

Real-time control of a robotic arm by neuronal ensembles

Eberhard E. Fetz

Chapin and colleagues demonstrate that simultaneous recordings from ensembles of cortical and thalamic neurons can be decoded in real time to allow a rat to control a robotic arm. These results may ultimately lead to the design of brain-operated prosthetic devices for human patients.

Extracting signals directly from the brain to control robotic devices has been a science fiction theme that seems destined to become fact. Neurons in the brain are constantly computing the signals required to control biological limbs. In principle, it should be possible to tap this information and use it to control a prosthetic limb. Taking a step toward this goal, Chapin and colleagues¹ demonstrate in this issue of *Nature Neuroscience* that the activity of ensembles of neurons in rats could be converted to a real-time signal operating a simple robotic 'arm', which the rats readily manipulated to obtain liquid rewards.

Chapin and colleagues first trained their rats to press a bar to move the single-hinged robotic arm in an arc to acquire a drop of water. With arrays of implanted electrodes, the authors simultaneously recorded the activity of several dozen neurons in motor cortex and thalamic areas activated during limb movements. Using principal component analysis, they found that a good predictor of the robotic arm movement could be derived from a prominent burst of activity preceding the bar press in many neurons. They summed the activity of 32 selected neurons, with appropriate weights, to derive a single time-varying 'neural population function' (NPF) appropriate for driving the robotic arm to retrieve the water. When they switched control of the robotic arm from the bar press to the NPF, they found that most rats continued to operate the arm and retrieve the

reward through neural activity. Interestingly, the associated bar-press movements often decreased or dropped out.

This study breaks new ground in several areas. Unlike comparable studies discussed below, this is the first demonstration that simultaneous recordings from large ensembles of neurons can be converted in real time and online to control an external device. An important factor in the success of these experiments was the ability to

Figure 1 schematizes the concept as it might be applied eventually to the human brain. Voluntary limb movements are normally controlled largely by neurons in motor cortex, whose activity is clearly involved in generating movements². The descending axons of the corticospinal neurons drive interneurons and motoneurons in the spinal cord. The cortical and spinal networks together compute the appropriate patterns of activity of motoneurons,

which directly contract arm muscles. This normal sequence can be disrupted by spinal cord lesions or neurodegenerative disorders like amyotrophic lateral sclerosis (ALS), which produces progressive paralysis. In such cases, the mind usually remains intact, and brain activity could in principle be used to operate prosthetic devices. Such activity could be derived from the large pyramidal cells in motor cortex, which present easy targets for microelectrodes. The recorded neural activity could be transformed by appropriate circuitry, such as the artificial

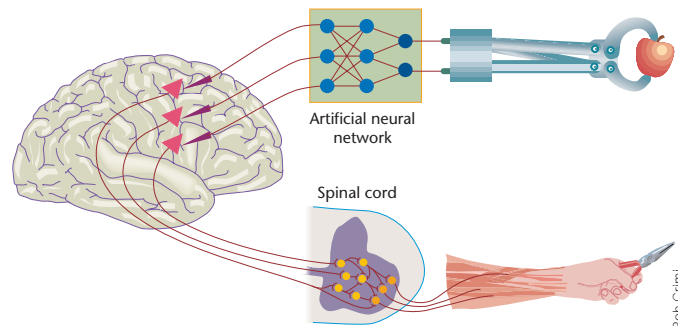


Fig. 1. Cortical neurons controlling voluntary arm movement could provide signals used to control a prosthetic arm. Large pyramidal neurons in motor cortex (red triangles) send axons to spinal cord, ending on interneurons and motoneurons. Motoneurons project to and contract arm muscles. Microelectrodes could record neural activity, which is transformed by an artificial neural network into signals required to operate a prosthetic arm.

monitor the activity of the same population of neurons over many weeks, which provided enough time to calculate the appropriate functions during normal motor behavior. These experiments also demonstrate the robust coding capacity of neural populations. Single neurons in the motor system are usually analyzed in terms of which parameter of movement their activity might encode—for example, muscle force, displacement, etc. This has engendered endless debates, which turn out to be largely irrelevant to the successful extraction of effective control signals from a population. Of course, these observations also have significant implications for possible clinical applications in neural control of prostheses.

neural network in the figure, into signals suitable for controlling a robotic arm.

Of course there is a large leap from showing that rats can operate a one-dimensional hinge with bursts of cell activity to enabling humans to continuously control a multi-jointed prosthetic limb under variable load conditions. Several labs are currently trying to solve the intervening problems.

The study of Chapin *et al.* extends the pioneering experiments of Humphrey and colleagues³, who showed that activity of a population of motor cortical cells could be used to predict the time course of several movement parameters. In monkeys performing reciprocal wrist movements, a weighted sum of the activities of cells could

Eberhard Fetz is in the Department of Physiology and Biophysics and Regional Primate Research Center, University of Washington School of Medicine, Seattle, Washington 98195, USA. e-mail: fetz@u.washington.edu

match wrist displacement, active torque or their rates of change (with different weights optimized for each parameter). Once derived, the weights could predict the time course of these parameters for additional, similar wrist movements. The prediction was reasonably close when only a few neurons were used, and the accuracy increased with the number of non-redundant cells included. In follow-up studies, Humphrey and colleagues have demonstrated that the activity of pre-recorded primate motor cortical populations could be used to control alternating movements of a robotic wrist offline^{4,5}.

Others have investigated how multidirectional movement parameters could be extracted from populations of motor cortex neurons. Lukashin and colleagues used previously recorded activity of a selected population of tuned motor cortex neurons to calculate isometric torques generated in two dimensions by a simulated arm⁶. Schwartz and colleagues have shown that the activity of populations of tuned motor cortex neurons can be used to reconstruct complex limb trajectories offline⁷ and have also demonstrated that simultaneously recorded populations of cells can provide real-time, offline control of a robotic arm reaching to targets in space.

Although most such efforts have focused on motor cortex neurons, Andersen and Shenoy plan to use neurons operating at earlier stages of motor preparation (R.A. Andersen, personal communication). Neurons in posterior parietal cortex are involved in generating plans to reach to visible or remembered targets and could provide signals representing a higher level of abstraction than motor cortex. Andersen and Shenoy are currently recording from the parietal reach region with a chronically implanted array of electrodes and will determine whether monkeys can use a population of posterior parietal cells to control the position of a virtual arm on a computer screen.

The raw recordings of randomly sampled neural activity are typically not optimal for direct control of a prosthesis, but two important factors will help. First, the transform can be optimized using a computing interface, such as an artificial neural network, to calculate appropriate control functions from the neural population activity. The simple weighted sum of activity, computed by a feed-forward convergent network, has proven remarkably effective in several studies^{1,3,8,9}, but recurrent networks could compute more sophisticated transforms, including history-dependent functions.

Secondly, the brain is flexible enough to allow subjects to learn to activate the recorded neurons in ways that provide optimal control. This flexibility, normally evident in the adaptive learning of complex movements, would also be expected to help subjects learn to better control prosthetic devices. Such flexibility was observed when monkeys learned to drive a meter arm to a reward level by activating neighboring motor cortex neurons in new combinations⁸ and by changing patterns of neural and muscle activity⁹. The monkeys readily learned in single online sessions to generate many different response patterns to drive the meter arm. In another demonstration of cortical flexibility, a recent study has shown that cortical cells can learn to represent a prosthetic tool as an extension of the limb¹⁰; many anterior parietal neurons that normally respond to objects approaching the forearm will extend their response fields to include a raking tool that the monkey has learned to use to retrieve food.

The normal delays between cortical activity and movements of a biological limb are about several hundred milliseconds. In contrast, signals taken directly from higher motor centers can generate effects more quickly, leading to interesting consequences. In the study of Chapin and colleagues, the neural recordings allowed the robotic arm to reach the goal before the bar press, and the rats soon dropped the unnecessary bar-press movements². Similarly, in previous experiments, monkeys were trained to generate bursts of motor cortical activity, which were often accompanied by limb movements; after repeatedly triggering the feeder by cell activity, the monkeys often discontinued the previously associated movements⁸.

A major hurdle in making successful neural prostheses is the technical problem of obtaining reliable long-term recording from isolated neurons in the brain. Such recordings involve invasive procedures, and the fidelity of single-neuron recordings from implanted electrodes tends to deteriorate with time. The problem is slightly easier if multiunit recordings are accepted, and these seem to provide adequate signals for extracting useful information⁵. Another approach involves implanting special 'cone' electrodes containing a nerve growth factor that lures developing neurites from neighboring cells into a pipette containing recording electrodes¹¹. These cone electrodes have yielded long-term recordings from a paralyzed ALS patient who learned to control the multiunit signals. A non-invasive alternative sources of brain signals is the scalp-recorded EEG¹². Subjects have

learned to control the position of a cursor by changing the frequency of the EEG¹³ or the DC level of cortical potentials¹⁴. However, the degree of control is limited, because the EEG has nowhere near the usable information coding capacity of neural populations. Another alternative source of signals is the EMG of proximal muscles, which may be available in amputees, but not in totally paralyzed patients. Although these alternatives are more accessible, the best source of detailed information would be populations of single neurons. Ultimately, an ideal solution would be a non-invasive imaging method with the spatial and temporal resolution to monitor cell activity.

Assuming that the technical problems of recording brain cells are eventually solved, where can we expect this work to lead? Given the possibility of reliably extracting real-time information from neural populations, we can imagine many symbiotic interactions between brains, computers and prosthetic devices. The annals of science fiction and current movie offerings are replete with imaginative scenarios. More realistically, the many locked-in ALS and quadriplegic patients would gain the welcome capacity to continue more meaningful lives. The extent to which these possibilities are realized will depend on overcoming some real-life technical obstacles, but these in principle seem ultimately surmountable.

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