Neuronal Functional Connectivity Dynamics in Cortex: An MSC-based Analysis

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Abstract—The activation of neural ensembles in the cortex is correlated with behavioral states and a change in neuronal functional connectivity patterns is expected. In this paper, we investigate this dynamic nature of functional connectivity in the cortex. Because of the time scale of behavior, a robust method with limited sample size is desirable. In light of this, we utilize mean square contingency (MSC) to measure the pairwise neural dependency to quantify the cortical functional connectivity. Simulation results show that MSC is more robust than cross correlation when the sample size is small. In monkey neural data test, our approach is more effective in detecting the dynamics of functional connectivity associated with the transitions between rest and movement states.

I. INTRODUCTION

It is generally believed that movements are induced by functional networks of cortical neurons working together. Current results in the Brain Machine Interfaces (BMI) literature support this neural ensemble hypothesis [1]. However, how to detect such neural ensembles is an open problem and has attracted significant attention from the community [2], [3].

When neural ensembles are active, their activity becomes statistically dependent (in other words, functionally connected). [4]. The most widely accepted form of dependency in neuronal ensembles is synchrony [5], [6], [2], and there are many methods to detect synchronous population of neurons [7], [8], [9]. However, there are other ways for neurons to show functional connectivity, one example being decorrelation of their activity [10]. Hence, it is more appropriate to use the more general concept of dependency rather than synchrony which becomes just a special case.

Another feature of neural ensembles is that they are not always active [1]. In the cortex, during different phases of behavior, distinct ensembles are reported to be active. Hence, the observed functional connectivity is also transient, which means that the pattern of functional connectivity changes over time.

In this paper, we assume that cortical neurons initiate the animal’s action and recruit other neurons synergistically in the corresponding neural ensemble to complete the movement. This changes the pattern of functional connectivity, and our goal is to detect such dynamic changes. We assume that the neural activity is locally stationary for a range of 1-2 seconds depending on the behavioral task. Therefore, a robust estimation method is desired due to a small window size because of the dynamic nature of functional connectivity (correlated with the time scale of behavior).

In this paper, we utilize mean square contingency (MSC) to measure the pairwise neural dependency to quantify the functional connectivity in the cortex. Simulation results show that MSC performs better in a small sample size regime, compared with the cross-correlation-based method. Furthermore, we apply this algorithm to monkey data recorded during a food reaching task. The results show that the estimated pattern of functional connectivity is effective in detecting the dynamics of neural ensembles in the cortex which is associated with the behavioral states.

II. MEAN SQUARE CONTINGENCY

Mean Square Contingency (MSC) is a Chi-square based measure of dependency, and it was first defined by Pearson for two discrete random variables [11]. For a test of independency, an observation consists of a pair of values and the null hypothesis is that the occurrences of these values are statistically independent.

MSC quantifies the difference between the observed frequencies and the theoretical frequencies under the assumption of independency. Each observed frequency is allocated to one cell of a two-dimensional array (known as contingency table) according to the values. If there are \( r \) rows and \( c \) columns in the table, the theoretical frequency for a cell given the independency assumption is \( E_{i,j} = P_{ij} P_{+j} P_{+i} = \sum_{k=1}^{c} P_{ik} P_{+j} \), and \( P_{+j} = \sum_{k=1}^{c} P_{k,j} \) are the marginal frequencies, and \( P_{i,j} \) is the observed (joint) frequency of the cell in row \( i \) and column \( j \) in contingency table. The MSC value, denoted by \( P \), is given by

\[
P = \left( \frac{\Phi^2}{1 + \Phi^2} \right)^{1/2},
\]

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where
\[
\Phi_2 = \sum_{i=1}^{r} \sum_{j=1}^{c} \frac{(P_{i,j} - E_{i,j})^2}{E_{i,j}} = \sum_{i=1}^{r} \sum_{j=1}^{c} \frac{P_{i,j}^2}{P_{i}+P_{j}+1} - 1 \tag{2}
\]
Note that \(0 \leq P \leq 1\). If the two random variables are independent, \(P = 0\).

In this paper, we treat the number of spike events in a bin of each neuron as a random variable. For each pair of neurons, we construct a contingency table to describe the observed frequency from the bins within a window. Functional connectivity between pairs of neurons is estimated by the dependency (MSC value) between the two spike trains.

III. SIMULATED DATA

To test the capability of MSC in estimating functional connectivity within a small window size, we first simulate a network of 4 leaky integrate-and-fire (LIF) neurons, where two independent input neurons synapse to two neurons that interact unidirectionally with a single synapse. A white Gaussian noise with variance \(10^{-8}\) is injected in each neuron to induce spontaneously spiking. The interacting neurons fire at a reasonable firing rate range (1Hz to 10Hz). For analysis, neuronal spike events are binned in non-overlapping windows of 100ms. The spike trains produced by two interacting neurons are recorded in two states. Two neurons are coupled via a simple synapse (C state) or two neurons are uncoupled (U state). We assume U state represents the null-hypothesis and C state represents the alternative-hypothesis. Dependency based on MSC and the Pearson’s correlation of two neurons are estimated over 100 trials in C and U states, respectively. The performances of two methods are compared as a function of the window size. Figure 1(a) shows the distributions of the test statistic of null and alternative hypotheses for MSC and cross correlation. When 100 samples are used, the area of the rejection region based on cross-correlation is a little larger than that based on dependency. For the distribution of dependency, the bias of null hypothesis is greater. However, when the window size narrows to 20, the distribution of cross-correlation spreads out because of the lack of samples. The distribution of dependency based on MSC is less affected by the decrease of the window size. In other words, MSC outperforms cross correlation when the window size is small.

To quantify the influence of sample size on MSC and cross-correlation, we calculate the statistical power of each method. The significance criterion is 0.05. The power with respect to sample sizes is shown in Figure 1(b). It is noticeable that the statistical power based on dependency is greater than the one based on cross-correlation when the window sizes are small, e.g., 10 and 20 samples. This robustness of MSC is significant and can be used to estimate the dynamical functional connectivity, because of the short time scale of behavior. However, when the number of samples lies between 30 and 40 samples, the two methods have similar performance. When the window size rises to 50, the power of cross-correlation becomes greater than the power of dependency.

IV. MONKEY DATA

The data for these experiments are collected in Dr. Nicolelis’ primate laboratory at Duke University (see [12] for details). For our experiments, neural data are recorded from an owl monkey’s cortex when the animal are performing a food reaching task. Multiple micro-wire arrays are used to record this data from 104 neural cells in the following cortical areas: posterior parietal cortex (PP), left and right primary motor cortex (MI), and dorsal premotor cortex (PMd). In tandem with the neural data recording, the 3-D hand positions are digitized when the monkey are conducting three repeated movements: rest to food, food to mouth, and mouth to rest (see Figure 2).

For dependency analysis, neuronal spike events are binned in non-overlapping windows of 100ms. The hand position data sets are digitally low-pass-filtered and downsampled to 10Hz.

(a) Distribution of the test statistic of null and alternative hypothesis for MSC and cross correlation. The gray areas represent the rejection region with significant criterion 0.05.

(b) Statistical power of the methods for different sample sizes

Fig. 1. Small sample size performance of MSC compared to cross correlation for detecting synaptic coupling between spiking neurons. Two spontaneously active LIF neurons are coupled via a simple synapse.
Our particular data set contains 104 neural channels recorded for 38.33 minutes. This time recording corresponds to a data set of $23000 \times 104$ time bins.

**V. The behavioral state analysis**

We apply MSC on the described monkey data to estimate the functional connectivity of pairwise neurons. The MSC-based dependency vector of all pairwise neurons at each time point is viewed as the pattern of the functional connectivity. The pattern of functional connectivity among 104 neurons is used to analyze behavioral states: rest state (R) and movement state (M). We also perform a single trial moving window analysis.

![Image](image.png)

Fig. 2. Example of reaching movement trajectory. Trajectory is segmented into M (movement) and R (rest). The data set contains 50 such trials.

**A. Block analysis: M state vs R state**

First, we test if the patterns of functional connectivity based on MSC are distinguishable between M and R states. The data are segmented into M and R classes according to the 3-D hand position, as shown in Figure 2. We set the estimation window size to be 2s (20 samples), since the average duration of the movement state is only 2s. We estimate the functional connectivity of pairs of neurons over 50 trials (20 samples for each data set) of M and R states, respectively.

To test if the functional connectivity structure is different in the M and R states, we assume the dependency at each time point is an observation of the distribution according to M or R state. The t-test is conducted on the dependency over the 50 trials for each pair of neurons. We set the risk level as 0.05. For comparison, the results of t-test based on MSC and that of cross correlation are illustrated in Figure 3(a) and Figure 3(b), respectively.

In fact, the dependency is always higher in M state with respect R state (Figures not shown), which is consistent with the active neural ensembles in the cortex. Hence, we call the set of neurons that modulate their functional connectivity from R to M state as ensemble neurons. On the other hand, there are neurons associated with the dark lines that have little influence on the M and R states. In contrast, the results for the cross correlation method in Figure 3(b) demonstrate only a small number of white spots distributed around the diagonal which means that the firing rate of these neurons are modulated with respect to M and R state, as observed in [13]. Most of the significant changes in the functional connectivity that are detected by MSC are not detected by cross correlation. The comparison between the two methods demonstrates that MSC is able to capture the dynamic changes of function connectivity more effectively than the cross correlation method.

**B. Moving window analysis**

Furthermore, we investigate the pattern of functional connectivity changes over time. The strengths of ensemble connections are estimated by a moving window (sliding 2s window by 0.1 steps). The result reveals that in a fine time scale, the efficiency of ensemble connections is enhanced in the transitions between R and M states.

To illustrate this temporal connectivity evolution, the time-varying connectivity patterns of the ensemble connections with neuron 93 are depicted in Figure 4(a). Neuron 93 is chosen as an example of ensemble neurons. Figure 4(a) demonstrates the dynamics of the connectivity associated with the behavioral state. The connection-efficiency increase indicates the transition from R to M states. To demonstrate this association better, we calculate the average dependency over connections. Note that each complete M state corresponds to a peak point on the time series of average dependency. Therefore, we conclude that the dependency based MSC is able to detect the dynamics of the functional connectivity associated with the changing behavioral states. Our results substantiate the assumption that cortical neurons which initiate the animal’s action will recruit other neurons synergistically in the corresponding neural ensemble.

In addition, the pattern in Figure 4(a) provides detailed information of the functional-connectivity dynamics. For example, we observed that the connection between neuron 93 and 94 is only associated with the movement on the y-dimension (blue line) and z-dimension (red line). We interpret these details by function differentiation. The diversity of durations and the delay of the temporal connectivity evolution is also demonstrated in Figure 4(a).

As a baseline comparison, we implement cross correlation on the same data. In Figure 4(b), it is worth noting that no association between the transition from R to M states and the connectivity pattern changes based on cross-correlation is...
Our simulation results demonstrate that MSC are more robust than cross-correlation when the sample size is small. In addition, we test this algorithm on in vivo monkey data for a food reaching task. We observe that MSC can identify the significant difference of the function connectivity in different phases of behavior. Our results suggest that the strength of ensemble connections is usually higher in a movement state, which substantiates the results of Freeman’s Mass Action.

The analysis of functional connectivity dynamics also helps us obtain the corresponding active neuronal ensembles in the cortex. If the dependency between a pair of neurons is always higher in a certain behavioral state than a baseline state, these two neurons may belong to the same active ensemble.

Moreover, MSC is able to detect the evolution of the connectivity associated with the transition of behavior states. Therefore, the pattern of the functional connectivity is capable of predicting the behavior states. In contrast, the result of cross correlation is incapable of detecting such dynamics with a small window size. With a relatively large window, although both methods are able to detect such evolution of the connectivity, the fine time resolution cannot be achieved. Because of its robustness, MSC is more suitable to measure the functional connectivity of real neuron data.

VI. CONCLUSIONS

In this paper, we utilize a dependency measure based on MSC to study the dynamic changes of the functional connectivity in the cortex associated with the behavior states. Because the sample size is limited by the time scale of behavioral state, the robustness of the functional-connectivity estimation with a small sample size is required to detect this dynamic nature.

Fig. 4. The time-varying connectivity patterns of the ensemble connections with neuron 93. In each sub-figure, the first figure shows the 3-D hand position time series. The second one is the dependency pattern of ensemble connections estimated by a moving window (sliding 2s window by 0.1s steps). The third one is the time series of average dependency over the ensemble connections. The bottom one the dependency pattern of ensemble connections estimated by a moving window (sliding 5s window by 0.1s steps)

observed with the 0.2s window. When the window increases to 0.5s, the ensemble connections estimated by MSC and cross-correlation are associated with the transition from R to M states. However, the time resolutions become worse. The comparison demonstrates the robustness of MSC in detecting the functional connectivity with small window size.

REFERENCES