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Multivariate Encoding Analysis of Medial Prefrontal Cortex Cortical Activity during Task Learning

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Abstract— **Studies have shown that medial prefrontal cortex (mPFC) is responsible for outcome evaluation. Some recent studies also suggest that mPFC may play an important role in goal planning and action execution when performing a task. If the information encoded in mPFC can be accurately extracted and identified, it can improve the design of brain-machine interfaces by better reconstructing subjects' motion intention guided by reward information. In this paper, we investigate whether mPFC neural signals simultaneously encode information of goal planning, action execution and outcome evaluation. Linear-nonlinear-Poisson (LNP) model is applied for encoding analysis on mPFC neural spike data when a rat is learning a two-lever-press discrimination task. We use the L^2-norm of tuning parameter in LNP model to indicate the importance of the encoded information and compare the spike train prediction performance of LNP model using all information, the most significant information and reward information only. The preliminary results indicate that mPFC activity can encode simultaneously the information of goal planning, action execution and outcome evaluation and that all the relevant information could be reconstructed from mPFC spike trains on a single trial basis.**

Keywords— brain machine interface, medial prefrontal cortex, neural encoding

I. Introduction

Brain-machine interface (BMI) technology [1] builds the communication pathway between brains and external devices. BMIs generally collect neural activities from motor cortical areas and translate them into motion intentions, which enable people with disabilities to control a neural prosthesis. Existing BMIs were designed to execute pre-defined tasks and have difficulty in adapting to a new task. To enable the neural prosthesis to learn a new task, it is important to study the task learning mechanism in brains and utilize it to improve the BMI design.

A wealth of studies [2]–[4] have suggested that the medial prefrontal cortex (mPFC), especially the anterior cingulate cortex (ACC), is critically involved in reward-guided learning. However, how mPFC functions in the learning process remains in dispute. The most widely accepted point of view is that mPFC is responsible for outcome evaluation. The predicted response outcome (PRO) model [5] and reward value and prediction model (RVPM) [6] addressed the role of mPFC in detecting discrepancies between actual and intended outcome. On the other hand, some recent studies suggest that mPFC may also play an important role in goal planning and action execution when performing a task. Holroyd *et al.* [7] proposed that mPFC gives the goal and plan at the beginning of the task and monitors the movement execution during the task. Shenhav *et al.* [8] proposed that mPFC integrates a variety of signals (including expected reward, costs, effort and so on) to determine whether, where and how much control to allocate during the task.

The accurate extraction of the mPFC encoding information can help the better reconstruction of subjects' motion intention during task learning. Previous study has used the reward information encoded in mPFC to improve the design of BMIs towards autonomous system. Shen *et al.* [9] proposed an internally rewarded reinforcement learning-based BMI decoder which extracted reward information from mPFC spikes and guided the choice of the movement. The proposed decoder in [9] has the advantage of autonomous task learning ability compared with traditional BMI designs. However, the information of goal planning and action execution encoded in mPFC has not been investigated on the single trial basis, which is particularly important for online BMI decoding during task learning.

In this paper, we are interested in investigating whether mPFC neural signals simultaneously encode information for goal planning, action execution and outcome evaluation. We perform multivariate encoding analysis using rat data, while a male Sprague Dawley (SD) rat was trained to learn a two-lever-press discrimination task according to audio cues. Neural signals of 16 channels from mPFC were collected during the task learning. Four kinds of information including start cue, movement preparation, movement execution and reward information are extracted from behavioral data and mapped into an eight-dimensional vector for encoding analysis. The linear-nonlinear-Poisson (LNP) model is applied to map the high dimensional information into spike trains of mPFC neurons. The L^2-norm of tuning parameter in LNP model is used to evaluate the importance of encoded information. In order to verify if mPFC activity encodes multiple information simultaneously. We compare the spike train prediction performance of LNP model that takes in 3 types of inputs including all information, the most significant information and only the reward information to see if mPFC encode multiple information simultaneously. Kalman filter is applied to verify whether the kinematics related to movement preparation,

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movement execution and reward information can be reconstructed from mPFC spike trains on a single trial basis.

The rest of this paper is organized as follows: Section II shows the detailed experiment design, data collection and preprocessing methods, mPFC neural encoding analysis and decoding evaluation. Section III shows the results of encoding comparison and decoding evaluation. Section IV gives the conclusions and future work.

II. Method

A. Behavioral Experiment Design and Data Preprocessing

All animal handling procedures and BMI experiments in this paper were conducted with approval from the Animal Ethics Committee at HKUST. Six male Sprague Dawley (SD) rats were first well trained on a one-lever-press task and then started to learn to perform a two-lever-press discrimination task. Each trial of the task was initialized by an audio cue (lasting 900ms) of either a high pitch (10kHz) or low pitch (1.5kHz), which was randomly generated. The rat needed to press the high lever when hearing the high-pitched cue and press the low lever when hearing the low-pitched cue. If the lever was correctly pressed within 5s after the start cue and held for 500ms, a feedback cue (lasting 90ms) with the same pitch would be presented and the subject would be rewarded with a water drop. Wrong pressing, early releasing and omission all led to an unsuccessful trial and the rat would neither hear the feedback cue nor get water reward. The inter-trial interval was set to be a random value ranging from 3 to 6s.

Two 16-channel microelectrode arrays were chronically implanted in the M1 and mPFC areas to record neural signals. Data acquisition and storage were accomplished by the neural recording system (Plexon Inc, Dallas, Texas). Here, we only use the data sampled from the region of mPFC. The raw signal was sampled at 40 kHz and digitally filtered using a 500 Hz four-pole high-pass Butterworth filter. The spikes were detected from the filtered waveforms with a -4σ threshold, where σ was the standard deviation of the histogram of the amplitudes. The offline sorter (Plexon Inc, Dallas, Texas) was utilized to sort the single neuron from each channel and the spike timing information was restored. Meanwhile, all the behavior events and their timings including the trial start cue presenting, lever pressing, lever releasing, feedback cue presenting were recorded by the behavior recording system (Lafayette Instrument, USA) and synchronized with the aforementioned neural recording system. All the time series were discretized with a resolution of 10ms. Here we use the data collected from one rat. With this 10ms bin size, 91.2% of the intervals with spikes had only a single spike. We selected the day when the success ratio of the rat showed a great improvement during the task learning procedure. On the selected day, there were a considerable number of successful and unsuccessful trials (we only use wrong pressing trials as unsuccessful cases), which are respectively 216 and 116.

To investigate what information mPFC activity encodes, we extract information for goal planning, action execution and outcome evaluation from behavioral events. Applying the similar methods of [10], we map discrete events data to continuous values in [-1,1] to represent the information including position, velocity, start cue and reward information. Fig. 1 shows the mapping results of four kinds of information. For each kind of information, we use a two-dimensional variable to describe how it changes over time. For example, we use P_x and P_y to represent position information, where the rest stage is set as [0,0] and holding low lever and high lever are set as [1, -1] and [1,1]. The different stages are connected smoothly with sigmoid function [10], as shown in Fig. 1(a). The velocity is obtained as the first derivative information of position and normalized within [-1,1], as shown in Fig. 1(b). The start cues of low and high pitch are set as [1, -1] and [1,1]. The reward presenting and no presenting are set as [1,0] and [0,1]. The state labels of start cue and reward information are obtained by Gaussian smoothing. Therefore, we have a total of eight variables served as the input of the encoding algorithm — $P_x, P_y, V_x, V_y, C_x, C_y, R_x, R_y$.

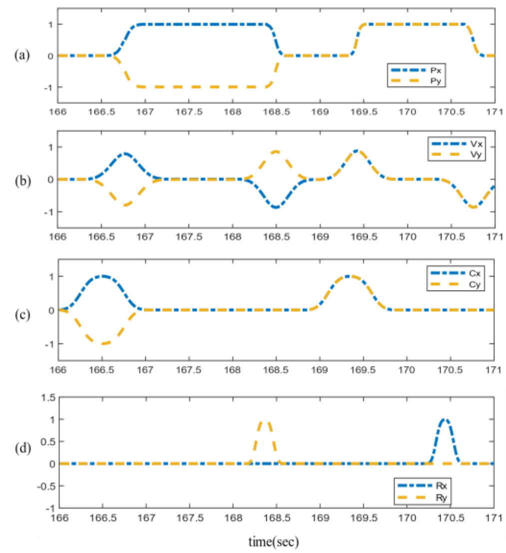

Fig. 1 The state label of (a) position (b) velocity (c) start cue (d) reward

B. Multivariate Encoding Analysis of mPFC spike trains

In this paper, we apply the linear-nonlinear-Poisson (LNP) model to conduct the encoding analysis and compare the spike prediction performance using different information inputs. The linear-nonlinear-Poisson (LNP) model [11] is able to relate the mPFC neural activities to high-dimensional information they may encode. Compared with other encoding models which use linear, exponential or Gaussian tuning function, LNP model builds the tuning characteristic of each single neuron without any prior assumption on the tuning properties [12]. As shown in Fig. 2, LNP model consists of three parts, including a linear filter, a nonlinear function and a Poisson model.

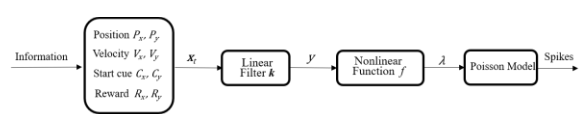

Fig. 2 The block diagram of the Linear-Nonlinear-Poisson model

The input $\boldsymbol{x}_t = [P_x, P_y, V_x, V_y, C_x, C_y, R_x, R_y]_t$ is a multi-dimensional encoding information vector sampled within a time window of [-150,150] ms centered at each time instance t. Firstly, the input vector $\boldsymbol{x}_t$ is optimally projected into a scalar y by a linear filter, where the tuning parameter $\boldsymbol{k}$

(representing a preferred direction in hyperspace) is estimated by spike-triggered regression [10]:

$$\boldsymbol{k} = (E[\boldsymbol{x}_t \boldsymbol{x}_t^T + \eta \boldsymbol{I}])^{-1} E_{\boldsymbol{x}_t|spike}[\boldsymbol{x}_t] \quad (1.)$$

where $E[\boldsymbol{x}_{win}\boldsymbol{x}_{win}^T]$ represents the autocorrelation of input vector and $E_{\boldsymbol{x}_{win}|spike}[\boldsymbol{x}_{win}]$ is the cross-correlation between the input and the binary spike observation. η is a regularization factor for avoiding ill-conditioning in the inverse computation. Then the produced scaler $y = \boldsymbol{k}^T \boldsymbol{x}_t$ is converted by the nonlinear function $f(y)$ estimated from the conditional probability density $p(spk|y)$ which implements the Bayes rule,

$$f(y) = p(spk|y) = \frac{p(spk,y)}{p(y)} \quad (2.)$$

where joint distribution $p(spk, y)$ and the corresponding marginal $p(y)$ are estimated by kernel density estimation using a Gaussian kernel. After estimating the two distributions from the training set and calculating the nonlinear function for every neuron, we can obtain the instantaneous firing rate λ_t of the Poisson model from the output of $f(y)$ and finally establish a mapping from the multi-dimensional information vector to the spike trains of mPFC.

To investigate whether the ensemble of mPFC neurons encode all the information as the input of LNP model, we examine the $\boldsymbol{k}$ of each neuron and calculate their L^2-norm of position $\boldsymbol{k}_p$, velocity $\boldsymbol{k}_v$, cue $\boldsymbol{k}_c$ and reward $\boldsymbol{k}_r$ individually, which represents the correlation with spike trains. For each neuron, we choose the input with the largest l^2-norm as one with the most significant information.

$$i^* = \arg\max_i(\|\boldsymbol{k}_i\|_2),\ i = 1,2,3,4 \quad (3.)$$

Here $\boldsymbol{k}_p, \boldsymbol{k}_v, \boldsymbol{k}_c, \boldsymbol{k}_r$ are indexed by $\boldsymbol{k}_1, \boldsymbol{k}_2, \boldsymbol{k}_3, \boldsymbol{k}_4$ and i^* is the index of the most significant information. After obtaining the most significant information, we compare the encoding performance under inputs with all information, the most significant information only, reward information only to see whether the neuron encode multiple information simultaneously.

C. Reconstruct kinematics and reward information

Here, the Kalman filter decoder [12] is utilized to verify whether the movement preparation, movement execution as well as reward information can be reconstructed from mPFC spike trains on a single trial basis.

In our approach, $\boldsymbol{x}_t = [P_x, P_y, V_x, V_y, C_x, C_y, R_x, R_y]_t^T$ is defined as the state variables described in section II A, and $\boldsymbol{z}_t$ is defined as the neural activity observation, where $\boldsymbol{z}_t$ is a 64×1 vector which contains the firing rates counted in 100ms time window of 16 channels, and each channel consists of current firing and 300ms historical firing. A detailed description of the Kalman filter configuration can be seen in [12]. We divide the original data into training set (75%) and testing set (25%). The training data is used to obtain the parameters of the Kalman filter, including state transition matrix, measurement matrix and noise covariance matrix. Here, the correlation coefficient is calculated to evaluate the decoding performance by comparing reconstruction states with the ground truth.

III. Result

In this section, we first present the selection on the most significant using l^2-norm of tuning parameter. Then we show the spike prediction result of LNP model on one neuron as an example and compare the encoding performance using high dimensional input, the input with most encoded information, as well as the reward information. Finally, we show the decoding results using Kalman filter.

We use mutual information to select the neurons which are most related to collected behavioral events [12]. After sorting the mutual information of all 18 mPFC neurons by descending order, we choose the top 10 neurons for encoding analysis. The L^2-norm of each tuning parameter is shown in Fig 3. Here we present three typical neurons in mPFC. For example, the L^2-norm of $\boldsymbol{k}_p$ (blue bar) and $\boldsymbol{k}_v$ (orange bar) of neuron 15 are larger than the L^2-norm of $\boldsymbol{k}_c$ (green bar) and $\boldsymbol{k}_r$ (gray bar), which indicates this neuron is mainly involved in motor control (action execution). Similarly, we can infer that the major information encoded by neuron 16 and 14 is respectively start cue (goal planning) and reward (outcome evaluation) information. These results provide preliminary evidence that mPFC neuron ensemble can encode all the aforementioned information simultaneously.

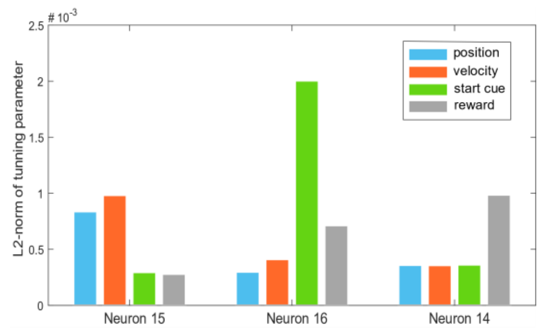

Fig. 3 The L^2-norm of tuning parameter of neuron 15, 16 and 14

The l^2-norm of tuning parameter is then used to determine the most significant information for each neuron. Fig. 4(a) shows a segment of the spike prediction of the neuron 12. The events labelled on the top include start cue presenting (blue), pressing (green) and reward presenting (purple). The gray bar represents the actual spike trains. The red thick line represents the firing rate estimated by smoothing the spike trains using Gaussian kernel. The blue, black and green dashed line represents firing rates predicted by the LNP model with all information, most significant information (position information for neuron 12) and reward information, respectively. We can see that the firing rates predicted by LNP model with all information are the closest to the ground truth. The prediction performance with the most significant information is worse than that with all information and better than that with reward information only. We calculate the correlation coefficient between actual spikes and the predicted firing probability using three different inputs. The correlation coefficient values averaged on 10 neurons are 0.61, 0.52 and 0.35 for LNP model with all information, the most significant information and reward information. We also employ Kolmogorov-Smirnov test (more details about KS-test can be seen in [10]) to evaluate how the prediction agrees with the observed spike

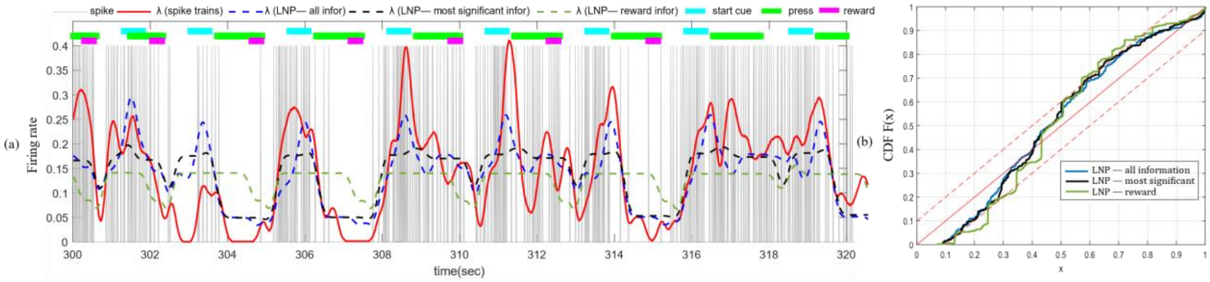

Fig. 4 Encoding analysis of neuron 12 (a) The spike prediction using different inputs (b) KS-test results using different inputs

train. As shown in Fig. 4(b), the KS statistics (neuron 12) of LNP model with all information, the most significant information, reward information are displayed by blue, black and green line respectively, and the 95% confidence interval is plotted by red dash line. We can observe only blue line keeps in the confidence range, which demonstrate that the prediction from LNP model with all information is closer to the real observation than other two predictions. All the above results, including correlation coefficient values and KS-test, demonstrate that mPFC activity may encode information for goal planning, action execution and outcome evaluation simultaneously.

Fig. 5 shows a segment of the decoding results, where we reconstruct position, velocity, cue and reward information simultaneously from mPFC activity. In Fig. 5(a)-(d), the desired signals (red thick line) of P_x, V_x, C_x, R_x are compared with the estimation (blue dash line) using Kalman filter. We can clearly see that all the estimation follows the change of desired signals well almost in every trial. We further perform the decoding on 10 segments of data, each contains 250 data samples. For position, velocity, start cue and reward information, the averaged correlation coefficients between the desired signal and estimation are 0.82, 0.76, 0.61 and 0.53. The decoding results show that the movement preparation, executed kinematics and reward information can be well reconstructed from mPFC neural signals.

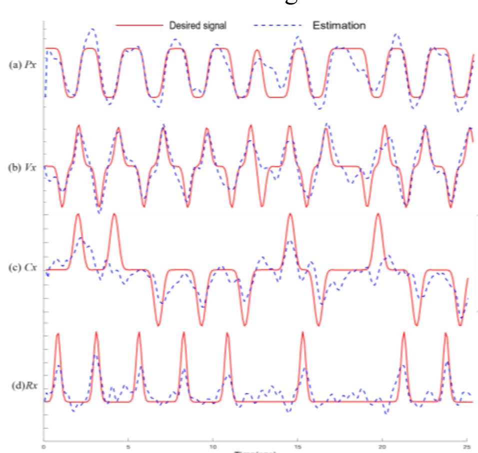

Fig. 5 Decoding results of kinematics and reward information

IV. Conclusion And Discussion

In this paper, we investigate whether mPFC neural spikes simultaneously encode information of goal planning, action execution and outcome evaluation. Four kinds of information including position, velocity, start cue and reward information are served as high dimensional input of the LNP encoding model. The LNP mode that takes in all information can achieve the most satisfactory spike prediction performance. Four kinds of information can be well reconstructed by Kalman decoder at the same time with high correlation coefficients. These results indicate that mPFC activity may simultaneously encodes goal planning, action execution and outcome evaluation and that all the relevant information can be reconstructed from mPFC spike trains on a single trial basis. In the future work, we plan to explore more subjects and utilize the information from mPFC to improve the decoding performance of BMIs.

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