Primer

Cognitive neural prosthetics

B. Pesaran[1], S. Musallam[2] and R.A. Andersen[2]

Paralysis affects millions of people, greatly impacting their lives. Causes of paralysis range from stroke and cervical spine injuries to neurodegenerative diseases such as multiple sclerosis and amyotrophic lateral sclerosis (Lou Gehrig's disease). In each of these conditions, the injury leaves the person unable to move without affecting their ability to think about moving. This is true even for patients that become locked-in; in this tragic condition people can lose the ability to control all or nearly all muscles, being unable to move or speak or even make eye movements, while maintaining consciousness and cortical processing.

Cortical neural prosthetics seek to help paralyzed patients by recording their thoughts directly from the brain and decoding them to control external devices such as computer interfaces, robotic limbs and muscle stimulators. These prosthetics 'read-out' signals by recording neural activity and are different from prosthetics for the deaf and blind that 'write-in' signals by delivering electrical stimulation. Broadly speaking, there are two different types of cortical prosthetics for paralyzed patients — motor prosthetics and cognitive prosthetics.

Motor-based prosthetics are mainly concerned with recording activity from motor cortical areas that is related to arm and hand movements. In this approach, recordings from cells have been decoded to position a cursor on a screen or move a robotic arm [1–3]. They have also been used to decode signals related to desired grip force of the hand [3]. Cognitive neural prosthetics are concerned with recording activity related to higher level cognitive processes that organize behavior. In this approach, recordings of neural activity have been used to decode the state of the subject, their goals and the expected value they place on those goals [4]. Decoding these and other cognitive processes directly means patients can have new ways to control their prosthetic device and their control can be more flexible.

Cognitive control signals are found in areas of the frontal and parietal cortices that are related to sensory-motor integration. These areas are involved in transforming sensory inputs into plans for action and are specialized for different movements [5]. For example, within the intraparietal sulcus of the posterior parietal cortex (PPC) there are areas specialized for planning eye movements (the lateral intraparietal area, LIP), reaching movements of the arm (the parietal reach region, PRR) and grasping movements of the hand (the anterior intraparietal area, AIP). Similar areas also exist in the frontal cortex, namely the frontal eye fields for eye movements and the dorsal and ventral premotor cortex (PMd and PMv) for arm and hand movements. Motor signals coexist with cognitive signals in these areas, so it is not the location of the recordings that distinguishes cognitive prosthetics from motor prosthetics. Instead, it is the type of information being decoded and how it is used to help patients.

In this primer, we shall examine the cognitive variables that can be used for cognitive prosthetics, and how the activity of single cells and local field potentials (LFP) encode these variables.

Goals

Representing the goals of our movements can be quite different from representing how we achieve those goals. The posterior parietal cortex and areas of the frontal cortex are part of a major pathway for visually guided movements that begins in visual cortex and ends in motor cortex. Activity in these areas does not represent movement plans according to the biomechanics of how we achieve our goals; the muscle and joint variables needed to acquire the target. Instead, activity in PRR encodes the goal of a reach in visual (eye) coordinates that are based on eye position [6]. PMd, which is a major frontal lobe projection target of PRR, encodes the goal of a reach based on both hand and eye position. It does so using a relative position code where the level of activity depends on the relative position of the hand and eye [7]. A similar relative coding is found in area 5 of the posterior

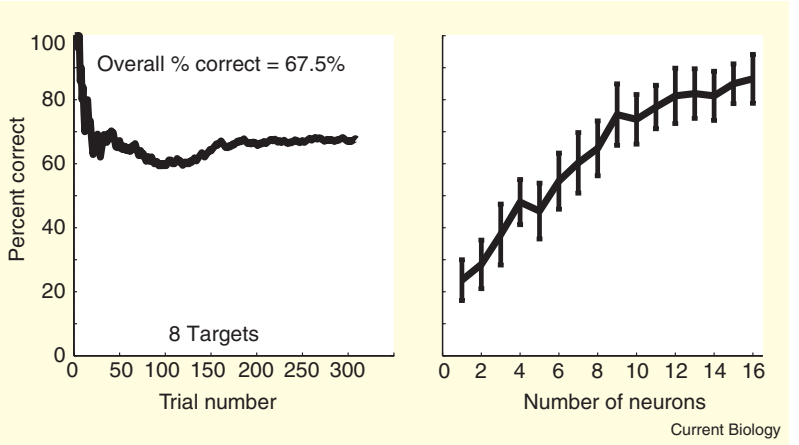

Figure 1. Goal decoding.

Left panel: cumulative performance of a brain control session using the memory period activity of 16 neurons recorded from PMd. Right panel: off-line decode using the same data, showing the effect of the number of cells on decode performance. The higher overall success rate for the offline decodes is due to a larger database being used. (Reproduced with permission from [10].)

Box 1

Local field potentials.

Extracellular electrodes can be used to record a variety of different signals from the brain. The principal distinction between these signals is whether their source is action potentials emitted by cells, or the synaptic events that accompany them. Action potentials are fast neural events typically lasting only a millisecond. Synaptic events are much slower, lasting tens of milliseconds and longer. Traditionally, different electrodes have been used to record these signals: Sharp microelectrodes inserted into the brain have been used to record action potentials while larger electrodes, often placed at the scalp, have been used to record the synaptic events in the form of an electro-encephalogram (EEG). In line with this, prosthetic research has focused on deriving control signals from EEGs recorded from the scalp [15] and single cell activity recorded with microelectrodes [16].

Each signal has advantages and disadvantages for prosthetic applications. An advantage of the EEG signal is that it is robust over time and is recorded non-invasively. A disadvantage is that it comprises signals summed over centimeters of brain and thus has limited specificity. Microelectrode recordings have spectacular specificity, recording the activity of one or a small number of neurons. This technique is invasive, however, requiring the insertion of the microelectrodes into the cortex. Other drawbacks of this technique are that the quality of the signal depends on the precise location of the electrode with respect to the neuron being recorded and the recorded signal degrades with time, in part due to the formation of scar tissue around the electrode tips.

While it is not possible to record action potentials without using microelectrodes, it is possible to record synaptic events without using scalp electrodes. Recordings of synaptic events using electrodes placed within or on the surface of the brain are called local field potentials (LFPs). In cases where both action potentials and field potentials are recorded using the same electrode, they can be separated by filtering the signal: action potentials are present at frequencies above 300 Hz and LFPs are present below 300 Hz.

Using LFPs is a new direction for prosthetic applications and offers an intermediate path between EEG and single cell activity. The EEG and single cell recordings sum activity over areas of very different scale: centimeters for the EEG and microns for cell recording. The LFP lies between these two scales of sampled activity. LFP activity is generated by current flows due to synaptic activity of hundreds or thousands of cells around the electrode tip [17]. Thus like single cell recordings it is invasive; however, it degrades less over time because the 'listening sphere' for LFPs is larger, and as a result less affected by local scarring. Also each recording electrode does not need to be placed precisely next to a neuron to record a signal, thus increasing the channel capacity of the implant. In this way, LFPs can balance the trade-offs inherent in using either single cell or EEG activity.

Despite this benefit, LFPs have received relatively little attention. This is, in part, because it has generally been believed that, like EEGs, the LFP signal does not contain a good deal of specificity because the listening sphere blurs activity from many neurons. However, recent research is leading to a revision of this view. Using signal-processing methods, a good deal of information can be decoded from LFPs about both cognitive and motor variables. Movement goals and cognitive states have been decoded using LFPs in posterior parietal cortex in monkeys [11,12] and in the ventral prefrontal cortex in humans [18]. Decodes of motor variables like the instantaneous direction of reach movements have also been made from the LFP in motor cortex of monkeys [19] and humans [20]. A particularly interesting aspect of these findings has been the observation that different variables are simultaneously encoded in the LFP signal in different frequency bands. For example, in parietal area LIP movement goals are encoded in the 25–90 Hz band while cognitive states are encoded below 20 Hz. Why this is the case is not known, but, along with other aspects of LFP activity, this is likely to be the subject of increasing scientific interest.

In summary, LFP activity can be used both to augment the usable lifetimes of microelectrode implants and increase the number of signals that can be decoded for prosthetic control. An important benefit of considering LFP activity is that it covers a wide range of neural signals between the extremes of single cell and EEG activity. This offers a great deal of flexibility that may be useful for engineering cortical prostheses that strike the right balance between ease-of-use and performance for a given situation.

parietal cortex [8,9]. These areas therefore encode reach plans in a high-level, cognitive manner that represents the goal of the movement itself. In contrast, activity in motor cortex encodes the direction to move the hand and so encodes the details of movement needed to acquire the goal. Cognitive prosthetics aim to decode movement goals themselves, leaving the determination of how to achieve those goals to other systems such as smart robotic controllers.

Brain-control experiments recording simultaneously from an ensemble of neurons from PRR or PMd have demonstrated that the goals of a reach can be decoded to position a cursor [10]. This recorded activity is interpreted with a computer algorithm and the cursor is positioned without the animals making any reach movements. This form of prosthetic can operate very quickly and goals can be decoded with relatively good accuracy in just 100 milliseconds. This approach also requires relatively few neurons [10]. The left panel of Figure 1 shows the cumulative success using eight target locations and the activity of 16 PMd neurons. The right panel shows an off-line analysis, using the same data, where different numbers of cells are used. Not surprisingly, decoding performance improves with the number of cells recorded, but good performance is possible with even a small number of cells.

Cognitive states

Our behavior is orchestrated so that the timing of different movements is coordinated. We can conceptualize this coordination using the idea of cognitive states. A simple example of movement-related cognitive states has two states; one when the subject is planning a movement and another when the subject is executing a movement. Having separate states for planning and executing separates the control of where we want to move from when we want to move. This is useful as sometimes we think about moving but do not

necessarily want to move straight away.

Local field potential (LFP, see Box 1) recordings from area LIP, an eye movement area in the posterior parietal cortex, have been used to identify which neural signals carry information about both the goal of a planned saccade, and whether the monkey is in the state of planning or executing a saccade [11]. The information about the saccade goal was carried by differences in the power in a higher frequency band (25–90 Hz), while information about the state of the animal was carried in the lower frequency band (0–20 Hz). Spikes were recorded at the same sites as the LFPs. A comparison of single trial decodes at individual recording sites showed that both LFPs and spikes could determine the direction of planned saccades in the preferred and non-preferred directions and with the same success rate (Figure 2A). Interestingly, the transition from planning to executing a saccade could be simply decoded with LFPs but not with spikes (Figure 2B).

Decoding different types of movements, such as eye movements and arm movements, will require additional cognitive states and recent work has shown such state information can be decoded from the PRR. LFPs in the PRR were found to carry information about both reach goals and five different cognitive states; baseline, planning a saccade, planning a reach, executing a saccade, and executing a reach [12]. Decodes of reach goals for eight directions were achieved for both spikes and LFPs, with spike decodes performing slightly better. Cognitive states were decoded with spikes and LFPs and in this case LFPs were better, similar to what was found in LIP. These results show cognitive prosthetics can simultaneously decode goals and a variety of states from the same brain areas.

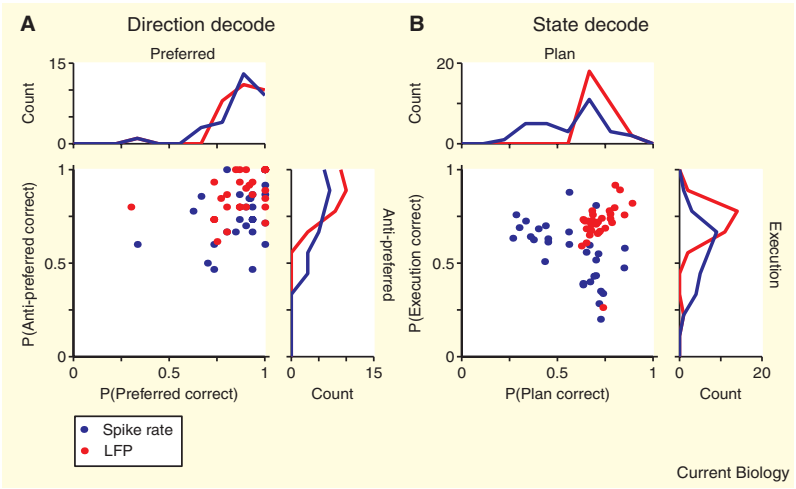

Figure 2. Single-trial decoding of cognitive states.

(A) Movement goal was decoded using spike rate (blue) and the LFP spectrum (red). Each dot represents a single cell or site. Horizontal axis is the probability that a saccade to the preferred direction is decoded correctly. Vertical axis is the probability that a saccade to the anti-preferred direction is decoded correctly. Line plots show the histograms of cell/site counts for each direction. (B) Movement state decode. Horizontal axis is the probability that the activity from the plan state is decoded correctly. Vertical axis is the probability that the activity from the execution state is decoded correctly. Line plots show the histograms of cell/site counts for each state. (Reproduced with permission from [11].)

Expected value

In addition to movement goals and states, another useful cognitive variable is the expected value we place on a given action. A number of brain areas represent expected value [13,14]. This activity is thought to be a central element for decision making; we choose the course of action that we expect will have the best outcome. Recent experiments have shown that expected value signals for fluid preference (Figure 3A,B), probability of reward (Figure 3C) and magnitude of reward (Figure 3D) can be determined from the activity of neurons in the PRR [10].

In these experiments, the animals were informed at the beginning of each trial whether to expect a preferred reward, such as orange juice, or a non-preferred reward, such as water. When the more valued reward was expected, the neurons had improved spatial tuning. In line with this finding, on-line decodes for goals improved when the monkeys expected a more preferred reward (Figure 3E). Additional offline decodes showed that both the movement goal and the expected reward could be simultaneously decoded from the same cells. Given the influence of decision-related variables on movement planning activity, decoding these variables may become an important new area for cognitive prosthetics.

Summary

A variety of cognitive variables can be decoded from neural activity and used for neural prosthetic control by subjects. These higher-level signals are complementary to motor variables that describe the details of movement. In the future, combining cognitive-based and motor-based approaches in a single prosthetic system could lead to the greatest benefits for patients.

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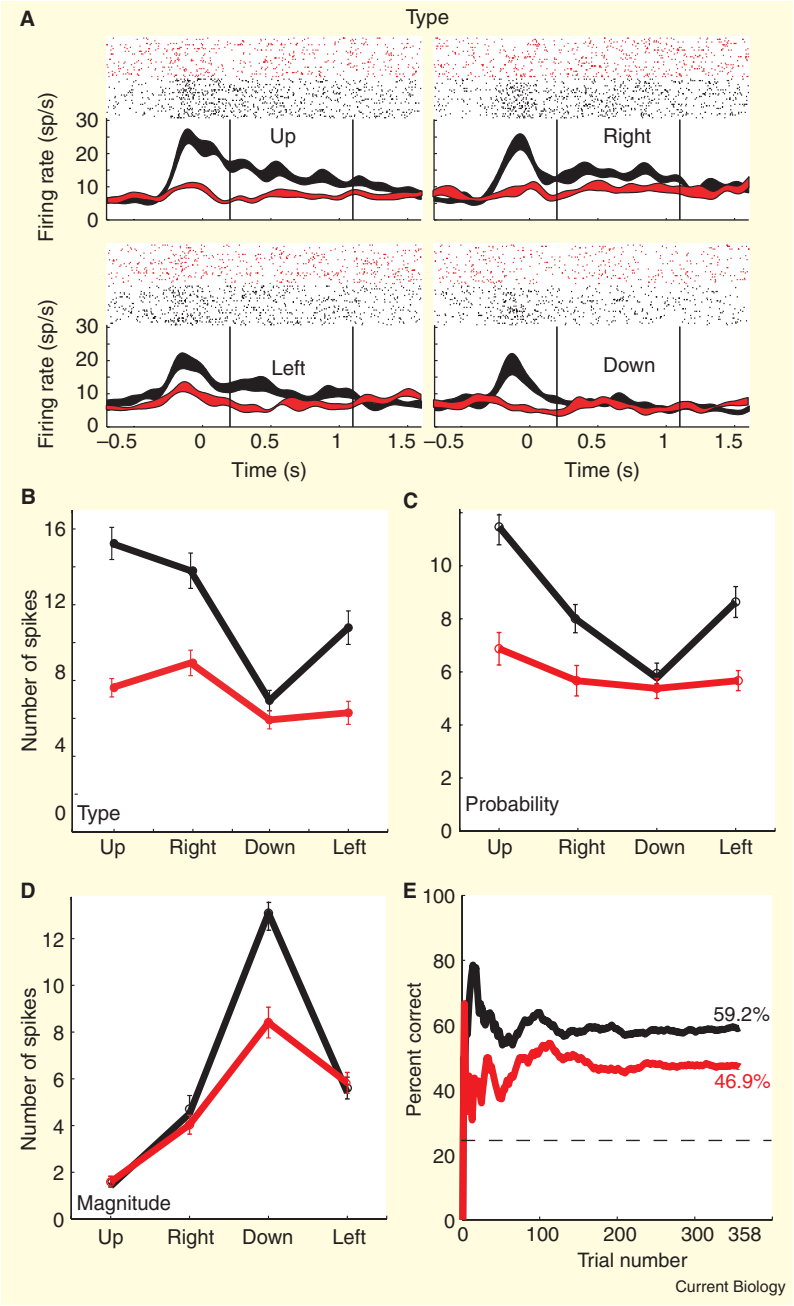

Figure 3. Expected value.

(A) Response of a neuron during brain control trials when the type of reward the monkeys expected to receive after completion of a successful trial was varied; orange juice (black) versus water (red). The direction of the intended reaches that elicited the responses is written on the figure. Rasters are aligned to the onset of the memory period. Vertical lines superimposed on the figures enclose the 900 ms memory segment used to calculate the tuning curves. (B) The neuron's tuning curve. Monkeys were instructed to form reach intention to a previously cued location. (C,D) Tuning curve calculated from the firing rates of two additional cells while the (C) probability and (D) magnitude of reward was varied. (E) Brain control results from one session during preferred (black) and non-preferred (red) reward conditions. Dashed line represents chance. Decode performance for the two reward conditions is indicated on the plot. (Reproduced with permission from [10].)

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[1]Center for Neural Science, 4 Washington Pl. Rm 809, New York University, New York, New York 10003, USA. E-mail: bijan@nyu.edu.
[2]Division of Biology, Caltech 216-76, Pasadena, California 91125, USA. E-mail: sam@vis.caltech.edu, andersen@vis.caltech.edu