Brain-Machine Interfaces
Lessons for Prosthetic Hand Control

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KEYWORDS

- Brain-machine interfaces • Fine motor control • Regression algorithms • Pattern recognition
- Calibration methods

KEY POINTS

- Brain-machine interfaces (BMI) directly access the nervous system to control arm and hand prostheses.
- BMI control algorithms are highly transferrable to peripheral recording techniques for myoelectric prostheses.
- Researchers investigating both brain-machine interfaces and myoelectric control face similar challenges controlling multiple degrees of freedom and acquiring clean calibration data from patients with injuries or disabilities.
- Solutions to these issues will likely be transferable between the 2 technologies.

INTRODUCTION

The loss of an upper extremity is a devastating injury that severely affects a person's ability to interact with the world around them. Hands remain our primary mechanisms for tool use and are important components of social interaction. Advances in robotics have yielded electronic prostheses that can mimic anywhere from 5 to 30degrees of freedom (DOF) of the human hand and provide adequate gripping force for functional tasks.[1–3] The clinical standard is to control these devices with surface electromyography (EMG), allowing users to use muscle activity for control. Dual-site control schemes are cumbersome and unintuitive, requiring a substituted pair of easily accessible agonist-antagonist muscle groups to trigger switches between hand and wrist movements and modulate single DOF. For some users, state of the art pattern recognition systems have eliminated the need for triggers or movement substitutions, and targeted muscle reinnervation

surgery expanded these benefits to users with more proximal amputations.[4,5] However, simultaneous control of multiple DOF has proved difficult.[6] Intuitive grasp selection has been demonstrated in controlled studies[5,7,8] and has only recently become available in commercial devices.

One of the main challenges of existing systems is the ability to extract specific motor commands from surface EMG, which represents a spatiotemporal summation of motor unit activity.[9] Classifiers, the algorithmic engine of pattern recognition systems, are adept at distinguishing movements from such summaries and can even remain accurate in systems with fewer input channels.[7,8,10] However, scaling to multi-DOF control requires distinguishing a rapidly increasing number of movement combinations. Hierarchical schemes have been proposed to alleviate this issue,[11] but the lack of independent control signals remains problematic.[6] Intuitive grasp and fine motor control is of high interest to prostheses users[12]

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but is difficult because many muscles responsible for thumb and finger movements are either lost due to the level of amputation or obscured by more superficial muscles. Peripheral nerve interfacing and surgically invasive recording techniques are being proposed to resolve these issues.[13–16] Extracting precise movement commands from electrophysiological activity is paramount to many rehabilitation and neuroprosthetic applications. In some of these cases, researchers are developing implantable devices and algorithms to solve problems that are fundamentally similar to the challenges experienced with traditional myoelectric prosthetic devices. Brain-machine interfaces (BMI) are being explored for movement assistance and control of robotic devices or computers for patient populations including persons suffering severe stroke, spinal-cord injuries (SCI), or amyotrophic lateral sclerosis. Here the authors discuss progress in BMI for neuroprosthetic control and how they could inform development of better implantable EMG control strategies for myoelectric hands.

DISCUSSION
Signal Acquisition

For patients suffering neurodegenerative diseases or injuries, for example, late-stage ALS or high-level SCI, severe damage renders the peripheral nervous system either an impossible or a poor source of information to extract motor commands for prosthetic control. For these applications, researchers are looking to the brain as an information source. The brain is the origin of intended movement commands for arm and hand control, and its somatotopy is reliably consistent between individuals to facilitate targeting these functions. Electroencephalography (EEG) is a noninvasive technique that records electrical brain activity from the surface of the scalp. Although useful for monitoring or diagnostic applications, EEG has not been widely adopted for neuroprosthetic control. The activity of a single neuron is too small to be recorded remotely through the skull, so EEG recorded reflects a summation of the synchronous activity of thousands or millions of pyramidal neurons.[17] The low conductivity of bone and the exponential decrease in voltage gradients as the recording electrode becomes more distant further reduces the signal specificity and lowers the signal to noise ratios (SNR), making signal interpretation difficult.[18] These properties make EEG ill-suited for prosthetic control applications, which require algorithms to confidently estimate, or "decode", movement intentions in real time. Over the past 2 decades, BMI researchers have capitalized on the availability and development of surgically invasive techniques for neuroprosthetic control to eliminate the need to record signals through the bone and improve SNR.

Recent surveys have shown that fast, accurate, and natural control of external prostheses or restoration of natural arm and hand control are priorities for patients with SCI considering surgically invasive procedures.[19,20] For motor control applications, intracortical electrodes have yielded the best performance in both nonhuman primate (NHP) and clinical studies.[21–23] The Utah Electrode Array (Blackrock Microsystems, Salt Lake City, Utah, USA) is clinically available in multiple configurations with 96 to 128 independent electrode shanks that penetrate 1.0 to 1.5 mm into the brain. When implanted into the motor cortex, penetrating shanks capture local field, single neuron, or multi-unit activity reflective of intended movement kinematics and dynamics.[24,25] Access to source signals provides engineers with the opportunity to develop systems that predict and actuate prosthetic devices without exceeding the time delay of natural movement. Neural firing rates can be counted by manual spike sorting to identify individual wave forms,[26] threshold crossings that aggregate units per channel,[27,28] or power in frequency bands that reflects motor neuron firing.[29–31] Signal processing techniques that capture individual neuron activity have yielded the best performance. Low-frequency (<300 Hz), local field potentials may be used to augment firing rates as a stable input but have not proved sufficient as a standalone feature.[32–34] Biological responses to the penetrating electrodes can lead to tissue scarring and cell death, which ultimately reduce signal quality and the longevity of the BMI.[35–37] Novel electrode designs, to minimize scarring and increase biocompatibility, are an active area of research to address this challenge.[38–40] Flexible electrode grids record electrocorticography (ECoG) from the surface of the brain and may alleviate some of the biological risks of penetrating electrodes, although the precision and speed of motor control has been lacking to date.[41] For intracortical and ECoG applications, multiple groups are developing implantable electronics to bring systems closer to clinical reality.[42–45]

For persons with amputations, activity of the peripheral motor system can be monitored via surface EMG and used to command prostheses. Commercially available systems predict movements based on compound muscle activation patterns. Depending on patient anatomy and prostheses capabilities, this approach may be sufficient. However, simultaneous control of wrist joints or dexterous hand functions has proved

difficult.[6] Access to movement-specific commands from the neuromuscular system can improve device control. Muscle tissue has proved to be a durable interface for implanted electrodes to record stable EMG for months and years,[14,16,46] and routine surgical techniques have used either transplanted or denervated muscle to provide a stable interface with the nervous system.[4,16,47] Intramuscular EMG is often preprocessed for input into control algorithms by band-pass filtering, rectification, and integration. Bandwidths and processing windows vary across studies but are similar to parameters used to isolate nearby muscle activity in surface EMG.[13,14,16] In a bipolar configuration, the mean absolute value of each filtered channel reflects a highly localized summation of motor unit activity specific to the implanted muscle. Like intracortical electrode grids, intramuscular EMG records motor impulses with a high spatial and temporal resolution. Therefore, it is not surprising that a similar algorithmic framework can be applied to control prostheses from downstream motor units in extremity muscles. This review focuses on intracortical approaches that have enabled dexterous control of natural limbs[48,49] or robotic prostheses.[22,50]

Regression Algorithms

Many patients have positive attitudes regarding invasive BMIs if they provide high levels of performance.[19,20] Most controllers accomplish this with linear regression algorithms that adhere to similar framework. Typically, regressors model the intended position or velocity of DOF as continuous variables that explain neural activity.[21,22,51] The regression algorithm, or "decoder", accepts firing rates as an input and usually outputs velocities in each DOF to control the virtual or physical prostheses. Velocity output is typically used regardless of whether or not neural activity is assumed to be tuned to position[21,52] and is suspected to produce a simple physical system for real-time control in the presence of noisy inputs.[53,54] Researchers have also noticed that executing algorithms on shorter time intervals (<100 ms) improves online performance, which may be contradictory to offline simulations,[55] and this is thought to be due to improvements in both the rate of visual feedback and control rate that improve error correction and movement planning.[23] To date, many BMIs use linear regressions to decode arm reaches, which are then mapped to provide 2 DOF cursor control in a virtual environment. However, clinical trials have demonstrated that the following framework can also be applied to control higher DOF robotic limbs[22,50] or functional electrical stimulation

(FES) systems.[48,49] More recently, both NHP and clinical studies have demonstrated that a linear framework can be extended to precisely control individual finger or grasp dimensions.[31,52,56]

Over the last decade, clinical BMI have most commonly used 2 linear algorithms: optimal linear estimation (OLE) with ridge regression and the Kalman filter (KF).[22,50] In the early 2000s, the first linear regressors in NHP used a full second of time history to produce a stable and accurate decoder.[57] However, basing motor commands on outdated neural activity reduces responsiveness and negatively affects real-time control. OLE resolves this issue by estimating firing rates based on the previous 450 ms but remains responsive by using an exponential filter to prioritize the most recent samples. Firing rates are collected in 33 ms time bins and input into the OLE to provide velocity predictions. The OLE is calibrated by first modeling the firing rate of each channel as a function of velocities, then finding inverse coefficients for the online decoder. The KF was first introduced in NHP in 2004 and models channel activity as a function of kinematics.[51] This model is then fused with a physical model, reflective of the intended movements, that recursively estimates position and/or velocity states at each time step. Here, the physical model enforces stability, whereas updates to the neural measurement ensure responsiveness. Typical KF implementations execute in intervals ranging from 20 to 100 ms. Both techniques depend on sampling channels that are tuned to different movement directions. Some neurons in the motor cortex may be highly specific to individual movements.[58] However, observing numerous broadly tuned channels may provide sufficient information for control, provided they are well modulated and can be represented by a linear model. In fact, the regularization method in OLE encourages activity from one neuron to be related to more than one kinematic variable. For both the KF and OLE, channels with sparse activity (<1 spike per second average firing rate) during the calibration session are usually ignored. These channels cannot be well represented by linear models, which provide optimal solutions when the predicted variables have normally distributed errors. Neuron spike events closely resemble a Poisson process, which significantly deviates from a normal profile for low firing rates. Evidently, motor prosthetic implementations have succeeded by leveraging profuse channels and large enough processing windows to avoid a problematic violation of this assumption. However, neural interfaces that operate on extremely rapid timescales would benefit from nonlinear techniques.[23]

Following its use in BMI, the KF has been applied to dexterously control multi-DOF hands using inputs from the peripheral motor system. The same framework was successful in both bipolar electrode configurations that measure motor unit activity in specific muscles[16] and referencing schemes that capture potential differences between muscles.[13] However, there are some minor differences between peripheral and BMI implementations. Intracortical electrode grids are designed to interrogate individual neurons in the brain with a high channel count to capture different motor functions. By comparison, intramuscular EMG systems often have lower channel counts but use larger electrodes that capture many nearby motor units. Concerns of sparse activity are therefore not applicable to well-placed EMG leads. Furthermore, because muscles can be individually targeted during surgical implantation,[14–16] engineers can be confident in the functional representation of individual channels. If desired, irrelevant channels can explicitly be masked from decoders instead of relying on automated screening techniques. In the abovementioned clinical studies, the position output of the KF was used to control individual wrist and hand DOF. Velocity control may be useful depending on hardware capabilities, although it is evidently not required. A strong relationship between individual muscles and finger movements produces a decoder that requires less smoothing or active modulation. Patients have used this framework to simultaneously control 3 to 6 wrist and hand DOF using research grade hardware or virtual reality environments.[13,16] The dexterity and precision of control may be limited with commercially available hands that do not offer position or velocity control of individual motors.

BMI and peripheral interfaces can be used to perform different tasks with a variety of end effectors. It is important to consider hardware differences when discussing the limitations of linear regression algorithms. For example, BMI often control computer cursors for communication.[59] In this case, errors may seldom be due to a lack of physical constraints, context changes, and comparatively few DOF. However, for both BMI and peripheral interfaces, directly controlling multi-DOF functional electrical stimulation systems or robotic limbs can prove more challenging. Hardware latency and noise can reduce precision, and a common issue with regression algorithms is the inability to independently activate DOF.[13,52,60] Many reaching and grasping movements use synergistic activations, so this issue may only be apparent for fine motor tasks. In BMI applications, motor neurons are broadly tuned to multiple movements, which can cause problems related to coactivations. Recording from a larger number of neurons theoretically results in better separability of DOF. However, even in EMG applications where specific muscles can easily be targeted, coactivations still cause difficulties for decoders;. This could be due to natural movement synergies required to stabilize joints, which are problematic if they are not properly incorporated into the algorithm. Without a more complete sampling of muscle activity in these contexts, decoders will broadcast these signals as movement commands.

Ultimately, the performance of regression algorithms may be most severely limited by channel count or, in other words, the number of information sources available for each DOF. Techniques to resolve these issues include nonlinear output thresholds[13] and hybrid controllers that use pattern recognition to suppress unwanted activations,[51,61] although these solutions may limit dexterity and increase exertion. Biomechanical models account for natural nonlinearities in muscle activation forces to improve decoder robustness.[62] However, the ability for a hand model to differentiate finger movements depends on the complexity of the model itself as well as muscle synergy mappings in undersampled configurations. Other nonlinear algorithms such as neural networks may one day learn to isolate DOF without sacrificing dexterity.[63] However, approaches with more advanced modeling capabilities may require higher quality calibration data in order to be effective in multiple contexts.[64]

Real-Time Pattern Recognition

Classifiers can be used in to detect movement states or discrete commands in real time. Reducing movement prediction to discrete states can also be useful when there are an insufficient number of channels modulated by a particular movement. In BMI, neural states can be detected to classify hand grasps for FES control.[49] In other implementations, classifiers have been used to improve the performance of virtual cursors by initiating stop or click states.[59,65] The Hidden Markov Model (HMM) has emerged as a common framework to optimize movement state predictions. The HMM represents neural dynamics by explicitly modeling transitions between several underlying latent states.[61] This capability allows the prediction of a click intention, as it occurs in the brain.[59] In addition to stop or click states, classifiers have also been used to suppress unintentional movements of regression controllers by selecting discrete trajectories.[51,61] In this framework, integration delays are extremely costly because they reduce controller

responsiveness and the patient's ability to make fine adjustments. Fortunately, the ability of the HMM to model and evaluate state changes over time allows it to operate on rapid timescales without sacrificing stability.[61] In addition to the HMM, deep learning architectures such as recurrent neural networks can recognize temporal dynamics to boost pattern recognition performance of fine motor movements, for example, distinguishing handwritten letters imagined by a patient withSCI.[66] This classifier required characters to be completed before a prediction could be issued, but it demonstrated that complex movements with high temporal variation can be easier to distinguish than less complex gross movements.

Movement classifiers are a natural fit for myoelectric hands that are designed to switch between hand grips rather than individual finger control. Some pattern recognition systems even offer grasp selection capabilities.[5,7,8] However, performance may degrade across different physical contexts.[10] Intramuscular EMG improves controller reliability by providing stable signals with a high signal-to-noise ratio.[15,67] However, it also may allow for techniques such as the HMM to confidently estimate grasp states on faster timescales. Furthermore, access to high resolution muscle signals could increase the number of movements that can be predicted by neural networks.. EMG implementations may differ from BMI in the following ways. For BMI applications, the HMM often characterizes movements with many (up to 20) underlying neural states.[61] To represent downstream muscle activity, only a few latent states may be required per movement. Naive Bayes is commonly used as the latent state model for the HMM because it can model many states without large amounts of training data.[68] However, most BMI implementations have been used for cursor control,[59,65] and myoelectric prostheses need to operate across a wider range of physical contexts. Because intramuscular recordings can provide independent movement signals,[16] it is possible that more robust underlying models can be used without sacrificing predictive power. Similarly, neural networks may be able to predict grasps from EMG with fewer nodes or layers than comparable BMI implementations. Although, as regression algorithms, they may require improvements to the calibration routine.

Calibration Techniques

The performance of both pattern recognition and regression algorithms depends on the quality of calibration data, and this may be especially true for neural networks that may require richer calibration data to take advantage of their increased fitting capabilities.[64] Many research groups use able-bodied participants to validate approaches. Although these volunteers are valuable to the development process, their performance may not directly reflect the capabilities of persons with amputations. A large portion of BMI research is also done with able-bodied NHP. In an able-bodied model, the ground truth of movement intention can be used for training. In that case, ill-fitted parameters can largely be ascribed to a lack of modulated neurons or poorly measured kinematics and motor noise.[69] On the other hand, kinematics cannot easily be measured for patients with injuries or motor system impairments. This can severely limit the quality of training data for fine finger and grasping movements.[64] Neural plasticity may naturally alleviate this issue, as it has been demonstrated that NHP can eventually learn to use BMI with suboptimal parameters.[70] However, advanced calibration techniques can improve performance either by improving initial training data quality or by reducing the learning curve.

Similar to commercial pattern recognition systems, BMI are calibrated by having the user mimic a computer animation or robotic hand to capture neural activity reflective of an intended movement. However, it has been documented that brain activity changes between observed, imagined, and attempted grasps.[71] Patients who lack peripheral motor abilities may have a difficult time consciously distinguishing between these brain states or precisely following movement cues in part due to broken feedback links. In this sense the quality of training data can depend on a patient's sensorimotor function. BMI researchers have found that training grasps with objects in place can improve decoder performance, possibly by encouraging consistent engagement of motor pathways.[56,72] To account for variations in attempted movement speeds, time warping techniques may prove useful by structurally aligning training data.[66] For myoelectric prostheses control, these upstream phenomena could manifest themselves in the improvements noticed with bilateral mirror training.[64]

In cases where an initial training dataset proves difficult to obtain, adaptive calibration techniques have proved effective for BMI. Adaptive calibration for regression algorithms can be completed in single or multiple stages and has shown effective double performance in virtual tasks for arm movements.[21–23] These techniques use goal-oriented supervised tasks, so online control errors and the intended movement can easily be identified and used to reweight parameters. Unsupervised

calibration may seem more convenient but requires a framework to automatically identify grasp errors.[73] Supervised techniques may also be preferred to focus on difficult movements and decrease adaptation time.[74] Most supervised approaches estimate the correct movement intention by rotating or aligning the velocity vector toward the goal.[21,22] Finger movements have a short range of motion, and motor cortex hand region neural activity has been shown to be strongly correlated with position as well as velocity. Although it is unclear if existing techniques provide an optimal intention estimate for grasp recalibration, they are still beneficial for BMI.[52] Closed-loop adaptation allows the decoder to recognize shifts in neural tuning between offline calibration and online control.[69] Users also adapt their own behavior to improve online performance of both BMI and EMG controlled devices.[74–76] For BMI, neuroplasticity may play a more prolonged role, reshaping activation patterns to best utilize a given decoder.[76] This type of motor learning is being explored for prosthetic and movement rehabilitation applications even though remapping muscle synergies may be difficult.[77–79] It is unknown how transferrable adaptive BMI techniques will be, as they are only recently being investigated.[74] The success of different calibration techniques for persons with amputations is likely to be individual. Advanced or adaptive calibration methods may not be required for skilled patients who also have excellent perception of their phantom limb but may be increasingly valuable for patients with more proximal or bilateral amputations.

SUMMARY

Intracortical BMI and implantable EMG technologies aim to provide fast and fluid control of upper-limb prostheses by interrogating motor neurons and peripheral motor units, respectively. These high-resolution signals can be fed into high-speed pattern recognition and regression algorithms to control digital cursors or robotic hands. Common solutions may exist to common issues such as unintended movement coactivations or collecting quality calibration data. In the future, BMI may be a rich source of algorithm inspiration, as the number of peripheral channels for EMG systems increases or stable nerve monitoring techniques are developed. Peripheral nerve interfaces may increase the appeal of myoelectric prostheses to patients with more proximal amputations. For patients with varying skill levels and sensorimotor function, enhanced and adaptive calibration techniques can reduce training time and may be essential to delivering high-performance prosthetic systems.

CLINICS CARE POINTS

- Brain machine interfaces allow patients to fluidly control robotic arms or reanimate previously paralyzed limbs.
- Implantable EMG systems can use similar algorithms to provide dexterous grasp control, although simultaneous and independent control of high DOF systems remain challenging.
- Software solutions are likely to be shared between these 2 technologies, although researchers and engineers must keep in mind some differences.
- Fully implantable electronic systems need to be developed to move both technologies from research to clinic.

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