ADAPTATION IN CORTICAL CONTROL OF ARM MOVEMENT

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Abstract: By simultaneously recording multi-neuronal activities through chronically implanted electrode arrays in motor and sensory cortices, arm movement trajectory, and muscle activities, we observed both spatial and temporal differences in neuronal activities during different phases of a reaching task. We also discovered that when developing an effective control strategy to overcome an externally applied perturbation, the direction of the movement and the arm configuration played an important role in determining which control strategy to apply. The results indicated that predictive trajectory compensation was often adopted while stiffness control was also utilized. *Copyright © 2002 IFAC*

Key words: Biomedical system, adaptive control, neural activity, perturbation, predictive control

1. INTRODUCTION

Developing a cortically controlled neuroprosthetic system has become achievable due to recent development in sophisticated neural implants for chronic recording and stimulation of brain activities, advanced signal processing and control algorithms, and a better understanding of the fundamental principles of neural control of posture and movement (Mussa-Ivaldi et al. 1988; Loeb, Levine et al. 1990; Nicolelis et al. 1997; Thoroughman and Shadmehr 2000). However, serious obstacles remain and include identifying where and how to get reliable control commands conveniently and consistently. Furthermore, it is crucial to have a better understanding of how neural commands or coding will be affected by external perturbations. Neuronal signals may change when such perturbation is encountered and may also adapt to the dynamics of a given perturbation. We will present a new approach to investigate the adaptation at the neural coding and movement execution levels.

Extensive research effort has been devoted to understand the underlying mechanisms of cortical control of arm movement, interactions among various structures in the central nervous system (CNS), especially cortical and subcortical brain areas, and information substrates from neuronal activity patterns in these brain areas when a subject is learning new motor tasks or adapting to changing task conditions (Caminiti et al. 1991; Kalaska and Crammond 1992; Georgopoulos 1994; Schwartz 1994; Crammond and Kalaska 1996). Neuronal signals recorded from these

areas have been used to predict the arm movement direction and velocity. Schwartz and his colleagues have successfully reproduced the hand trajectories using neuronal signals recorded from monkey's motorcortex when the animals performed various unrestrained tracing motions in three dimensional space (Moran and Schwartz 1999). Their work showed that the population of motor cortical neurons represented direction and velocity of hand movement with approximately 80-120 ms lead time. Recently, Nicholelis et al. (2000) reported their successful reproduction of controlling movement along a straight line by using neural network and linear filtering algorithms on neural activity simultaneously recorded from populations of cortical neurons. However, the successes of these investigations were based on the animals performing well-trained regular tasks. If the task is perturbed, will the cortical neuron activity patterns change? If so, will the same decoding algorithms accurately predict the compensatory hand motion? How will the change occur and what adaptation process might we observe if we subject the animals to repeated perturbations? Will the adaptation changes be permanent even after the removal of the perturbation? These are some important questions we need to address in order to develop a robust system for neuroprosthetic applications.

Perturbation paradigms are effective to test the performance of neural controllers in biological systems when responding to externally applied disturbances. These perturbations have consisted of constant bias forces (Georgopoulos et al. 1992),

complex force fields that depend on the reach velocity (Shadmehr and Mussa-Ivaldi 1994), or transient impulse perturbations (Lacquaniti et al. 1991; Weber et al. 1998). Data from these experiments have revealed the remarkable capacity of neural control systems to compensate for various types of external disturbances. In general, this compensation is provided by an adaptive control system that utilizes both sensory feedback and direct cortical control (Hayashi et al. 1990; Lacquaniti et al. 1992; Bhushan and Shadmehr 1999). However, the exact mechanism of adaptation and coordination between descending cortical control and sensory feedback control remain elusive.

This paper will describe the design of a new perturbation mechanism under which the arm can move freely without any constraint. Combined with multi-unit recording through chronically implanted microelectrodes from various cortical areas, we have investigated the real-time response of cortical neurons to repeated perturbations, adaptation of the response from these neurons to the perturbation, and the development of a control strategy to reduce the perturbation effect on arm movement. The data generated from these experiments present unique opportunities to address several important questions in understanding cortical control of movement, such as the time course of response changes in cortical neurons as the monkey learns to anticipate the perturbation, the choice of control strategies adopted by the CNS to compensate for the perturbation, the relationship between adapted behavior and modified cortical activity, the effect of modified cortical spike patterns on the directional tuning properties, and the residual changes, if any, in cortical spike patterns after the removal of perturbations. These questions have direct implications for the development of a practical and robust neuroprosthetic system.

2. EXPERIMENTAL DESIGN AND DATA ANALYSIS

The Institutional Animal Care and Use Committee approved the behavioral paradigm and surgical procedures. The guidelines for general animal care by AAALAC and the Society for Neuroscience were followed.

2.1 Behavioral Tasks and the Perturbation

Three rhesus monkeys (maccaca mullata) were trained using operant conditioning to perform a three-dimensional center-out reaching task in which eight targets were located at the vertices of a 13 cm cube (see Figure 1). The start position for each movement was at the center of the cube and the 8 targets were presented in a randomized block design with 5 replications of each, for a total of forty successful trials (1 block = 40 trials). A successful trial required an appropriate sequence of actions.

The start of a trial began with the illumination of the center light (*Center-on*), and the monkey was trained to push and hold the center button for a minimum center-hold-time (CHT = 100 – 500 ms) to ensure the hand stationary until a target was presented. The center light then was extinguished and 1 of the 8 targets was illuminated (*Target-on*) at random order. The *Reaction-Time* (RT) from Target-on to Center-release had to be between 200 and 750 ms. The monkey reached to and depressed the illuminated target button within the allowable *Movement-Time* (MT <= 600 ms). The target button was to be held for a minimum *Target-Hold-Time* of 100 ms (THT = 100 to 500 ms), before the animal would receive a
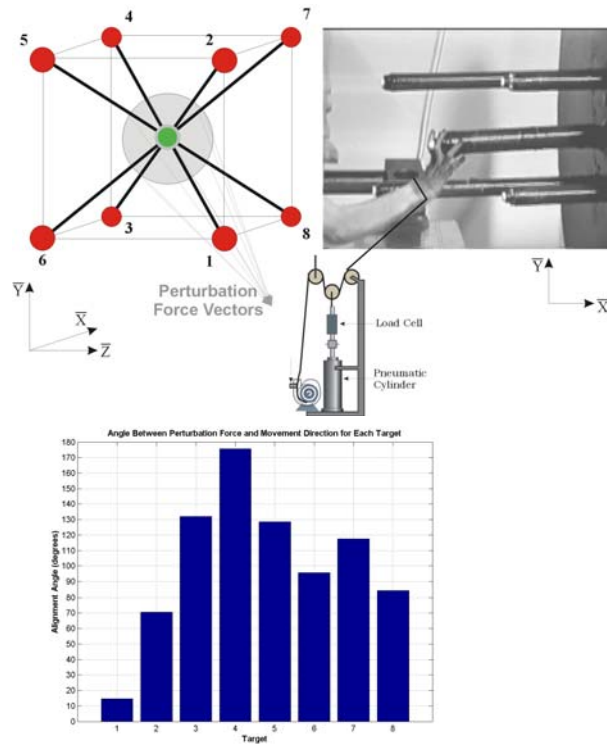

Figure 1: The apparatus for the reaching task is shown with the perturbation mechanism. Lighted push-button switches (1 cm diameter) are positioned on the ends of two short (14 cm) and two long (27 cm) rods located at the 4 corners of a 13 cm square and represented four of the eight vertices of a cube. Rotating the plate 180 degrees produces the remaining four targets. The monkey begins a trial by holding the center-button, then reaching for a lighted target. During the reach, a pneumatic cylinder is actuated to apply a pulling force to the wrist when the hand moves 20 mm from the start position (indicated by the gray circle). The gray vectors clustered around target 1 indicate the direction of the perturbation force for each target. The bar graph illustrates the alignment angle between the perturbation and reach directions for each target.

reward. The movement time is further divided into three smaller periods: movement initiation (LT), perturbation (PT) and the target acquisition (TAT).

To study the sensory feedback and descending cortical control of arm movement, we designed an apparatus that can deliver a transient perturbation force for any given duration at any prescribed time during a 3-D reaching movement. The apparatus consisted of a pneumatic cylinder, a recoil-mounted string attached to the subject's wrist, and a series of pulleys to guide and change the direction of the perturbation force (see Figure 1). A strain-gauge force transducer was mounted on the pulley attached to the cylinder and measured the tension in the string. The signal was sampled at 500 Hz. The hand and arm movement were monitored in real-time (Optotrak System, Northern Digital, Inc.) and sampled at 200 Hz. The perturbation trigger was set after the hand moved 20 mm from the center-hold position.

2.2 Chronic, Simultaneous Multi-unit Recording from Motor and Sensory Cortices

Four arrays of microwires (4x16 stainless steel or tungsten electrode arrays, 50 micron tip diameter) were permanently implanted in the arm areas of the left motor and sensory cortices of a rhesus macaque. Extracellular field potentials were recorded on a 96 channel MAP (Plexon, Inc., Dallas, TX). A threshold crossing marked the occurrence of a sorted action potential (spike), and spike times from all active channels were recorded in a data file along with behavioral event times. Sorted waveform samples (800 us clip) were also recorded throughout the experiment to track the stability of the neural recordings within a single experimental session and across multiple days.

Intra-cortical micro-stimulation (ICMS) was used to assess the functional connectivity of each electrode array. Brief (< 5 seconds) trains of cathodal current pulses (200 us, 300 Hz, 50 – 200 uA) were injected through a single electrode in the array while the arm was visually inspected for muscle twitches in response to the stimulation. The threshold current and location of evoked muscle twitches was recorded on an anatomical map of the dorsal and ventral surfaces of the arm. During a recording session, we used passive manipulation of the arm to test the responsiveness of each cell to movement and tactile stimulation. These response properties were compared with the ICMS results to produce a general map of the cortical region recorded by each array. We marked the location of each electrode array in the cortex by making small, electrolytic lesions (5 uA dc for 5 seconds) at three points in each implanted array.

2.3 Data Analyses

To document any adaptation in cortical control strategy and learning of perturbation dynamics, we designed an experiment that consisted of four phases completed over a five-week span: normal, perturbation, adaptation and extinction. We established the baseline data during the *normal* phase (unperturbed, 240 – 640 trials in 6-16 blocks/day. The pneumatic cylinder was activated but no perturbation force was applied. This was done to de-sensitize the animal to the sound emitted by the pneumatic valves and cylinder.

We began the *perturbation* phase on the last day of the normal trials. On this day, the subject would experience the first actual perturbation after 2 – 4 blocks (80 – 160 successful movements) of unperturbed trials. Then, the perturbation was applied on each consecutive reaching movement until the end of the day to establish the pattern of responses to the perturbation in cortical neurons, muscles, and arm movement trajectories.

The *adaptation* phase of the experiment consisted of 8 – 12 perturbation days for the three monkeys in which the perturbation was applied on consecutive trials after the first 80-240 unperturbed trials each day. At irregular intervals, we also disengaged the perturbation force during a reach to a randomly selected target (catch trials: 1 in 40).

On the last perturbation day, we disengaged the pneumatic cylinder after six perturbation blocks (240 trials) were completed. This marked the beginning of the *extinction* phase, and 2 more days of experiments were performed without perturbations.

Cortical, kinematic, and EMG data from each trial were grouped by each of the eight targets and the following experimental condition 1) normal, 2) perturbed, 3) catch, and 4) extinction. We aligned the data to the trigger for perturbation onset, which was a time reference at a central point in each experimental trial. This alignment preserved the time scale of the data across trials, which is important for comparing the temporal profile of cortical data with the observed behavioral measurements. For the cortical data, we computed average firing rates in each epoch by dividing the number of spikes in each epoch by the epoch duration. Combinations of these epochs were also used. These data allowed us to compare event-related cortical activity across perturbation conditions and target directions.

3. RESULTS

3.1 Perturbation Effects Are Different on Movements towards Different Directions

The hand position during the center-hold time was subtracted from the entire trajectory to locate the initial hand position at the origin (0,0,0). Normal and perturbed hand trajectories to four of the 8 targets are
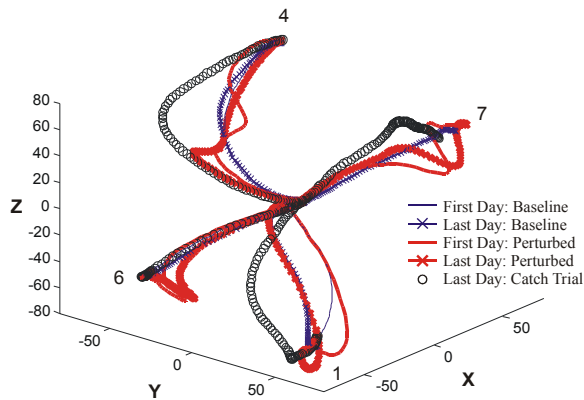
Figure 2: Hand paths to targets 1, 4, 6, and 7 are shown for different experimental conditions: normal unperturbed (thin lines), first day when the perturbation was introduced (thick lines), adapted (after many days of repeated perturbations, thick lines with cross), and catch trials (single no perturbation among repeated perturbations, circles). Notice the lack of predictive trajectory compensation to target 6.

shown in Figure 2. The normal trajectories exhibited consistent reach paths to each target. The thin traces show the hand paths during the first set of perturbation trials and demonstrate the transient displacements induced by the perturbation. The thick traces show the hand paths for those movements with the perturbation. Lines with crosses are movement paths from the later days after the subjects had learned the dynamics of the perturbation. The hand paths in the normal and perturbed trials were similar during the early phase of the reach, but the perturbation created a large deviation during the latter half of the movement.

Recall from Figure 1 that the direction of the perturbation pulling force and the directions of reaching movement toward the eight targets formed a range of angles. As a result, the effect of perturbation was different for the eight movement directions. When the movement direction was aligned with the perturbation direction, the effect would either assist or resist the movement (targets 1 and 4). When the movement direction was perpendicular to the perturbation direction (targets 6 and 8), the effect would be to divert the movement direction (*pure direction* perturbation). During movements to the remaining targets, a *hybrid* perturbation force is produced by the acute (target 2) or oblique (targets 3, 5 and 7) angle between movement direction and perturbation force vectors. The variety of effects from this perturbation would generate a rich set of data to investigate the control of arm movement to compensate for different external disturbances.

After a few days of exposure to the same perturbation, the subjects learned the timing and the dynamic effect of the perturbation on the arm movement, and developed a control strategy to overcome or reduce the disruption of the perturbation to the reach trajectory. This control action is reflected in the improved success rate of reaching the targets within the allowed time duration and less deviation in movement trajectory. To test for anticipatory correction of the expected disturbance we inserted a few unperturbed trials to "catch" the effect of erroneous anticipations. By comparing the catch trials to the normal and perturbed trials, we can identify signs of predictive, feedforward compensation. The adapted trials to targets 4 and 7 showed an anticipatory correction as the hand path deviated from the normal trajectory opposite to the expected perturbation. This trajectory compensation was not observed for target 6 and not clear for target 1, suggesting that different control strategies may have been used to counteract the perturbations to these targets.

3.2 Neural Response and adaptation to Perturbation

The peri-event time histogram in Figure 3 illustrates the spiking activity patterns of a single neuron recorded on the first and tenth perturbation days. The data are aligned at the onset of the perturbation and extend 500 ms in both directions to include the initiation and the perturbation phases of the reaching
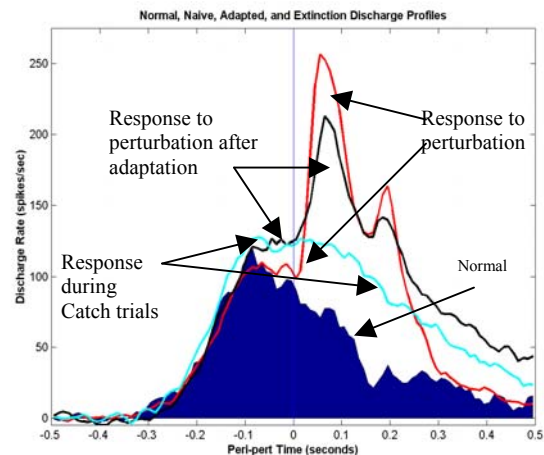

Figure 3: The accumulated histogram from 1 neuron on the first and last perturbation days. The histograms are aligned on the perturbation trigger (t = 0, approximately 110 ms after the movement initiation). The filled area histogram represents the normal discharge profile without experiencing any perturbation, and the histogram with the highest peak is from the first set of perturbation trials (naïve). The histogram with reduced response to the perturbation shows the discharge profile on the eighth perturbation day (adapted). The histogram from a catch trial in the last perturbation day is also shown.

movement. The filled area is the normal spike frequency pattern for the reaching task. The original and later adapted responses of the neuronal population are shown as indicated. The neuronal spike pattern during a catch trial (a no perturbation trial among repeated perturbation trials) is also shown.

The histograms demonstrate a consistent activity pattern from the cortical neuron during the task time; activity starts to increase around t = -.3 seconds and peaks near the point of movement initiation (t = -.1 seconds). The timing of the perturbation response is also consistent between the naïve and adapted trials, but the peak of the response is smaller after adaptation. The movement-onset activity peak is followed by a reduction in activity before the perturbation in naïve trials. After adaptation, this dip is not present or reduced significantly. Instead, the activity maintains a tonic rate until the perturbation evokes a response at the same latency observed in the naïve trials. This tonic activity is also evident in the extinction trials, and is probably related to anticipation of the perturbation.

One obvious change in neuronal activity after the introduction of the perturbation is the increased spike frequency during the complete movement cycle. The difference between the early and adapted responses to the same perturbation is mainly reflected in the increased activity prior to the perturbation onset (on the left of the vertical line) and decreased reflexive (feedback) response after the perturbation. The Wilcoxan rank-sum test indicated that the increase in firing rate between the movement initiation and the perturbation trigger was significant (alpha = .01).

4. DISCUSSION AND CONCLUSION

Sensory feedback may be used in shaping descending control commands after the neural controller adapts to a new task or environment. These new control commands can provide the feedforward compensation needed to improve performance of the new task. To investigate the development of feedforward compensation strategies, many recent studies have employed perturbation paradigms to study adaptations in control as subjects experience consistent perturbations. Human and non-human (Gandolfo et al. 2000) primates have been shown to adapt to perturbations. Thoroughman and Shadmehr (2000) found that error-driven feedback produced in a response to a novel force field perturbation shifted earlier in time as the subjects adapted to the perturbation, indicating that the perturbation compensation shifted from a feedback to a feedforward strategy.

In our research paradigm, we developed a perturbation mechanism that can be applied at any time during a natural 3-D movement with any desired perturbation duration. Multi-unit cortical activity was recorded chronically, allowing us to track the activity of a large population of neurons throughout the adaptation study. Changes in the discharge rate of motor and somatosensory cortical neurons are of specific interest in this study. A combination of no perturbation, repeated perturbation, random perturbation, and catch trials allowed us to investigate the real time learning and adaptation process in neural control of movement.

Arm kinematics and cortical neuron activities were recorded to measure changes in the control strategy used to execute the reach task. Task performance was quantified in terms of the reach kinematics and success rate. Marked improvement in the success rate is illustrated across the adaptation days, providing clear evidence for adaptation to the trajectory perturbation. The corrective movements made after release of the perturbation are more controlled after adaptation as demonstrated by the much smaller deviation in the hand paths. Since the perturbation is consistent, it becomes a fixed part of the task and the subjects learn to anticipate the perturbation. As a result, the subjects are able to plan a corrective strategy rather than try to resist the disturbance with a simple stiffness control strategy. The catch trials exemplify the development of a feedforward strategy to compensate for the expected perturbation.

Similar to the results of Evarts and Tanji (1976), two components of the perturbation response have been identified in the neural activity in motor cortex. A reflex component appears at a constant latency across all of the perturbation days. During adaptation, a volitional component of the perturbation response develops as the animal learns to anticipate the perturbation. It is likely that this component is related to the planned corrective movement that was observed in the catch trials. The histograms in Figure 3 show that after adaptation, the cell still shows a reflex response at 80 ms from perturbation onset. However, there is also increased activity in the pre- and post-perturbation intervals. These changes reflect the adaptation in control that has taken place throughout adaptation.

From Figure 2 we identified at least two different control strategies adopted by the neural control system: anticipatory trajectory compensation and stiffness modulation. The adaptive trajectory compensation is easily seen in the shift of hand trajectory direction before the perturbation onset (Figure 2, movement to targets 1, 4 and 7). No such shift was observed in hand trajectory to target 6 even though the performance was drastically improved as measured by the success rate. The changes in cortical neuron activity patterns were not conclusive on any major difference between the cumulative histograms when moving to target 6 from other targets.

Individual neuron activity patterns remain to be analyzed for further clarification.

An analysis of the arm configuration during the adaptation process indicated that coordinated joint angles changed more when moving to target 6 than to other targets. Figure 4 shows the phase plots of shoulder flexion-elbow flexion for targets 6 and 7. The effect of the adopted arm configuration when
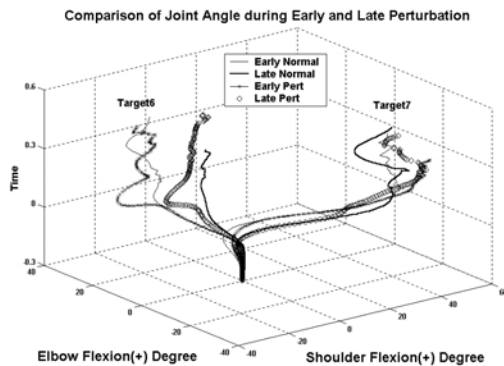

Figure 4. The phase plots of elbow flexion-shoulder flexion when moving to target 6 or 7. A significant change in arm posture after the adaptation is observed for target 6. When moving towards target 7, the change in arm posture is not as significant.

moving to target 6 increased the arm stiffness against the perturbation.

This preliminary data analysis demonstrates that our research approach has produced a rich data set for exploring control of arm movement at the cortical and muscular levels. Further analysis is necessary to evaluate the time-course of the adaptation that shifts the mode of control from feedback to feedforward perturbation compensation.

5. ACKNOWLEDGEMENT

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