FUNCTIONAL GROUPING OF NEURONS OF THE PRIMARY MOTOR CORTEX DURING INDIVIDUATED FINGER MOVEMENTS: A CLUSTER ANALYSIS STUDY

A.V. Poliakov* & M.H. Schieber. University of Rochester, Rochester, NY 14642 158.5

1. Abstract

Neurons related to individuated finger movements often exhibit activity modulation for more than one of the movements performed. Hypothesizing that groups of neurons with distinct activity patterns might reflect functional organization of the primary motor cortex (M1), we implemented clustering techniques to group neuronal activity patterns formally. Such analysis could reveal functional groups of neurons related, for example, to individual movements, to particular muscles or muscle groups, or to other hypothetical movement primitives that the CNS may utilize to compose more complex movements from simpler ones.

Activity of single neurons was recorded in the M1 hand area while monkeys performed twelve individuated finger and wrist movements -- flexions or extensions. Cluster analysis of these neuronal populations in three animals revealed that the distribution of neuronal discharge patterns was non-random, and that identifiable clusters were indeed present. We consistently found: i) a large cluster of neurons with broad field increases in firing rate (i.e. activity increased during most of the twelve movements); and ii) a smaller cluster of neurons with broad field decreases in firing rate. Other clusters consisted of groups of neurons with more selective movement fields. These varied from animal to animal, suggesting that functional groups of neurons related to particular muscles, movements, or other movement primitives are not a basic feature of M1 organization. Clusters may form, however, in relation to movements difficult for that particular animal. Neurons within a distinct functional cluster were spread widely across the M1 hand area. Cortico-motoneuronal neurons, which produce post-spike effects in the spike-triggered averages of rectified EMG, were present throughout the neuronal population, but tended to be less frequent in the clusters of broad field firing rate increase, and especially broad field decrease.

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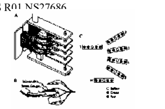
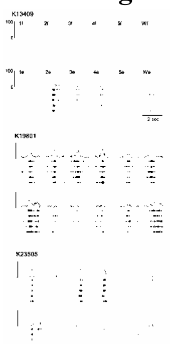


2. Methods

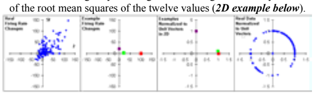
Data for the present study were collected from three rhesus monkeys--K, A and C--trained to perform a visually-cued individuated finger movement task (Schieber, 1991). In brief, the monkey's right hand was placed in a pistol-grip manipulandum that separated each finger into a different slot (***A, above***). At the end of each slot, each fingertip lay between two microswitches (***B***). By flexing or extending a digit a few millimeters, the monkey closed the ventral or dorsal switch, respectively. The monkey viewed a display of light-emitting diodes (***C***) that cued him to flex or extend one finger, closing only one switch at time, for a reward. Each instructed movement is denoted by the number of the instructed digit (1 = thumb to 5 = little finger; w=wrist) and the first letter of the instructed direction (f = flexion, e = extension). As the monkey performed the finger movement task, spike trains of single neurons were recorded with microelectrodes inserted into the primary motor cortex via a surgically implanted recording chamber.

3. Problem: Diverse Discharge Patterns



A striking feature of neurons in the population from each monkey was the wide variety of discharge patterns observed across the different individuated finger and wrist movements. The figure ***at left*** shows raster and histogram displays of the discharge of three typical neurons--K13409, K19801 and K23505--recorded from monkey K during each of the 12 instructed movements.

We characterized each task-related neuron's firing rate modulation during each instructed movement as the change in firing for each movement, calculated by subtracting the average firing rate during a 200 msec baseline period (1000 to 800 msec prior to switch closure) from the average firing rate during the 100 msec immediately prior to switch closure. Each neuron's discharge across the instructed movements then could be characterized by a 12-dimensional vector consisting of the neuron's firing rate change during each of the twelve movements. For monkey A, discharge measures for the six movements not performed were set to zero. To search for neurons with similar relative patterns of discharge across the movements, rather than similar absolute discharge, we normalized each neuron's vector to unit length by dividing each discharge measure by the sum of the root mean squares of the twelve values (***2D example below***).



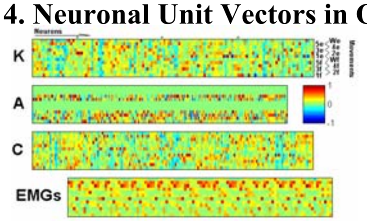
5. Clustering

To apply cluster analysis to our neuronal populations, a measure of similarity between any two neurons had to be established. Since a 12-dimensional vector was assigned to every neuron, we defined the similarity of two neurons, S_{ij}, as the Euclidean distance in 12-dimensional space between the endpoints of their unit vectors $\mathbf{v}_i$ and $\mathbf{v}_j$.

$$S_{ij} = \sqrt{(\mathbf{v}_i - \mathbf{v}_j)^T(\mathbf{v}_i - \mathbf{v}_j)} = \sqrt{\sum_{k=1}^{12}(v_{ik} - v_{jk})^2}$$

Thus defined, similarity ranged from 0 to 2. The utility of normalization to unit vectors now can be appreciated by considering 3 hypothetical neurons: neuron A that discharged 100 spikes/sec during movement 2e only; neuron B that discharged 10 spikes/sec during movement 2e only; and neuron C that discharged 10 spikes/sec during movement 5f only. Without normalization, neuron B would be more similar (closer) to neuron C than to neuron A, because both have relatively low discharge. After normalization, however, neurons A and B are similar (close) because they both discharge only for movement 1f. Agglomerative, hierarchical techniques were implemented for clustering. To apply these techniques to *N* neurons, we started with *N* clusters, each containing a single neuron. An *N* x *N* symmetric matrix of similarities, ***S***, then was calculated, and the pair of clusters closest to each other was identified. These were merged to form a new cluster. As each step merged two clusters, C_i and C_j ($i>j$), the neurons of cluster C_j were taken out of their original order location in the neuronal population and placed next to the neurons of cluster C_i. Then the similarity matrix was updated, and the next step of clustering was performed, etc., until all neurons were merged into one cluster.

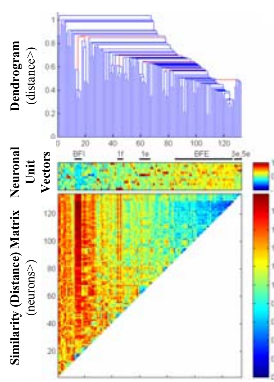
4. Neuronal Unit Vectors in Original Order



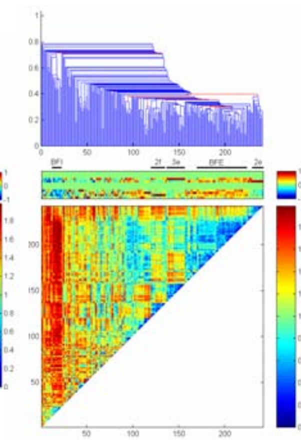
The figure ***at left*** illustrates the diversity of discharge patterns across the different instructed movements observed for all task-related M1 neurons in monkeys K, A and C (*N* = 133, 241, 177, respectively). The diversity of these discharge patterns precluded our using inspection to classify the neurons into categories such as "thumb-related" or "flexion-related" neurons. (EMGs are shown as a comparison control.)

Above, each neuron is represented by a column; the columns are arranged according to the order in which the neurons were recorded, from left to right. Each of the twelve instructed movements is represented by a row. The columns and rows define cells in which the normalized firing rate change of that neuron (column) during that instructed movement (row) is displayed using a color scale from +1 (dark red) to -1 (dark blue). The twelve cells in the column for each neuron thus summarize the neuron's discharge pattern across the twelve instructed movements by displaying the values of the 12-dimensional unit vector representing that neuron's normalized increase (yellow to red) or decrease (light to dark blue) in discharge during each movement, from 1f (bottom) to We (top).

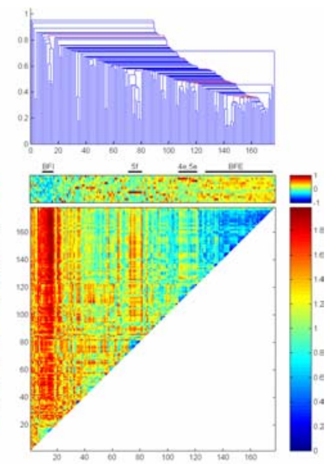
Monkey K



Monkey A



Monkey C

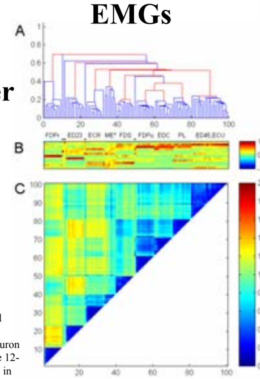


Comparison Controls

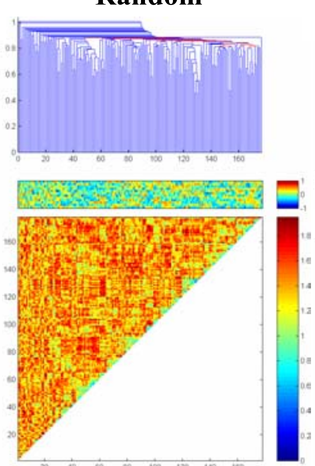
For comparison with the cluster analyses of the real neuronal populations, we show clustering of 3 control populations:

1) **EMGs** recorded from 9 muscles in 10 sessions along with the raw microelectrode recording (ME) in each session.
2) An imaginary population in which 12 **Random** numbers evenly distributed from -1 to +1 were used to generate the vector for each of neuron.
3) An imaginary population in which the actual firing rate changes from monkey C's neurons (distribution shown in inset D) were randomly **Reshuffled**, destroying the linkage between particular values in a given neuron.

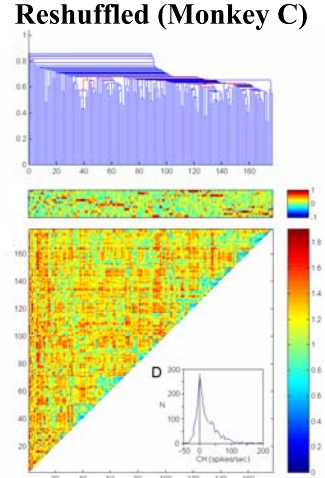
EMGs



Random



Reshuffled (Monkey C)



6. Clustering Results

<u>Two broad field groups were found in each of the three monkeys:</u>

1) A large group of neurons whose discharge *increased* for many or all movements (Broad Field Excitation, **BFE**)
2) A small group of neurons whose tonic discharge ***decreased*** for many or all movements (Broad Field Inhibition, **BFI**)

BFE and BFI groups were identified consistently in all 3 monkeys using different discharge measures and clustering algorithms.

BFE and BFI groups were not present in the Random or Reshuffled controls.

<u>A few small groups with more specific movement fields were found in each monkey.</u>

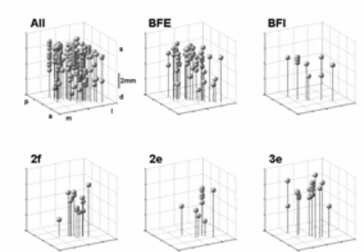
Specific field groups differed from monkey to monkey: Monkey K had 1f, 1e and 3e,5e groups; Monkey A had 2f, 2e and 3e groups; Monkey C had 4f and 4e,5e groups.

Specific field groups were less robust to changes in discharge measure and clustering algorithm. The groups listed above were found using at least 4 of 6 different combinations of discharge measure (change, cumulative sum, or final firing rate) and clustering algorithm (single linkage or average linkage).

Specific field groups appeared when the data from each monkey was reshuffled (see example from monkey C below).

<u>Functional groups of neurons were not spatially segregated in the M1 cortex</u> (see *below*).

7. Spatial Location of Groups



Above, members of each group identified in monkey A-- BFE, BFI, 2f, 2e and 3e--are plotted as spheres of constant size in a separate three-dimensional lollipop diagram. An additional plot shows the location of all neurons in the population. Each sphere is centered at the location of the neuron it represents in a constant reference frame, oriented as if viewing the cortex in the anterior bank of the central sulcus from the frontal pole of the hemisphere, with the motor face representation to the viewer's far right, leg representation to the far left. a - anterior, p - posterior, m - medial, l - lateral, s - superficial (toward the hemispheric surface), d - deep.

8. Conclusions

We found little evidence of functional neuronal groups in M1 that might represent different fingers, muscles or movements, or more abstract constructs such as virtual fingers, movement primitives or principle components.

The limited functional grouping of M1 hand area neurons suggests that M1 neurons act as a network of highly diverse elements in controlling individuated finger movements.