Interpretation of inter-spike interval statistics through the Markov switching Poisson process

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Abstract

Inter-spike interval statistics are often used to characterize spike sequences. Each of lower order statistical coefficients itself characterize a spike sequence well. But it is hard to understand the meanings of their combinations. The interval histogram can partly make it clear, but in practical experiments, we can not often obtain enough length of data to estimate the histogram. Moreover, interval statistics do not directly give us an information about the mechanism of spike event generation. In the present study, we attempt to interpret the combination of inter-spike interval statistics in comparison with a simple stochastic process designed to describe spike events. We define the Markov switching Poisson process, where the state switches in Markov manner between two Poisson processes (one is active state, and the other inactive) at each spike event. Through the Markov switching Poisson process, we interpret the differences in interval statistics of the biological spiking data between middle temporal (MT) area and prefrontal (PF) area of monkey cortex. Most MT data are found to be interpreted as spike sequences whose balance of staying time is biased to inactive state. It is also found that the mean staying time relative to the mean inter-spike interval is shorter than that of typical PF data. The staying time scale can be considered as time scale of temporal correlation in the incoming synaptic inputs. This implies that the differences between the two area originates in the time scales of synaptic inputs correlations.

1 Introduction

Inter-spike interval statistics are often used to characterize spike sequences. The coefficient of variation (CV) of intervals characterize spiking irregularity[1][2]. The skewness coefficient (SK) of intervals characterize the degree of anomalous long intervals[3][4][5], which is one of the reflects of long time scale correlation[6]. The two statistical coefficients are described by the moments up to the third order. The correlation coefficient (COR) of consecutive intervals characterize serial correlation of interval sequence[6][7]. These statistical coefficients do not characterize all of the properties of the spike sequence. If a biological spike sequence consists of a very large number of intervals, then we can employ higher order statistical coefficients in addition to these coefficients, or serial correlations at larger lag than 1, or we can construct a detailed interval distribution function as a histogram. However, an available biological sequence does not consist so large number of intervals. The reliabilities of statistics, which depend on the statistical fluctuation for finite data, generally become lower as the order becomes higher. So higher order statistics are not practical.

Spike count statistics also contain reliable low-order statistics. Physiologist often use spike frequencies corresponding to the first order statistics of spike counts. The second order statistics of spike counts are sometimes used to characterize the spiking variabilities[8][9][10] and other spiking properties[11][12]. But the width of time window to count spikes has significant effect on statistics values of spike counts. It is difficult to deal with the effects of window width theoretically, except for the first order one. So more than second order statistics of spike counts are not easy to use.

Accordingly we take up low order statistics of inter-spike intervals, CV, SK, and COR. Each of the coeffi-

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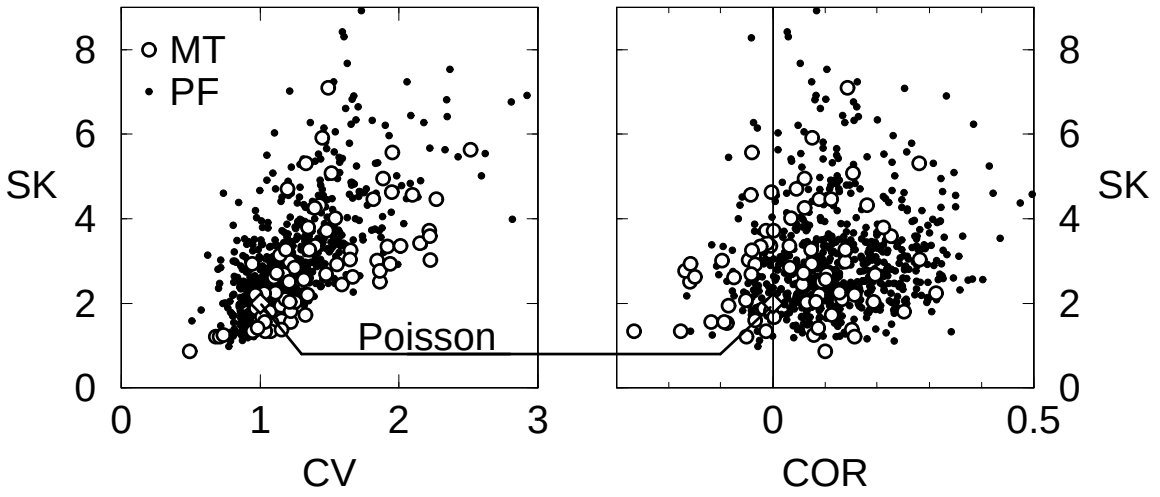

Figure 1: Each dot or circle represents the statistical coefficients (CV, SK) values (in left plot) and (COR, SK) values (in right plot) estimated from biological spike sequences. A large circle represents (CV, SK, COR) estimated from MT data, and a small dot represents that of PF data. The values (CV, SK, COR) = (1, 2, 0) are given by the Poisson process (random sequence).

cients characterizes a spike sequence. But they do not directly give us an information about the mechanism of spike event generation. There are a large number of trials to determine the conditions that a single neuron model can reproduce interval statistics of cortical neurons [1] [2] [5] [6] . But it is essentially ill-posed inverse problem, so any conclusions are specific to an assumed model. If a complex model is assumed, it is difficult to catch the essence of the problem. For the sake of interpretation of inter-spike interval statistics, it is desirable that the assumed model is as simple as possible. It is not necessary to try biological reality. So we assume a simple stochastic process designed to describe spike events, free from the spiking mechanisms of biological neurons.

2 Inter-spike interval statistics

We take up three statistical coefficients of inter-spike intervals characterizing a spike sequence: the coefficient of variation CV, the skewness coefficient SK, and the correlation coefficient of consecutive intervals COR, defined as,

$$\mathrm{CV} \equiv \frac{\sqrt{\overline{(T-\overline{T})^2}}}{\overline{T}},$$

$$\mathrm{SK} \equiv \frac{\overline{(T-\overline{T})^3}}{\sqrt{\overline{(T-\overline{T})^2}}^{\,3}},$$

$$\mathrm{COR} \equiv \frac{\overline{(T_i-\overline{T})(T_{i+1}-\overline{T})}}{\overline{(T-\overline{T})^2}},$$

where T represents an inter-spike interval, and $\{T_1, T_2, ..., T_i, ..., T_n\}$ is an interval sequence. The notation $\overline{\cdots}$ represents an averaging operation through an interval sequence: $\overline{T} = \frac{1}{n}\sum_{i=1}^{n} T_i$. The coefficient of variation CV is a measure of variability of intervals, which shows a measure of spiking irregularity[1]. The skewness coefficient SK is a measure of the asymmetry of the interval distribution, which shows a measure of anomalous long intervals[3][5]. The correlation coefficient COR is a serial correlation coefficient at lag 1 in an interval sequence, which shows a measure of temporal correlation[6][7].

In this paper, we examine two kinds of spiking data recorded from neurons in two area of monkey cortices: the middle temporal (MT) area and the prefrontal(PF) area.

The MT data are obtained from an anesthetized monkey in front of a cathode-ray tube[13]. Random dots displayed in the whole screen are flowing for 10 sec in a constant direction of 12 directions. MT neurons exhibit sustained activity during random dots flowing, and the level of the sustained spike rate largely depends on the flow direction. We use only the final 9 sec of 10 sec in order to avoid the possible initial transient changes. The 240 spike sequences are obtained from 20 neurons (20 neurons $\times$ 12 di-

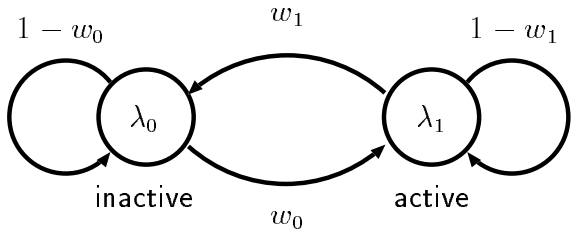

Figure 2: Schematic representation of Markov switching Poisson process.

rections). For reliable statistical analyses, we adopt only the sets including more than 100 spikes. The 74 sequences of 240 contain more than 100 spikes.

The PF(prefrontal) data are obtained through a delay response task experiment [5][14]. In the experiment, a rhesus monkey is required to make a specific saccade eye movement in response to a visual cue stimulus which is presented in advance to a 3 second delay period during which cue stimulus is absent. PF neurons exhibit sustained activity during the delay period. In some neurons, the level of the sustained spike rate largely depends on the choice of the cue stimuli. We use only the middle 2 sec in the delay period of 3 sec in order to avoid the possible initial and final transient changes. The 2 sec spike sequences are classified according to the cues and the neurons, and 1864 sets (233 neurons $\times$ 8 cues) of spike sequences are obtained. Each 2 sec spike sequence includes too few spikes to estimate the statistical coefficients. So we link spike sequences belonging to one set one trial to the next, and we obtain a long spike sequence from one set. We analyze the 666 sequences containing more than 100 spikes, for reliable statistical analyses.

Figure 1 shows the statistical coefficients (CV, SK, COR) estimated from MT and PF data. A large circle represents (CV, SK, COR) estimated from MT data, and a small dot represents that of PF data. There are slight differences between MT and PF data. The MT data are biased to small SK relatively to the CV, while many PF data exhibit large SKs relatively to their CVs, The MT data are biased to small or negative COR, while the PF data are biased to large positive COR. In this paper, we attempt to interpret these differences in comparison with a simple stochastic process designed to describe the spike event generation.

3 Markov switching Poisson process

Each of the statistical coefficients, CV, SK, and COR shows us properties of a spike sequence very well. But it is difficult to understand the meanings of the combination of them. They do not directly show informations about the mechanisms of spike event generation. Therefore, we assume a simple spike event process to reproduce the inter-spike interval statistics (CV, SK, COR)s of cortical neurons. The statistics (CV, SK, COR) are mapped to the model parameters of the spike event process, values of which can give us some informations about spike event generation. It is desirable for the sake of catching the essence that the assumed model is as simple as possible. The most simple spike event process is Poisson process. It is the unique uncorrelated spike event process without need of any hidden variables. In Poisson process, a spike event occurs at random due to the constant rate λ. Poisson process gives an exponential interval distribution, and the statistical coefficients (CV, SK, COR) = (1, 2, 0). We can see in Figure 1 that many of the biological (CV, SK, COR)s are around that of Poisson process (1,2,0), but not a few data exhibit (CV, SK, COR) values far different from that of Poisson process. The differences are found to be significant[6]. So now we need a higher class of spike event processes.

In this paper, we assume the Markov switching Poisson process. At each moment, a spike event occurs due to a Poisson process, but the event rate λ can switch between 2 values, $\lambda_0, \lambda_1 (\lambda_0 \leq \lambda_1)$, due to constant probabilities at every spike events. Schematic representation is in Figure 2. The transition probability w_0 is the probability of switching from the inactive state λ_0 to the active state λ_1, and w_1 is the probability of switching from the active state λ_1 to the inactive state λ_0. The Markov switching Poisson process is simple and easy for consideration, though it can describe large class of spike event processes, for instance, bursting-like spike patterns, or temporally correlated spike sequences with long time scale. It is a kind of the modulated Poisson processes, but does not belong to the doubly stochastic Poisson process (Cox process)[16]. In the doubly stochastic Poisson process, the spike rate varies independently from its spike events, while the rate changes of Markov switching Poisson process depend strongly on its spike event.

The model has 4 parameters, $\lambda_0, \lambda_1, w_0, w_1$. The model can be also characterized by 4 time scales: the mean intervals of each state, τ_0, τ_1, and the mean staying time in each state, s_0, s_1, described by the followings,

$$\tau_0 = 1/\lambda_0 \ , \qquad s_0 = 1/w_0\lambda_0 \ ,$$
$$\tau_1 = 1/\lambda_1 \ , \qquad s_1 = 1/w_1\lambda_1 \ .$$

These 4 parameters have one-to-one correspondence to the interval statistics (CV, SK, COR) and the mean interval, $\overline{T}$, in addition. They satisfy the following

equations,

$$\begin{aligned}
\frac{s_0+s_1}{s_0/\tau_0+s_1/\tau_1} &= \overline{T}\ , \\
\frac{s_0\tau_0+s_1\tau_1}{s_0+s_1} &= \frac{\mathrm{CV}^2+1}{2}\,\overline{T}\ , \\
\frac{s_0\tau_0^2+s_1\tau_1^2}{s_0+s_1} &= \frac{\mathrm{SK}\ \mathrm{CV}^3+3\ \mathrm{CV}^2+1}{6}\,\overline{T}^2\ , \\
\frac{(\tau_0-\tau_1)^2}{s_0+s_1} &= \frac{\mathrm{CV}^2(1-2\ \mathrm{COR})-1}{2}\,\overline{T}\ .
\end{aligned}$$

The solution $(\tau_0, \tau_1, s_0, s_1)$ for $(\overline{T}, \mathrm{CV}, \mathrm{SK}, \mathrm{COR})$ exists when the statistics satisfy the following inequality,

$$1 < \frac{(\mathrm{CV}^2+1)^2}{4} < \frac{\mathrm{SK}\ \mathrm{CV}^3+3\mathrm{CV}^2+1}{6}\ ,$$

$$1 < \mathrm{CV}^2(1-2\ \mathrm{COR})\ .$$

The whole grey regions in Figure 3a represent the projection of the conditions on CV-SK plane.

4 Projection to the model parameters

Now, we try to interpret the interval statistics (CV, SK, COR) through the Markov switching Poisson process. One of the characteristic differences in (CV, SK, COR) between MT data and PF data is the value of SK relative to CV. So we define two CV-SK regions (see Figure 3a),

Region A: $\mathrm{SK}-2 \geq 6(\mathrm{CV}-1)$ (dark gray) ,
Region B: $\mathrm{SK}-2 \leq 3(\mathrm{CV}-1)$ (light gray) .

The region A belongs to characteristic PF data, and the region B belongs to characteristic MT data. Another characteristic difference between MT data and PF data is the COR value. So we use 4 slices at $\mathrm{COR} = -1, 0, 1, 2$ in (CV, SK, COR) space. The 8 slices (2 region $\times$ 4 COR values) are mapped to the parameters of the Markov switching Poisson process.

The region A and B are projected on the plane of the staying time balance, $s_1/(s_0+s_1)$, and the staying time scale, $(s_0+s_1)/\overline{T}$ (Figure 3b). The difference between the region A and B can be seen well by the balance in the mean staying time of active and inactive state, $s_1/(s_0+s_1)$. The region A, with large SK relative to CV, appears to be biased to the active state by means of staying time. This kind of spike sequences can be generated if its state is mainly active and sometimes becomes inactive. On the other hand, the region B, with small SK relative to CV, appears to be biased to the inactive state. This kind of spike sequences can be generated if its state is mainly inactive and sometimes becomes active. They may sometimes look like bursting pattern.

The differences also appear in the staying time scale over the mean inter-spike interval, $(s_0+s_1)/\overline{T}$. Spike sequences belonging to the region A are staying in each state longer than those of the region B, when COR is positive. In other words, spike sequences with larger SK relative to CV have longer scale temporal correlations, when COR is positive. We can also see in Figure 3b a trivial result that the larger value its COR has, the longer it is staying in each state.

The biological ($\overline{T}$, CV, SK, COR)s are mapped on the same plane in Figure 3c. Each circle and dot correspond respectively to the statistics ($\overline{T}$, CV, SK, COR) estimated from the MT data and the PF data. We can see that MT data are apt to have parameters that the staying time balance is biased to inactive state and correlation time scale is relatively small.

Summary of results:

1. Large SK value relative to CV means that the balance of staying time is biased to the active state.
2. Large SK or large COR means that the staying time is long relative to the mean inter-spike interval.
3. The MT data exhibit inactive-biased balances and short staying time scale relatively to the PF data

5 Discussion

If the state changes in the model are considered to correspond to level changes of incoming synaptic inputs to the neuron, then the staying time scale is interpreted as correlation time scale of incoming inputs, and the staying time balance represents the difference in distribution shapes of input rate. The properties of incoming inputs reflect collective activities of presynaptic neurons. We can see the differences in the staying time balance and staying time scale between the MT data and the PF data. In both cases, experimental conditions are constant during recording, by means of either stimulus or behavior. So the area differences may imply the difference in structure properties of cortical networks or in current states of neuronal assembly.

There is also possibility that the state changes occur in a single neuron. A typical case can be see in a bursting neuron (see [17] for review). The first spike leads to a bursting state and back to a normal state in about a few 10 msec. We can not find such a short

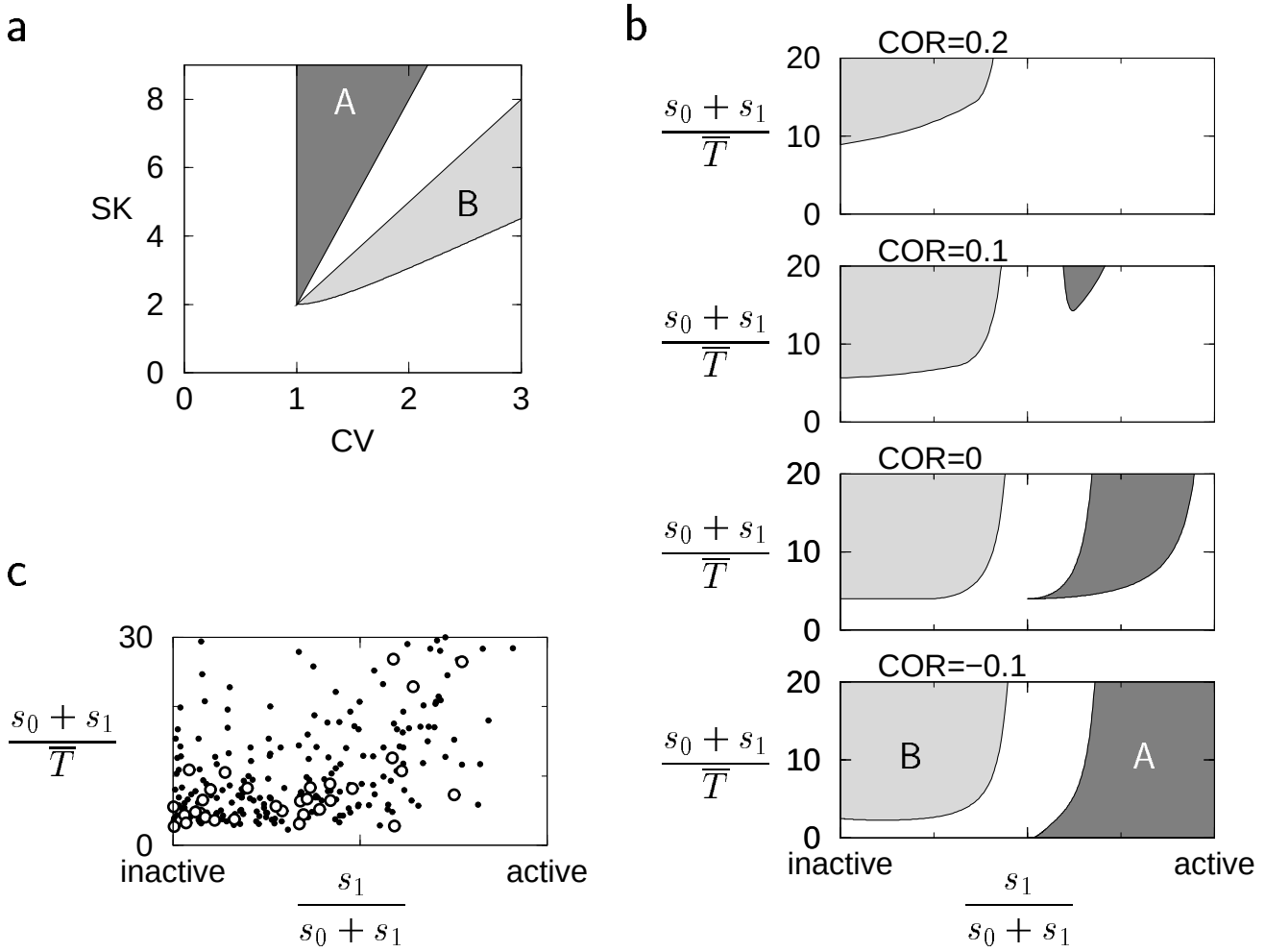

Figure 3: a: The definition of two characteristic CV-SK region: Region A (dark gray) and Region B (light gray). The whole region of gray parts can be reproduced by the Markov switching Poisson process. b: The projection on the model parameter plane of the staying time balance, $s_1/(s_0+s_1)$, and the staying time ratio, $(s_0+s_1)/\overline{T}$, of the regions corresponding to the region A and the region B defined in a. The 4 plots differ in COR value, respectively COR $= 2, 1, 0, -1$. c: The projection on the same plane as b of the statistics (CV, SK, COR) estimated from the biological data. The circles represent those of the MT data and the dots represent those of the PF data.

staying time in active state, s_1, among the present data. So we can say that the prepared biological data do not contain data from typical bursting neurons. However, we can not deny the possibilities that the state changes occur in a neuron by neuronal variables such as membrane sensitivities, ion densities, or others.

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