

Real-Time Control of the Hand by Intracortically Controlled Functional Neuromuscular Stimulation

Eric A. Pohlmeyer, Eric J. Perreault, Marc W. Slutzky, Kevin L. Kilgore, Robert F. Kirsch, Dawn M. Taylor and Lee E. Miller

Abstract—The purpose of this study was to develop an animal model to evaluate the efficacy of a brain machine interface (BMI) to control a neuroprosthesis intended to restore hand function via functional neuromuscular stimulation (FNS). We have implemented the system in a single primate, whose limb could be temporarily paralyzed by a reversible peripheral nerve block. Recordings from the primary motor cortex were obtained from a 100-electrode array in the intact monkey, and used to predict the activity of a variety of wrist and hand muscles. These predictions were calculated in real-time, and used as inputs to a 4 channel neuromuscular stimulator for electrically activating the paralyzed muscles. Here we demonstrate that the BMI can be used to restore voluntary control of wrist flexion following muscle paralysis.

I. INTRODUCTION

FUNCTIONAL neuromuscular stimulation has proven to be an effective means for restoring movement control following spinal cord injury [1]. Most of systems have focused on stance, bowel or bladder control, or basic grasping movements using low dimensional control signals. However, the restoration of more complex tasks, such as dexterous object manipulation, 3-dimensional reaching, or inter-limb coordination would require access to more control sources than are currently unavailable from severely disabled patients. Ironically, it is most difficult to obtain such control sources from the individuals who are most likely to benefit from them. For example, patients with spinal cord injuries at the C4 level or above are generally paralyzed from the shoulders down and would need restoration of full arm and hand movement to achieve functional reach and grasp [2]. Unfortunately, these patients have fewer options for command signals as only the head and neck area remain under volitional control.

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E.A. Pohlmeyer is with the Dept. of Biomedical Eng., Northwestern University, Chicago, IL 60611 USA. (e-pohlmeyer@northwestern.edu).

E.J. Perreault is with the Depts. of Biomedical Eng. and Physical Med. and Rehab., Northwestern University, Chicago, IL 60611 USA. (e-perreault@northwestern.edu).

M.W. Slutzky is with the Depts. of Physiology, Neurology, and Physical Med. and Rehab., Northwestern University, Chicago, IL 60611 USA. (mslutzky@northwestern.edu).

K.L. Kilgore is with the Dept. of Orthopaedics, MetroHealth Medical Center, Cleveland, OH 44109 USA. (klk4@case.edu).

R.F. Kirsch is with the Dept. of Biomedical Eng., Case Western Reserve University, Cleveland, OH 44106 USA. (rfk3@cwru.edu).

D.M. Taylor is with the Dept. of Biomedical Eng., Case Western Reserve University, Cleveland, OH 44106 USA. (dxt42@cwru.edu).

L.E. Miller is with the Depts. of Physiology and Biomedical Eng., Northwestern University, Chicago, IL 60611 USA. (lm@northwestern.edu; 1.312.503.8677).

BMI provide one possibility for providing higher dimensional control sources for FNS applications. The goal of this project is to test the efficacy of a BMI for controlling an FNS system. To accomplish this goal, we have developed a non-human primate model that includes an intracortical micro-electrode array, a reversible peripheral nerve block, and an FNS system to activate several muscles of the wrist and hand. This paper presents our initial evaluation of this system's performance in restoration of the monkey's ability to control voluntary wrist flexion force despite the temporary paralysis.

II. METHODS

A. Behavioral Tasks

A single, male Rhesus monkey was trained to perform a variety of tasks that required either grasp force (including palmar, lateral, and precision grasps) or isometric wrist flexion/extension forces. Grasp force was measured using a pair of force sensitive resistors mounted on each of the devices. Wrist force was measured by a pair of strain gauges mounted on an aluminum cantilever strapped to the monkey's arm. The monkey faced a video monitor on which a moving cursor provided visual feedback of the applied forces. Targets were also displayed on the monitor, appearing pseudo-randomly at one of several different levels. Under normal conditions, the monkey was required to move the cursor into the target within 1.5 seconds in order to receive a liquid reward. During nerve block, this period was increased to 3.0 seconds. A trial consisted of matching a single target, and the monkey acquired 1000 or more such targets in a typical session. Data files were collected while the monkey reached toward and grasped a series of the devices in random order.

In addition to the standard force tracking paradigm, we also measured the maximum amount of force that the monkey would generate voluntarily (MVC) for each device. This estimate was important in order to gauge both the depth of the peripheral nerve block, and the efficacy of the FNS. Unlike similar paradigms with cooperative human subjects, this required the use of a non-monotonic sequence of increasing target force levels, by which means the monkey was coaxed to exert increasingly high force without giving up. This method typically proved capable of generating consistent estimates of MVC within 3-4 minutes.

B. Surgery

After the animal had become familiar with the tasks,

surgical procedures were undertaken to implant the necessary hardware. All surgery was conducted under isoflurane gas anesthesia. The antibiotic, cefazolin was given pre- and post-operatively, and Buprenex, an opioid analgesic, was also administered postoperatively. Dexamethasone was given prior to the cortical implant surgery to control intra-cranial pressure.

An array of 100 silicon microelectrodes (Cyberkinetics, Inc.) was implanted in the primary motor cortex (M1), just anterior to the crown of the central sulcus, and approximately in line with the superior ramus (medial edge) of the arcuate sulcus. This location includes both proximal and distal representation of the arm within M1.

In a separate surgery, silicone cuffs were placed around the median and ulnar nerves just proximal to the elbow. Cannulae from these cuffs were routed subcutaneously to sub-dermal injection ports located more proximally on the arm. Each nerve was dissected free of surrounding tissue, in order to expose approximately 2 cm length. The cuffs then were formed by using sutures to shape 1 mm thick Silastic sheets into tubes around the exposed nerves. Before closing each incision, we injected saline into the corresponding port to ensure that it was patent, and to determine its dead-space volume.

C. Cortical and Muscle Recordings

Neural data were recorded using a multi-channel acquisition processor (MAP; Plexon, Inc.) with a sampling rate of 40 kHz. EMG and force signals were recorded at 2000 Hz using the same system. For offline analyses, the waveforms of the neuronal signals were discriminated using Offline Sorter (Plexon, Inc.). For the real-time experiments, spike-shape templates were created by more coarsely clustering the waveforms (using just the first two principal components) of a set of training data. The templates were subsequently used to classify spikes as they were acquired in real-time. Both well-isolated, single-unit signals, as well as multi-unit signals were recorded, and treated equivalently in all analyses.

In initial EMG prediction experiments, muscle activity was measured using surface electrodes. Surface recordings were made from the medial deltoid (MDI), biceps (Bic), and triceps (Tri). An electrode was also placed on the forearm, above the digit flexor musculature, sampling primarily flexor digitorum sublimis (FDS). This recording probably included some activity from the adjacent wrist flexors as well. The EMG signals were amplified and band-pass filtered before being sampled.

In later experiments involving muscle stimulation, we inserted percutaneous, intramuscular electrodes that were used for both recording and stimulation. Individual stainless steel wires (Cooner, AS632) were inserted through the skin using a 22 gauge hypodermic needle with the monkey under ketamine-xylazine anesthesia. Stimulus pulses were passed through the wires during insertion in order to find sites of low threshold activation. When a satisfactory response was

obtained, the needle was withdrawn, and the leads carefully taped down to the skin, and routed proximally up the monkey's arm. Leads were typically placed in flexor carpi radialis and ulnaris (FCR and FCU), palmaris longus (PaL), and flexor digitorum profundus (FDP) and superficialis (FDS). The monkey was placed in a jacket while the leads remained in place (typically 1-3 weeks). Bipolar recordings from these electrodes were made across two such leads inserted into each muscle.

D. Muscle Activity Prediction

For offline data analyses, the neural data were converted into continuous, 100 Hz signals by counting the number of action potentials within successive 10 ms bins. Likewise, EMG data were full-wave rectified, low-pass filtered (4-pole, 10 Hz) and downsampled to match the sampling rate of the neuronal discharge signals. Multiple-input impulse responses were calculated between these discharge rate signals and each of the recorded muscles:

$$z(t) = \sum_{k=1}^N \sum_{\tau=0}^{M-1} h_k(\tau) x_k(t - \tau) \quad (1)$$

Each input x_k was convolved with its impulse response, h_k , where h_k was a causal linear filter of length 0.5 s relating it to the output $z(t)$. As a result, the system output was simply a result of a weighted, linear combination the recent history of N neural signals. Six minutes of data were used to estimate the filters using a least squares regression process. Efficient methods for the calculations have been described elsewhere [3].

Although we recorded as many as 64 neural signals, a subset of 16 were used for the EMG prediction experiments. We have described a formal optimal selection process elsewhere, that identifies the unique contribution of each neuron to the prediction of a particular output [4]. Briefly, that process ranks neurons using an iterative process to determine the magnitude of their unique information with respect to a particular output signal. A simplified version of this process was used to select the signals used to control the BMI during the real-time experiments.

Having determined an optimal set of filters to fit each muscle, additional neural data were used to generate predictions of novel EMG data and thereby cross-validate the filters. The quality of these predictions was evaluated by calculating the coefficient of determination (R^2) between 1 minute lengths of predicted and actual EMG signals.

E. Peripheral Nerve Block

In order to test the monkey's ability to activate its muscles voluntarily via cortically controlled FNS, it was necessary to temporarily paralyze the forearm musculature. The median and ulnar nerves innervate the intrinsic hand muscles and the extrinsic wrist and digit flexors. The extensor muscles are supplied by the radial nerve. A complete block of the median and ulnar nerves at the elbow will eliminate essentially all wrist and digit flexor force, while leaving intact control of shoulder and elbow

movement, and most wrist and digit extension. Injection of either Lidocaine or Bupivacaine into the implanted nerve cuffs provided the most effective and convenient means to elicit the nerve block, but by the time of the closed-loop experiments, the cannula of the ulnar cuff had become obstructed. Under these conditions, the monkey was briefly anesthetized with isoflurane, and percutaneous injections were made in the vicinity of each nerve. The precise injection sites were determined when appropriate movements were evoked by low current ($< 500 \mu\text{A}$ @ $100 \mu\text{s}$ pulse width) stimulation through the uninsulated tip of the 24 gauge Stimuplex injection needle (B Braun Medical Inc).

F. Muscle Stimulation

Muscle contractions were evoked through the percutaneous leads using monopolar, bi-phasic pulses of between 2 and 10 mA current from a 4-channel stimulator. Pulse-width modulation (5-200 μs) was used to control stimulus intensity. Each time a set of wires was inserted, a series of tests were run to determine the threshold and spillover (activation of adjacent muscles) points for each lead. Finally, during closed loop FNS control, real-time EMG predictions above a threshold level were mapped linearly into stimulator pulse-width commands using the four muscles that produced the greatest wrist flexion force.

III. RESULTS

A. Prediction of Muscle Activity Based on Signals from Primary Motor Cortex

The ability to record from the brain and predict muscle activity is central to our efforts to produce a neuroprosthesis capable of driving appropriate muscle activity in paralyzed muscles. Fig. 1 illustrates several examples of these predictions. The rectified and filtered activity of four

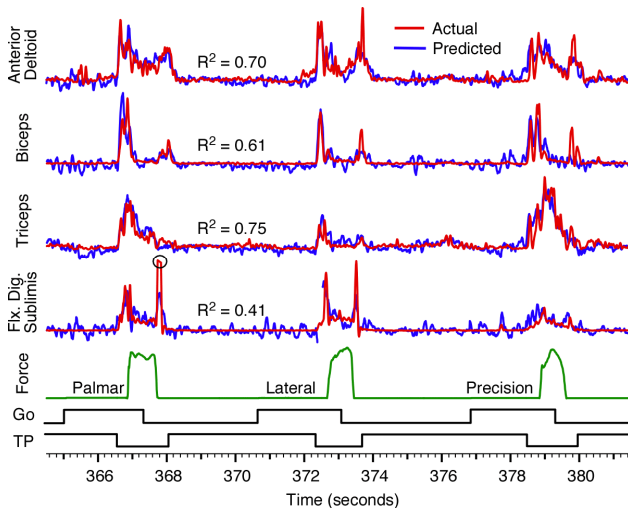


Fig. 1. Recorded EMG and EMG predicted on the basis of recordings from 16 M1 neurons as a monkey made a series of 3 reaches to grasp different devices. Cross-validated results calculated from data not used to construct the linear filters. Circle marks a saturated burst of EMG.

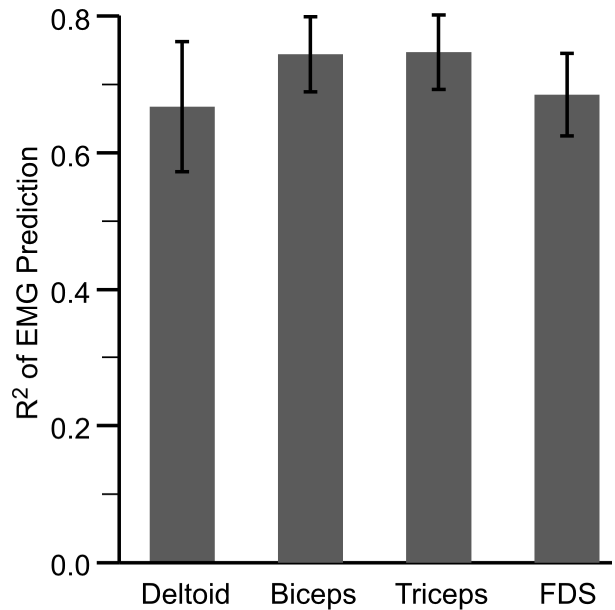


Fig. 2. Summary across all data sets of R^2 for results like those shown in Fig. 1, using optimally chosen sets of 16 neurons.

muscles is pictured in red as the monkey performed a sequence of three different grasps. At the bottom are records of the grip force, the Go cue, and a record of when the monkey's hand was on the touch pad (TP). Shown in blue are the EMG predictions. In general, the predicted signals matched the actual signals remarkably well, capturing the varying patterns of activity across the different grasps. It is important to note that these are continuously recorded signals from a series of grasps, not averages across trials. The predictions were clearly noisier during the quiescent periods between reaches than were the actual signals, which was a product of the non-zero spontaneous rate of most neurons. The accuracy of each prediction is indicated by the R^2 value above each signal. This represents a measure for the entire minute of continuously recorded data of which these three reaches are representative.

Fig. 2 summarizes the EMG prediction results for a larger data set obtained from this monkey while performing a task that required reaching to press one of four different buttons with the arm either supinated or pronated. The quality of the predictions in Fig. 1 was quite similar to this performance, with the exception of FDS, which was unusually low. The high quality of the predictions is important in itself, but the fact that both distal and proximal muscles were accurately predicted is equally important. This suggests that a single array, at least in the monkey, should be sufficient to provide high quality predictions for proximal, as well as distal muscles of the arm.

B. Transient Paralysis of Wrist and Digit Flexors

Having developed the ability to predict muscle activity, it was also necessary to develop methods to weaken or paralyze the monkey's forearm musculature temporarily. The temporary block was important, because it provided the ability to record initially from the intact muscles in order to

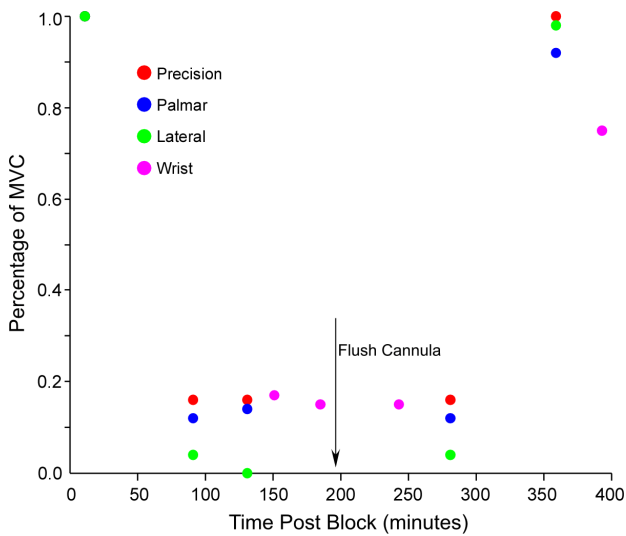


Fig. 3. Magnitude and duration of the loss of flexion force following injection of Bupivacaine into the cannulae leading to cuffs implanted on the median and ulnar nerves. Lidocaine caused a more rapid onset, but shorter acting block.

calculate the filters between neuronal discharge and muscle activity. The implanted nerve cuff and cannulae proved effective for blocking voluntary muscle activity. This was evaluated by comparing MVCs measured before and after the block. Results from a Bupivacaine block (1-1.5 cc, 0.75%, 1:200,000 epinephrine) on precision, palmar, and lateral grasp, as well as wrist flexion force are shown in Fig. 3. In all these tasks, voluntary force was reduced by more than 80% of the pre-block levels. Voluntary control began to return to normal levels approximately 5 hours after the anesthetic was initially administered, about 90 minutes after the cannulae were flushed. Blocking either nerve alone proved to be inadequate, as significant voluntary control of force remained. Lidocaine typically resulted in blocks lasting from 1-2 hours in duration.

C. Open-loop Control of Dynamically Modulated Muscle Activity

Finally, we needed the means to activate muscles by electrical stimulation, adequate to produce significantly more force than the monkey was capable of generating voluntarily during the nerve block. Ideally it should also be possible to grade this force dynamically. As an initial open-loop means to test these methods, we recorded EMG signals from four wrist flexor muscles as the monkey performed a series of wrist flexion trials. In a later session, while the monkey was anesthetized with ketamine, these signals were converted to pulse-width commands and used to control stimulus trains delivered to percutaneous leads placed in the same set of muscles. Fig 4 shows the result of this experiment. The black traces indicate the voluntarily controlled force measured along with EMG signals in the first session. The red traces indicate the force produced later, by stimulating muscles electrically. Dynamically, the two traces match one another quite well. Although the force

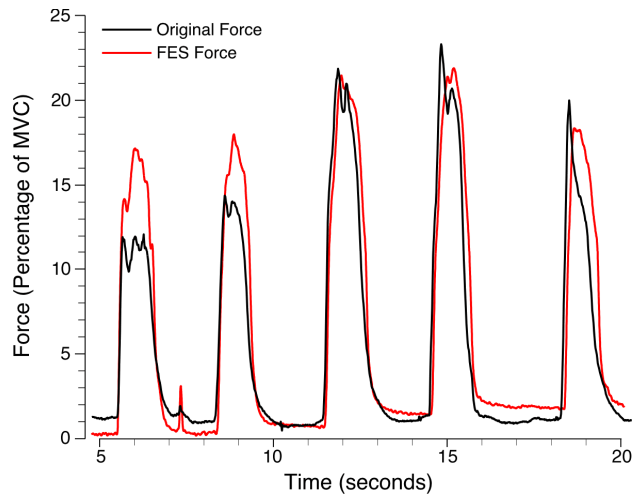


Fig. 4. Dynamically modulated wrist flexion force produced by pulse-width modulated stimulus trains delivered to four different muscles contributing to wrist flexion. The monkey was anesthetized with ketamine, and each input was driven by actual EMG signals previously recorded during the same task.

was modulated well, there were some scaling differences between the low and high forces. It should be noted that we were not controlling all of the muscles that would have normally been contributing to wrist flexion force. This may have contributed to the scaling mismatch.

D. Closed-loop, Voluntary Control of Wrist Flexion Force

Finally, a session was conducted in which the monkey performed the wrist flexion task during a nerve block, while the stimulator control signals were provided by M1 recordings and real-time predictions of muscle activity. The filters had been calculated using data collected in a session on the previous day. Fig. 5 presents results from this initial closed-loop test of the system. The top trace shows the real-time EMG predictions used to control FDP stimulation. Stimulation to the three other wrist flexors (FDS, FCU, PaL)

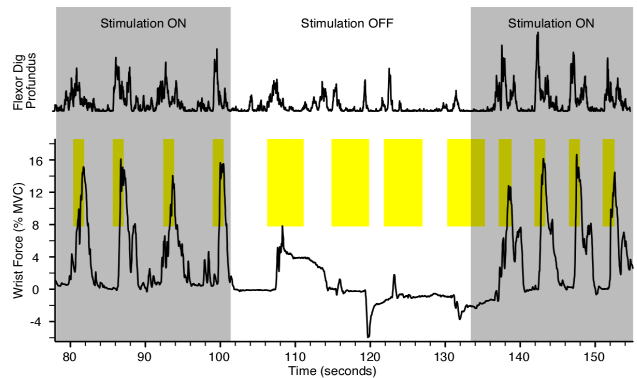


Fig. 5. Wrist flexion force produced voluntarily by the monkey with a temporarily paralyzed arm. Yellow rectangles denote the force targets the monkey was required to achieve. Real-time predictions of 4 muscles were calculated, and used to modulate the pulse-width of stimulus trains to those 4 muscles. Under these conditions, the monkey was able to do the task only with the assistance of the FNS neuroprosthesis.

was quite similar, since these muscles all acted as close synergists during this one-dimensional task. The bottom trace shows the measured wrist force. Positive deflections correspond to wrist flexion. The yellow bars indicate the timing and magnitude of the force targets displayed to the monkey.

When the stimulator was on, the animal reached the targets with a movement time that was about twice as long as in his normal behavior. In contrast, when the stimulator was off, the peripheral nerve block prevented the monkey from generating adequate force to complete the task successfully. Consequently, the targets remained on throughout the maximum allowable reach time (3 seconds). These targets required the monkey to generate peak forces of approximately 10-15% of his normal MVC. We did not attempt a formal determination of MVC during the closed-loop control, but forces significantly higher than those used in this experiment appeared to be very difficult or impossible for the monkey to generate. It is important to note that some of the forces generated with the stimulator off were the result of inertial forces generated at the wrist, by the animal swinging his arm in an attempt to complete the task.

IV. DISCUSSION

We have demonstrated that it is possible to make predictions of muscle activity based on recordings from the primary motor cortex. The accuracy of these predictions compares quite favorably to predictions of kinematic signals reported by a number of other studies, despite the greater bandwidth of the EMG signals [5-7]. We have used such predictions to control the output of a four-channel muscle stimulator in real-time. This provided voluntary control of wrist force to a monkey whose forearm flexor musculature had been paralyzed by a peripheral nerve block. Although the forces the monkey generated under these conditions were well below normal, the stimulation allowed the monkey to generate forces well above what he was capable of without stimulation. It is important to note that the monkey was able to make use of the closed loop system almost immediately, without the need for any retraining.

We were restricted to the use of percutaneous leads for muscle stimulation with this animal. This caused several limitations. First, the electrode placement was less precise and less stable than what can be achieved with chronic, subcutaneous implants. Chronic implants should allow greater, more consistent force production. Second, because the leads exited the skin near the implanted muscles, it was not practical to use any intrinsic hand muscles. This prevented control of more dexterous hand movements. However, in other applications, we have surgically implanted EMG electrodes in several hand muscles, including those of the thumb, index, and little fingers. We intend to use chronically implanted stimulating electrodes, including several in the hand, in future monkeys.

Despite these limitations, our demonstration serves as an ideal proof of concept that intra-cortical signals can

provide a natural means to control an FNS prosthesis. We are working to demonstrate similar ease of control of movements involving a larger number of degrees of freedom. If this can be achieved, patients with C5-C6 spinal injuries, such as those for whom the Freehand FNS system was designed [8], would be obvious candidates to benefit from such a system. Patients with higher cervical injuries would stand to benefit even more, as they have greater deficits, but fewer control options.

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