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Cover Page Footnote

I would like to thank Dr. Joon Yun for his guidance during this independent research project. He served as an invaluable sounding board for all my ideas and encouraged me to challenge current scientific thought.

Turning Science Fiction into Reality: Enhanced Motor Learning for Prosthetic Limbs

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ABSTRACT

In science fiction, prosthetic limbs appear as seamless extensions of the human body that function as if the limbs were made of flesh and bone. With recent technological and scientific advancements, the prosthetic limbs of today are beginning to resemble those we once only imagined. Patients are now able to perform simple, everyday tasks like drinking from a glass of water. However, there are many limitations to this technology, including lack of fine motor movement, absence of reflexes, and missing sensory feedback from the prosthetic limb. These restrictions prohibit prosthetics patients from having the same experience as someone with a biological limb. This paper touches upon the limitations of prosthetics today and applies the findings of current neuroscience research to address these shortcomings to identify potential solutions and areas for further research.

BACKGROUND

One of the greatest challenges in creating prosthetic limbs is translating brain signals to produce a wide range of smooth motor movements rather than slow, jerky motion. Brain-computer interfaces (BCIs) allow neuronal signals to be read and processed by computer algorithms in order to instruct a robotic arm to perform the desired task. In the past decade, there has been a transition away from recording neurons in the motor cortex, the brain region traditionally associated with controlling muscle movements. While at first it seems reasonable to read signals from the motor cortex and alpha motor neurons—after all those are the neurons responsible for instructing muscles to contract or relax—prosthetic limbs controlled by microchips reading from just the primary motor cortex produce choppy and slow movements. A robotic arm is built of entirely different materials and the set of instructions given to a human bicep do not perfectly translate to instructions for how a mechanical arm should move. In addition, prosthetics that rely on EMG signals from residual limb muscles have limited controllable degrees of freedom, which greatly impedes the types of movement they can perform and negatively affects the reliability and intuitiveness of the prosthetic limb (Pasquina et al., 2015). In current prosthetic technology, there is also an absence of feedback loops relative to those present in the control of natural neural systems. The lack of haptic feedback raises two issues: the central nervous system's innate error correction circuits are not harnessed—which if utilized could increase the accuracy of prosthetic limb movement—and prosthetics patients lack the full experience of having a limb that can "feel." There are several physical limitations regarding amputation technology and understandings of neural plasticity that make it difficult to incorporate haptic feedback, but recent advancements in this area are yielding promising results (Srinivasan, 2020).

Another limitation of prosthetics is the recording technology available to read in signals from the brain cortex and the spinal cord. Recent advancements in BCI technology have begun to solve this problem and now allow scientists to record neural signals from many areas with low power consumption. The Stanford Bio-X group has pioneered wireless BCI technology that requires less power to function compared to similar BCIs, and it enables recording from a much larger number of channels (Pandarinath et al., 2017). This would allow a prosthetic to receive input from many different regions of the brain and spinal cord, which could improve motor function and make the experience of having a prosthetic more closely resemble that of having a biological limb.

LOOKING BEYOND THE MOTOR CORTEX

The ability to record from several regions of the brain makes it possible to capture a patient's intent of how they wish to move, rather than the muscle-specific instructions the motor cortex sends to individual muscle groups. A patient's intent or desire to move can be translated into code that instructs a mechanical arm to perform the task. This shifts the focus to premotor or supplementary motor regions of the brain, which play a role in higher-level motor planning rather than specific muscle movement instruction. The posterior parietal cortex (PPC) is one such region that is often implicated in reaching behaviors and thought to be involved in higher-level motor planning (Hauschild et al., 2012). Robotic arms controlled by microchips implanted in the PPC are able to perform relatively smooth actions guided just by a patient imagining the action in their mind (Hauschild et al., 2012). The success in translating neural activity in the PPC into prosthetic limb movement is a promising first step. Further investigation of the features of PPC cognitive processing may prove effective in finding analog regions of the brain from which we can record additional higher-level motor planning. A study recording neuronal activity in the intraparietal sulcus of a monkey's PPC investigated the function of the lateral intraparietal area (LIP) and posterior reach region in tracking attention and movement goals (Bisley et al., 2003). The monkey was presented with two stimuli: a target cue indicating where a monkey should reach or look once the "go" signal was given, and a distractor that was not related to the movement goal but still captured attention. The neural responses in the LIP show that although the distractor captured attention even though it was not related to the movement goal, there was increased LIP activity when the placement of the distractor was beneficial to the movement goal (i.e. located such that the monkey could respond to the target more quickly). That result indicates that a combination of attention and movement goal is encoded in the PPC. This supports the pre-motor theory of attention, which proposes that attention plays a preliminary role in planning motor actions (Rizzolatti et al., 1998).

Assuming there is merit in the pre-motor theory of attention, it makes sense to look at other regions of the brain that are involved in attention to investigate the possibility that they may aid in creating smooth motor movement in prosthetic limbs. One such area that is involved in attention is the prefrontal cortex, which has both anatomical and functional connectivity with regions of the parietal cortex. A study using BOLD imaging demonstrated that there are intrinsically coupled brain networks in the intraparietal sulcus (IPS) and medial prefrontal cortex when using the posterior cingulate cortex as a seed (Fox et al., 2005). The positive network included the medial prefrontal cortex and was correlated with seed regions that were activated during attention and working memory tasks. The negative network including the IPS was anti-correlated with the regions of the seed that were activated by these same tasks. Three branches of the superior longitudinal fasciculus anatomically link areas of the prefrontal and parietal cortex in the dorsal attention network (connecting the IPS and frontal eye field) and the ventral attention network (connecting the temporal parietal junction and the medial and inferior frontal gyrus) (Bartolomeo et al., 2012). The fronto-parietal pathways of a human subject's brain were imaged during an attention task involving motion detection, revealing parallel pathways of correlated activity between parietal regions and the FEF and SEF of each hemisphere (Szczepanski et al., 2013). Diffusion tensor imaging revealed anatomical connectivity made of distinct fiber tracts for each of these fronto-partietal pathways. All of these studies implicate areas of the PFC as potential regions that could be involved in attention and intent to move. A neuroprosthetics group at Caltech stated they were focusing less on external related motor areas and more on higher-level internal intention and thoughts in order to build prosthetics that carry out smoother movements to accomplish desired tasks (Aflalo et al., 2015). Distinct regions of the PFC appear to be involved in different kinds of attention processing: in a study regarding emotional control, the medial PFC was activated during self-regulating processing and the lateral PFC was more external and sensitive to sensory and motor stimulus (Oschner et al., 2004). Experiments could determine whether recording from one of these areas, for example the more internally focused medial PFC, results in clearer decoding of movement intent and therefore more efficient and accurate prosthetics. In addition, working memory is often described as a form of sustained attention, and studies show that neurons in the dorsolateral prefrontal cortex display firing rates that encode working memory (Goldman-Rakic, 1995). Further research should test regions of the prefrontal cortex including the FEF, SEF, dlPFC, and medial frontal gyrus for signals of movement intent. Readings of neural activity from these areas coupled with readings from the parietal cortex may increase the response time and accuracy of prosthetic limb movement.

The differential equations that govern control systems could be useful in characterizing higher-level motor planning occurring in these supplementary motor areas. Consider higher level motor planning to be the second part of a second order control system with a characteristic transfer function of:

$$C(s)/R(s) = n^2/(s^2+2ns+n^2)$$

If we use the unit step signal as the input to the system, we can solve the above equation to get the outputs in the time domain. When the function =0, the response is a continuous time signal with constant frequency and amplitude. When the function =1, the response approaches the step input in steady state. When the function is 0<<1, the amplitude of the response decreases. When the function is >1, the response is over damped and never reaches the step input in its steady state. These outcomes display that higher order control systems—which represent more layers of feedback loops in motor processing and planning—respond faster and more accurately but the tradeoff is an increased risk of instability. If pushed outside of the bounds within which they are supposed to operate, these higher order control systems can behave unpredictably. This highlights a potential pitfall of including higher-level motor planning regions in the calculations for prosthetic movement: increasing the number of feedback layers introduces possible instability.

REFLEXES

Another current gap in prosthetic limb technology is the absence of reflexive behaviors. Currently, engineers design prosthetic limbs so they can execute movements patients consciously desire to perform. But if we want to give individuals with prosthetic limbs a normal life with all the abilities of someone with biological limbs, prosthetic limbs must have reflexes. Reflexive movements play a crucial role in our day-to-day lives, from blocking a ball about to hit our face to pulling back from a hot surface. Incorporating reflexes into prosthetic limbs may not even require reading from entirely new regions of the brain, as top-down and bottom-up control processing occur in many of the same regions (Buschman and Miller, 2007). Regions in the brain in fronto-parietal attention network (LIP in parietal lobe and FEF and IPFC in prefrontal cortex) were recorded while participants performed two tasks: one was a "pop out" visual task that evoked bottom-up attention and the other was a visual search task that evoked top-down attention (Buschman and Miller, 2007). The same areas of the parietal and prefrontal cortex were activated in each task, but the two regions (parietal versus prefrontal cortex) were activated in the opposite order when performing the pop out versus visual search task. There is also above-baseline local field potential coherence between neurons in the parietal and prefrontal cortex during these tasks, indicating the neurons in each region are communicating with each other at the micro level. This study found the neuronal coupling occurs in different frequencies—beta frequency band or gamma frequency band—depending if the participant is engaging in a top-down versus bottom-up attention task, respectively (Buschman and Miller, 2007). All of this information can be used to incorporate reflexes into the coding of prosthetic limbs. By identifying the region of the brain that was activated first and the frequency band being used by neurons to communicate, we could decode whether someone is intending to focus on a stimulus—like in the search task—or if it is grabbing their attention like the pop out task. It is possible that reflexive behaviors are initiated in the brain by bottom-up stimulus, such as detecting an object flying at you out of the corner of your eye. Differentiating neural activity into "intent" and "reflex" could allow us to prioritize

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which movement a prosthetic limb should perform first. For example, it would be better for a prosthetic arm to block a ball about to hit the patient's face before moving a chess piece in a game they are playing. It is worth researching other regions of the brain involved in subconscious motor movement in order to determine if the neural activity in these regions can be used to decode reflexive actions. There are also other reflexes that may not even be initiated by the brain. For example, a prosthetic arm could be coded to pull back from a hot surface without ever consulting the brain. However, in this case it would be important to connect the prosthetic limb back to the brain to inform it about the limb's actions so a patient can then make decisions based on that information.

In order to incorporate reflexes into prosthetic limb technology, we must understand the levels of computation taking place in different parts of the central and peripheral nervous system that contribute to the execution of a reflexive movement rather than a voluntary one. One study analyzed the nonlinear connectivity of the human stretch reflex by using a novel tool in cross-frequency phase coupling (Yang et al., 2016). In the experiment, a sequence of periodic physical perturbations was applied to a participant's wrist at a frequency high enough to require a reflexive response. Because the perturbations were occurring too quickly for a voluntary response, any reaction in the wrist muscles was due to the stretch reflex. Participants were also asked to maintain a specific hand and wrist position during the experiment, so they were exerting some voluntary motor control. Since the experiment involved reflexes, somatosensory input, and voluntary motor movements, regions of the brain, spinal cord, and periphery were all involved. Both cortical sources for sensory registration and motor activity were measured in this experiment. This is necessary in order to apply this study to prosthetics because the combination of sensory and motor registration allows someone to "feel" what is happening in their limb and allows the brain to utilize its current circuits that adjust motor movement based on sensory input. The study showed that while sensory input reaches the brain and is processed in the somatosensory cortex, the brain only weakly contributes to the muscle stretch reflex. This means that peripheral neurons are informing the brain of what is happening, but the motor reflex itself is coming from other parts of the nervous system, such as the spinal cord. Not only should we expand the recording regions beyond just the motor and supplementary motor cortices, but we should also include regions of the spinal cord. The fact that spinal cord signals--not signals from cortex--cause the stretch reflex suggests that the prosthetic should be coded to mainly provide sensory input and receive motor signals from the spinal cord in order to create a reflexive movement.

Recording signals from the spinal column and incorporating them into prosthetic technology is feasible: a 2019 study demonstrated that single and multi-neuronal signals can be recorded from the surface of the dorsal root ganglia via a non-penetrating electrode array, as opposed to recordings made by intrusive extracellular electrodes (Kashkoush et al., 2019). This novel technique has a slightly lower signal to noise ratio than traditional extracellular recording methods, but it does not require penetration of the dorsal root ganglia. The Kashkoush study only discusses the ability of electrode arrays to measure the sensory information passing through the dorsal root and does not deal with the ventral horn. It is possible that ventral horn neurons can be measured with electrode arrays, which could perhaps more finely tune a prosthetic reflex response because this region houses motor neurons. However, even with only the information from the dorsal root ganglia, it could be possible to program the prosthetic such that it takes the sensory input and executes the correct reflex without the spinal cord motor information.

A potential issue with this approach is that there is nonlinear connectivity between sensory and reflex muscle responses (Yang et al., 2016). While the sensory and motor pathways in the transcortical reflex loop can be distinguished from one another using nonlinear directional phase coupling, there is interaction between the two pathways beyond a simple interneuron connection. Understanding these specific interactions could be key to designing a prosthetic such that it interacts with the nervous system as a biological limb would. Measuring neuronal coherence may help solve this issue. A study on cognitive neural prosthetics showed that local field potentials capture broader network activity than spike recording (Andersen, 2011). Instead of focusing on individual neuronal spiking, measuring the frequency of radiation emissions can be used to determine a brain "state" and see what regions of the brain are communicating. It is also possible that different frequencies operating on the same physical neuronal pathways generate interference patterns that are secondary feedback loops arising from activation of certain neural responses. Researching these harmonics and constructive interference patterns may give insight into computations occurring in the brain above the synaptic level.

INCORPORATING SENSORY FEEDBACK

An important next step in prosthetics is developing sensors for a prosthetic limb and connecting them to brain regions, such as the sensory cortex, so an individual can "feel" what is happening in the limb. Connecting the limb back to the brain in this way would complete a circuit that would potentially allow for learning and correction of errors to occur more quickly and effectively. There is precedent that repetition of a task with visual feedback improves the accuracy of tasks completed with a BMI. In one study, goal-oriented movement signals were recorded in a monkey's brain and used to control the positioning of cursors on a computer screen during a task (Mussalam et al., 2004). Over the course of several weeks, the monkeys became more accurate in positioning the cursors by only using their thoughts and intentions of moving the cursors to achieve a reward. It is possible that increasing the amount of feedback and diversifying the sources of feedback, for example sensory information in addition to visual, could speed up the learning process of performing tasks with a BMI. Previous studies have shown that direct brain stimulation can simulate a physical sensory experience, which means it is possible to create the illusion of "feeling" parts of a prosthetic limb (Romo et al., 2000; Houweling and Brecht, 2008). Not only would this create a more "normal" experience for a prosthetics patient, but it could also allow a prosthetic limb to provide the brain with sensory information and potentially tap into several preexisting error correction and learning networks. The basal ganglia is one such region of the brain directly involved in motor learning and is connected to the entire cerebral cortex (Lanciego et al., 2012). The PPC receives proprioceptive input from neurons in the primary somatosensory cortex (S1), which suggests that sensory information is usually processed when making a decision to move (Hauschild et al., 2012). Because the brain is already wired to integrate sensory information into these higher-level learning networks, providing the necessary input from the prosthetic limb could harness existing brain networks and lead to the best possible limb performance.

"An understanding of the neuroscience behind visuomotor processing and motor learning combined with sophisticated robotic design can turn science fiction into reality."

PROPRIOCEPTION

Another key component of restoring "life-like" function to a prosthetic limb is including proprioception: the sense of oneself that allows us to know where our limbs are in space. The Herr Lab at MIT has recently developed a lower leg prosthetic that fuses with the nervous system of the body such that the prosthetic foot has proprioceptive abilities (Stolyarov, 2017). The bionic foot developed by Herr and his team is capable of small reflexive movements that biological feet perform when walking up stairs or on uneven surfaces. By combining their prosthetic with a novel amputation surgery that preserves agonist-antagonist muscle dynamics, the prosthetic successfully links the sensory and motor system together such that it utilizes the already-existing error correction and reflex circuits in the nervous system (Srinivasan, 2021). This is promising evidence that mechanical limbs can feasibly be integrated into pre-existing motor and sensory circuits. While the current technology provides a certain level of basic reflexes required to carry out movement tasks such as walking, it could be possible to build upon this technology to create upper-limb prosthetics that also harness the innate circuitry provided by our body. A next step would be to integrate the prosthetic at the spinal cord level, eventually allowing the prosthetic to execute all kinds of reflexes that involve the central nervous system and some higher-level processing. Given that the bionic foot developed by Herr's lab gives people proprioception and the sense that the mechanical foot is their own, it is possible that fully integrating the sensory and motor pathways of a prosthetic with the spinal cord will also provide patients with a sense of feeling without additional electrical inputs to the sensory cortex. Thus, this would limit the amount of invasive brain or spinal cord surgery necessary when implementing a prosthetic.

ENHANCED LEARNING MECHANISMS

Every prosthetics patient faces the challenge of adapting to their new limb and learning how to use it as they would a biological one. However, new technology may expedite the process of learning how to use a prosthetic limb and increase brain plasticity. Halo Neuroscience is a company that creates headphones to deliver transcranial direct current stimulation (tDCS) to certain regions of the brain in order to enhance learning and performance of various physical tasks (Halo Neuroscience, 2016). In a study performed by Halo researchers, this technology was used to deliver bi-hemispheric tDCS to the primary motor cortex of an individual doing a chord configuration task, which requires learning precise finger movements. The individuals using Halo's headphones had faster and more accurate synchronizing of finger movements during the task over time compared to the controls (Halo Neuroscience, 2016). Halo's headphones could potentially aid patients with new prosthetic limbs and speed up the process by which they learn to use their prosthetics. If added to physical therapy programs, these devices could allow patients to use their prosthetics more accurately in a shorter amount of time.

While this paper is mainly focused on the electrical domain, the chemical domain may be just as important in decoding and implementing prosthetics. For example, many motor learning circuits involve certain neuromodulators. Dopamine is one such neuromodulator that is a key part of the motor control loop involving the basal ganglia and thalamus (Jahanshahi et al., 2015). Moreover, neuromodulators like dopamine can enhance neuroplasticity, which is directly involved in feedback loops and motor learning (Kroener et al., 2009). Manipulating the levels of neuromodulators like dopamine might accelerate the motor learning process for patients learning how to use prosthetic limbs.

CONCLUSION

The field of prosthetics has made remarkable advancements in the past decade, now allowing patients to control a robotic arm with nothing but their thoughts. We currently have the technology to allow paralyzed individuals to perform simple, everyday tasks like picking up a glass of water in relatively smooth and efficient movements (Singer, 2020). While the prosthetic limbs of our world today are quite a few steps behind those we see equipping characters in Star Wars, that ideal is not too far out of reach. An understanding of the neuroscience behind visuomotor processing and motor learning combined with sophisticated robotic design can turn science fiction into reality. While significant hurdles still remain, there are endless opportunities for further research that has the potential to create a world in which prosthetics function as seamlessly as one's own limbs.

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