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Brain-Machine Interfaces in Rat Motor Cortex: Neuronal Operant Conditioning to Perform a Sensory Detection Task

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Abstract- **A chief concern in the pursuit of controlling a neuroprosthetic device using direct brain signals is the question of how many bits of information are achievable through a direct brain-machine interface (BMI) via implantable microelectrode devices. This experiment begins to address this issue with implementation of a simple, software based decoding algorithm that allows the brain to adapt to the rules imposed upon it, To test this algorithm, two chronic 16-channel Michigan silicon microelectrode arrays were implanted into the primary motor cortex of two rats to record simultaneous unit spike activity. The animals were trained to perform an auditory detection task by modulating the recorded cortical spike activity in a prescribed manner. Both non-adaptive and adaptive neural decoding algorithms were evaluated. With the implementation of a non-adaptive decoding algorithm, the rats' behavioral (cortical) responses plateaued at approximately 75% correct; however, with the implementation of an adaptive algorithm, the rats' behavioral responses relatively quickly increased to 91% correct. The neural recordings suggest that the brain is able to modulate detailed cortical responses in accordance with the prescribed operant conditioning rules.**

Keywords **– extracellular recording, microelectrodes, motor cortex, operant conditioning, neuroprosthesis**

I. Introduction

Advanced control-related neuroprosthetic systems tend to be limited by the paucity of available control signals. One strategy for increasing the control signal bandwidth is to interface with the motor control system at progressively higher levels of the system, such as neurons in the motor cortex. [1]. Seminal studies, first pioneered in the 1960s [2] and continuing through the present period [3] have experimentally demonstrated that movement related signals in the primary motor cortex are coded through the combined actions of large populations of tuned neurons. With progressive technological advances, high-precision microelectrode arrays have allowed researchers to tap into this rich source of information available in the motor cortex. In a previous study in rats, it was demonstrated that a lever could be controlled with cortical unit responses decoded using a relatively computationally-intensive artificial neural network algorithm [4]. In this study, we investigated the extent to which recorded cortical units can be operantly conditioned to meet criterion responses in accordance with computationally simple adaptive and non-adaptive spike decoding algorithms. The adaptive algorithm continuously adapts during each recording session on a trial-by-trial basis. The results of this pilot study suggest a robust capacity for cortical unit response modulation in a relatively simple binary (1 bit) detection task. The cortical responses were found to adapt over days to the criterion rules. This convergence was accelerated using an adaptive decoding algorithm provided that the algorithm adapted more slowly than the cortical responses. A companion paper reports the effects of a related adaptive algorithm in a more complicated discrimination task [5].

II. Methodology

1) *Animals and Apparatus*: Two male Sprague-Dawley rats (280-320 grams) maintained at 80% of their free-feeding body weights were initially trained to lever press for food in a standard operant-conditioning chamber (Coulbourn, Allentown, PA, USA) inside a sound-dampened enclosure. The auditory stimuli were delivered via a speaker (Yamaha NS-10M Studio, Yamaha Corporation, Buena Park, CA) located 1 m directly above the test chamber. The acoustic environment was found to approximate a free field. One retractable 2.5-cm lever positioned approximately 8 cm from the chamber floor served as the manipulandum. Single 45-mg pellets (P.J. Noyes Co., Lancaster, NH) were used as reinforcers. They were delivered into a 2.5-cm by 2.5-cm food tray located at the opposite wall of the lever. A 28-volt bulb in the upper front of the chamber provided the only ambient lighting. Rats were housed separately under a reversed 12-hour light/dark schedule.

2) *Electrode Arrays, Surgical Procedure, and Neural Recordings:* Two 16-channel chronic silicon-substrate microelectrode arrays were implanted into each rat [6]. These "Michigan" microelectrode assemblies were provided by the Center for Neural Communication Technology funded by the NIH National Center for Research Resources. Each electrode had four separate shanks (200 μm inter-shank spacing) with four recording sites spaced evenly along each shank (200 μm inter-site spacing). The electrodes were implanted into the forelimb area in one hemisphere of the rats' primary motor cortex (approximate stereotaxic coordinates of AP: +3.0um, ML: 2.5um, as described in [7]). This electrode geometry provided simultaneously sample from cortical depths of a region spanning 600 μm below the surface. Anesthesia was administered using intra-peritoneal injections of an anesthetic cocktail (Ketamine, Xylazine, and Acepromazine). The craniotomies created were rectangular in shape spanning approximately 3mm in the anterior-posterior direction, and 2mm in the medial-lateral direction. After the electrodes were hand inserted, ALGEL® was applied, as described in [8,9], followed by dental acrylic (Co-Oral-Ite Dental Mfg. Co.). The animals were allowed 48 hours to recover from surgery.

During each experimental session neural electrophysiological data from the 16 electrode channels sampled at 40 kHz were simultaneously amplified and

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bandpass filtered (450 – 5000 Hz) on a Multichannel Neuronal Acquisition Processor (MNAP; Plexon Inc, Dallas, TX). Operator-controlled unit discrimination criteria were established at the beginning of each recording session prior to behavioral training. Multichannel spike times were transmitted with nominal delays via a local TCP/IP connection to a second computer running the Matlab-based neural decoding software and the experiment control system (Tucker-Davis Technologies, Gainesville, FL).

3) *Psychophysical Detection Task:* Prior to electrode implantation, rats were trained to perform a Go/No-Go auditory detection task for food rewards in about two weeks. Reinforcements have been shown to encourage higher levels of cortical neuron modulation [2]. Each experimental session was composed of 300 trials, in which each trial consisted of a 10 second inter-trial interval, a 1 second stimulus setpoint, and a response window of up to 4.5 seconds. For each trial, a setpoint consisting of a 1 kHz tone at 70 dB SPL was presented. To receive a reward the rat was required to press the lever within the response window time frame. After the electrodes were implanted the rats could receive a reward by two different means. A reward was granted if the lever was pressed or if the appropriate neural response was achieved. The appropriate neural response is described in the following paragraphs

In the first phase of this experiment, a non-adaptive algorithm was implemented that used the average modulation computed from the combined neural output from all the electrode sites that recorded discriminable units. The baseline firing rate for each microelectrode channel was determined by binning the neural data during the last 1.8 seconds of the inter-trial interval into 90 ms bins and calculating an average firing rate and standard deviation.

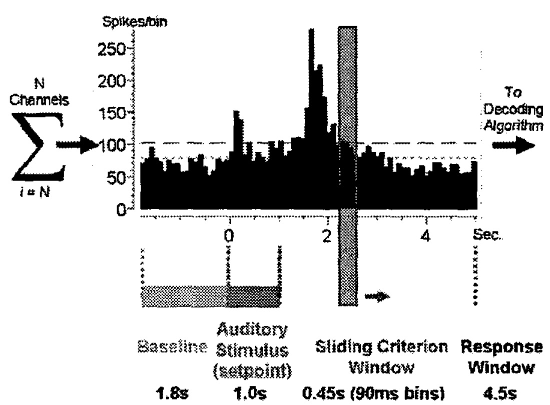

Fig. 1. Experimental control algorithm with time sequence. The input to the algorithm consists of the weighted combination (non-adaptive algorithm: weights = 1; adaptive algorithm: weights = % of modulation present) of all recorded channels.

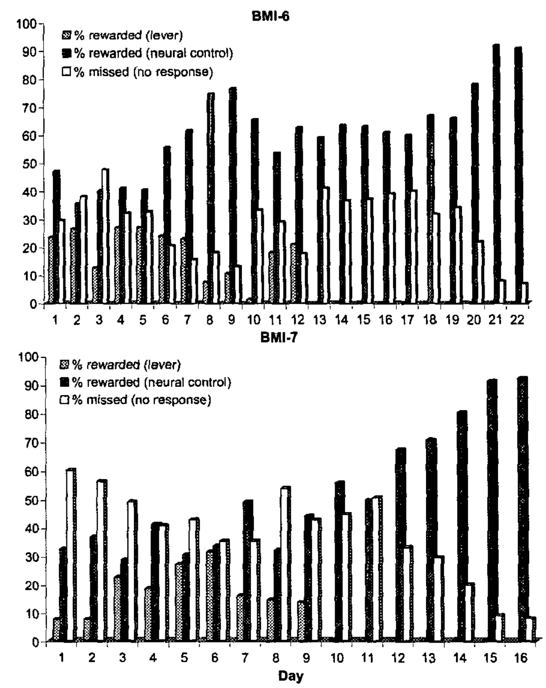

Fig. 2. Behavioral results from two different rats. Data represented are: 1) rewards granted from lever presses, 2) rewards granted from direct neural control, and 3) misses (no response). All days (excluding the final two) represent data collected using the non-adaptive control algorithm. The final two days for each animal represent data collected using the adaptive algorithm.

Immediately after the baseline time period, the setpoint was presented. The response window data was divided into 90 ms bins, and a 450 ms window, sliding in 90 ms increments, was used to calculate an average response firing rate for each channel. The baseline firing rate average for each channel was then subtracted from the response window average. In order to receive a reward, the rat had to modulate its motor cortical firing rate two standard deviations above or below the baseline and maintain it for 450 ms. If the average response of the sorted channels fulfilled this criterion the rat was rewarded and the trial would end. Fig. 1 illustrates the basic components of this algorithm.

In the second phase of this experiment, an adaptive algorithm was implemented. The aforementioned linear combination described was still used; however each channel was now assigned a weight that represented the level of modulation for each channel. The weights were modified based on the average criterion-baseline firing ratio of the last 10 correct trials for that set point. Each weight converged to the corresponding channel's percent modulation with respect to the presented set point according to the following rules: no firing rate modulation resulted in a zero weight, increased modulation resulted in a positive weight, and a decreased modulation resulted in a negative weight. Set point weights were carried over from day to day. This allowed for the algorithm to adequately account for sparse modulation patterns and also allow channels with the greatest modulation to dominate the neural response.

III. Results

A. Behavioral Results

Immediately prior to implantation, the rats' performances on the lever pressing task peaked at approximately 85% correct trials. The remaining 15% of the trials were classified as "misses" (no response). Once implanted, the rats could respond to the setpoint by either pressing the lever or providing the appropriate neural response. Fig. 2 shows the behavior data from two rats. The three values plotted over time are: % rewards from lever presses, % rewards from neural control, and % misses (no response). These results show that over time the rewards granted for neural control increased and the rewards for lever presses decreased. This demonstrates an extinction of a lever press for reward and an association of neural modulation for reward. In as short as 6 days, the rats were clearly positioning themselves close to the food delivery tray without moving toward the lever at all. The lever seemed to be used only as a last resort if the rat missed several trials in a row. As time increased, the number of lever hits continued to decrease until it only accounted for 10-20% of the rewards. Once this occurred the lever was completely turned off. In less than two weeks, using a non-adaptive control algorithm, food delivery to the rat was solely under neural control. Once the rat had plateaued at approximately 75% neural control rewards, the previously described adaptive algorithm was implemented. In Fig. 2 the final two days from each animal utilized the adaptive algorithm. In these days, the rat's performance immediately jumped to 91% neural control rewards.

B. Neural Responses

Single unit activity was present on 84% of the channels with spikes amplitudes ranging from 100 to 800 μV peak-to-peak. An example of a one-second recording is shown in Fig. 3. This recording represents the duration of time during a one second stimulus presentation. An increase in firing rate of this neuron is first noticeable at approximately 400 ms after the onset of the stimulus. In order to better understand what the response of each neuron in the recorded neural population is doing with respect to the auditory setpoint, peri-stimulus time histograms (PSTHs) were constructed from spike times relative to the preceding auditory setpoint (cue). Fig. 4 shows five different modulating channels from rat BMI-6 that showed significant modulation. Each of these plots represents the duration of time included in the baseline, setpoint, and response window. The time of each setpoint is considered

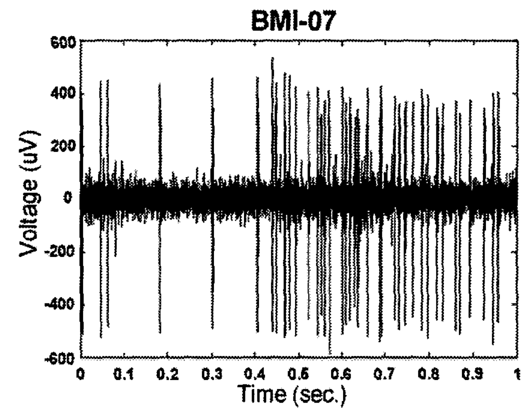

Fig. 3. A one second snap shot of spike activity recorded from an implanted Michigan probe. A one-second stimulus onset begins at time zero. An increase in neural modulation can be see begins at approximately 0.4 seconds.

time zero. The dotted line in each plot represents the mean firing rate over these intervals and the dashed lines represent two standard deviations above and below the mean. The PSTH's on day 1 show a minimal amount of coordinated modulation. With daily training, over a period of a week, this modulation becomes more distinct. On day 8 the rat significantly uses neural control over lever presses to achieve awards (Fig. 2), and the corresponding PSTHs exhibit more pronounced and narrow narrow peaks representative of short periods of increased firing rates relative to the setpoint (Fig. 4). The data indicate that the cortical activity tends to repeat a similar type of modulation pattern over the course of the 300 trials in the recording session.

IV. Discussion

In the first phase of this pilot study, the use of a non-adaptive algorithm evaluated the rat's ability to positively modulate the recorded neural population. Without adapting this particular decoding algorithm, the effects of non-modulated neurons would tend to wash out the effects of modulated neurons thereby making them less significant. Additionally, negatively modulating neurons would detract from the overall average of the firing on the array. The results of this experiment have demonstrated that even with a simple non-adaptive algorithm, rats can be operantly trained to modulate motor cortex unit responses in a goal-directed manner. Following the implementation of an adaptive algorithm, the performance of the rat increased by 16%. By adapting the algorithm, the signal-to-noise ratio was improved: the contributions of modulated neurons were enhanced and non-modulated neurons were attenuated.

V. Conclusion

We have shown that the underlying structure of rat cortex can be augmented in a useful way and the rate at which the rat can learn to modulate neural output is within a week's

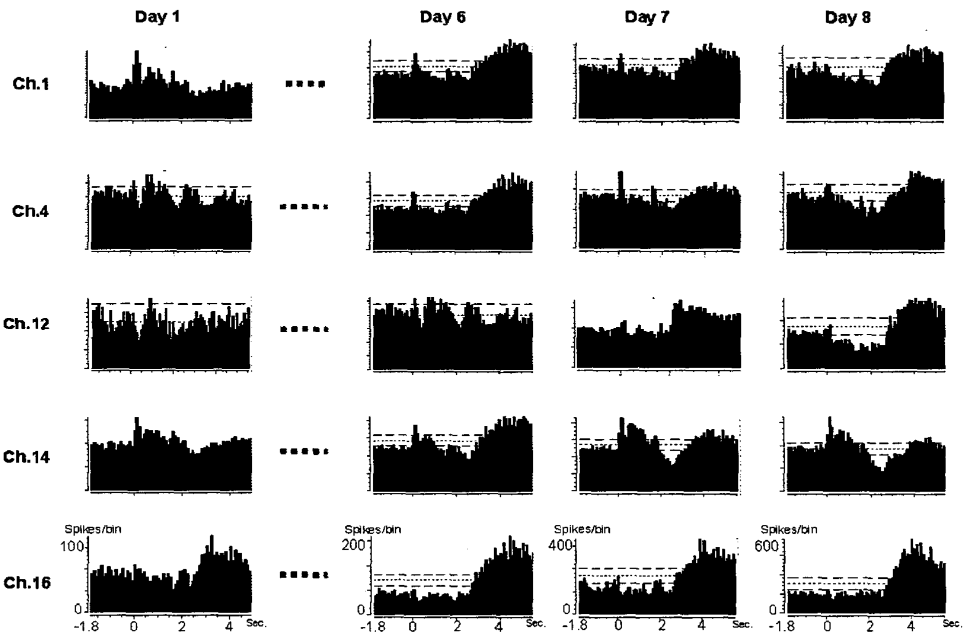

Fig. 4. Five channels representing a period of 8 days post-implant are shown that had significant modulation in neural activity (BMI-6). The modulation characteristics become more tightly shaped with daily training of the rats. By day 8, this rat has almost completely stopped using the lever presses for rewards and instead used direct neural control. Each of these plots represents a single day comprised of 300 trials. The dotted line in each plot represents the overall mean and the dashed lines represent two standard deviations above and below the mean.

time (given the relatively simple and arbitrary rules we have imposed on the recorded units) with training periods lasting approximately an hour each day. We conclude that rats are able to learn over 5-6 days to modulate their neurons, in some cases as high as 20 times, in a coordinated way in order to satisfy the rules presented to them in this paradigm. These numbers demonstrate that the use of rats in an experiment of this nature is a viable resource and has several applications in the investigation of cortical interfaces for neuroprosthetic control. The results from this experiment begin to suggest that by focusing in on the specific modulatory characteristics of individual neurons within larger populations of neurons, we can extract useful bits of information as a result of the rat's behavior. These experiments have laid the foundation towards extracting multiple bits of information directly from the cortex of an awake and behaving animal.

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