c) DIV 30.

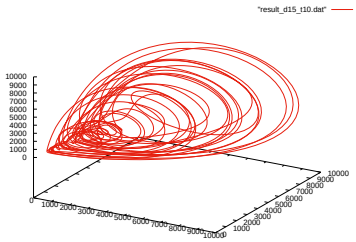
Figure 2: Time series data of cultured neurons.

The attractor of dynamical systems can be reconstructed topologically in the embedding space from Takens' theorem [7]. The state vectors in the reconstructed m-dimensional embedding space are defined by

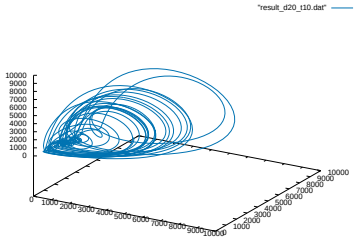
$$y(t) = \{x(t), x(t+\tau), ..., x(t+(m-1)\tau)\} \qquad (1)$$

where $x(t)$ means a scalar time series and τ is the delay time.

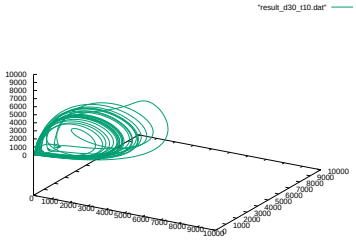
Figure 3 shows the analysis results when neuronal time-series data is embedded in 3-dimensional space with time delay $\tau = 10$. From this figure, we confirm that all three cultures exhibit a clear network structure, because the orbit draws in a certain range and is not random. Furthermore, in the case of the neurons at DIV 15 (Fig. 3(a)), the size of the attractor is larger and the behavior of the orbit is complex. As the culture matures, the attractor size becomes smaller and the complexity of the orbit becomes weaker.



(a) DIV 15.



(b) DIV 20.



(c) DIV 30.

Figure 3: Attractor reconstruction ($\tau = 10$). x-axis: $x(t)$, y-axis: $x(t+\tau)$, z-axis: $x(t+2\tau)$.

3. Attractor reconstruction for Izhikevich neuron model

3.1 Izhikevich neuron model

Izhikevich neuron model efficiently produces a wide variety of neuron spiking and bursting dynamics. The Izhikevich neuron model is described by the following equations.

$$\begin{aligned} \frac{dv}{dt} &= 0.04v^2 + 5v + 140 - u + I_{ex} \\ \frac{du}{dt} &= a(bv - u) \end{aligned} \tag{2}$$

$$\text{if } v > 30 \text{ mV, then } v \leftarrow c \text{ and } u \leftarrow u + d.$$

where v represents the membrane potential of the neuron, u represents a slow membrane recovery variable, accounting for the activation of K^+ ion currents and inactivation of Na^+ ion currents. I_{ex} denotes the excitatory input current.

In the computer simulations, 1,000 neurons were coupled randomly. The ratio of excitability and inhibitory neuron is 0.8 and 0.2, respectively. The parameters of the Izhikevich neuron model are fixed with a=0.02, b=0.2, c =-50 and d=8. By using these parameters, the Izhikevich neuron model produces tonic spiking as shown in Fig. 4.

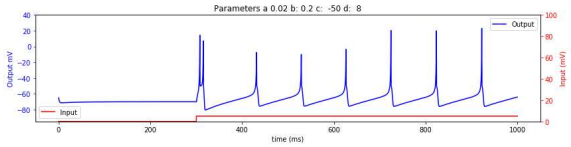
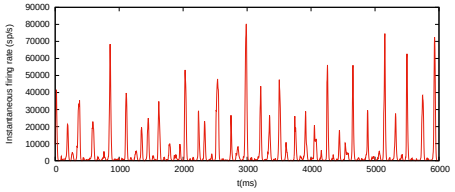


Figure 4: Tonic spiking of the neuron network model.

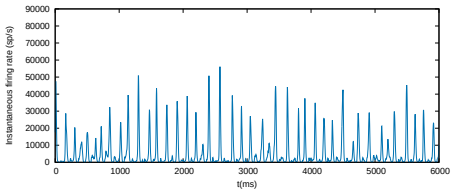
The coupling probability (p) of the network and the coupling strength (γ) of excitability neurons are important parameters for modeling the development of neurons. Figure 5 shows the network activity of 1,000 neurons, resp. the firing rate during a fixed bin, for different values of the coupling probability and strength. Table 1 summarizes the three different parameter sets. Figure 5(a) uses a high coupling probability and weak coupling strength. While, Fig. 5(c) uses low coupling probability and strong coupling strength.

Table 1: Parameters

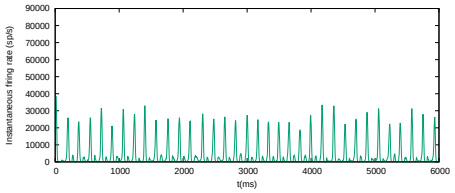
	p	γ [mV]
Figure 5 (a)	0.20	1.6
Figure 5 (b)	0.08	2.2
Figure 5 (c)	0.03	2.5



(a) p=0.20, γ=1.6[mV].



(b) p=0.08, γ=2.2[mV].



(c) p=0.03, γ=2.5[mV].

Figure 5: Time series data of the simulated neuronal network.

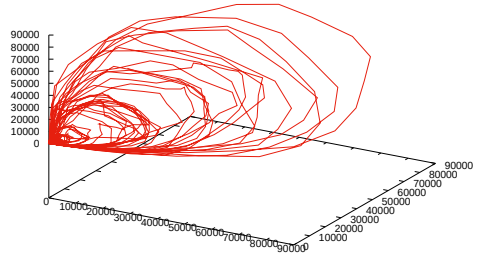
3.2 Attractor reconstruction

Finally, we apply the attractor reconstruction to neuron data obtained from the simulated Izhikevich neuronal network model. The simulation results of the attractor reconstruction in a 3-dimensional space are shown in Fig. 6, where the time delay is set to τ=3. Even though the mathematical neuron model is used, a similar development process is observed as with the biological neuronal data.

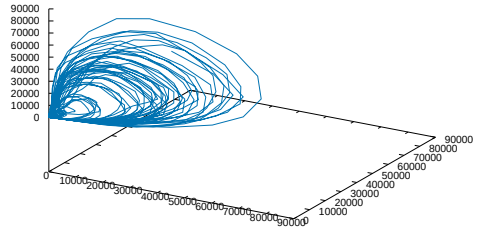
Namely, we confirm that all three cultures exhibit a clear structure, because the orbit draws in certain range and is not random. Furthermore, in the case of the neurons of Fig. 5(a), the size of the attractor is larger and the behavior of the orbit is complex. The attractor size becomes smaller and the complexity of the orbit becomes weaker with a lower coupling probability and a stronger coupling strength, similar as observed with the cultured neurons.

4. Conclusions

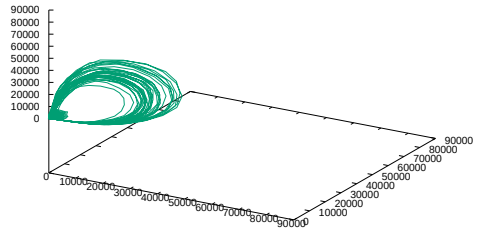
In this study, we applied the proposed technique, which is a visualization method of whole network characteristics for neuron data obtained from Izikevich neuron model. By using an attractor reconstruction technique, we obtained the attractors of actual measured neuronal data and also simulated neuronal data in a 3-dimensional space. From the observed results, we confirm that the Izhikevich neuron model, with



(a) p=0.20, γ=1.6[mV].



(b) p=0.08, γ=2.2[mV].



(c) p=0.03, γ=2.5[mV].

Figure 6: Attractor reconstruction of the simulated neuronal network($\tau = 3$). x-axis: $x(t)$, y-axis: $x(t+\tau)$, z-axis: $x(t+2\tau)$.

appropriate parameters, may exhibit similar network properties as during the development of brain function in cultured neuronal cells.

In future works, we would like to use neuron data with different parameters of the Izikevich neuron model. We are also interested to classify neuronal data using the techniques described here and apply such techniques also for applications in drug development, such as observing and classifying effects of pharmacological compounds on neuronal networks.

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