Neuron Firing Features

Gaia Bellone & Shuhei Okumura

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Introduction

We are working on a neuroscience project with Dr. MARC SOMMER, an assistance professor in the department of neuroscience at Center for the Neural Basis of Cognition (CNBC) at University of Pittsburgh. His lab studies how different brain areas interact with each other. Most of their work focuses on the circuits that allow us to see and move our eyes. Using neurophysiological methods on a single neurons recording, electrical microstimulation, and reversible inactivation, they study signal processing in the brains of awake, behaving rhesus monkey.

The goal of this project is to understand if there is any relationship between the structure of the spikes of the signals propagate from the neurons and their function. Because neurons represent and transmit information by firing sequences of spikes in various temporal pattern, we will try to identify and classify neurons based on firing spikes characteristics. The neurons typi-

cally respond to a stimulus by producing complex spike sequences that reflect both the intrinsic dynamics of the neuron and the temporal characteristics of the stimulus. Neuronal responses can vary from trial to trial even when the same stimulus is presented repeatedly, for this reason they are typically treated probabilistically, and characterized, for example, from the probability that a spike occurs at a particular time during a trial. Another useful statistic for characterizing spiking patterns is the inter- Spike interval (ISI) distribution, the probability density of the time intervals between adjacent spikes. The spike waveform widths and the spontaneous firing rate, the rate of spontaneous activity of the neuron (that is, activity not caused from stimuli) can give us additional information about the neurons identity. There are two major types of neurons, inhibitory and excitatory. Inhibitory neurons have short spike periods, on the other hand, excitatory neurons some what longer spike periods. Inhibitory neurons have high spontaneous firing rates, while the excitatory have lower ones. Because the statistical charactestics of the spike patterns are therefore rich of information, our work will be to study these for identifying and classifying neurons in subcategories, concentrating on the characteristics of the ISI distribution.

Experiment

During the experiment, the monkey faced a tangent screen on which visual stimuli were projected by an LCD monitor. Visual stimuli were 0.3×0.3 blue

or red spots ($(0.6cd/m^2)$) with dim ambient room light. Personal computers controlled the presentation of visual stimuli and recorded at 1 kHz the eye position the occurrence of action potentials, and the timing of task events.

Each task is composed of 3 parts, the control period, the visual stimulus and the movement. The control period is at the very beginning of the trial. This is when the animal is just looking around, just waiting, and not engaged in a formal task. Then there is the usual stimulus given by the spotlight, and in the end the saccade movement. A rapid intermittent eye movement, as that which occurs when the eyes fix on one point after another in the visual field. At the end of each trial, the monkey is rewarded.

The Control data, the data from the control period, are critical because they tell us how much the processes of the neurons fluctuate in the steady state, when nothing in particular is happening in the visual world or with regard to eye movements.

Data

Our dataset is composed of all the single neuron data from one brain structure, the mediodorsal thalamus (MD). All of these data were from the Control period of the task. There were inserted certain numbers as delimiters, i.e. labels to show where one trial ends and the next one begins. Here is the code: 7773, 8883, and 9993 show the ends of trials. So if you see something like

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12
15
222
5
197
7773
132
4
21
7773
12
29
8883
8883
144
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etc., this means that there were five sequential ISIs during the Control period of the first trial: 12, 15, 222, 5, then 197. Then the trial ended (7773) and the monkey did something else for a few seconds. Then another trial began in which the following ISIs occurred during the Control period: 132, 4, and 21. Then that trial ended (7773). Sometimes there is no ISI during a trial (hence the two 8883s in a row). Sometimes there is only 1. Considering the structure of the dataset, we have decided to ignore this subdivision, and working on each file as it is a big task, and not a sequence.

Even if we have the ISI distribution for 40 neurons, we decided to carry out our analysis only for 24 of them, because we think that we need at least 30 data points for each neuron for having a significant estimate. Moreover, because these data come from a specific time period lasting 100 ms, every data point greater than 100 ms have to be excluded.

Analysis

A stochastic process that generates a sequence of events, such as action potentials, is called a point process. In general, the probability of an event occurring at any given time could depend on the entire history of preceding events. If there is no dependence at all on preceding events, so that the events themselves are statistically independent, we have a Poisson process. The Poisson process provides an extremely useful approximation of stochastic neuronal firing. In particular we are assuming that the process that generates a sequence of spikes is the homogeneous Poisson process, for which the firing rate is constant over time.

The probability density of time intervals between adjacent spikes (ISI) for a homogeneous Poisson spike train is an exponential. This is why we start our analysis by trying to fit the exponential model.

First we plotted the histogram and the QQ-plot for all the 24 neurons separately. Here the histogram and the QQ-plots are shown for 4 neurons with data points more than 100. In the histogram plots, in Figure 1, the green line corresponds to the nonparametric density estimate and the blue line is the estimated exponential density. It is clear that the peaks of these two density estimates are different. The peak for the non parametric density is shifted to the right of the exponential density in all four plots. The left tail of the nonparametric density is totally different from the exponential density. From this plot we can say that the exponential model might not be adequate

in this case.

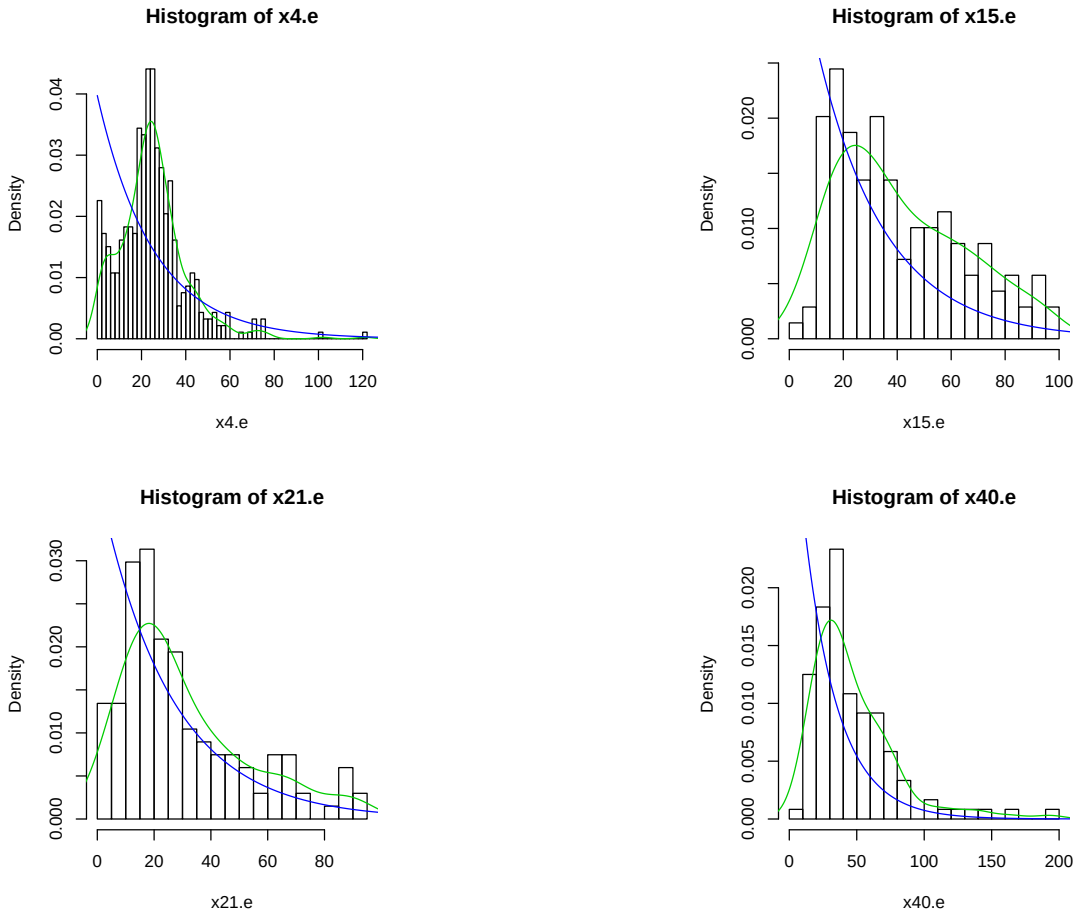

Figure 1: Histogram

Next we look at the QQ-plots for these four neurons in Figure 2. For the neurons X15 and X40 the right tail is uniformly lower than the estimated exponential density whereas for X4 the left tail is substantially different. So the QQ-plot also confirms that the exponential model is not adequate in this case.

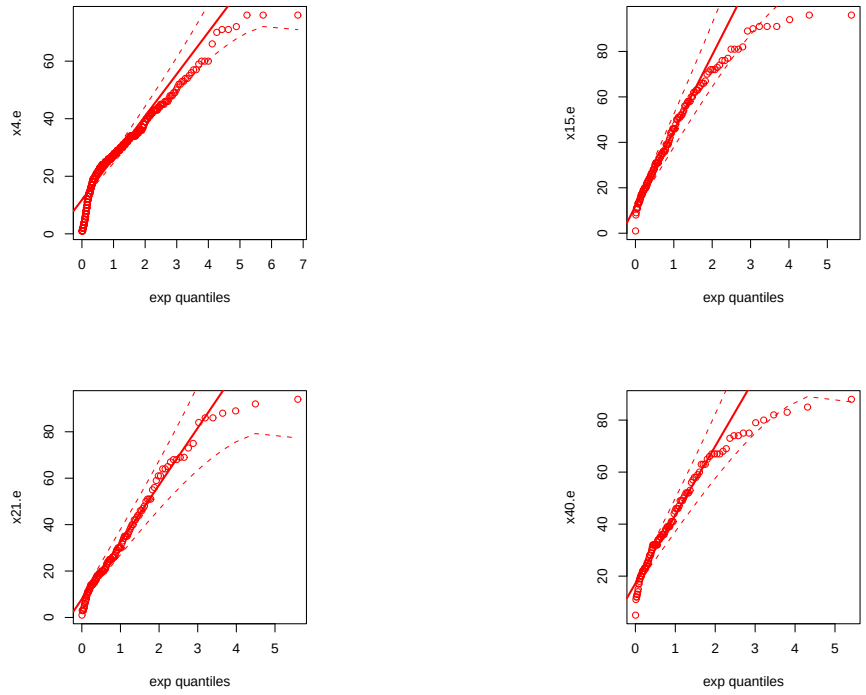

Figure 2: QQ plot

Now we do some quantitative analysis. We calculated the coefficient of variation for all the neurons. If they really come from exponential distribution then their coefficient of variation should be close to 1. We constructed a confidence interval for the coefficient of variation based an the 24 neurons and it is of the form $[0.5612426, 0.6491892]$. We can see that 1 does not fall in this interval. So this also suggests that the exponential model might not be a good fit in this case.

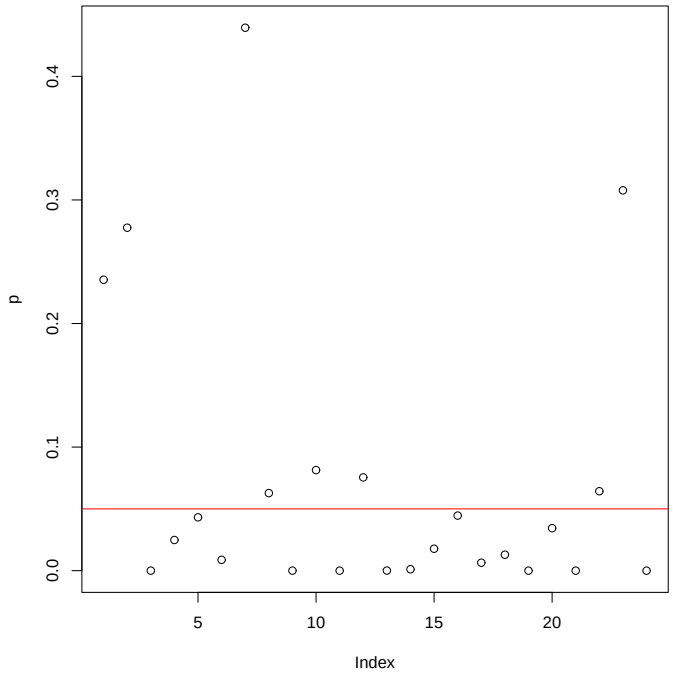

Figure 3: Plot for p-value of Kolmogorv Smirnov test

We do the Kolmogorov-Smirnov test for all the 24 neurons. The p-values for all the 24 tests are plotted in Figure 3. Here we can see that most of the p-values are below 0.05, which means that the null hypothesis that they come from an exponential distribution is rejected. That means from these tests we can infer that most of the neurons do not follow an exponential distribution. Since we want the same probability model for all the neurons we can infer that exponential model does not fit well in this case. Because the exponential assumption doesn't seem to be good enough from our analysis, we are trying to understand better how a neuron can fire.

The action potential (spike) generation also depends on the recent history of cell firing. For a few milliseconds just after an action potential has been fired, it may be virtually impossible to initiate another spike. This is called the absolute refractory period. This could be a reason why a model based only on a simple exponential distribution cannot be a good assumption for the distribution of the ISI.

Conclusion

From the analysis conducted so far, we can infer that an exponential model is not adequate to describe the ISI distribution.If we consider the influence of the refractory period on the ISI distribution, we can think to a mixture model that reflects the cumulative effect of the refractory period and the distribution of the ISI.

In the literature, the refractory period is assumed to be distributed normally with a lower end point at 0 since a length cannot be a negative value. And actual ISI's are distributed as exponential. Thus we are now aiming to estimate a mixture model comprising of the normal and exponential distributions from the data.

In addition to refractory period, neurons' bursting behaviors will have to be considered. A neuron produces spikes both on a regular basis and on an irregular basis, switching the two modes with some probability. And each mode is assumed to be distributed as an exponential. Therefore, our model now has a combination of a normal and two exponentials. We will use the EM algorithm to estimate the parameters of all the distributions in the mixture model. Finally, we are going to move on to classification of the neurons.