OPTIMAL ORDER OF HIPPOCAMPAL PLACE CELL MODELS CONSTRUCTED USING EXPANSIONS OF ZERNIKE POLYNOMIALS AND POWER SERIES

Sleim Mohamed I. MARGHAM [1], Murat OKATAN [2,3]

[1]Biomedical Engineering Program, Istanbul Technical University, Türkiye
[2]Institute of Informatics, Istanbul Technical University, Türkiye
[3]Department of Artificial Intelligence and Data Engineering, Istanbul Technical University, Türkiye

ABSTRACT

Hippocampus is a brain region that is important for the encoding and retrieval of episodic memories. The spiking activity of hippocampal place cells depends strongly on spatial location. Their position-dependent firing rate is usually modeled as a parametric function of 2-D or 3-D space. Yet, no study to date has optimized such functions using a rigorous statistical model selection procedure. Here, we model the position-dependent firing rate of hippocampal place cells using two different series expansion models and determine the optimal model type and order. Our results indicate that the optimal order is much higher than those used in earlier studies. We have observed that the models of some cells are reminiscent of the firing patterns of grid cells. These findings are important for elucidating the origins of place cell activity, for accurate assessments of the amount of position information encoded in this activity, and for the inference of position using neural decoding algorithms.

Index Terms— Point Process Likelihood Models, Spike Train Decoding, Computational Neuroscience, Generalized Linear Models, Grid Cells

1. INTRODUCTION

Hippocampal place cells were discovered by O'Keefe and Dostrovsky while they were recording single units (neurons) from the CA1 region of a rat's hippocampus [1]. These single units seemed to increase their firing rate when the rat was in a particular location of the experimental environment and its head was pointing toward a particular direction. Subsequent studies strongly supported these earlier observations and revealed that some hippocampal neurons fired predominantly when the subject was located in a particular subregion of the environment [2], [3]. Such neurons were called 'place cells' and the subregion of the environment where they fired was called their 'place field' or 'firing field' [2].

Early studies characterized the position-dependent firing of the place cells using 2-D 'firing rate maps' [3]. These firing rate models were obtained as the ratio of 2-D histograms, where a spike histogram was divided by a time-in-location histogram. The number of pixels in the map represented the number of model parameters. Subsequent studies showed that it was possible to infer the position of the subject just by comparing the ensemble firing rate vector of a group of place cells to the average firing rate vectors derived from the cells' firing rate maps [4]. Later studies pointed out that this "spike train decoding" could be performed recursively using Bayesian statistical methods [5], [6]. In these methods, the position-dependent firing rate model was formulated as a parametric function of the position coordinates using much fewer parameters than the firing rate maps [5]–[7]. While these studies demonstrated the success of the Bayesian spike train decoding paradigm, the optimality of the firing rate models remained unaddressed. The fact that those models used as few as five to 10 parameters, compared to the tens to hundreds of pixels used in firing rate maps, suggests that they may have been content with substantially fewer parameters than what would be optimally required. It is therefore the goal of the present study to determine the optimal order of those parametric firing rate models within a likelihood-based neural modeling framework.

2. METHODS

This section starts by explaining the data used in the present analysis. Then, the conditional intensity function models of place cell spike trains are presented. The log-likelihood function of the model parameters and its maximization using the Generalized Linear Models are explained. The section ends with the presentation of model selection using Akaike's Information Criterion (AIC_c).

2.1. Data

Studies that explore the position-dependent spiking of hippocampal place cells record the place cell spike trains and the position coordinates of the subject's head simultaneously, while the subject exhibits spatial behavior. The spike trains are recorded using microelectrode arrays that are chronically implanted into the brain. The microwires of the

microelectrodes are attached to a connector (head stage) that interfaces them with the recording system. The position of the subject's head is measured using a video camera [3].

The data used here were downloaded from Cajigas [8]. These data were collected from a Long-Evans rat that was freely foraging for randomly delivered food pellets in an open circular environment of 70 cm diameter with 30 cm high walls and a fixed visual cue [5], [9], [10]. The rat was well familiarized with the environment prior to data collection, which implies that place fields were formed and stabilized to a large extent. Simultaneous activity of 37 place cells was recorded for 23 min using a microelectrode array that was implanted into the CA1 region of the hippocampus. The sampling rate was 31.25 kHz per electrode. The position of the rat's head was measured at 30 Hz by a camera tracking the location of two infrared diodes mounted on the head stage.

2.2. Conditional intensity function models

For a spike train that is recorded between times $t = 0$ and $t = T$, let τ_i, $1 \le i \le n$, denote the spike times, such that $0 < \tau_1 < \tau_2 < \cdots < \tau_{n-1} < \tau_n \le T$. For $t \in (0, T]$, define $N(t)$ as a right-continuous function that jumps 1 at the spike times and is constant otherwise [11]. It follows that $N(t + \Delta t) - N(t)$ reports the number of spikes observed in the time interval $[t, t + \Delta t)$. By choosing Δt sufficiently small, such that $N(t + \Delta t) - N(t) \le 1$ for all $t \in (0, T]$, the conditional intensity function (CIF) of the spike train is defined as in Eq. 1 [12]:

$$\lambda(t|H_t) = \lim_{\Delta t \to 0} \frac{Pr(N(t + \Delta t) - N(t) = 1|H_t)}{\Delta t}. \quad (1)$$

Here, $H_t = \{0 < \tau_1 < \tau_2 < \cdots < \tau_k < t\}$ is the history of the spike train up to time t. The specification of $\lambda(t|H_t)$ completely characterizes the stochastic structure of the point process [12]. It is assumed that the probability of observing a spike in an interval can be arbitrarily small but non-zero. Since $\lambda(t|H_t)$ is a probability divided by a time interval, $\lambda(t|H_t) > 0$ at all times.

2.2.1. Bivariate Gaussian and Zernike Polynomials

To model the position-dependent firing of the hippocampal place cells, parametric models have been proposed for the CIF as a function of the position coordinates $x(t) = [x_1(t), x_2(t)]'$ of the rat's head, without considering the activity history [5], [6]. One of these models is the bivariate Gaussian function [5]:

$$\lambda_G(t|x(t), \xi) = exp\left(\alpha - \frac{1}{2}(\tilde{x}_1(t) - \mu_1)'W^{-1}(\tilde{x}_2(t) - \mu_2)\right), \quad (2)$$

where, $W = \begin{bmatrix} \sigma_1^2 & 0 \\ 0 & \sigma_2^2 \end{bmatrix}$ is a scale matrix, $\mu = [\mu_1, \mu_2]'$ is the place field center, α determines the firing rate at the place field center, $\xi = [\alpha, \mu, W]$ is the parameter vector, $\tilde{x}_1(t) = (x_1(t) - c_1)/R$, $\tilde{x}_2(t) = (x_2(t) - c_2)/R$, R is the radius of the circular environment and $c_1 = c_2 = R$.

Another model is an exponentiated linear combination of Zernike polynomials [6], [7]:

$$\lambda_Z(t|x(t), n_{max}, \beta) = exp\left(\sum_{n=0}^{n_{max}} \sum_{m=-n}^{n} \beta_{n,m} Z_n^m\big(r(t), \phi(t)\big)\right), \quad (3)$$

where, n_{max} is the order of the polynomial, $\beta = \{\beta_{n,m}\}$ is the parameter vector and $Z_n^m\big(r(t), \phi(t)\big)$ is given by [13]

$$Z_n^m\big(r(t), \phi(t)\big) = \begin{cases} R_n^m\big(r(t)\big)cos\big(m\phi(t)\big) & m \ge 0 \\ R_n^m\big(r(t)\big)sin\big(|m|\phi(t)\big) & m < 0, \end{cases} \quad (4)$$

where, $0 \le r(t) \le 1$, $0 \le \phi(t) \le 2\pi$ and, for $(n - m)$ even,

$$R_n^m\big(r(t)\big) = \sum_{l=0}^{(n-|m|)/2} \frac{(-1)^l (n - l)!}{l!\left(\frac{n+m}{2} - l\right)!\left(\frac{n-m}{2} - l\right)!} r^{n-2l}, \quad (5)$$

whereas for $(n - m)$ odd $R_n^m\big(r(t)\big)$ is zero, with m=0, ±1, ..., ±n, $r(t) = \sqrt{\tilde{x}_1^2(t) + \tilde{x}_2^2(t)}$ and $\phi(t) = tan^{-1}\big(\tilde{x}_2(t)/\tilde{x}_1(t)\big)$.

In previous studies the Zernike polynomials model was used with n_{max}=3 to keep the model complexity low [6], [7], [9], therefore this value was not optimized using a model selection criterion in those studies.

In these models, exponentiation serves a dual purpose: first, it ensures that the CIF is always strictly positive regardless of the values of the position coordinates or the model parameters, second, exponentiation makes the CIF a Generalized Linear Model (GLM) with Poisson distribution and logarithmic link function [14], [15]. Since GLM is available in many statistical data analysis software packages, the estimation of the parameters of these models can be readily performed using those packages.

2.2.2 Power Series Expansion

The bivariate Gaussian is a particular case of the bivariate power series expansion. Just as it is done using the Zernike polynomials, the CIF can be formulated as an exponentiated linear combination of the terms of the bivariate power series:

$$\lambda_P(t|x(t),P_1,P_2,\beta) = exp\left(\sum_{p_1=0}^{P_1}\sum_{p_2=0}^{P_2}\beta_{p_1,p_2}\tilde{x}_1^{p_1}(t)\tilde{x}_2^{p_2}(t)\right), \quad (6)$$

where, P_1 and P_2 determine the model order and $\beta = \{\beta_{p_1,p_2}\}$ is the parameter vector. $\tilde{x}_i(t)$ are obtained from $x_i(t), i = 1,2$, as in Section 2.2.1. Previous studies used $P_1 = P_2 = 2$ [16], but this value was not optimized using a model selection criterion.

2.3 The log-likelihood function and AICc

Given a CIF $\lambda(t|x(t),\beta)$, the log-likelihood function of β under a given set of spike times is [17]:

$$l(\beta|x,N) = \sum_{i=1}^{N(T)} log\big(\lambda(\tau_i|x(\tau_i),\beta)\big) - \int_0^T \lambda(u|x(u),\beta)du, \quad (7)$$

where, x and N denote $x(t)$ and $N(t)$ for $t \in (0,T]$.

Because the position variable is sampled at 30 Hz, $x(t)$ is constant between position sampling times. Let Δ_x denote the position sampling period and let $u_s = s\Delta_x$ denote the position sampling times for $s = 0,1,\dots,S$, such that $S\Delta_x < T \leq (S+1)\Delta_x$. Then the log-likelihood function becomes

$$l(\beta|x,N) = \sum_{s=0}^{S} c_s log\big(\lambda(u_s|x(u_s),\beta)\big) - \Lambda_s, \quad (8)$$

where, c_s is the number of spikes observed in the interval $[u_s,u_{s+1})$ for $0 \leq s < S$, c_S is the number of spikes observed in the interval $[u_S,T)$, $\Lambda_s = \lambda(u_s|x(u_s),\beta)\Delta_x$ for $0 \leq s < S$ and $\Lambda_S = \lambda(u_S|x(u_S),\beta)(T-u_S)$.

This is the log-likelihood function of a GLM with Poisson distribution and logarithmic link function, to within a model-independent constant term [14], [15]. The maximum likelihood estimate (MLE) $\hat{\beta}$ of β is computed by maximizing $l(\beta|x,N)$ with respect to β. We perform this computation using the fitglm function of MATLAB (R2021b) (MathWorks, Inc., Natick, MA, USA), where the dependent variable is the vector c_s, the independent variables are the expansion terms in Eq. 3 or Eq. 6 evaluated at $t = u_s$, for $0 \leq s \leq S$, and the offset vector is $[o_1,\dots,o_{S-1},o_S]$, where $o_s = -log(\Delta_x)$ for $0 \leq s < S$, and $o_S = -log(T-u_S)$.

Once $\hat{\beta}$ is obtained, the AICc of the model is [18]:

$$AIC_c = -2l\big(\hat{\beta}|x,N\big) + 2K + \frac{2K(K+1)}{N(T)-K-1}, \quad (9)$$

where, K is the number of estimated parameters in the model. For the Zernike polynomials model, $K = (n_{max}+1)(n_{max}+2)/2$, for the power series model, $K = (P_1+1)(P_2+1)$.

For each place cell, $\lambda_Z(t|x(t),n_{max},\beta)$ is fit to the spike train for $n_{max} = 0,1,\dots,n_{opt}+q$ such that AIC_c is minimized at n_{opt} and AIC_c at $n_{opt}+q$ exceeds the AIC_c at n_{opt} by at least 10. An AIC_c difference (ΔAIC_c) of 10 or more is considered to indicate that the model with the larger AIC_c is clearly worse than the model with the minimum AIC_c [18]–[20]. Zernike polynomials were constructed using the Zernike polynomial MATLAB functions of Fricker [21].

Similarly, for each place cell, $\lambda_P(t|x(t),P_1,P_2,\beta)$ is fit to the spike train for $P_1 = 0,1,\dots,P_{1,opt}+q_1$ and $P_2 = 0,1,\dots,P_{2,opt}+q_2$ such that AIC_c is minimized at $(P_{1,opt},P_{2,opt})$ and ΔAIC_c at any of $(P_{1,opt},P_{2,opt}+q_2)$, $(P_{1,opt}+q_1,P_{2,opt})$ or $(P_{1,opt}+q_1,P_{2,opt}+q_2)$ is at least 10. For the 37 cells analyzed, the model type and order of the AIC_c-best model is determined.

3. RESULTS

Two models are considered equivalent in relative goodness-of-fit if their $\Delta AIC_c \leq 4$ [18]–[20]. The optimal power series and Zernike polynomials models had $\Delta AIC_c \leq 4$ for six cells, the optimal power series model was clearly better for 17 cells ($\Delta AIC_c > 10$) and the Zernike polynomials model was clearly better for 9 cells. In the remaining five cells, the power series model was the better model for two cells. Figure 1 illustrates the firing rate functions of two cells, where the better model is either the power series model (top panels) or the Zernike polynomial expansion model (bottom panels).

The optimal order for the Zernike polynomials model was three for only one cell and ranged between three and 25 with a median value of 14, indicating that the optimal order of this

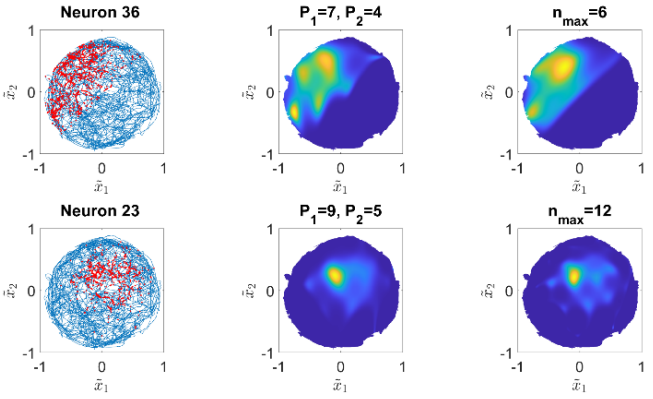

Figure 1. Spike position data and firing rate (Eq. 3 or Eq. 6) plots of the cell 36 (top) and cell 23 (bottom). The blue trace in the leftmost graphs shows the trajectory of the rat's head during the experiment. Red dots indicate the locations at spike times. The best fitting model was the power series expansion model for cell 36 ($\Delta AIC_c = 90.7$), whereas it was the Zernike polynomial expansion model for cell 23 ($\Delta AIC_c = 88.4$). The firing rate is plotted at positions within the area enclosed by the rat's trajectory.

model is much higher than three for almost all place cells. The minimum, median and maximum ΔAIC_c of the model of order three was 0, 228 and 1387, respectively, with $\Delta AIC_c \leq 4$ for only cell 34. The number of parameters used per cell ranged between 10 and 351, with a median value of 120.

The optimal order for the power series model was higher than $P_1 = P_2 = 2$ for 36 cells. The minimum, median and maximum ΔAIC_c of the model of order $P_1 = P_2 = 2$ was 0, 326 and 1387, respectively, with $\Delta AIC_c \leq 4$ for only cell 34. The median values of $P_{1,opt}$ and $P_{2,opt}$ were 9 and 10, respectively. Their minimum values were 2 and 2, while their maximum values were 22 and 23, respectively. The number of parameters used per cell ranged between 9 and 340, with a median value of 135.

4. DISCUSSION AND CONCLUSIONS

Our results show that most hippocampal place cells encode more position information than that represented by Zernike polynomial expansion models of order $n_{max} = 3$ or power series expansion models of order $P_1 = P_2 = 2$. Therefore, future place cell analyses and decoding algorithms may be constructed using higher order models, which may improve the characterization of the position-dependent firing properties of these cells and reduce decoding error.

The power series expansion is computationally simpler to construct than the Zernike polynomials expansion. In decoding algorithms, the derivative of the log-likelihood function needs to be computed, which is relatively easier to compute for the power series compared to the Zernike polynomials. Our results suggest that the power series expansion model was clearly the better model for almost half of the place cells. Because of these reasons, we suggest that both the power series expansion and the Zernike polynomials expansion models may be used to fit place cell spike trains and the one with the smaller AIC_c may be used for decoding.

In a few cells, as in Fig. 1, the optimal model suggested the presence of multiple regularly-spaced local peaks, which resemble the hexagonal firing patterns of entorhinal grid cells [22]. It has been suggested that place cells may be formed as a result of input from grid cells [23]. The prevalence and significance of these patterns and their potential link to the entorhinal grid cells may be explored in future studies.

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