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Selecting the signals for a brain–machine interface

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Brain–machine interfaces are being developed to assist paralyzed patients by enabling them to operate machines with recordings of their own neural activity. Recent studies show that motor parameters, such as hand trajectory, and cognitive parameters, such as the goal and predicted value of an action, can be decoded from the recorded activity to provide control signals. Neural prosthetics that use simultaneously a variety of cognitive and motor signals can maximize the ability of patients to communicate and interact with the outside world. Although most studies have recorded electroencephalograms or spike activity, recent research shows that local field potentials (LFPs) offer a promising additional signal. The decode performances of LFPs and spike signals are comparable and, because LFP recordings are more long lasting, they might help to increase the lifetime of the prosthetics.

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Abbreviations

EEG	electroencephalogram
LFP	local field potential
LIP	lateral intraparietal area
M1	primary motor cortex
PMd	dorsal premotor cortex
PRR	parietal reach region

Introduction

Brain–machine interfaces, which connect brain tissue to machines, have many applications in medicine. These interfaces are bidirectional: they can 'write-in' signals to the brain, typically through electrical stimulation, or 'readout' signals by recording neural activity. Examples of great successes with 'write-in' devices have been cochlear prosthetics [1,2] for deaf patients and deep-brain stimulation [3] for Parkinson's disease patients.

Recently, there has been considerable progress in designing 'readout' prosthetics to assist paralyzed patients. Because patients can often still think about moving the goal is to record these movement intentions, interpret them and use them for the control of external devices. Researchers have demonstrated that monkeys can control the trajectory of cursors on a computer screen without the animals making any movements [4,5••,6]. Signals related to desired grip force have also been decoded and used to control the size of a cursor [5••]. One-dimensional cursor movements have been accomplished using spike activity recorded from a paralyzed human [7]. These recordings have been made largely, but not exclusively, from the motor cortex, a part of the brain that normally encodes parameters of limb movements.

These experiments raise the natural question of what other signals can be decoded from the brain and used for neural prosthetic applications. Two high-level cognitive signals have recently been shown to be viable for prosthetic control [8••]. These brain signals specify the goal of an intended movement and the value of the reward the subject expects to receive for successfully completing a task. The goal signals can be used to operate external devices such as a computer, robot or vehicle and the expected value signal can be used continuously to monitor a patient's preferences, motivation and mood. Because expected value signals are important for forming decisions, they might also be used to augment decodes of the decisions of patients. Moreover, these results suggest that a large number of high-level cognitive signals, from emotions to speech, can be decoded from different parts of the brain to increase the ability of paralyzed patients to communicate and interact with the outside world.

A second new direction concerns the nature of the electrical signals recorded from the brain for prosthetic applications. Until now, the electroencephalogram (EEG) [9] or recorded action potentials from single neurons have been used [10•]. A third type of signal, the local field potential (LFP), is now showing considerable promise [11,12•,13]. Although the precise source of LFP activity is not well understood, this signal is predominantly generated by excitatory synaptic potentials in the vicinity of the electrode tip [14,15]. It has several advantages, similar to EEG, it is easy to record and robust over time, and similar to single-cell recordings, it provides highly specific information.

Goal

One major pathway for visually guided movements begins in the visual cortex and proceeds to the posterior parietal cortex [16] and then to motor areas in the frontal lobe [17]. Within the posterior parietal cortex, there is an

anatomical specialization for function. The lateral intraparietal (LIP) area is specialized for saccadic eye movements [18], the parietal reach region (PRR) for reach [19] and the anterior intraparietal area for grasp [20].

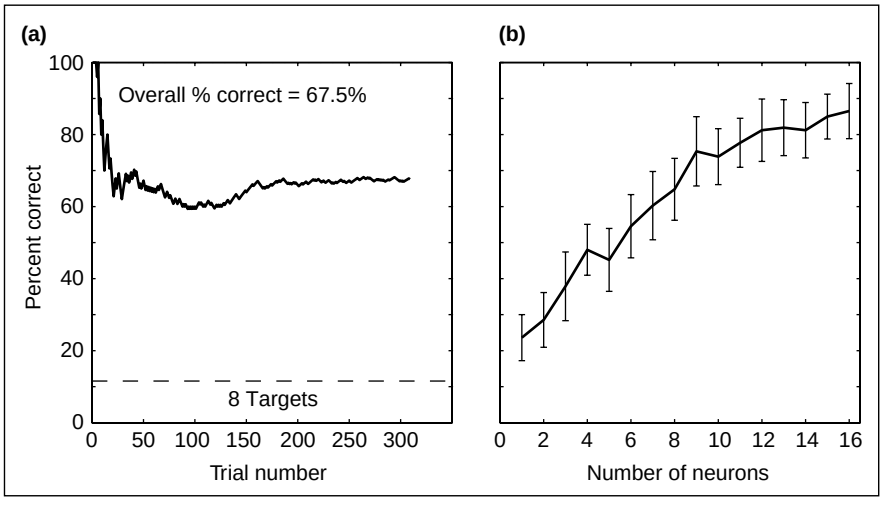
Activity in PRR indicates the goal of a reach in visual (eye) coordinates [21]. Thus, it codes reach plans in a high-level, cognitive fashion. For example, PRR neural activity codes the intention to reach to an object at a particular location in space, whereas motor cortex codes the direction to move the hand. The apparent homolog of PRR has been determined in humans using functional magnetic resonance imaging [22,23]. One of the frontal-lobe projection targets of PRR, the dorsal premotor cortex (PMd), also appears to contain a subset of cells that code reaches in this more cognitive form [24–26,27••].

Recent experiments recording simultaneously from an ensemble of neurons have demonstrated that the goals of a reach can be decoded in brain control experiments from monkey PRR and PMd [8••]. This recorded activity is interpreted with a computer algorithm and used to position a cursor on a computer screen without the animals making any reach movements. This form of prosthetic can operate very quickly; goals can be decoded with relatively good accuracy in just 100 ms. This approach also requires relatively few neurons [8••,28]. Figure 1 (left-hand panel) shows the cumulative success using eight target locations and the activity of 16 PMd neurons. The right-hand panel of Figure 1 shows an offline analysis, using the same data, where different numbers of cells are used. Not surprisingly, the more cells recorded, the better the decode but good performance is achieved even with a small number of cells. Although the cells in PRR code goals in retinal coordinates, early data suggest that eye movements do not adversely affect the decodes [8••]. This could be the result of a combination of factors: PRR activity compensates for eye movements [29], PRR neurons carry eye position information [30] and eye–hand coordination is highly stereotyped [31].

Expected value

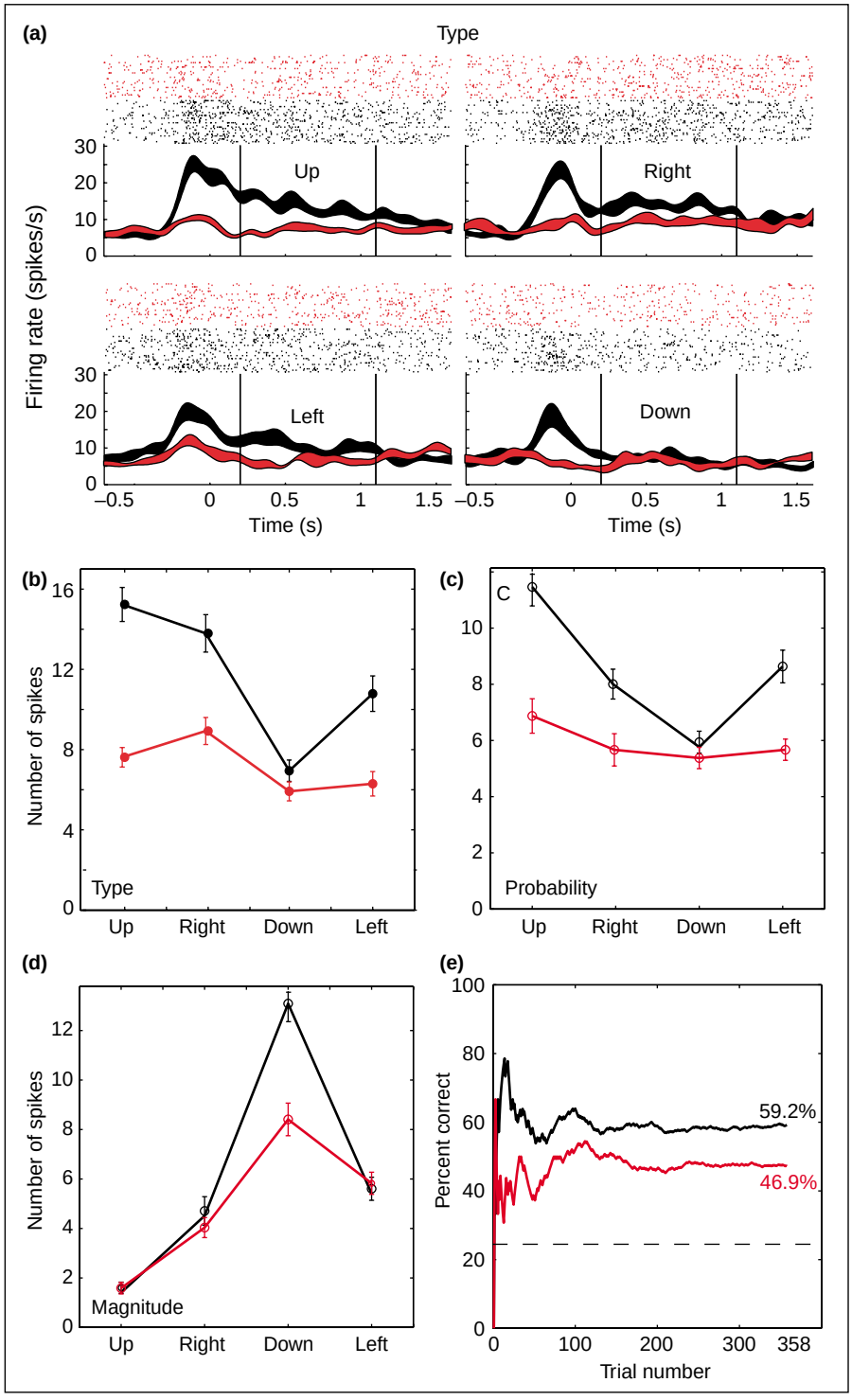
Several brain areas represent the expected value of reward [32••,33,34]. This activity is thought to be a central element for decision making; we choose the course of action that we expect will have the best outcome. Recent experiments have shown that expected value signals for fluid preference (Figure 2a,b), probability of reward (Figure 2c) and magnitude of reward (Figure 2d) can be determined from the activity of PRR neurons [8••]. The animals were informed at the beginning of each trial whether to expect a preferred (e.g. orange juice) or nonpreferred (e.g. water) reward. When the more valued reward was expected, the neurons had improved spatial tuning. As a result, the online decodes for goals improved when the monkeys expected a preferred reward (Figure 2e). Moreover, offline decodes showed that both the target location and the expected reward could be simultaneously decoded. These results show that more than one cognitive variable can be read out from the same population of neurons at the same time. Whether these signals code expected value *per se* or motivation that is a consequence of expected value, is an interesting question for future research [35]. However, from a prosthetics perspective, either signal will be very useful.

Figure 1



Decode performance increases with the number of recorded cells. **(a)** Cumulative performance of a brain control session using the memory period activity of 16 neurons recorded from the PMd. **(b)** Offline 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 a result of a larger database being used. Reproduced with permission from [8••].

Figure 2



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) and **(b)** its tuning curve. Monkeys were instructed to form reach intention to a previously cued location. The direction of the intended reaches that elicited the responses is included in the subparts of 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. **(c,d)** Tuning curves 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 nonpreferred (red) reward conditions. The dashed line represents chance. Decode performance for the two reward conditions is indicated on the plot. Reproduced with permission from [8••].

Local field potentials

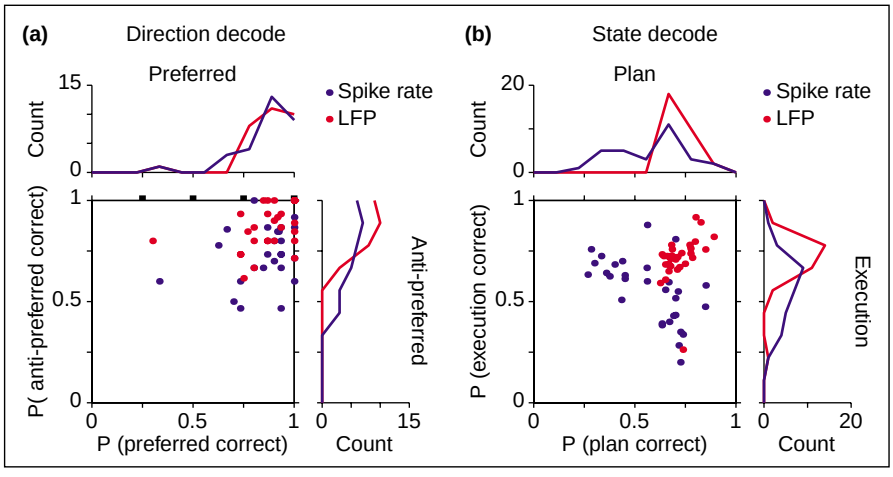
A second new direction concerns the electrical signals that are recorded. Prosthetic applications have traditionally used EEGs [9], which are brain waves recorded from the scalp, and single-cell activity recorded with microelectrodes [10]. The advantage of the EEG signal is that it is robust over time and is recorded noninvasively. 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. However, this technique is invasive, requiring the insertion of the microelectrodes into the cortex. Another drawback of this technique is that the recorded signal degrades with time, in part owing to the formation of scar tissue around the electrode tips [36]. Nonetheless, advances in electrode design are showing promising results in extending single-cell recording time [37–39].

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. This signal comprises the activity of hundreds or thousands of cells around an electrode tip inserted into the cortex or placed on the cortical surface. Thus, like single-cell recordings, it is invasive; however, it degrades less over time because the 'listening sphere' for LFPs is large, and as a result is less affected by local scarring. It was generally believed that, like EEGs, the LFP signal lacks specificity because it is a sum of the activity of many neurons. However, recent research has indicated that, using signal-processing methods, a good deal of information can be decoded from LFPs, and thus these signals can be used to augment the usable lifetimes of microelectrode implants.

LFP recordings from LIP, a region in the posterior parietal cortex involved with planning eye movements, carry information about both the direction of a planned saccade and whether the monkey is in the state of planning or executing a saccade [11]. The direction information was carried by differences in the power in a higher frequency band (30–100 Hz) and the state of the animal 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 nonpreferred directions, and with the same success rate (Figure 3a). Interestingly, the transition from planning to executing a saccade could be simply decoded with LFPs but not with spikes (Figure 3b). The direction tuning in the higher frequencies (gamma band) might result from the columnar organization for eye movement direction in LIP [40].

PRR also carries information in the LFPs about the direction of planned reaches and five behavioral states, including baseline, planning a saccade, planning a reach, executing a saccade and executing a reach [41]. Direction decodes for eight directions were achieved for both spikes and LFPs, with spike decodes performing slightly better. States were decoded with spikes and LFPs, and in this case LFPs were superior. Decodes for the direction of

Figure 3



Single-trial decoding of a movement plan. **(a)** Direction was decoded using spike rate (blue) and the LFP spectrum (red). Each dot represents a single cell or site. The horizontal axis represents the probability (P) that a saccade to the preferred direction is decoded correctly. The vertical axis represents the probability that a saccade to the anti-preferred direction is decoded correctly. Line plots show the histograms of cell or site counts for each direction. **(b)** State decode. The horizontal axis represents the probability that the activity from the plan state is decoded correctly. The vertical axis represents the probability that the activity from the execution state is decoded correctly. Line plots show the histograms of cell or site counts for each state. Reproduced with permission from [11].

reach movements from LFPs have also been made from the motor cortex of monkeys [12•] and humans [13,42].

Conclusions

A goal of neural prosthetic research is to design a system that can decode several control signals. Among the control signals that have been demonstrated so far are motor parameters of desired trajectory [4,5••,6] and grip force [5••,43] and high-level cognitive variables of goals and expected value [8••]. Similar approaches could in principle be extended to speech, emotions and, in fact, any number of cognitive variables.

Although it would be ideal to decode a large number of cognitive signals, it is not yet clear which cortical areas, or how many areas, need to be implanted to achieve this goal. The same signals often exist in more than one area; for example, goal signals can be extracted from the PRR and PMd [8••], and movement trajectories from motor, premotor and the parietal cortex [5••,44]. However, some areas appear to be better than others for a particular function [5••,27••]. More than one signal can be decoded simultaneously from an area; examples are goal and expected value from the PRR [8••] and trajectory and grip force from the motor cortex [5••]. The animals also learn to improve their performance in brain control tasks over a period of weeks [5••,6,8••,45]. This plasticity suggests that a cortical area can be trained to perform more than one function.

The above considerations suggest that not many areas are needed. However, neural network simulations indicate that the more tasks a single network is trained on, the more poorly it performs, especially if the tasks are computationally, fundamentally different [46]. Such an observation would argue for sampling several areas — ideally those that are naturally designed for processing the desired cognitive variables. Another potential advantage of a multi-area approach is to increase the number of channels for communication. For example, a subject could use a cursor and letter board to spell out words. However, electrodes within speech areas would in principle enable the direct decoding of speech without the need for a cumbersome letter board. Likewise, the patient could use the cursor to answer questions about emotional state, something that healthy subjects continuously convey by body language and voice inflections. Again, a direct readout from emotion centers would provide for continuous communication of emotional state. Moreover, in both of these examples the motor cortex would then be freed to perform other tasks concurrently. Thus, it would be desirable to use more than one cortical area to increase the ability of patients to communicate and manipulate the outside world.

LFPs can extend the lifetime of implants. They can provide almost as much information as spikes for some parameters, and are even better for others [11,12•]. Using LFPs in the posterior parietal cortex produces a better decode performance for action planning and execution states. Similar improvement might be found for decoding attentional state because attention-driven changes in LFPs have been observed with negligible changes in spike rate [47].

Why do decodes using LFPs sometimes outperform those using spikes? One possibility is that LFPs represent an average of activity of many neurons, and as such are less noisy. This is likely to be the case when the recording electrode is within a cortical column formed by cells with similar response properties. Another possibility is that LFPs and spikes might carry somewhat different information. For example, recorded spiking activity is biased toward the activity of larger cells, which are more likely to have connections with other brain areas, whereas LFPs are generated by local synaptic activity [14,15]. Therefore, spikes might largely represent the outputs of an area and LFPs might largely reflect the inputs to an area and local processing within an area.

Thus, two categories of signals seem ripe for future progress in the development of neural prosthetics. Signals conveying different cognitive functions are a rich source of multiple channels for communication. It will be particularly important to see what cognitive signals can be conveyed by human paralyzed patients using cortical prosthetics. LFPs have the potential to prolong the lifetime of electrode implants and, in some cases, particularly those related to cognitive states, they can improve the decode performance. In other cases, they can provide a second source of signal, which, when combined with spikes, can achieve more robust decodes.

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