AN INTRODUCTION TO NEURAL INTERFACES

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INTRODUCTION

Multiple neurological disorders (e.g. traumatic and non-traumatic spinal cord injury, motor-neuron disease, neuromuscular disorders, and brainstem strokes) can result in severe and devastating paralysis. Patients cannot perform simple activities and remain fully dependent for care. Especially in patients with high cervical injuries, advanced amyotrophic lateral sclerosis (ALS) or brain-stem strokes, the effects are especially devastating and often leave patients unable to communicate. While there has been extensive research into each disorder, little has proven to be clinically effective for rehabilitation of long-term disability.

Brain-machine interfaces (BMIs) offer a promising means to restore motor function [1-6]. In the patients described above, while the pathways for transmission of signals to muscles are disrupted, the brain itself is functional. Thus, BMIs can restore function by communicating directly with the brain. For example, in a 'motor' BMI, a subject's intention to move is translated in real-time to control a device. As illustrated in Figure 1, the components of a motor BMI include: (1) recordings of neural activity, (2) algorithms to transform the neural activity into control signals, (3) an external device driven by these control signals, and (4) feedback regarding the current state of the device.

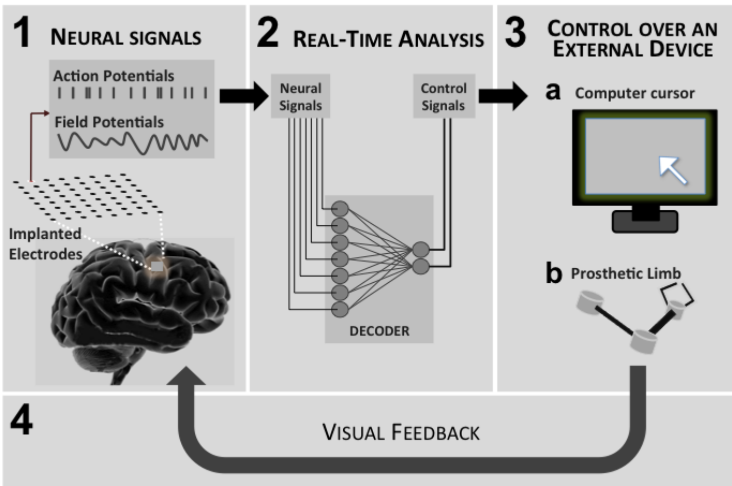

Figure 1: Components in a Brain-Machine Interface (BMI)

What signals can be recorded from the brain?

Many sources of neural signals can be used in a BMI (Figure 2). While EEG signals can be obtained non-invasively, other neural signals require invasive placement of electrodes. Three invasive sources of neural signals include electrocorticography (ECoG), action potentials or spikes and local field potential (LFP). Spikes and LFP are recorded with electrodes that penetrate the cortex. Spikes represent high-bandwidth signals (300-25000 Hz) that are recorded from either single neurons ('single unit') or multiple neurons ('multiunit' or MUA). LFPs are the low frequency (~0.1 to 300 Hz) components. In contract, ECoG is recorded from electrodes that are placed on the cortical surface. ECoG signals may be viewed as an

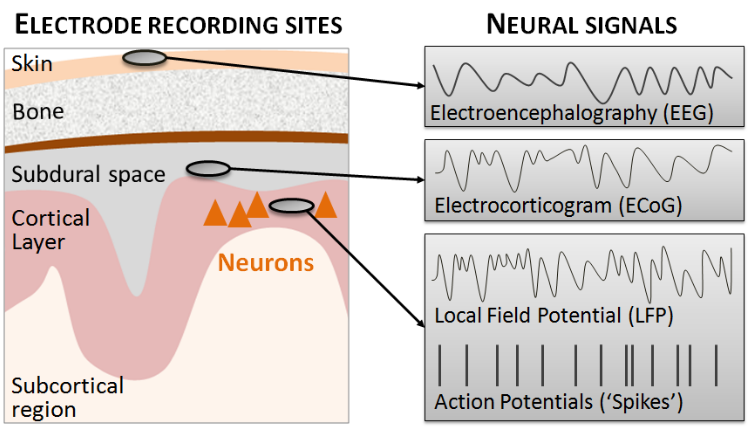

Figure 2. Sources of neural signals. EEG is recorded from the skin surface. ECoG, LFP and action potentials are recorded through electrodes placed invasively through the skull.

intermediate resolution signal in comparison to spikes/LFP and EEG. It is worth noting that there is still considerable research into the specific neural underpinning of each signal source and what information can be ultimately extracted regarding neural processes.

Decoding Neural Signals from Motor Cortex

There is a long history of monitoring neural signals from motor cortex [7-10]. While the initial body of work focused primarily on single neurons, there was also initial efforts to interpret the neural representation in small groups of neurons (i.e. neural 'ensembles') [11]. Over the past decade the advent of chronic multielectrode recoding technology has allowed for the simultaneous monitoring of large sets of neurons from multiple motor areas. Initial studies simultaneously recorded over 100 neurons in non-human primates and demonstrated the ability to predict limb motion in real-time [2,10,12,13]. While these initial efforts focused on spike recordings, subsequent work examined the contribution of other signal sources such as LFP and ECoG [14-16]. The topic of decoding has increasingly gained prominence in the field of neuroscience and neural engineering. Ultimately, the ability to 'read out' patterns of ensemble neural activity can help elucidate the 'neuronal code' and reveal how information is distributed over cortical and subcortical regions and how it flows among regions. From the perspective of BMIs, efficient decoding of neural activity will allow optimal interpretation of a user's intention.

'The decoder'

A critical component of a BMI is the transform of neural activity into a reliable control signal (i.e., the decoder shown in panel 2 in Figure 1. The decoder is an algorithm that converts the neural signals into control signals. There is considerable uncertainty as to the exact properties of a decoder that may best facilitate stable, long-term prosthetic control. One important distinction between classes of decoders is biomimetic versus nonbiomimetic [17,18]. In the case of biomimetic decoders, the transform attempts to capture the natural relationship between neural activity and a movement parameter [13]. In contrast, nonbiomimetic decoders can be more arbitrary transforms between neural activity and prosthetic control [18,19]. It had been hypothesized that learning prosthetic control with a biomimetic decoder is more intuitive. Recent evidence, however, increasingly reveals that learning is critical for achieving improvements in the level of control over an external device (e.g., a computer cursor, a robotic limb) for either type of decoder [3,4,18,20]. This is linked to the notion of learning an 'internal model' for natural motor control of a limb [18]. Our results also suggest that long-term stability is important for developing an internal model for the decoder. Of course, it is important to point out that requirements for learning a novel transform could have limitations. For example, it remains possible that for neural control of devices approaching the complexity of natural movements, this process would be insufficient.

What can be controlled using neural signals?

A central goal of the field of BMIs is to improve function in patients with permanent disability. This can consist of a range of communication and assistive devices such as a computer cursor, keyboard control, wheelchairs, or a robotic limb. In the ideal scenario, the least invasive method of recording neural signals would allow the most complex level of control. Moreover, control should be allowed in an intuitive manner that resembles the neural control of our natural limbs. There is currently active research into developing and refining techniques to achieve the most complex control possible using each signal source.

One measure of complexity is the degrees of freedom that are controlled. For example control of a computer cursor on the screen (i.e. on the 'x' and 'y' axis) represents 2 degrees of freedom (DOF). Control of a fully functional prosthetic upper arm that approaches our natural range of motion would require approximately 7 DOF. If the functionality of the hand and fingers are included, then an even more complex level of control would be required.

There has been a large-body of research on the use of non-invasive recording of EEG signals [5,21-24]. Studies suggest that 2 DOF control using EEG is feasible [21]. There are also promising reports of patients with advanced ALS communicating via email using EEG based BCIs. Known limitations of EEG based BCI's include its 'signal-to-noise' ratio (due to filtering of neural signals by bone and skin) and contamination by muscle activity [5,22]. Ongoing research aims to test usability in a more general non-research setting as well as targeted use in patients with disability.

Numerous studies now indicate that BMIs using invasive recording of neural signals can allow rapid control over devices with multiple DOF [10]. The vast majority of this research has been conducted using recordings of spiking activity via implanted microelectrode arrays. Initial preclinical studies have been performed largely in able-bodied non-human primates [2,10,25]. Initial studies demonstrated the feasibility of control over a computer cursor. More recently, there has been demonstration of real-time control of a robotic arm with 4 DOF control that allows for self-feeding [26]. Importantly, there are ongoing efforts to translate this research into the clinical arena (see subsequent document from Dr. Leigh Hochberg). While a neural interface that is based on the fundamental unit of the nervous system is quite appealing (i.e. spiking activity from single neurons), a challenge is achieving long-term stable recordings [18]. There is active research in this arena including the development of novel techniques for neural recordings as well as using multi-unit activity as a proxy signal [27].

ECoG based signals offer another promising alternative for BMIs. ECoG electrodes record field potentials (reflecting aggregate activity of groups of neurons) [5,14,16]. Current studies further suggest that ECoG signals can be stably recorded over long periods of time [28]. Initial studies in able-bodied subjects demonstrated control over multiple DOF [14]. Preliminary reports also suggest that ECoG based devices can be used in patients with disability. However, key questions regarding ECoG signals are: (1) the amount of neural information that can be extracted and (2) its ultimate ability to permit control over complex neuroprosthetic devices.

What does controlling an external device mean?

It is increasingly clear that learning control through a BMI is directly analogous to acquiring a new skill [16,17,22]. Such learning is also associated with modifications to the neural circuitry. Thus, BMIs also offer a powerful framework to study neural computations and plasticity in awake-behaving subjects. Continued research into the neural basis of learning BMI control will likely generate novel ideas to model the interplay of brain areas for learning and memory. This research should also improve techniques to enable neuroprosthetic control in a manner equivalent to the neural representation for natural limb control.

Summary and Challenges

BMIs have the potential to revolutionize the care of neurologically impaired patients. While in its infancy, there have been multiple proof-of-principle studies that highlight possibilities. Combined basic and clinical efforts will ultimately lead to the development of products that are designed for patients with specific disabilities. As outlined earlier, each signal source has strengths (e.g. non-invasive versus invasive, recording stability) and weaknesses (e.g. bandwidth or the amount of information that can be extracted). With additional research a more precise delineation of these strengths and weakness should occur. For example, one hypothesis is that control of complex devices with high DOF will only be possible using invasive recordings of high-resolution neural activity such as spikes from small clusters of neurons. As these limits become increasingly clear it should allow targeted clinical translational efforts that are geared to specific patient needs and preferences (e.g. extent of disability, medical condition, non-invasive versus invasive). For example, patients with high cervical injuries (i.e. above C4, where the arm and the hand is affected) have different rehabilitation needs than patients with lower cervical injuries (i.e. below C5-C6, where the primary deficits is the hand and fingers).

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