Explicit Markov counting model of inter-spike interval time series

G. Mijatović1, T. Loncar Turukalo1, L. Negyessy2, F. Bazsó3, E. Procyk3, L. Zalányi2, J. Minich4, D. Bajić1

1Department of Telecommunications and Signal Processing, University of Novi Sad, Serbia
2 Institute for Particle and Nuclear Physics, Wigner Research Centre for Physics, Budapest, Hungary
3 Inserm U846 Stem Cell and Brain Research Institute, University of Lyon, France
4 SU-Tech, College of Applied Sciences, Subotica, Serbia

gorana.mijatovic@yahoo.com, tatjana.turukalo@ktios.net, negyessy@gmail.com, bazso@mail.kfki.hu,
zala@rmki.kfki.hu, jminich@vts.su.ac.rs, dragana.bajic@gmail.com

Abstract— In this paper the inter-spike intervals (ISI) time series are recorded in awake, behaving macaque monkeys and their differences are modeled as a counting explicit finite Markov chain. The average length of time series was 3050 samples. The parameters investigated were: the state probability, the transition probability and normalized count histogram of the Markov chain, as well as ISI interval and ISI difference associated to each state of Markov model separately. As a control parameter, for each series pseudorandom Gaussian and uniform series with same mean and standard deviation, as well as isodistributional surrogates were generated. An unexpected conclusion is that the state and the transition probabilities, as well as the count histogram, correspond to the exact values are shown in Section IV and compared to the artificially generated data, with the outline for the future investigations.

Keywords: Inter-spike intervals, Markov models, counting model.

I. INTRODUCTION

One of the techniques for studying the nervous system is to observe the signal measured at the cellular level. The very first methods used low impedance microelectrodes (<1MΩ) with tips exposed a bit farther from the spike generating sources in order to prevent the predominance of action potentials in recorded signals.

Extracellular recordings yield two signals by the means of frequency band separation: high pass filtered recording with cutoff frequency of 300 to 400Hz results in multiple-unit spiking activity (MUA); low pass filtered recorded signal with cutoff up to 300Hz yields local field potential (LFP) which represent mostly slow events reflecting cooperative activity in neural populations.

The data obtained by high impedance electrodes (1-5 MΩ) can isolate the activity of single neurons. Single-unit recording technique still remains the method of choice in many behavioral experiments with awake animals [1]. Estimation of spiking activity from recorded signal relies on the assumption that their frequency content substantially differs. A usual method for spiking activity analysis is to observe the interval between the successive spikes – inter spike interval (ISI).

Inter spike intervals were subject of many studies, most of which were based assuming the Poisson distribution. Novel approaches, however, contradicts this assumption [2-5].

This paper investigates the possibility of the counting Markov model application within the ISI time series analysis. The counting models have been investigated in cardiovascular time series (pulse intervals and systolic blood pressure), revealing strong psychological correlations [6]. It was the main trigger for extending the application of these models to ISI time series.

The paper is organized as follows: after the brief introduction considering experimental procedures and signal recording and pre-processing (Section II), the model itself is described and the parameters defined in Section III. The results considering the probabilistic parameters, as well as for the absolute and differential ISI values are shown in Section IV and compared to the artificially generated data, with the outline for the future investigations.

II. METHODS

A. Experimental procedures and tasks

As stated elsewhere [7], housing, surgical, electrophysiological, and histological procedures in this experiment were carried out according to the European Community Council Directive (1986) and Départemental des Services Vétérinaires (Lyon, France). The details on surgical, experimental and task procedures are given in detail in [7]. In brief, two male rhesus monkeys were trained in the problem solving task (PS). Monkeys had to find by trial and error which target, all incorrect trials up to the first correct touch and a repetition period wherein the animal was required to repeat the correct touch several times.

Neuronal activity was recorded using epoxy-coated tungsten electrodes (1–4 MΩ at 1 kHz; FHC Inc, USA). One to four microelectrodes were placed in stainless-steel guide tubes and independently advanced into the cortex through a set of micromotors (Alpha-Omega Engineering, Israel). Recording locations were confirmed by anatomical MRI and histology [7].

B. Extracellular recordings

Raw recordings were filtered using high pass filter (two poles Butterworth) with cutoff at 250Hz and low pass (4
pole Butterworth) with cutoff set to 3KHz for MUA and 280Hz for LFP. Neuronal activity (MUA) was sampled at 12.5 kHz and LFP at 781.25 Hz. Single unit activity was identified using online spike sorting (MSD, AlphaOmega). Since the amplitude of waveforms depends on the electrode position with respect to recorded cells, LFP data was normalized prior to analysis.

The spike signatures are clearly visible on bottom LFP waveform, as well as the presence of high frequency content. The inference on the spike position based only on LFPs is even possible using the simple threshold algorithm on the first derivative of LFPs with almost the same accuracy as this algorithm works on MUA.

Total of 98 records were collected, among which the short ones that would not ensure statistically significant data were removed. The remaining 67 ones were of average length of 3050 ISI samples.

III. MODEL

Recorded time series consisted of signals \( ISI_i, i=1,\ldots, n \), out of which \( n-1 \) signal differences (increments) were derived:

\[ \Delta_i = ISI_{i+1} - ISI_i, i = 1,\ldots, n - 1 \]  

ISI intervals can be increasing or decreasing, according to their differences, as shown in Fig. 1.

The corresponding counting model is a finite ergodic Markov chain. Each state corresponds to a single signal difference \( \Delta \). The state denoted “\( k \)” correspond to the \( k \)th difference of the same sign that has occurred in a row. State denoted with “1” corresponds either to the first difference in a row, or to a “solitary” difference, i.e. a difference preceded and followed by a difference of the opposite sign.

It should be noted that the model is different from the model introduced in [6] as the positive and the negative states are not evaluated jointly as in [6], but separately. The gray states in Fig. 2 correspond to positive ISI differences, and the white states to the negative differences.

![Figure 1. Spike time series with increasing and decreasing inter-spike intervals (ISI)](image1)

\[ \Delta_i = ISI_{i+1} - ISI_i \]

**INCREASING**

- \( IS1 \)
- \( IS2 \)
- \( IS3 \)
- \( IS4 \)

**DECREASING**

- \( ISb_1 \)
- \( ISb_2 \)
- \( ISb_3 \)
- \( ISb_4 \)

Figure 1. Spike time series with increasing and decreasing inter-spike intervals (ISI)

![Figure 2. Counter model](image2)

The classical parameters of the model are state selection probabilities \( P(i), i=1,\ldots,L \) and \( Q(i), i=1,\ldots,L \) for positive and negative states respectively, as well as the state transition probabilities shown in Fig. 2.

Sequences of \( m=1,\ldots,L \) successive all positive or all negative increments form a ramp (row) of the length \( L \). Count histogram (number of ramps of specific length) is also one of the features of this model. Finally, for each state, a mean ISI value and the mean difference value are evaluated.

IV. RESULTS

The possibility of bursts in spiking activity is investigated estimating their probability density functions. The pdfs of all the ISI time series were monomode, so there was no need for application of burst detecting algorithms [8,9].

The classical probabilistic parameters were estimated from the time series. They were compared to the formula values. The detailed theoretical derivation of formulae is presented in [6]. The theory is strictly valid for uniform distribution. It is also valid for any stream of i.i.d. random variables, proven by Kolmogorov-Smirnov and Wald-Wolfowitz test and aided with Central limit theorem [6].

\[ P(n) = Q(n) = \frac{n+1}{(n+2)!} \]  

(2)

\[ p_{n+1} = q_{n+1} = \frac{n+2}{(n+1)\cdot(n+3)} \]  

(3)
\( h(n) = 100 \frac{(n+1)^2 + n}{(n+3)!} \) \hspace{1cm} (4)

Eq. (4) presents row histogram normalized per 100 samples (number of rows of length \( n \) per 100 ISI samples). The formulae values and values estimated from ISI series are presented in Fig. 3(a), 3(b) and 3(c).

Figure 3(a). Transition probabilities

Figure 3(b). State probabilities

Figure 3(c). Number of ramps per 100 samples

Figure 4. Autocorrelation function

Figure 5: State distribution of signal amplitudes – a) Original ISI signal; b) Surrogate ISI signal; c) Pseudorandom Gaussian series; d) Pseudorandom uniform series; Legend is given in Fig. 5(b)
prevents statistical significance.

The accordance of the probabilistic formulae does not mean that ISI series are streams of i.i.d. random variables, as the autocorrelation function with sidelobes confirms as well (Fig. 4).

For this reason, the statistics of ISI amplitudes are associated with each state of the model. Each one was investigated considering the following state parameters: a) positive or negative; b) ramp (row) length; c) the order of state. Then for each one of 67 signals an isodistributional surrogate data [10] were generated, as well as the pseudorandom Gaussian and uniform series with the same mean and standard deviation as the source ISI series.

The results are presented in Fig. 5. The complete procedure is repeated for signal differences, presented in Fig. 6. Negative differences are presented as absolute values for “negative” states. The rows (ramps) longer than six are not presented, since the number of their appearance was not enough to ensure statistical significance.

The maximal ramp length was 8, the same for all investigated data.

V. DISCUSSION AND CONCLUSION

The behavior of ISI time series, although unexpectedly in good accordance with the formulae derived for the differences of series of i.i.d. random variable, exhibit different behavior when the amplitudes and the differences are associated to the model.

Positive and negative ISI differences are asymmetrical. Positive differences increase with increasing states, with the last difference in a row equaling the value of the solitary difference. The longer the ramp, the lower the difference. Negative difference decrease with increasing states and the values overlap (Fig. 6a). The starting point for positive differences is lower than for the negative ones (Fig 5a).

The absolute value of positive and negative solitary $\Delta$ is the same, but the ISI level at which they occur is different. The interpretation is that if absolute value of ISI is high, it is expected that the difference that follows it would tend to decrease its high level, and vice versa.

The $\Delta$ signal in uniform series remain constant within a ramp of specific length, similar to Gaussian series.

The physiological meaning of the ISI time series associated to states remains to be investigated. Although in other biomedical data series the results were in a good correlation with psychological observation, the study on ISI time series requires more data for comparison, with physiological rather than pseudorandom origin. The future study would investigate exact behavior of the animals and correlate their signals to the states of the observed model.

Figure 6: State distribution of signal differences

a) Original ISI signal; b) Surrogate ISI signal; c) Pseudorandom Gaussian series; d) Pseudorandom uniform series
ACKNOWLEDGMENT

This research is supported in part by grants TR32040, Serbian Ministry of Science, and by Bilateral cooperation Serbia-Hungary “Statistical characterization of neural behavior in the cerebral cortex of behaving animals”.

REFERENCES


