## **REAL-TIME CONTROL OF A CORTICAL NEURAL PROTHESIS**

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Brain Computer Interfaces primarily use non-invasive devices – EEG-based methods - to interact with the central nervous system. Since the 1960's, with the development of the phrenic nerve stimulator, implantable devices that interact with the peripheral nervous system have been widely accepted. More recently, as signified by the FDA approval of a deep brain stimulator for movement disorders, interest has shifted towards direct communication with the brain. Research being conducted at Arizona State University, as a part of the NIH's Neural Prosthesis Program, is developing a cortical motor prosthesis. The goal is to design a system to record and analyze the activity of neurons in the motor cortex, and implement this as a control system for a robotic arm. One potential benefit of this type of system includes a more accurate and versatile means of manipulating an artificial limb. We have demonstrated, in an initial step, the feasibility of this approach.

Neurons in the cerebral cortex typically display broad cosine tuning, and those in the motor cortex have been shown to be broadly tuned to the direction of hand movement. These neurons will fire most rapidly for movements in their 'preferred direction', and least when movements are in the opposite direction. Knowing the parameters that describe a given neuron, very little information about of the action of the hand can be derived. When analyzed as a population, using a population vector or pattern recognition, a reconstruction with a high correlation to the true instantaneous velocity of the hand can be formed. The foundation of this work has been established using single-unit recording techniques; the same level of accuracy has yet to be proven in real-time using multi-unit recording. Technological advances are improving the ability to record and process the activity of multiple cells simultaneously. Concomitant with this, analytic techniques designed to extract information inherent in simultaneous recordings are making it possible to extract the information encoded in the neural signal with fewer numbers of cells. With this, we are progressing towards the goal of online robotic control.

When a large number of neurons is present, a vector sum of weighted preferred directions (a population vector) should well describe the task being performed. With fewer, relatively noisy cells, pattern recognition can provide a better estimation of the information present in the cortical signal. A new method is being developed to use a principal component analysis (PCA) to find the patterns of co-activation that can identify the ensemble activity throughout each movement. To do this, the cross-covariance of each neuron's activity with one another is calculated. After performing the PCA, the eigenvectors of the covariance matrix illustrate the patterns that best identify the group activity at any given moment. Once new cortical activity is related to known movements, an instantaneous velocity can be assigned.

Rhesus monkeys, implanted with chronic electrode arrays, were trained to perform a 3D center-out reaching task in a cubic workspace. Normalized neural activity from over 30 task-related, simultaneously recorded neurons was grouped to find the temporal patterns of co-activation. A PCA was employed to define these patterns and reduce the data to a handful of unique identifiers. This constituted the calibration process. Every 20ms, a sliding window of activity from all of the neurons was multiplied by the previously derived eigenvectors. This new set was compared with the training data in principal component space. The instantaneous velocity from the training data set to which the new data most closely matched was assigned for that time instant. No velocity was given if the pattern matched a point in time not associated with movement. Adding these velocities tip-to-tail formed the trajectory.

The system used to access the neural activity and the chronic electrode arrays were available commercially. Recordings from each microwire in the electrode assembly (NB Labs, Denison, TX) were obtained using a JFET buffer amplifier that connects to a multi-channel neural recording system (Plexon Inc., Dallas, TX). The recording system provided channel-selectable, variable gains (up to 30,000x) and bandpass filtering (50-12,000 Hz), before sampling each channel at 40,000 samples/sec. On-line spike discrimination was controlled interactively by the investigator by applying standard techniques to isolate the neural activity from the background noise. The system saved spike waveforms and timestamps for all of the channels simultaneously, and can be accessed in real-time using client programs. This architecture has been extended to include online analysis of the cortical signal and will eventually be used to drive the robotic arm.

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Using the system described above, client programs can be written which can make the necessary calculations to relate the neural activity to a control signal at 50 Hz. To run a robotic arm, an on-off signal, direction, and speed must be derived at every instant in time, and can be related back to the original arm movement for comparison. Over a two-month time period, the system correctly predicted when the hand was in motion over 80% of the time – with the most consistent errors occurring at the beginning and end of the movements. Comparing the angle formed between the true and the derived movements, a daily average angle ranged from less than 33 degrees to over 60 degrees. Endpoint prediction, being dependent on the prediction of movement onset, termination, and the instantaneous velocity at each movement interval, varied more substantially. The average displacement difference from the best day was approximately four cm off from the true endpoint, which lies 10 cm from the center of the cube.

Research is being directed at the formation of a real-time control signal to drive a cortical motor prosthesis. Although the accuracy of the current system is limited, it does provide three-dimensional motion control, deriving direction, speed, and movement initiation and termination, from the firing activity of motor neurons. Using the system described above, the conversion from neuronal activity to movement on a millisecond time-scale is attainable. Visual feedback should allow for learning and cortical remodeling. Once the animal is allowed to interact with the robotic arm as the task is being performed, we expect that the ability to control this device should improve. Therefore, further refinements in technology coupled with the addition of biofeedback should aid us in accomplishing our goal of an implantable, intracortical BCI.