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Bayesian nonparametric analysis of neuronal intensity rates

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ABSTRACT

We propose a flexible hierarchical Bayesian nonparametric modeling approach to compare the spiking patterns of neurons recorded under multiple experimental conditions. In particular, we showcase the application of our statistical methodology using neurons recorded from the supplementary eye field region of the brains of two macaque monkeys trained to make delayed eye movements to three different types of targets. The proposed Bayesian methodology can be used to perform either a global analysis, allowing for the construction of posterior comparative intervals over the entire experimental time window, or a pointwise analysis for comparing the spiking patterns locally, in a predetermined portion of the experimental time window. By developing our nonparametric Bayesian model we are able to analyze neuronal data from three or more conditions while avoiding the computational expenses typically associated with more traditional analysis of physiological data.

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1. Introduction

The fundamental statistical question in this work, and in a wide range of similar studies involving distinct experimental conditions, revolves around the calibration of the similarities of multiple firing patterns along with the identification of sharp differences between them. This idea is motivated from the observation that the presence or the absence of firing activity is considered as the main marker of the degree of involvement of the neuron in the studied behavior. Our interest is in developing a method whereby the overall pattern of activity across multiple conditions can be described which will allow us to better define exactly what role these neurons play in variable sensorimotor contexts. Consequently, it would be useful to devise a suitable statistical methodology to address such comparative inquiries, mainly on two fronts: first, a global analysis over the entire experimental time window, enabling neurophysiologists to decide whether the neuron should be considered for further study; second, a pointwise analysis, to pinpoint differential patterns at specific time points in the experimental time interval. The method proposed in this work is well suited to address these scientific goals.

The need for a comparative study of spiking patterns in multiple conditions may be justified by investigating the neuronal activities presented in Fig. 1, where a peri-stimulus time histogram (PSTH) for a single neuron recorded from an awake, behaving monkey is plotted under three experimental conditions described below. A 4000 ms window is considered. The time is aligned on a saccadic eye movement. Condition 1 ("Space" condition on the top panel) reflects a trimodal firing pattern: a peak in firing activity in about 1000 ms prior to the saccade, followed by a significantly less-pronounced peak at the saccade time, yielding to yet another strong peak at about 1500 ms after the saccade time. The response in condition 2 ("Dot" condition on the middle panel) is inherently different: a series of comparably weaker bursts of activity, more like a random noise, nonetheless with a seemingly noticeable decline in firing activity at the saccade time. Finally, in condition 3 ("Ring" condition on the lower panel) a multimodal pattern is suggested with the most noticeable peak at the saccade time. We now can restate the main objectives of this work in the context of the data presented in this figure: 1 – Are the differences and similarities in the spiking patterns of the three conditions in Fig. 1 statistically significant or should they be interpreted as perturbations due to chance and hence be ignored? 2 – When studied in predetermined slices of the entire time segment, could such differences shed light on the sensorimotor properties? These are among the questions that motivate the statistical strategies we adopt in order to compare the firing patterns of each neuron in multiple conditions. Here, we address the above two questions by developing a Bayesian

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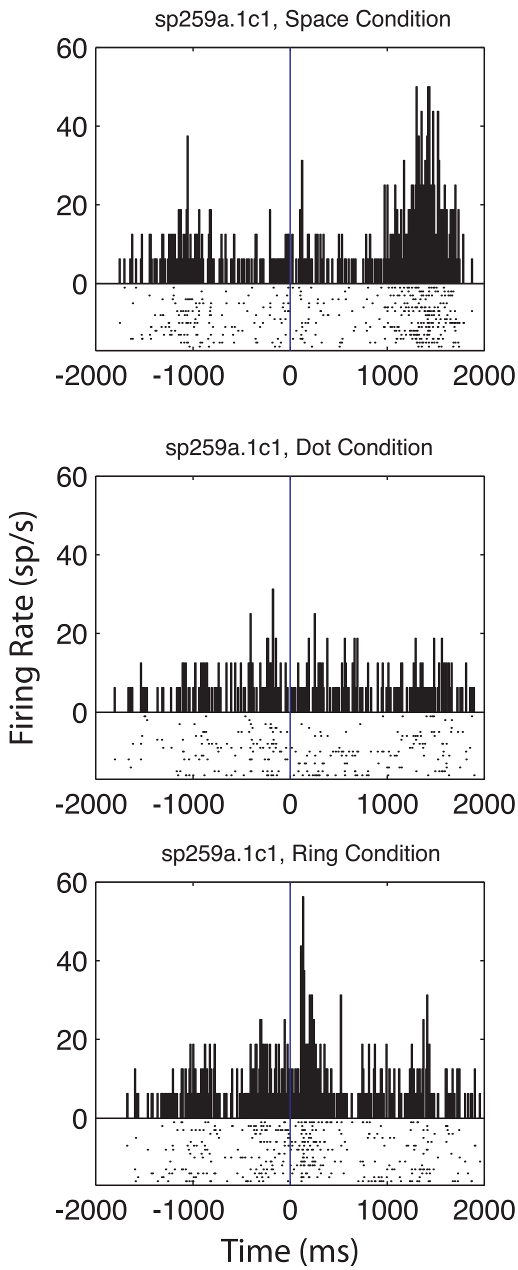

Fig. 1. Neuron sp259a.1. PSTH is shown for three experimental conditions (conditions 1, 2, and 3). A 4000 ms window is considered. The time is aligned on the spatial cue onset. Conditions 1 (Space, top panel), 2 (Dot, middle panel), and 3 (Ring, lower panel) demonstrate different responses.

nonparametric model that allows us to compare neuronal intensity rates under a number of distinct experimental conditions within a coherent probabilistic framework for inference.

The outline of the paper is as follows. Section 2 develops the methodology with technical details on implementation included in an Appendix A. In Section 3, we provide more details for the experiment used to illustrate the proposed methodology, and in Section 4, we present the results from the analysis of the corresponding data. Finally, Section 5 concludes with an overview and discussion.

2. Models

In Section 2.1, we discuss the stochastic model underlying our approach and provide a brief review of the class of models from the field of Bayesian nonparametrics that provides the foundation for the proposed methodology. Section 2.2 develops the modeling approach for comparison of neuronal spiking patterns under multiple experimental conditions.

2.1. Motivation and background

2.1.1. Poisson process modeling for neuronal firing intensities

Stochastic modeling and statistical estimation techniques for the analysis of data from single-recording neurophysiological experiments have received considerable attention in the neuroscience, as well as the statistics literature (see, e.g., Brillinger, 1992; Ventura et al., 2002; Kass et al., 2005). Predominantly, the focus of statistical modeling approaches is on the temporal evolution of the neuronal firing activity. Historically, the stochastic modeling of spike trains may be traced back to the original forms of the so-called Integrate and Fire (IF) models (Gerstein and Mandelbrot, 1964; Stein, 1965). In these stochastic models, the output is taken as a one-dimensional voltage while the inputs consist of current and membrane conductance. The error is typically captured by a Brownian motion, representing the stochastic feature of the model. As noted in Paninski et al. (2010), from the statistical point of view, the IF model may also be studied via hidden Markov (or state space) models in which the unobserved (hidden) voltage is modeled through a Markovian process evaluated at the observed spiking times (Brown et al., 1998; Volgestein et al., 2009).

An alternative approach, leading eventually to the methodology proposed in this paper, is to view the spike train as a realization of a point process, a random sequence of times associated with spike occurrences, and subsequently model the spike counts with a time-varying intensity function formulated through a Non-Homogeneous Poisson Process (NHPP) as described below. Reviews of the analysis of neuronal data using point processes, from either a single neuron or from multiple neurons, can be found in, e.g., Brillinger (1992), Brown et al. (2004), and Kass et al. (2005).

Let $N_{(t_a,t_b)}$ denote the number of spike occurrences in the time interval (t_a, t_b). By definition, a NHPP point process model is constructed over two conditions:

(a) For any interval (t_a, t_b), $N_{(t_a,t_b)}$ follows a Poisson distribution with mean $\int_{t_a}^{t_b} \lambda(u)du$. Here, $\lambda(\cdot)$ is the NHPP intensity function, a non-negative and locally integrable function (i.e., $\int_D \lambda(u)du < \infty$ for any bounded subset D of the positive real line).
(b) For any non-overlapping intervals, (t_a, t_b), and (t_c, t_d), the random variables $N_{(t_a,t_b)}$, and $N_{(t_c,t_d)}$ are independent.

Subsequently, if a generic set of n spike times, $\{s_1, \ldots, s_n\}$, observed in time window (A, B), is assumed to arise from a NHPP, the corresponding likelihood for the intensity function is given by $e^{-\int_A^B \lambda(u)du} \prod_{i=1}^{n} \lambda(s_i)$.

Statistically, the problem of modeling the spike trains will then revolve around estimating the NHPP intensity function $\lambda(\cdot)$ from which inference on several features of the neuronal spiking pattern can be obtained. In this paper, we adopt a Bayesian nonparametric point of view for such an estimation problem developing a practically important methodological extension of the approach proposed in Kottas and Behseta (2010). This approach and the relevant class of nonparametric Bayesian prior models are reviewed in the following section.

2.1.2. Background on Bayesian nonparametric mixture models

A nonparametric modeling approach for the NHPP intensity treats the entire function $\lambda(\cdot)$ as the unknown parameter, which under the Bayesian paradigm, necessitates placing a prior over a space of functions (i.e., over an infinite dimensional parameter). The field of Bayesian nonparametrics deals with the problem of

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