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Discrete stimulus estimation from neural responses in the turtle retina

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Abstract

In this paper, we investigate the decoding of flashed, full-field visual stimuli while recording from a population of retinal ganglion cells. We present a direct statistical method for determining the likelihood that a response was evoked by a particular stimulus, and use this method to estimate stimuli based on microelectrode array recordings in the turtle retina. This method uses the well-known time-varying Poisson model of neural firing, along with extensions to accommodate neural refractory periods. Unlike other approaches commonly used for Poisson processes, the specific formulation presented here is bin free and requires few user-specified parameters. Statistical dependency issues and the effects of stationarity on the estimation method are also discussed.

Keywords: Stochastic; Retina; Model; Stimulus; Discrimination; Turtle (*Pseudemys scripta elegans*)

1. Introduction

The entire visual experience of vertebrates is conveyed in the spatiotemporal patterns of action potentials that are output from their retinal ganglion cells. Early research into retinal encoding determined that ganglion cells can be placed into broad response classes (Granda & Fulbrook, 1989; Hartline, 1938) and that they had relatively localized, structured receptive fields (Kuffler, 1953). However, the responses of individual ganglion cells can exhibit significant variability to identical sets of visual stimuli and similar responses for very different stimuli (Reich, Victor, Knight, Ozaki, & Kaplan, 1997). These responses can also include stochastic variations due to the inherent noise in phototransduction and neural transmission processes, especially at near threshold levels. Because of these variabilities and ambiguities, it is generally recognized that populations of ganglion cells are required to reliably encode the visual scene. Nevertheless, the specifics of how these cells work together and how their firing patterns can best be interpreted are still the subject of much investigation. The exploration of methods for estimating stimuli based on the neural response is one approach to understanding these processes.

Neural responses to discrete stimuli are commonly analyzed with Peri-Stimulus Time Histograms (PSTHs). These plots average out the per-trial variability and provide the prototypical responses for a particular stimulus. Based on observed differences in the responses, one can create a variety of bin counting and vector representations that allow the stimuli to be determined from the neural response (Awiszus, 1997; Becker & Kruger, 1996; Gawne & Richmond, 1993; Geisler & Albrecht, 1997; Oram, Foldiak, Perrett, & Sengpiel, 1998; Salinas & Abbott, 1994). Ideally, however, a method is desired for directly evaluating the likelihood that the spikes from a single trial came from a certain prototypical response without ad hoc vector representations (Sanger, 2002).

Statistical methods for point processes can provide insight and a mathematical framework for studying this class of problems (Brown, Barbieri, Eden, & Frank, 2003; Johnson, 1996; Kass & Ventura, 2001; Perkel, Gerstein,

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& Moore, 1967). They provide a language for describing both the distribution of possible responses to stimuli and the likelihoods of different stimuli given an observed neural firing pattern. In this paper, we present a method for estimating the most likely stimuli among discrete sets on the basis of the neural response, and we apply this method to the responses of turtle retina ganglion cells. For the forward encoding model of the time-varying spike response, this method uses the well-known inhomogeneous Poisson process combined with a refractory renewal period following each spike. This combined model has also been called the Inhomogeneous Markov Interval or IMI process by Kass and Ventura (2001). Unlike most Poisson estimation methods used for neural signal decoding (Rieke, Warland, de Ruyter van Steveninck, & Bialek, 1997), the presented method is essentially bin-free and can include neural refractory periods in the estimation. Using this approach, we show that a discrete set of eight color stimuli can be decoded with an accuracy of 78% with recordings from a population of 18 cells. Performances from simulated cell populations constructed from the data are also presented.

When stochastic estimation methods are applied to a neural system, the statistical dependencies between cells and the stationarity of the responses over time must be determined (Johnson, 1996). Several researchers have proposed the existence of higher-order or synchrony codes that could be used among groups of cells in a variety of cortical and sensory neural systems (Abeles, 1991; Softky, 1995), including the retina (Meister, Lagnado, & Baylor, 1995). In this study, we used the normalized Joint PSTH (Aertsen, Gerstein, Habib, & Palm, 1989) to examine the correlation structure of the responses. This analysis found no significant correlations, and the cells were therefore treated as statistically independent coders of information for the estimation analysis. However, generalizations of the estimation method for correlated spike trains are discussed. In this study, we also examine the impact of the stationarity of the recorded responses on the model building and estimation performance.

2. Methods

2.1. Preparation

Recordings were made from ganglion cells in isolated turtle (*pseudemys scripta elegans*) retinas with isolation performed as described by Perlman, Normann, Chandler, and Lipetz (1990). In these experiments, a 100-electrode extracellular array with 1.5 mm electrodes in a 10×10 grid with 400 μm inter-electrode spacing was used. The retina was placed on a glass slide (photoreceptor side down), held in place by a millipore filter border, and superfused with an oxygenated (95% O_2, 5% CO_2) buffer solution (110 mM NaCl, 2.6 mM KCl, 2.0 mM $CaCl_2$, 2.0 mM $MgCl_2$, 22 mM $NaHCO_3$, and 10 mM D-glucose) delivered at 0.5 ml/min. Light stimuli were provided by a Hitachi Superscan Pro 620 monitor with a vertical refresh rate of 100 Hz and stimulus updates were performed between refreshes. The monitor image was focused by a 55 mm camera lens (f2.8) and prism system to produce a 6×6 mm image on the photoreceptor layer of the retina. Once the retina was in place, the electrode array was lowered into the ganglion cell layer of the retina until single unit activity became apparent. The data acquisition system allowed simultaneous online extraction of the spike timing and waveforms from all 100 electrodes in the array (Guillory & Normann, 1999). Multi-unit recordings were obtained and the single unit waveforms were classified offline using MATLAB implementations of the clustering algorithm described by Shoham, Fellows, and Normann (2003).

While unit activity was recorded, full-field light stimuli were presented in trials consisting of a 200 ms ON period followed by a 300 ms OFF period before the next trial. The light stimuli were randomly selected from an equally probable discrete set of eight stimuli composed of 100:1 contrast, ON–OFF binary combinations of the red, green, and blue channels of the monitor (ON intensities of 1.4, 2.0, and 1.5 mW/m^2, respectively). These intensities and color variations were selected as a simple stimulus set that could be differentiated by the pentachromatic visual system of the turtle. These color combinations appear to the humans as black (no stimulus), red, green, blue, cyan, magenta, yellow, and white. Data were collected from three retinas with a total of 16,000 stimulus presentation trials per retina. For the cells recorded and analyzed in this study, PSTHs were constructed for each stimulus color in the data set. Raster plots of the spikes across all trials and separate PSTH plots for the first and second halves of the data sets were generated and visually compared to provide an empirical index of response stationarity (Awiszus, 1997).

2.2. Estimation method

To perform statistical estimation, a forward model for neural encoding must be selected, and the model employed here begins with the non-homogenous Poisson process. This is the simplest model with the fewest assumptions for capturing a time-varying likelihood of event generation, and it uses a stochastic rate function $\lambda(t)$ as its only parameter. In this method, the rate function for each cell and stimulus was estimated by applying a unit-area Gaussian smoothing kernel (Szucs, 1998) to the PSTHs generated from training data sets. The width (σ) of this Gaussian filter and the number of training trials represent the only two free parameters for the presented method.

For a non-homogeneous Poisson process, the likelihood that a given set of observed events came from specific time-varying rate function can be directly calculated by (Snyder & Miller, 1991)

$$P(X \mid \lambda(t), t_0, t_1) = \left[\exp\left(-\int_{t_0}^{t_1} \lambda(t)\mathrm{d}t\right)\right]\left(\prod_{i=1}^{n} \lambda(x_i)\right), \quad (1)$$

where $P(X|\lambda(t), t_0, t_1)$ is the probability that the set of n events (X) over the time period t_0 to t_1 was generated by the rate function $\lambda(t)$, and $\lambda(x_i)$ is the value of the rate function at the times of the occurrence (x_i) of the n events. For time periods where no events occurred, the $\prod$ term is omitted.

For neural spike events within a trial, the stochastic rate $\lambda(t)$ over the trial is a function of the stimulus, and under the Poisson model, Eq. (1) for a single cell becomes:

$$P(X_c|s) = P(X_c \mid \lambda_c(s,t)) = \left[\exp\left(-\int_0^T \lambda_c(s,t)\mathrm{d}t\right)\right]\left(\prod_{i=1}^{n} \lambda_c(s,x_{c,i})\right), \quad (2)$$

where $P(X_c|s)$ of observing the set of spikes X_c from cell c for stimulus s, $P(X_c|\lambda_c(s,t))$ is the probability that the observed set of spikes (X_c) from cell c over the period of the trial $[0,T]$ was generated by the time-varying response function $\lambda_c(s,t)$ of cell c for stimulus s, and $\lambda_c(s,x_{c,i})$ is the value of the rate function at the times of the n spikes in the trial ($x_{c,i}$) for cell c. The intuitive interpretation of Eq. (2) is that the first term represents the penalty for not getting spikes when they are expected and the second term represents the reward for detecting spikes when likely. Although variations of the Poisson model have been widely used for modeling and estimating spike timing (see Rieke et al., 1997, for a summary), most of these focus on the likelihoods of observing specific spike counts in different bins within a trial. The continuous likelihood function shown in (2) does not require bins to be defined by the user, it only requires a description of the rate function ($\lambda(t)$) within the trial. This continuous form is recently