Neural Ensemble Activity From Multiple Brain Regions Predicts Kinematic and Dynamic Variables in a Multiple Force Field Reaching Task

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***Abstract*—In everyday life, we reach, grasp, and manipulate a variety of different objects all with their own dynamic properties. This degree of adaptability is essential for a brain-controlled prosthetic arm to work in the real world. In this study, rats were trained to make reaching movements while holding a torque manipulandum working against two distinct loads. Neural recordings obtained from arrays of 32 microelectrodes spanning the motor cortex were used to predict several movement related variables. In this paper, we demonstrate that a simple linear regression model can translate neural activity into endpoint position of a robotic manipulandum even while the animal controlling it works against different loads. A second regression model can predict, with 100% accuracy, which of the two loads is being manipulated by the animal. Finally, a third model predicts the work needed to move the manipulandum endpoint. This prediction is significantly better than that for position. In each case, the regression model uses a single set of weights. Thus, the neural ensemble is capable of providing the information necessary to compensate for at least two distinct load conditions.**

***Index Terms*—Brain–machine interface (BCI), manipulandum, motor learning, reaching movements.**

I. Introduction

Despite more than 40 years of neurophysiological investigation, the precise mechanisms by which the mammalian motor cortices "encode" movement remains controversial (for review see [1] and [2]). Recently, we and other researchers have developed a new approach to this problem by using implanted electrode arrays to record simultaneously from populations of motor cortical neurons (as opposed to recording them in serial order). These neural populations are then mathematically subject to linear or nonlinear regression fits so as to optimally predict the actual motor output. This neural population output can then be used in a brain–machine interface (BMI) wherein the subject uses its brain activity to directly control a computer cursor or a robot arm. Because such BMIs offer the possibility of restoring motor function in paralyzed people [3]–[6], it is now vitally important to determine how motor cortical neural populations encode the different variables that are involved in movement, including dynamics as well as kinematics.

Previous investigations have involved the use of reaching paradigms in primates working against torque manipulandi while recording from small groups of neurons to determine how the neural activity changes with load conditions [7], [8]. Such work, however, has not yet definitively demonstrated that a BMI can decode the neural activity recorded from an animal working against multiple load conditions. Here, we present the first such results obtained by recording from multielectrode arrays in rats trained to move a manipulandum against different forces. These results show that neural populations in the motor cortex can predict both the position and the force of a robotic manipulandum even while the animal works against more than one dynamical environment. Moreover, it can predict the work (position x force) that is needed to move the manipulandum.

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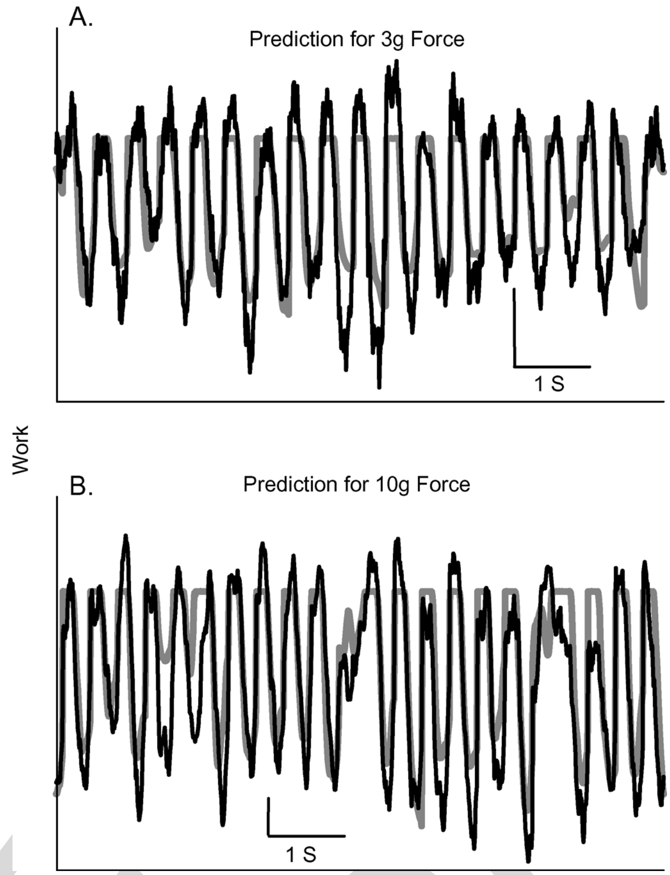

Fig. 1. In (A) and (B), we have plotted the work needed to move the manipulandum in gray and the regression model prediction from the neural data in black. Note the scale differences between (A) and (B):$r = 0.89$ for the prediction to the work variable and $r = 0.87$ for prediction of the position variable (data not shown).

II. Methods

Seven female rats between 280–350 G were implanted with 32 channel microwire arrays that spanned 5 mm in the rostro-caudal direction and approximately 1.5 mm in the medio-lateral direction. The surgical techniques and the torque manipulandum have been described in our previous work [9]. In short, animals were anesthetized with pentobarbital and isoflurane and placed in a stereotactic apparatus. A craniotomy was made over the motor cortex such that the implant could be centered 2.5 mm lateral of the midline and +2 mm rostral to bregma. After removal of the dura the implant was driven down approximately 1.5 mm into the cortex and sealed into place with acrylic attached to bone screws. Following experimentation, animals were anesthetized with ketamine/xylazine in preparation for intracortical microstimulation by passing current through the recording electrodes in order to confirm electrode placement in the arm and hand region of the motor cortex. Since we did not exclude any units from these recordings, it also included single units from adjacent "nonmotor" areas (as determined via microstimulation mapping).

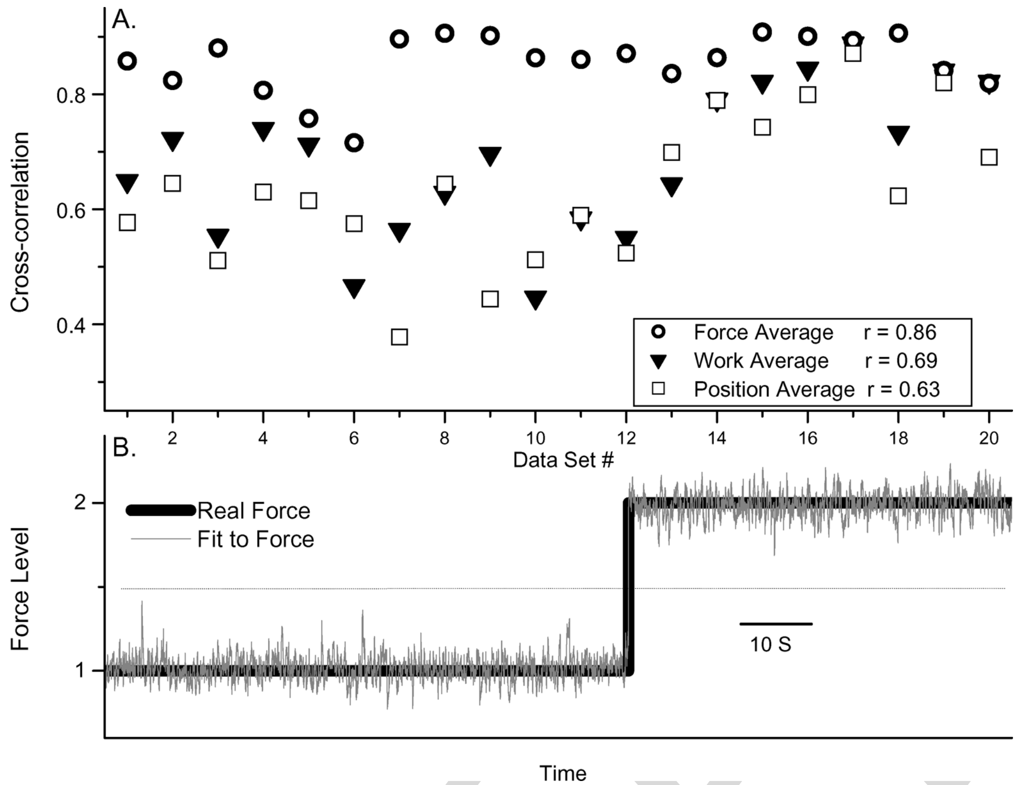

Fig. 2. In (A), we have plotted the cross-correlation values between each of the three variables of interest's real values, and those for the predictions of the models. In (B), we have plotted the real force state produced by the manipulandum as a binomial variable of either 1 or 2 was well as the model's fit to this data.

A. Behavioral Paradigm

Before undergoing surgery, rats were trained to grasp a one degree-of-freedom torque programmable manipulandum and to make reaching movements to a remembered location [9]. Upon reaching (or passing) the target, a light flashed signifying success and the rat received a water reward. Rats were water deprived for approximately 15 h before each experiment, and were provided with food *ad libitum*. All experiments adhered to the SUNY Downstate Medical Center animal welfare protocols. During the training stage, the manipulandum produced a constant force field directed away from the targeted reach. These self-paced movements were made at the animals' natural velocity. These animals were allowed to over-train on this task for several weeks before they underwent surgery. After a week of postoperative recovery, the rats were reintroduced to the reaching task. In this second phase, the manipulandum produced the same type of constant force field, but alternated between a large force (10 G) and a small force (3 G) in blocks of random length (ranges 2–16 movements for the 10 G force and 9–23 for the 3 G force). Overall, 63% of trials involved the 3 G force and 37% the 10 G force.

B. Linear Model and Statistics

We used three simple linear regression models: one to predict the position of the manipulandum handle; another to predict the state of the force field that is 10 G or 3 G force, and a third to predict the work needed to move the manipulandum handle. In each case, we first regressed the neural data to the time series of the selected variable. For prediction, we simply used the regression coefficients and filtered the incoming neural data in the following manner:

$$\hat{y} = b + \sum_{i=1}^{i=M} \sum_{\tau=1}^{\tau=10} (\alpha_i(\tau) * N_i(t-\tau))$$

where $\hat{y}$ is the predicted position, work, or force, b is the y intercept, $\alpha_i(\tau)$ are the filter coefficients for the N_i's that represent the neural activity for the ith neuron (of which there are M) at times $t-\tau$. In general, we used 80% of a data set for fitting the parameters and the other 20% for assessing our prediction. We used the cross correlation between the real data and the prediction, to determine the accuracy of the linear fit. All neural data were smoothed using a 200-ms moving average with a step size of 10 ms. Data starting at 250 ms before the reaching movement until 250 ms after reaching onset were used for the analysis. The smoothing window size was chosen after an exhaustive search for the optimal length, although it should be noted that shorter window lengths of 100 ms produced similar results. Since the reaching movements were often finished in as little as 100 ms, a step (bin) size of 10 ms was employed to ensure successful fitting of the fine details of the movement. This analysis was fully causal, that is, we only used information from the past to predict the future states of the variables.

III. Results

We collected 20 data sets from seven rats making 2579 reaching movements. The animals held the handle of a robotic manipulandum that produced a constant resistive force field of either 3 or 10 G. Fig. 1 shows the results from one rat that made 307 movements during this session. Although the paradigm was run in a block fashion (see methods) we have concatenated a subset of 3 G movements in the top panel [Fig. 1(A)] and a subset of 10 G movements in the bottom panel [Fig. 1(B)]. Here, the plotted variable is the work (the force field times the displacement) needed to move the handle. The light gray line represents the actual work and the black line represents the model prediction. Note that the scales of Fig. 1(A) and Fig. 1(B) are different, though the prediction appears qualitatively similar for the two force conditions.

The cross correlation between the data and the model prediction was $r = 0.89$ for the work variable and $r = 0.87$ for the position variable (data not shown).

In Fig. 2, we have plotted the cross-correlation value between the real data and the model prediction for each data set, and for each of the three variables of interest. The average crosscorrelation between the real force and the predicted force was 0.86, 0.69 for work and 0.63 for the position. The difference between the model predictions for force was significantly better than the other two variables (ANOVA $p < .01$), and the model predictions for the work variable was significantly better than for position (paired T-test $p < 0.05$).

The data used in Fig. 1 came from data set 17. To allow comparison between the individual animals the data set/animal numbers were as follows: data sets 1–4, 5–7, 8–9, 10, 11–12, 13–17, 18–20 were from animals 1–7, respectively. In Fig. 2(b) we have plotted the force field variable as a binomial variable in time (black line) as well as the model prediction (gray line). Note that the force level could be predicted with 100% accuracy by using a simple threshold (dotted line).

IV. Discussion

In this paper, we present the first demonstration that a BMI can successfully predict a range of movement related variables while a subject works against at least two dynamical constraints. These conditions were chosen to reflect those that one would experience in a real world environment. In order for a brain-controlled neuroprosthetic arm to function correctly, the user must be able to control the arm while transporting a wide variety of objects, not only including objects of differing mass, but a great range of natural and human-made objects with unpredictable dynamics. Our current demonstration that neuronal populations in the rat motor cortex can be used to predict two alternating force fields represents a first step towards designing BMIs that can handle a universal set of load dynamics. Thus, a BMI using the same population of cortical neurons could be used to predict not only the kinematics of a reaching movement, but also the forces associated with moving the manipulandum endpoint. In the data presented here, our prediction of work was significantly better than that of position, and thus using control variables that incorporate both position and force such as work may provide better and more natural BMI control.

It should be noted that it is possible to use positional data to control a robotic arm, but this may not be natural and could lead to difficulties. However, if the BMI user is actually controlling a variable such as work, they would have the ability to set the strength of their own movements rather than relying on preset values of a robotic position controller. In general, previous BMI demonstrations have acted as position controllers and have not included any force information. We propose that BMIs that can handle both position and force variables (plus the composite work variable) provide an approach to developing the next generation of natural and efficient robotic prostheses.

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