31st Annual International Conference of the IEEE EMBS
Minneapolis, Minnesota, USA, September 2-6, 2009

Estimation and Visualization of Neuronal Functional Connectivity in Motor Tasks

Lin Li, Sohan Seth, Il Park, Justin C. Sanchez, Member, IEEE and Jose C. Principe, Fellow, IEEE,

***Abstract*—In brain-machine interface (BMI) modeling, the firing patterns of hundreds of neurons are used to reconstruct a variety of kinematic variables. The large number of neurons produces an explosion in the number of free parameters, which affects model generalization. This paper proposes a model-free measure of pairwise neural dependence to rank the importance of neurons in neural to motor mapping. Compared to a model-dependent approach such as sensitivity analysis, sixty percent of the neurons with the strongest dependence coincide with the top 10 most sensitive neurons trained through the model. Using this data-driven approach that operates on the input data alone, it is possible to perform neuron selection in a more efficient way that is not subject to assumptions about decoding models. To further understand the functional dependencies that influence neural to motor mapping, we use an open source available graph visualization toolkit called Prefuse to visualize the neural dependency graph and quantify the functional connectivity in motor cortex. This tool when adapted to the analysis of neuronal recordings has the potential to easily display the relationships in data of large dimension.**

I. INTRODUCTION

BRAIN machine interfaces (BMI) interpret and translate neural activity into computer control commands. BMIs can be done with the firing patterns of the primary motor, premotor, or posterior parietal cortices to reconstruct arm and hand kinematic parameters (i.e. position, velocity, and acceleration). Thus far, a majority of developments have been centered around linear and nonlinear models to discover the functional relationship between neural activity and a primate's behavior by presenting recordings of neural activity collected simultaneously with behavior and using a statistical learning criterion [1] [2] [3].

However, hundreds of neural inputs introduce model overfitting; extra degrees of freedom not related to the mapping can result in poor generalization. This explosion in the number of free parameters also puts a computational burden in finding the optimal solution especially when the goal is to implement the BMI in low-power and portable hardware.

For this reason, it is important to rate the importance of neurons in neural to motor mapping. Only the neurons, whose activation is associated with outcomes important to the animal's behavior, will be chosen as the input of the model. There are two major groups of importance assessment methods, model-dependent and model-independent. For model-dependent methods, a linear or nonlinear model is trained with the firing pattern as the input and the recorded animal behavior as the desired signal. The weights of the trained model can be used to quantify the neural importance [4].

In contrast with model-dependent methods, model-independent methods are a more challenging paradigm in the sense that their aim is to measure the importance of neurons without using the animal's behavior, i.e. neural data alone. However, it has great potential in real applications. The hypothesis is that the motor cortex neurons which initiate the animal's action recruit synergistically others to implement certain movements. Therefore functional connectivity *between* pairwise neurons can serve as a significant cue to assess the importance of neurons, which may reveal the modulation of this neuron to the behavior.

Cross-correlation is the standard in neural data analysis but it is incapable of describing nonlinear functional connections [5] [6]. In this paper we use dependence between pairwise neurons to derive a measure of neuron's importance. The dependence not only reflects the neuron's importance for certain movement but also reveals the extent of the functional neural assemblies in motor cortex. Another significant issue is how to display the functional connectivity based on dependence in a visually meaningful way. There are not many good methods to visualize connectivity in high dimensional neural recordings. In this paper, we are investigating a new approach to solve this problem. We implement an open source graph visualization toolkit called Prefuse [7] to create a visualization for neural dependency as a graph to display the complex functional dependencies in motor cortex. Compared with traditional representation of neural sensitivity [8], the graph visualization with high intelligibility and interactivity exhibits advantages to evaluate neuron's relation and diversification as a function of different movements.

II. BEHAVIOR EXPERIMENTS AND NEURONAL RECORDINGS

The data for these experiments was collected in Dr. Nicolelis primate laboratory at Duke University. For our experimental data, neural data was recorded from an owl monkey's cortex as it performed a food reaching task. Multiple micro-wire arrays recorded this data from 104 neural cells in the following cortical areas: posterior parietal cortex (PP), left and right primary motor cortex (M1), and dorsal premotor cortex (PMd). Concurrently with the neural data recording, the 3D hand position was digitized as the monkey made three repeated movements: rest to food, food to mouth, and mouth to rest. The monkey's arm is motionless in space for a brief amount of time while it reaches for food or places food in its mouth [1][9].

For dependence analysis, neuronal spike events were

This work was supported in part by the U.S. National Science Foundation under Grant #CNS-0540304 and #PFI- 0650161.

binned in nonoverlapping windows of 100ms and behavioral datasets,were digitally low-pass filtered and downsampled to 10Hz. Our particular data set contains 104 neural channels recorded for 38.33 minutes. This time recording corresponds to a dataset of 23000x104 time bins.

The data sets were segmented into movement and rest classes. In addition, each reaching movement is segmented in three phases: rest/food, food/mouth, and mouth/rest, as shown in Fig.1

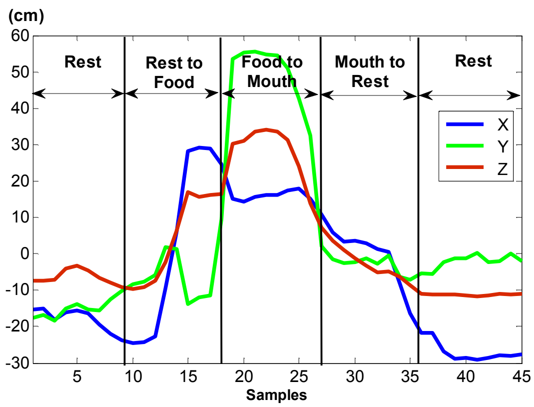

Fig. 1. Reaching movement trajectory One movement segmented into rest/food, food/mouth, and mouth/rest motions

III. MEASUREMENT OF DEPENDENCE OF PAIRWISE NEURONS

A. Mean Square Contingency (MSC)

In this paper, we use Mean Square Contingency (MSC) [10] as a measure of dependence. The concept of mean square contingency was first introduced by Pearson for two discrete random variables. Let X and Y be two random variables that can take values x_i for i = 1, . . .,m and y_j for j = 1, . . . , n respectively. Then MSC (ϕ) is defined as

$$\begin{aligned}\phi^2 &= \sum_{i=1}^{m}\sum_{j=1}^{n}\left(\frac{P(X=x_i,Y=y_i)}{P(X=x_i)P(Y=y_i)}-1\right)^2 P(X=x_i)P(Y=y_i) \\ &= \sum_{i=1}^{m}\sum_{j=1}^{n}\frac{P^2(X=x_i,Y=y_i)}{P(X=x_i)P(Y=y_i)}-1\end{aligned} \quad (1)$$

Where $P(X,Y)$ is the joint probability, $P(X)$ and $P(Y)$ are the marginal probabilities .

B. MSC of Pairwise Neurons with lags

The interaction among neurons associated with certain behavior only happens in a short time window [5]. Therefore, we use a small lag (500ms) as the maximum lag value for each neuron. We treat the binned data of each neuron as a discrete time series and compute the MSC between different lags of these time series. The MSC of pairwise neurons with different lags is defined as

$$\phi^2{}_{rs}(m,l) = \sum_i\sum_j \frac{P^2(X_r(n-m)=x_i, X_s(n-l)=y_j)}{P(X_r(n-m)=x_i)P(Y_s(n-l)=y_j)}-1 \quad (2)$$

where, X_r and X_s represent the binned data of two neurons, while m and l represent the lag for each neuron and n is the current time. The dependence value between two neurons is defined as the maximum of MSCs over all lags as (3),

$$C_{rs} = \max_{m,l}(\Phi_{rs}(m,l)) \quad (3)$$

To simpify the analysis, a threshold for dependence in MSC is empirically set at 0.1. When the MSC value between two neurons is over the threshold, these two neurons are considered to be functionally connected. In this way, a functional graph of neurons based on dependence is created. One neuron is reqresented by a vertice. If two neurons are functionally connected, there is one edge between these two vertices.

If a neuron is important to a given action, it will be involved in a temporal functional neural assembly that causes the action. In this case, more temporal functional dependence will exist between this neuron and others. Therefore, the degree of connectivity, i.e. the number of edges that connect to it, is defined as the neuron's importance.

IV. FUNCTIONAL CONSTRUCTION GRAPH VISUALIZATION

A. Prefuse

Prefuse is a software framework for information visualization in Java. As such, it is designed to simplify the creation of visualizations. A potential visualization builder needs only to compose their product into a pipelined series of prefuse components. Prefuse makes some assumptions about what kind of visualizations can be made. It assumes that the underlying data is a graph. Therefore we believe Prefuse is an ideal candidate for our visualization needs .

B. Design

1) Nodes

A node is defined by 3 keys according to the neuron's properties.

Labels: These represent the index for neurons.

Colors: These represent the neuron's brain area. The neural recordings are collected from four cortical regions (posterior parietal (PP) – Area 1, primary motor (M1) – Area 2, premotor dorsal (PMd) – Area 3, and (M1/PMd-ipsi) – Area 4). These four areas are respectively colored blue, purple, grey and green.

Sizes: These represent the node degree that is the importance of neurons.

2) Layout

Positions graph elements based on a physical simulation of interacting forces; nodes repel each other, edges act as springs, and drag forces (similar to air resistance) are applied. The strengh of drag forces are regulated by the user. This algorithm can be run for multiple iterations for a run-once layout computation or repeatedly run in an animated fashion for a dynamic and interactive layout.

In addition, the layout of the neurons has important priorities. First, the most important neurons distribute in the local center of the graph. Second, if two neurons are closed to each other in the graph, they might not be neighbors but the set of neurons they connect to are highly overlapped, which means they are likely to belong to the same functional neural assembly Therefore, the layout can be interpreted as the functional neural connectivity of the collected data.

3) Interactive Controls

In this graph, there are 104 nodes and 864 edges. We created three interactive controls to help us understand and analyze the abundant information contained in the graph.

Hovering the mouse: When the user places the mouse over some neuron, its neighbors, the neurons highly dependent on it, are highlighted in orange.

Focusing items: When the user clicks a neuron, this neuron is fixed. The fixed neuron is highlighted in red. Then the layout is updated.

Distance filter: It sets all items within a specified graph distance from the selected node visible; all other items will be set to invisible.

V. RESULTS

To test whether dependence of pairwise neurons is a useful measure of neuron's importance for the task, we compared our results with the sensitivity analysis of a recurrent MLP (RMLP) in BMIs [8].

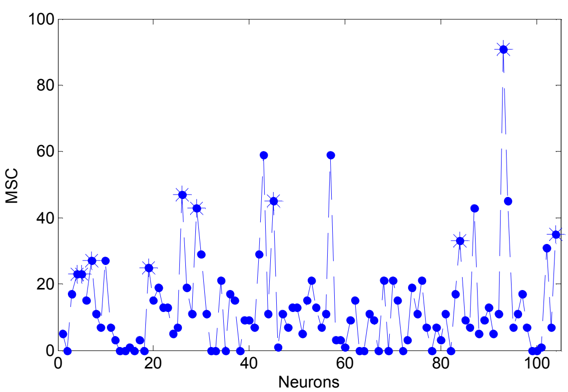

Fig. 2. The dependence score of 104 cells. The points noted with stars are the ten highest sensitive neurons obtained by using RMLP model..

Fig. 2 shows the dependence scores of 104 neurons in the food/mouth segment of the segmented movement of Figure 1. Of the 104 neurons, 6 of the 10 highest-ranking neurons for sensitivity in the RMLP are common in our dependence measure.

With respect to the cortical contribution to the three phases of the movement, the results from two methods are also in agreement. We caculated the mean dependence over neurons in each area for each movement to assess the area of importance to each phase and the results are presented in Table 1.

TABLE I

THE MEAN OF DEPENDENCE FOR EACH CORTICAL REGION WITH RESPECT TO THREE PHASES

Area	Rest to Food	Food to Mouth	Mouth to Rest
PP	9.697	8.546	9.697
M1	10.289	9.571	12.143
PMd	5.519	6.333	7.852
M1/PMd-ipsi	11.609	12.522	13.565

There are two trends observed in the hand trajectory reconstruction when using the RMLP model. PP captured rest/food, but showed a poor fit in food/mouth. For our interdependence measure, PP's high dependence score appears in rest/food and mouth/rest phases, and in food/mouth phase PP has the lowest score. Another trend from RMLP model is M1/PMd-ipsi captures the food/mouth and mouth/rest, but misses the beginning of movement. In our results, the dependence scores of M1/PMd-ipsi in food/mouth and mouth/rest phases are greater than that in rest/food phase.

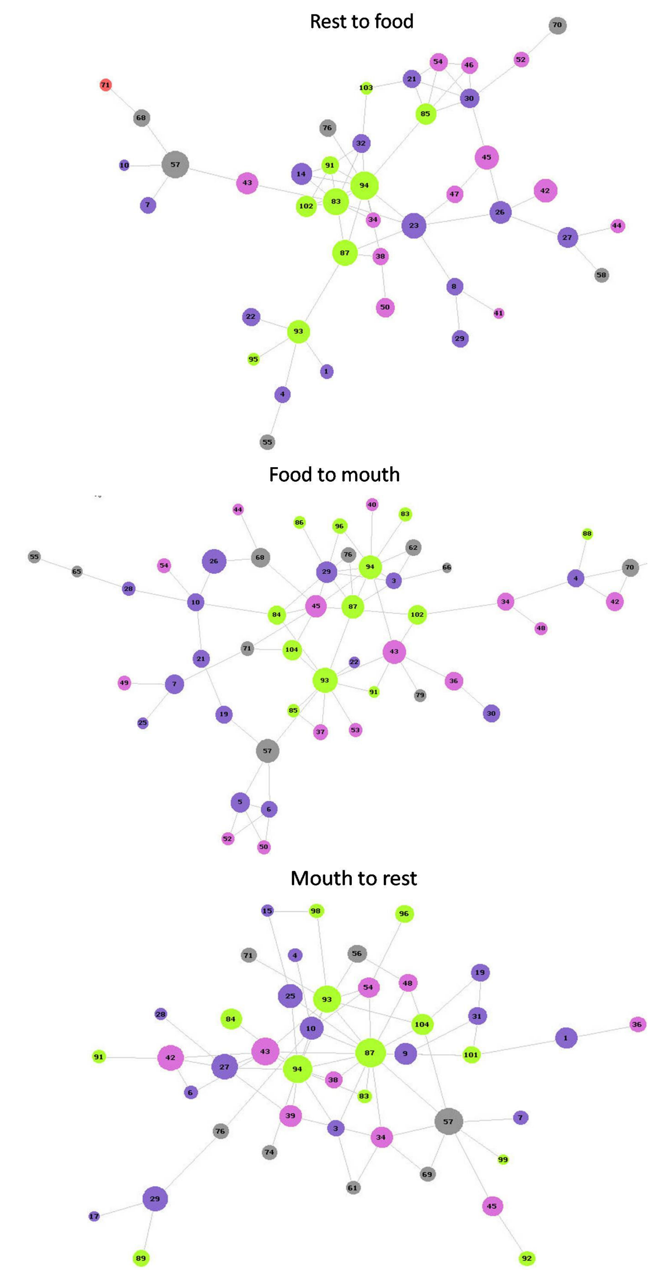

Fig. 3.Interdependency graphs of neurons for three reach movements.

To further understand the difference of the dependence of pairwise neurons, we compare the functional construction graph of the three different movement segments.

From Figure 3, it is interesting to observe that the network of neurons are different among the three phases of movement .

As a whole, there are several local centers of connectivity in the food / rest graph. While in the mouth / rest, the neurons in the graph become more closely related, and lose the local nature. Another aspect taken from the graphs is the inter area connectivity. In contrast with the food/mouth, there is more connectivity present between neurons in PP and neurons in other cortical regions. However, for M1/PMd, more inter area connections happen in mouth/food than in food / rest.

Besides the difference in the global functional construction, the specific changes of the functional connection for each neuron can also be analyzed as shown in Figure 4 for neuron 93. Evident changes happen not only in the number of connections but also the neighbors of each neuron. However, we have not pursused yet a systematic evaluation of these relationships.

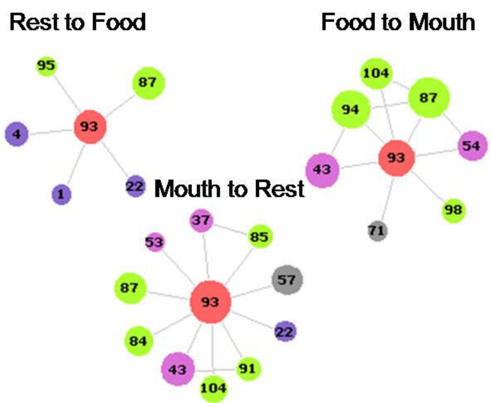

Fig. 4.Functional construction graphs of neurons based on dependence for three reach movements, when cell 93 is fixed and the distance of filter is 1.

VI. Conclusion

This paper implements a measure of pairwise neural dependence based on mean square contingency to measure the importance of neurons in neural to motor mapping. The appeal of this measure is its simple implementation and its properties to quantify dependence. The Prefuse toolkit is used to create visualization for neural dependence on a graph to quantify the functional connectivity of motor cortex. The visualization technology provides abundant information about functional connectivity and also the specific functional connections in each part of the movement. It also helps us find out the factors that contribute to the variation of the importance ranking for three different movements without using the movement data. Our method and hypothesis can only detect neural assemblies when sufficiently many neurons from the same assembly are recorded. Since the number of neurons sampled was relatively small (104), we might have missed a few neural assemblies that are important for the movement.

Comparing our importance ranking with the ranking by sensitivity through a RMLP model, we conclude that the dependence of pairwise neurons finds a great majority of the same neurons, but the ranking is not exactly the same. This can be expected since we do not use the neural data to build the functional connectivity, so having the extra information of the movement may change the ranking. In fact, this comparison can be understood in light of the differences between PCA and optimal filterning.

The functional connectivity graph based on dependence of pairwise neurons reveals a dynamic organization of the motor cortex according to the type of movement. In contrast with the rest/food graph with several local centers, the local nature is lost in the mouth/rest graph. Considering the inter area connectivity, PP increases its inter area connections during rest/food and mouth/rest phases, but it is M1/PMd that shows higher interconnectivity during food/mouth and mouth to rest phases. In addition, not only the number of functional connections but also neighbors directly connected change according to the different phases of the movement.

Acknowledgment

The data utilized in this study was collected by J. Wessberg and M.A. Nicolelis in the primate's laboratory at Duke University.

References

[1] M. A. L. Nicolelis, D.F. Dimitrov, J.M. Carmena, R.E. Crist, G Lehew, J. D. Kralik, and S.P. Wise, "Chronic, multisite, multielectrode recordings in macaque monkeys," *PNAS*, vol. 100, no. 19, pp. 11041 - 11046, 2003.

[2] J. Wessberg, C. R. Stambaugh, J. D. Kralik, P. D. Beck, M. Laubach, J. K. Chapin, J. Kim, S. J. Biggs, M. A. Srinivasan, and M. Nicolelis et al., "Real-time prediction of hand trajectory by ensembles of cortical neurons in primates," *Nature*, vol. 408, pp. 361-365, 2000.

[3] J.C. Sanchez, S. P. Kim, D. Erdogmus, Y. N. Rao, J. C. Principe, J. Wessberg, and M. Nicolelis, "Input-output mapping performance of linear and nonlinear models for estimating hand trajectories from cortical neuronal firing patterns," *International Workshop for Neural Network Signal Processing*, pp. 139-148, 2002.

[4] J. C. Sanchez, J. M. Carmena, M. A. Lebedev, M. A. L. Nicolelis, J. G. Harris, J. C. Principe, "Ascertaining the importance of neurons to develop better brain-machine interfaces," *IEEE Trans. Biomedical Engineering*, vol. 51, no. 6, June. 2004.

[5] E. Samlinas, and T. J. Sejnowski, "Correlated neuronal activity and the flow of neural information, " *Nature Reviews Neuroscience*, vol. 2, pp. 539-550, Aug. 2001

[6] E.Ahissar, E. Vaadia, M. Ahissar, H. Bergman, A.Arieli, and M. Abeles, "Dependence of cortical plasticity on correlated activity of single neurons and on behavioral context," *Science*, vol. 257, pp. 1412-1415, Sep. 1992

[7] J. Heer, S. K. Card, and J. A. Landay, "Prefuse: a toolkit for interactive information visualization," *Conference on Human Factors in Computing Systems*, pp. 421-430, 2005.

[8] J. C. Sanchez, "From cortical neural spike trains to behavior: modeling and analysis," Ph.D. dissertation, Dept. Elect. Eng., Univ. of Florida, May, 2004

[9] S. Darmanjian, S. P. Kim, M. C. Nechyba, J. Principe, J. Wessberg, and M. A. L. Nicolelis, "Bimodel Brain-Machine Interface for Motor Control of Robotic Prosthetic," *IEEE Machine Learning For Signal Processing*, pp. 379-384, 2006.

[10] A. Renyi. On measure of dependence, 1959, ch. 10, PP. 441-451