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REVIEW ARTICLE

Advanced technologies for intuitive control and sensation of prosthetics

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Abstract

The Department of Defense, Department of Veterans Affairs and National Institutes of Health have invested significantly in advancing prosthetic technologies over the past 25 years, with the overall intent to improve the function, participation and quality of life of Service Members, Veterans, and all United States Citizens living with limb loss. These investments have contributed to substantial advancements in the control and sensory perception of prosthetic devices over the past decade. While control of motorized prosthetic devices through the use of electromyography has been widely available since the 1980s, this technology is not intuitive. Additionally, these systems do not provide stimulation for sensory perception. Recent research has made significant advancement not only in the intuitive use of electromyography for control but also in the ability to provide relevant meaningful perceptions through various stimulation approaches. While much of this previous work has traditionally focused on those with upper extremity amputation, new developments include advanced bidirectional neuroprostheses that are applicable to both the upper and lower limb amputation. The goal of this review is to examine the state-of-the-science in the areas of intuitive control and sensation of prosthetic devices and to discuss areas of exploration for the future. Current research and development efforts in external systems, implanted systems, surgical approaches, and regenerative approaches will be explored.

Keywords Limb loss · Peripheral nerve · Muscle · Osseointegration · Brain–machine interface · Regenerative

1 Introduction

Persons with limb loss still have limitations that have not yet been overcome by available prosthetics. Most prosthetics devices delivered today, both lower and upper limb, are passive in nature in that they require power from the user to actuate. Powered systems are also available to persons with limb loss. These devices rely on external power and microprocessor control to actuate, either based on sensor data gathered from the device (position, force, acceleration, etc.) or from human physiological signals. Although both of these types of devices can provide significant levels of function and quality of life for those with limb loss they do not provide intuitive control or sensory perception. Additionally, many of these devices, more specifically upper extremity

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prostheses, both passive and powered, are abandoned due weight, appearance, and lack of function [1].

The US Government has invested significantly in advancing prosthetic technologies over the past 25 years, mostly through research and development funding through the Department of Defense (DoD), Department of Veterans Affairs (VA) and National Institutes of Health (NIH). Other federal agencies have also invested in prosthetic development as well as understanding health aspects of persons undergoing and/or living with limb loss. The goal of this review article is to express the interests of the DoD, VA, and NIH in investing in the advancement of prosthetic technologies, specifically in the realm of intuitive control and sensation, to demonstrate advances that have been made with research funding from those agencies, and to discuss the short and long term visions of these agencies towards optimizing function, performance and quality of life for Service Members, Veterans, and Civilians with limb loss.

Notably, when exploring the limb loss landscape and the prescription and use of prosthetics and surgical interventions undergone by the limb loss population there is a significant dearth of epidemiological information. Because limb preservation, amputation, device provision, and rehabilitation occur across a diverse clinical care environment, limb loss data is fractured across many health record systems that lack interoperability. The NIH and the DoD have partnered to establish a Limb Loss and Preservation Registry. The registry will collect information from electronic health records (EHRs) to detail limb loss prevention, etiology, acute care, and cost of services. The registry will use EHRs when possible to also capture device provision, rehabilitation, and quality of life for individuals living with limb loss. The goal of this registry is to improve and optimize care and outcomes for individuals living with limb loss or limb difference.

1.1 Department of Defense

The Global War on Terror, specifically Operation Iraqi Freedom (OIF), Operation Enduring Freedom (OEF), and Operation New Dawn (OND) has led to over 1700 Warfighter amputations as a result of combat operations [2]. Additionally, other Warfighters undergo amputation as a result of failed limb salvage resulting from combat injuries, and other non-combat injuries. The DoD has issued guidance that allows Warfighters with amputations to continue to seek care in the Advanced Rehabilitation Centers stating "DoD must ensure sustainment of the highest quality delivery of health care and health research…" [3].

The two main DoD agencies that are responsible for the majority of strategic planning and execution related to prosthetic technologies are the US Army Medical Research and Materiel Command (USAMRMC) and the Defense Advanced Research Projects Agency (DARPA). USAMRMC executes research appropriations on behalf of the Defense Health Agency, which is responsible for health and readiness of the fighting force and aims for increased readiness, better health, better care, and lower cost within the Military Health System. DARPA investments in this area are in higher-risk transformative research programs that are revolutionary and contribute directly to national security. DARPA's Biological Technologies Office (BTO), in particular, funds neuro-technology programs that both restore capability to wounded warriors and equip the warfighter to better defend the Homeland.

The ultimate goal for the DoD in funding advancements in prosthetic technologies is twofold; first is to provide Warfighters who are putting their lives at risk every day in defense of our Constitution the assurance that they will receive the highest level of care if they are injured, and second to allow Warfighters with limb loss the ability to return to pre-injury levels of performance including return to active duty and deployment.

1.2 Department of Veterans Affairs

The Veterans Health Administration within the Department of Veterans Affairs is responsible for the care of over 90,000 Veterans with amputation [4]. In contrast to the population of persons with traumatic (conflict-related and non-conflict-related) amputation in the DoD, the majority of Veterans with amputation who receive care from VHA are older (mean age of 68) and have amputations that are predominantly the result of disease processes such as peripheral vascular disease and diabetes. Care for these Veterans is provided through an integrated Amputee System of Care (ASoC) that provides specialized expertise in amputation rehabilitation incorporating the latest practices in medical rehabilitation management, rehabilitation therapies, and advances in prosthetic technology across the full continuum of care. The ASoC is comprised of 7 Regional Amputation Centers, 18 Polytrauma/Amputation Network Sites, 106 Amputation Care Teams, and 22 Amputation Points of Contact. Through care coordination and close collaboration with both Primary Care and other Specialty Care services, these amputation care teams assure that all medical, rehabilitation, and prosthetic needs of the Veteran are met in order to optimally restore desired function following amputation.

Within the Veterans Health Administration, the Office of Research and Development (ORD) oversees a primarily investigator-initiated intramural research program focused on improving the health care of our Veterans. ORD collaborates with the ASoC (clinical care delivery) and Prosthetics and Sensory Aids Services (device purchase and provision) to ensure that research funding is in alignment with Veteran healthcare needs and goals. Prosthetics has always been a core area of research within VA, which funds a wide range of prosthetics-related research including basic science, device development, clinical trials, care delivery, and health systems research.

1.3 National Institutes of Health

As part of its mission to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability, the National Institutes of Health supports research on advancing control and sensation of prosthetic limbs through the National Institute of Neurological Disorders and Stroke (NINDS), the National Institute of Biomedical Imaging and Bioengineering (NIBIB), and the National Center for Medical Rehabilitation Research (NCMRR) at the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD). The last 10 years have shown significant advances in seamless integration and embodiment of upper and lower prosthetic limbs. NIH-funded activities have focused on the key challenges: attachment, weight, actuators, sensors, power, aesthetics, and algorithms for intuitive control. While not specifically highlighted here, it should be noted that many of the breakthroughs of the past decade build upon many more decades of basic science research that was supported by the NIH. To share knowledge, leverage resources, and avoid duplication of efforts, NIH has collaborated with other federal funders through venues such as the Interagency Committee for Disability Research. In this overview, we provide a cursory summary of NIH's comprehensive research portfolio and encourage readers to visit the NIH Reporter (https://projectreporter.nih.gov/reporter.cfm) for more information.

2 External systems

Active prosthetic systems, i.e. those that are actuated with some kind of power and/or have microprocessor control, have traditionally been controlled by users through human physiological signals that have been collected non-invasively. Although electromyography (EMG) is the most common physiological signal acquisition modality that is used in upper extremity prostheses, other techniques have been explored. Lower extremity prosthetic systems that are controlled with microprocessors have traditionally leveraged data captured though inertia and force sensors that are either onboard the device itself or captured via the remaining limb of the user.

In the last decade, there has been a concerted effort to non-invasively measure user intent, to intuitively control the many degrees of freedom of the state-of-the-art prosthetic devices or to switch between modes of use with a minimal cognitive load. On this front, the field has advanced from simple binary and sequenced controls to proportional EMG controls [5, 6], fusion of EMG and IMU based methods [7, 8], pattern recognition [9], slip detection [10], and machine learning [11, 12] techniques. These advances have resulted in better task execution of upper limb grasping tasks [5] and identification of user intent to transition between states (sitting, standing, walking, stair climbing) in the lower limb [13]. Moving from wet or gel electrodes to dry electrodes will enable easier and more repeatable measurements of EMG signals from residual limbs [14].

Another factor limiting adoption and use of prostheses is the comfort and fit of the prosthetic socket. Investigators are developing sockets to improve comfort and performance [15–17]. Advances in 3D scanning and sensors embedded within the socket are leading to new innovations in building a socket that is innately customized to the user and able to measure the health of the residual limb. There are ongoing clinical trials to demonstrate that 3D scanning and modeling of a limb can produce a more comfortable fit. Adding temperature, pressure, and metabolite sensors within the socket hold the promise of notifying the user when problems arise with fit or limb health [18, 19].

2.1 Electromyography

Electromyography (EMG) is the current standard of care for controlling powered upper extremity prosthetic systems. The most common method includes sensors that are fabricated into the prosthetic socket that identify with specific residual musculature (both in those with transradial and transhumeral amputation). This requires users to activate their muscles with specific magnitude and timing to control their terminal device. Pattern recognition systems have become more common in the past 5 years. These systems "learn" muscle activation patterns based on calibration trials of users attempting to mimic natural hand motions and positions [20]. Outcomes have demonstrated improved function in clinical tests and patient satisfaction. Future work is being conducted to continue to improve algorithms that will improve intuitive control and to reduce or eliminate calibration requirements.

Research has also been conducted to translate use of EMG to those with lower limb loss [21–24]. The use of these systems is not as prevalent however because there are significantly fewer microprocessor controlled prosthetic ankles and knees available compared to upper extremity systems. Results of these studies demonstrated that persons with lower limb loss using prosthetic devices that are driven partially by EMG have the capacity to improve intent recognition, especially in non-reciprocal level-ground gait (i.e. stairs, ramps, and sit-to-stand).

Future work in the field of EMG is exploring how to improve high fidelity signal acquisition from residual musculature to improve intuitive control. One method that is being explored is the use of flexible epidermal electrodes that can conform to any shape of residual limb, which will reduce the need for calibration/re-calibration and contain a high volume of electrodes to sample all musculature, which can improve terminal device control [25].

2.2 Ultrasound

Ultrasound presents some capabilities compared to other capture modalities including the ability to sample deep muscles, spatially recognize individual muscles and provide intuitive proportional control. Preliminary work has demonstrated feasibility of ultrasound to sample muscle activity from subjects with transradial amputation, decode the data using proprietary control algorithms, and proportionally control a simplistic linear movement in a virtual test [26]. Further work will need to be done in this area to overcome limitations of ultrasound use, specifically size, power requirements, interface, and calibration.

2.3 Inertial measurement units (IMUs)

IMUs are small electronic devices that measure triaxial linear accelerations, rotational velocities, and occasionally magnetic fields to determine spatial position/orientation and motion. IMUs have been used to control advanced prosthetic devices, specifically the DEKA/LUKE arm. They are typically placed on the top of the users' shoes and foot motions are used to control additional degrees of freedom of the upper-limb prosthetic device. While this control schema is limited in that it can't be used by those with lower limb or balance impairment or while ambulating, it was recently found to be more effective than EMG pattern recognition for controlling the DEKA/LUKE arm for persons with transradial amputation [27].

2.4 Haptic feedback

A significant aspect missing from external systems is sensation. It is not sufficient for artificial limbs to have dexterous control if the users feel the limbs are 'other', or just a tool. Improving embodiment, the sense of a prosthetic limb belonging to the body, is thought to be a key enabler of recovery and prosthetic use. Understanding grasp force, proprioception, and other aspects of touch are impossible with previously mentioned control strategies as they are only capable of recording and not stimulating. Although vibration as a means of sensory substitution has long been employed in other applications, it has only recently been demonstrated to improve movement control when the muscles used for prosthetic control are given vibratory feedback [28]. Results from additional studies have demonstrated that these systems are feasible and provide some guidance on limb contact and position during various activities [29–31]. In order to provide sensory input, there is a need for innovation in sensors to transduce tactile information in a more biomimetic fashion. This has led to the development of sensorized synthetic skin to mimic mechanoreceptors in human skin [32]. More research is needed to demonstrate the ability of these systems to affect the function and health outcomes of prosthesis users.

Despite these advances, further refinements are required to make prosthetics usable to more people with amputations. While completely intuitive control is still the goal, at present user training and rehabilitation remains a key component of the device development pathway [33]. Surveys of prosthetic users still cite weight, cost, durability, and ease of use as barriers to widespread implementation [34].

3 Training

Training that allows users to leverage advanced devices as quickly and efficiently as possible is most commonly complete with the assistance of Occupational Therapists and simple computer interfaces. This may include training individual muscles to contract with various levels of magnitude and timing and to co-contract with other muscle groups [35].

New training paradigms must also be created for advanced technologies. Resnik et al. implemented a novel training program for patients with shoulder disarticulation using the Gen 3 DEKA Arm. The training focused on skilled unilateral movement as opposed to using the device as an assistant to an intact limb and can be used as a framework for future advanced devices [36].

Recent advances have sought to make training, specifically for upper extremity myoelectric prosthesis use both more accessible, robust and effective. Winslow et al. [37] have designed a mobile, game based platform that allows for home use and for clinicians to both prescribe levels of difficulty and track outcomes. Woodward and Hargrove [38] are designing a system that will challenge users in a virtual environment to improve pattern recognition controlled prostheses.

4 Implanted peripheral systems

Given the limitations of state-of-the-art surface EMG techniques to discern sufficient information to control multiple DOF prosthetics, the improved precision of implantable electrodes for cortical and peripheral recordings has shown great promise over the past 10 years. Technological advances, recently led to the first in human demonstrations of fully implanted myoelectric sensors to control a prosthetic hand with the Implantable MyoElectric Sensors (IMES) system [39]. A branched lead system for a distributed set of longitudinal intrafascicular electrodes built on cochlear implant technology [40, 41] is currently undergoing a clinical trial.

Implanted peripheral interfaces have enabled sophisticated bidirectional interaction with prosthetic limbs. These systems involve an electrical interface to the severed peripheral nerve as well as electrodes embedded in the residual muscles of amputees. Interfaces to the nerve include both penetrating [42] and non-penetrating electrodes [43–45], with trade-offs to consider between invasiveness, longevity, and selectivity. To provide sensory feedback, the electrodes stimulate the peripheral nerve to induce cutaneous and proprioceptive percepts. To correlate these percepts to sensation at specific locations on the prosthetic limb, researchers conduct mapping experiments where they test various stimulation parameters and ask the research participant to report where the sensation is felt on the missing limb. Current research into the best stimulation paradigms is ongoing [46], and vary from simple linear models to more sophisticated biomimetic techniques [47]. Beyond the restoration of somatosensation, electrical stimulation can reduce phantom limb pain [48] and contributes to the sense of limb embodiment [48–50], among other psychosocial benefits [51].

Motor control for an implanted peripheral system translates the descending neural command signal from the nerve and/or the muscles into movement commands for the prosthesis. Rather than relying on pattern recognition, the system involves direct control using either neuromusculoskeletal models [52, 53] or machine learning methods [49, 54, 55]. For the latter, the algorithm is trained by having the participant imagine making movements with his or her limb, often while watching the prosthesis move in virtual reality or physical space. Researchers have successfully decoded multiple degrees of movement using activity from the muscle alone, the nerve alone, and combinations of the two signals [55–57].

Other researchers have sought methods to improve packaging and interconnects, eliminating wires connecting implanted electrodes [58, 59], to harness alternative power sources, such as ultrasound via the neural dust platform [60], to improve wireless power transmission [61], and to stimulate and block neural signals in new ways [62, 63].

Under the DARPA Hand Proprioception and Touch Interfaces (HAPTIX) program (with additional prior and ongoing research from VA, NIH and USAMRMC), researchers are developing a fully implantable prosthetic system that does not require percutaneous leads. The final system is agnostic to the prosthetic limb, and includes the electrodes, implanted stimulation and recording devices, external processors, and algorithms for motor control and sensory feedback. The technology will be evaluated in a year-long take home trial, and teams have already begun to assess home use of the system [64]. The program has also funded efforts to develop metrics that quantify the benefit of sensory feedback for prosthetic limbs [65–69]. These metrics are important for system evaluation and may help to inform future payers. Future research in implanted peripheral systems will involve continuing to explore what types of sensory feedback are the most useful, and improving the longevity, reliability, and resolution of the interface.

5 Brain–machine interfaces

Bidirectional brain–machine interfaces (BMIs) for prosthetic limbs involve translating neural activity from the brain into motor control commands, and stimulating the brain to provide relevant sensory feedback [70]. Among other successes, researchers have demonstrated the ability to use neural activity from the motor cortex of a paralyzed patient to control sophisticated prosthetic limbs [71–73]. Research participants can also use BMIs to control other applications, such as a computer, a wheelchair, or even their own paralyzed arm [74, 75]. With regard to sensation, stimulating somatosensory cortex produces sensory percepts that correlate to locations on the paralyzed or amputated limb [76]. Similar to the peripheral interfaces described above, these sensations provide valuable feedback to the user about his or her interactions with the environment. Future work includes continuing to refine control algorithms and stimulation paradigms and working toward a bidirectional system for use outside of the lab.

6 Surgical techniques and osseointegration

In addition to the systems described above, researchers have also developed a number of surgical techniques that provide unique advantages to neural interfaces for prosthetics. One example is targeted muscle reinnervation (TMR), a procedure that involves rerouting amputated nerves into residual muscles, typically located in the chest or upper arm, which are repurposed after limb loss. Once the amputated nerves have reinnervated into these host muscles, the EMG signal from the new locations is used for successful and intuitive prosthetic control [77]. Analogously, targeted sensory reinnervation (TSR) involves isolating the sensory fascicles from the nerve and attaching them to cutaneous nerves next to where they innervate the skin [78]. Therefore, TMR also creates an opportunity to provide sensation to reinnervated skin, although recent studies show deficits in the integration of multisensory interaction. Specifically, "—although touch sensation on the missing limb can be reliably evoked in TMSR patients—this information is not integrated with visual bodily cues. Indeed, viewing a hand, while performing a tactile spatial discrimination task on the reinnervated skin region, did not improve tactile perception in TMSR patients" [79]. The cortical reorganization that occurs following an amputation should be incorporated into controls schemes and rehabilitation protocols to optimize the functionality from this surgical intervention.

Similar to targeted muscle reinnervation is the regenerative peripheral nerve interface (RPNI). Rather than moving the nerves to a new location, RPNI development involves creating muscle grafts and surgically attaching them to the end of the severed nerves. The nerve integrates into the graft, which serves as an amplifier for the descending neural signal. This larger control signal can in turn be used for individuated finger movement for a prosthetic hand [80, 81]. Stimulating the RPNI may also be useful for restoring sensory feedback.

Another novel surgical construct is the agonist–antagonist myoneural interface (AMI). The AMI involves connecting an agonist and antagonist muscle–tendon mechanically in series, so that one when component contracts (e.g. the agonist), the other (e.g. antagonist) stretches [82]. AMIs can be created during an amputation or post-hoc. EMG signals from the AMI are used for prosthetic control, and a separate AMI is typically constructed for each degree-of-freedom. The push and pull of the two components also provides proprioceptive feedback back to the individual that inherent to the natural muscle. These proprioceptive signals allow a prosthesis user to intuitively move the limb without relying on visual feedback. Functional electrical stimulation of the AMI can also be used to provide torque feedback to the user.

Direct skeletal attachment of a prosthetic limb to a percutaneous osseointegrated implant has been shown to be equivalent or superior to sockets in most studies thus far [83]. The potential benefits include an elimination of socket-related issues, much faster and easier donning and doffing, improved range of motion, and an improved mechanical connection between the prosthetic device and user. The risks include the requirement for one or two surgical procedures and the concomitant healing time and rehabilitation required, as well as the ongoing risk of infection caused by the percutaneous component and potential for device failure/removal. Persons with amputation may weigh these risks and benefits differently for their own needs and desires, but 28% of unilateral and 13% of bilateral upper-limb amputees were willing to consider osseointegration surgery [84].

Along with TMR and the RPNI, the osseointegrated neural interface (ONI) is another surgical solution to improving peripheral neural interfaces. The ONI involves rerouting the severed nerve into the medullary canal of residual bone, which provides insulation and a solid support framework that reduces both movement artifacts and crosstalk [85, 86]. The nerve may be interfaced to an electrode array of choice, and these signals can subsequently be routed through the metal osseointegrated interface that ultimately connects to a prosthesis. Beyond facilitating prosthetic control, the ONI, along with TMR and the RPNI, help to address and prevent neuromas. Additionally, this could eliminate the need for some implanted components like batteries and transcutaneous inductive charging coils and using hardwired rather than wireless communications could also improve system reliability and data security.

7 Regenerative techniques

Regenerative techniques show promise for increasing the dimensionality of peripheral neural interface, though they often involve cutting a nerve in two, and are therefore uniquely applicable for amputees. One such technique is the use of a tissue-engineered electronic nerve interface, or TEENI, which includes flexible polymer-based electrode threads embedded in a hydrogel nerve bioscaffold [87]. To place the construct, the surgeon cuts the amputated nerve at the distal end and installs the TEENI between the residual nerve and the nerve that was cut. Nerve tissue subsequently regenerates around the electrodes. Integration with the flexible construct encourages mechanically compatibility. Because the regenerative approach does not require implanting each thread into the nerve, the design may have the potential to scale to high channel counts.

Other regenerative methods include the sieve electrode designs. Similar to TEENI, the sieve requires transecting the nerve to place the technology. Implantation involves placing a disk between the two segments of nerve that includes holes and contacts throughout. The nerve then regenerates through the holes and makes a physical connection with the contacts. Recent investment in modeling micro-channel sieves has demonstrated their potential use for both stimulation and recording [88, 89]. Future work for regenerative methods include testing resolution and reliability and animal models to establish the proof-of-concept to translate the technology into humans.

8 Discussion

The US Government, specifically the DoD, VA, and NIH have invested research and development funding towards the advancement of intuitive control and sensation of prosthetics. While the target populations for these agencies may differ: Active Duty Warfighters, Veterans, or the General Public, the overall objective is to provide the highest possible function, performance, quality of life, and health outcomes that will allow those with limb loss to accomplish their goals.

Along with greater focus on intuitive control and sensation over the past decade, there has also been greater collaboration and discussion between federal agencies, with the overall goal of being transparent and avoiding redundancy of efforts and the intention of moving the science forward as quickly and safely as possible, to deliver solutions to the limb loss community. Collaborative efforts include not just DoD, VA, and NIH but also other federal agencies that fund research in this area such as the National Institute on Disability, Independent Living, and Rehabilitation Research (NIDILRR), and the National Science Foundation (NSF), and federal agencies responsible for regulation and policy such as the Food and Drug Administration (FDA), Centers for Medicare and Medicaid Services (CMS), and National Institute for Standards and Technology (NIST).

These federal agencies have also supported the development of large centers across the country with the intention to drive change forward quickly through impactful research and translation of findings to enhance the standard of care. The Extremity Trauma and Amputation Center of Excellence (EACE) is a joint DoD-VA organizations, the VA has additionally established both the Amputation System of Care and the Center for Limb Loss and MoBility (CLiMB), and both NIDILRR and NCMRR have funded several Centers that are conducting and supporting research focused on or relevant to the limb loss population.

Initiatives within these agencies and others will produce solutions and knowledge that will benefit this limb loss population. The NIH has launched The Brain Research through Advancing Innovative Neurotechnologies BRAIN Initiative and the Stimulating Peripheral Activity to Relieve Conditions (SPARC) Common Fund Program. The BRAIN Initiative is aimed at revolutionizing our understanding of the human brain and the SPARC Program is developing next generation tools and technologies for neural interfacing with the peripheral nervous system. DARPA has initiated the Next-Generation Nonsurgical Neurotechnology (N^3) program. This program aims to develop a high-resolution, portable neural interface system that is either completely noninvasive or only minutely invasive to enable practical applications of neurotechnology for able-bodied individuals. The VA has developed the VHA Innovation Ecosystem which seeks to align interests and improve the efficiency of innovation resources across the enterprise. USAMRMC introduced the Accelerating Innovation in Military Medicine (AIMM) Program which supports highly innovative high-risk research with the potential to accelerate critical discoveries or major advancements that will significantly impact military health and medicine.

While significant advancements have been made over the past quarter-century, there are still gaps that remain in delivering a prosthetic system to people living with limb loss that reproduces the abilities of an anatomical limb. Challenges may be related to the technology, including power capabilities, data transfer and signal fidelity acutely and long term, to the patient, including safety, infection, interface and comorbidities that may cause complications, or to the environment, including occupation and psychosocial factors.

The federal government will continue to invest in research and development efforts toward delivering prosthetic systems to fully restore the function, performance, health and quality of life of those living with limb loss. Achieving this goal will contribute to the mission of each agency involved. Collaboration between federal agencies investing in this area will continue, to ensure that each agencies' goals can be achieved as quickly and efficiently as possible, and to deliver the best possible solutions to the limb loss community.

Compliance with ethical standards

Conflict of interest The authors declares that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

References

1. Biddiss EA, Chau TT. Upper limb prosthesis use and abandonment: a survey of the last 25 years. Prosthet Orthot Int. 2007;31(3):236–57.
2. Amputee Database. Extremity Trauma and Amputation Center of Excellence. 2018.
3. Dickey NW. Sustainment and advancement of amputee care. Defense health agency/defense health board falls church United States. 2015.
4. VSSC Amputee Data Repository Cube. VHA Amputation System of Care. 2019.
5. Dalley SA, Varol HA, Goldfarb M. A method for the control of multigrasp myoelectric prosthetic hands. IEEE Trans Neural Syst Rehabil Eng. 2012;20(1):58–67.
6. Smith LH, Kuiken TA, Hargrove LJ. Real-time simultaneous and proportional myoelectric control using intramuscular EMG. J Neural Eng. 2014;11(6):66013–66013.
7. Bennett DA, Goldfarb M. IMU-based wrist rotation control of a transradial myoelectric prosthesis. IEEE Trans Neural Syst Rehabil Eng. 2018;26(2):419–27.
8. Huang H, Zhang F, Hargrove LJ, Dou Z, Rogers DR, Englehart KB. Continuous locomotion-mode identification for prosthetic legs based on neuromuscular-mechanical fusion. IEEE Trans Biomed Eng. 2011;58(10):2867–75.
9. Tkach D, Huang H, Kuiken TA. Study of stability of time-domain features for electromyographic pattern recognition. J Neuroeng Rehabil. 2010;7(1):21–21.
10. Ray Z, Engeberg ED. Human-inspired reflex to autonomously prevent slip of grasped objects rotated with a prosthetic hand. J Healthc Eng. 2018;2018:1–11.

11. Gailey A, Artemiadis P, Santello M. Proof of concept of an online EMG-based decoding of hand postures and individual digit forces for prosthetic hand control. Front Neurol. 2017;8:7.
12. Twardowski MD, Roy SH, Li Z, Contessa P, Luca GD, Kline JC. Motor unit drive: a neural interface for real-time upper limb prosthetic control. J Neural Eng. 2019;16(1):16012.
13. Spanias JA, Simon A, Finucane SB, Perreault E, Hargrove LJ. Online adaptive neural control of a robotic lower limb prosthesis. J Neural Eng. 2018;15(1):16015.
14. Yamagami M, Peters KM, Milovanovic I, Kuang I, Yang Z, Lu N, Steele KM. Assessment of dry epidermal electrodes for long-term electromyography measurements. Sensors. 2018;18(4):1269.
15. Fatone S, Caldwell R. Northwestern University Flexible Subischial Vacuum Socket for persons with transfemoral amputation-part 1: description of technique. Prosthet Orthot Int. 2017;41(3):237–45.
16. Fatone S, Johnson WB, Tran L, Tucker K, Mowrer C, Caldwell R. Quantification of rectifications for the Northwestern University Flexible Sub-Ischial Vacuum Socket. Prosthet Orthot Int. 2017;41(3):251–7.
17. Kahle JT, Highsmith MJ. Transfemoral sockets with vacuum-assisted suspension comparison of hip kinematics, socket position, contact pressure, and preference: ischial containment versus brimless. J Rehabil Res Dev. 2013;50(9):1241–52.
18. Han S, Kim J, Won SM, Ma Y, Kang D, Xie Z, Lee KT, Chung HU, Banks A, Min S, Heo SY, Davies CR, Lee JW, Lee CH, Kim BH, Li K, Zhou Y, Wei C, Feng X, Huang Y, Rogers JA. Battery-free, wireless sensors for full-body pressure and temperature mapping. Sci Transl Med. 2018;10(435):eaan4950.
19. Tran L, Caldwell R, Quigley M, Fatone S. Stakeholder perspectives for possible residual limb monitoring system for persons with lower-limb amputation. Disabil Rehabil. 2018;1–8.
20. Hargrove LJ, Miller LA, Turner K, Kuiken TA. Myoelectric pattern recognition outperforms direct control for transhumeral amputees with targeted muscle reinnervation: a randomized clinical trial. Sci Rep. 2017;7(1):13840.
21. Au SK, Bonato P, Herr H. An EMG-position controlled system for an active ankle-foot prosthesis: an initial experimental study. In: 9th international conference on rehabilitation robotics, 2005. ICORR 2005; 2005.
22. Young AJ, Kuiken TA, Hargrove LJ. Analysis of using EMG and mechanical sensors to enhance intent recognition in powered lower limb prostheses. J Neural Eng. 2014;11(5):56021.
23. Alcaide-Aguirre RE, Morgenroth DC, Ferris DP. Motor control and learning with lower-limb myoelectric control in amputees. J Rehabil Res Dev. 2013;50(5):687–98.
24. Huang S, Ferris DP. Muscle activation patterns during walking from transtibial amputees recorded within the residual limb-prosthetic interface. J Neuroeng Rehabil. 2012;9(1):55–55.
25. Tian L, Zimmerman B, Akhtar A, Yu KJ, Moore M, Wu J, Larsen RJ, Lee JW, Li J, Liu Y, Metzger B, Qu S, Guo X, Mathewson KE, Fan JA, Cornman J, Fatina M, Xie Z, Ma Y, Zhang J, Zhang Y, Dolcos F, Fabiani M, Gratton G, Bretl T, Hargrove LJ, Braun PV, Huang Y, Rogers JA. Large-area MRI-compatible epidermal electronic interfaces for prosthetic control and cognitive monitoring. Nat Biomed Eng. 2019;3(3):194–205.
26. Dhawan AS, Mukherjee B, Patwardhan S, Akhlaghi N, Levay G, Holley RJ, Joiner WM, Harris-Love M, Sikdar S. Proprioceptive Sonomyographic Control: a novel method of intuitive proportional control of multiple degrees of freedom for upper-extremity amputees. bioRxiv; 2018. p. 387290.
27. Resnik LJ, Acluche F, Borgia M, Cancio J, Latlief G, Phillips S, Sasson N. EMG pattern recognition compared to foot control of the DEKA Arm. PLoS ONE. 2018;13(10):e0204854.
28. Marasco PD, Hebert JS, Sensinger JW, Shell CE, Schofield JS, Thumser ZC, Nataraj R, Beckler DT, Dawson MR, Blustein DH, Gill S, Mensh BD, Granja-Vazquez R, Newcomb MD, Carey JP, Orzell BM. Illusory movement perception improves motor control for prosthetic hands. Sci Transl Med. 2018;10(432):eaao6990.
29. Fan RE, Culjat MO, King C-H, Franco ML, Boryk R, Bisley JW, Dutson E, Grundfest WS. A haptic feedback system for lower-limb prostheses. IEEE Trans Neural Syst Rehabil Eng. 2008;16(3):270–7.
30. Fan RE, Wottawa C, Mulgaonkar A, Boryk RJ, Sander TC, Wyatt MP, Dutson E, Grundfest WS, Culjat MO. Pilot testing of a haptic feedback rehabilitation system on a lower-limb amputee. In: 2009 ICME international conference on complex medical engineering; 2009.
31. Sie A, Realmuto J, Rombokas E. A lower limb prosthesis haptic feedback system for stair descent. In: 2017 design of medical devices conference; 2017.
32. Osborn L, Nguyen H, Betthauser J, Kaliki RR, Thakor NV. Biologically inspired multi-layered synthetic skin for tactile feedback in prosthetic limbs. In: 2016 38th annual international conference of the IEEE Engineering in Medicine and Biology Society (EMBC); 2016.
33. Powell MA, Kaliki RR, Thakor NV. User training for pattern recognition-based myoelectric prostheses: improving phantom limb movement consistency and distinguishability. IEEE Trans Neural Syst Rehabil Eng. 2014;22(3):522–32.
34. Engdahl SM, Christie BP, Kelly B, Davis A, Chestek CA, Gates DH. Surveying the interest of individuals with upper limb loss in novel prosthetic control techniques. J Neuroeng Rehabil. 2015;12(1):53–53.
35. Dawson MR, Carey JP, Fahimi F. Myoelectric training systems. Expert Rev Med Devices. 2011;8(5):581–9.
36. Resnik L, Klinger SL, Korp K, Walters LS. Training protocol for a powered shoulder prosthesis. J Rehabil Res Dev. 2014;51(8):vii.
37. Winslow BD, Ruble M, Huber Z. Mobile, game-based training for myoelectric prosthesis control. Front Bioeng Biotechnol 2018;6:94.
38. Woodward RB, Hargrove LJ. Adapting myoelectric control in real-time using a virtual environment. J Neuroeng Rehabil. 2019;16(1):11.
39. Pasquina PF, Evangelista M, Carvalho AJ, Lockhart J, Griffin S, Nanos G, McKay P, Hansen M, Ipsen D, Vandersea J, Butkus J, Miller M, Murphy I, Hankin D. First-in-man demonstration of a fully implanted myoelectric sensors system to control an advanced electromechanical prosthetic hand. J Neurosci Methods. 2015;244:85–93.
40. Pena AE, Kuntaegowdanahalli SS, Abbas J, Patrick J, Horch KW, Jung R. Mechanical fatigue resistance of an implantable branched lead system for a distributed set of longitudinal intrafascicular electrodes. J Neural Eng. 2017;14(6):66014.
41. Jung R, Abbas JJ, Kuntaegowdanahalli S, Thota AK. Bionic intrafascicular interfaces for recording and stimulating peripheral nerve fibers. Bioelectromagnetics. 2018;1(1):55–69.
42. Lachapelle JR, Bjune CK, Kindle AL, Czarnecki A, Burns JR, Grainger JE, Segura CA, Nugent BD, Sriram TS, Parks PD, Keefer E, Cheng JJ. An implantable, designed-for-human-use peripheral nerve stimulation and recording system for advanced prosthetics. In: 2016 38th annual international conference of the IEEE Engineering in Medicine and Biology Society (EMBC); 2016.
43. Schiefer M, Tan D, Sidek SM, Tyler DJ. Sensory feedback by peripheral nerve stimulation improves task performance in individuals with upper limb loss using a myoelectric prosthesis. J Neural Eng. 2016;13(1):16001–16001.

44. Tan DW, Schiefer MA, Keith MW, Anderson JR, Tyler DJ. Stability and selectivity of a chronic, multi-contact cuff electrode for sensory stimulation in a human amputee. In: 2013 6th international IEEE/EMBS conference on neural engineering (NER); 2013.
45. Charkhkar H, Shell CE, Marasco PD, Pinault GJ, Tyler DJ, Triolo RJ. High-density peripheral nerve cuffs restore natural sensation to individuals with lower-limb amputations. J Neural Eng. 2018;15(5):56002.
46. Graczyk EL, Schiefer MA, Saal HP, Delhaye BP, Bensmaia SJ, Tyler DJ. The neural basis of perceived intensity in natural and artificial touch. Sci Transl Med. 2016;8(362):362ra142.
47. Saal HP, Bensmaia SJ. Biomimetic approaches to bionic touch through a peripheral nerve interface. Neuropsychologia. 2015;79:344–53.
48. Petersen BA, Nanivadekar AC, Chandrasekaran S, Fisher LE. Phantom limb pain: peripheral neuromodulatory and neuroprosthetic approaches to treatment. Muscle Nerve. 2019;59(2):154–67.
49. George JA, Brinton MR, Duncan CC, Hutchinson DT, Clark GA. Improved training paradigms and motor-decode algorithms: results from intact individuals and a recent transradial amputee with prior complex regional pain syndrome. In: 2018 40th annual international conference of the IEEE Engineering in Medicine and Biology Society (EMBC); 2018.
50. Page DM, George JA, Kluger DT, Duncan C, Wendelken S, Davis T, Hutchinson DT, Clark GA. Motor control and sensory feedback enhance prosthesis embodiment and reduce phantom pain after long-term hand amputation. Front Hum Neurosci. 2018;12:352.
51. Graczyk EL, Gill A, Tyler DJ, Resnik LJ. The benefits of sensation on the experience of a hand: a qualitative case series. PLoS ONE. 2019;14(1):e0211469.
52. Gritsenko V, Hardesty RL, Boots MT, Yakovenko S. Biomechanical constraints underlying motor primitives derived from the musculoskeletal anatomy of the human arm. PLoS ONE. 2016;11(10):e0164050.
53. Pan L, Crouch D, Huang H. Musculoskeletal model for simultaneous and proportional control of 3-DOF hand and wrist movements from EMG signals. In: 2017 8th international IEEE/EMBS conference on neural engineering (NER); 2017.
54. Dantas H, Warren DJ, Wendelken S, Davis T, Clark GA, Mathews VJ. Deep learning movement intent decoders trained with dataset aggregation for prosthetic limb control. IEEE Trans Biomed Eng. 2019.
55. Yang Z, Nguyen AT, Jiang M, Tong W, Tam W, Zhao W. 15-DOF motor decoding based on a high performance PNS interface and deep neural network. Program No. 271.02.2018 Neuroscience Meeting Planner. San Diego, CA: Society for Neuroscience, 2018. Online.
56. Wendelken S, Page DM, Davis T, Wark HAC, Kluger DT, Duncan C, Warren DJ, Hutchinson DT, Clark GA. Restoration of motor control and proprioceptive and cutaneous sensation in humans with prior upper-limb amputation via multiple Utah Slanted Electrode Arrays (USEAs) implanted in residual peripheral arm nerves. J Neuroeng Rehabil. 2017;14(1):121.
57. Clark GA, Wendelken SM, Page DM, Davis TS, Wark HAC, Normann RA, Warren DJ, Hutchinson DT. Using multiple high-count electrode arrays in human median and ulnar nerves to restore sensorimotor function after previous transradial amputation of the hand. In: Conference proceedings: ... annual international conference of the IEEE Engineering in Medicine and Biology Society. IEEE Engineering in Medicine and Biology Society. Annual Conference; 2014.
58. Ersen A, Sahin M. Polydimethylsiloxane-based optical waveguides for tetherless powering of floating microstimulators. J Biomed Opt. 2017;22(5):55005–55005.
59. Yin M, Borton DA, Komar J, Agha N, Lu Y, Li H, Laurens J, Lang Y, Li Q, Bull C, Larson L, Rosler D, Bezard E, Courtine G, Nurmikko AV. Wireless neurosensor for full-spectrum electrophysiology recordings during free behavior. Neuron. 2014;84(6):1170–82.
60. Neely RM, Piech DK, Santacruz SR, Maharbiz MM, Carmena JM. Recent advances in neural dust: towards a neural interface platform. Curr Opin Neurobiol. 2018;50:64–71.
61. Lee B, Yeon P, Ghovanloo M. A multicycle Q-modulation for dynamic optimization of inductive links. IEEE Trans Ind Electron. 2016;63(8):5091–100.
62. Roldan LM, Eggers TE, Kilgore KL, Bhadra N, Vrabec T, Bhadra N. Measurement of block thresholds in kiloHertz frequency alternating current peripheral nerve block. J Neurosci Methods. 2019;315:48–544.
63. Fisher LE, Tyler DJ, Triolo RJ. Optimization of selective stimulation parameters for multi-contact electrodes. J Neuroeng Rehabil. 2013;10(1):25–25.
64. Graczyk EL, Resnik L, Schiefer MA, Schmitt MS, Tyler DJ. Home use of a neural-connected sensory prosthesis provides the functional and psychosocial experience of having a hand again. Sci Rep. 2018;8(1):9866.
65. Blustein D, Wilson A, Sensinger J. Assessing the quality of supplementary sensory feedback using the crossmodal congruency task. Sci Rep. 2018;8(1):6203.
66. Shehata AW, Scheme EJ, Sensinger JW. Evaluating internal model strength and performance of myoelectric prosthesis control strategies. IEEE Trans Neural Syst Rehabil Eng. 2018;26(5):1046–55.
67. Thumser ZC, Slifkin AB, Beckler DT, Marasco PD. Fitts' law in the control of isometric grip force with naturalistic targets. Front Psychol. 2018;9:560.
68. Valevicius AM, Boser QA, Lavoie EB, Murgatroyd GS, Pilarski PM, Chapman CS, Vette AH, Hebert JS. Characterization of normative hand movements during two functional upper limb tasks. PLoS ONE. 2018;13(6):e0199549.
69. Beckler D, Thumser Z, Schofield J, Marasco P. Fitts' Law in the control of isometric grip force with naturalistic targets. Front Psychol. 2018;9:560.
70. Collinger JL, Gaunt RA, Schwartz AB. Progress towards restoring upper limb movement and sensation through intracortical brain–computer interfaces. Curr Opin Biomed Eng. 2018;8:84–92.
71. Collinger JL, Wodlinger B, Downey JE, Wang W, Tyler-Kabara EC, Weber DJ, McMorland AJC, Velliste M, Boninger ML, Schwartz AB. High-performance neuroprosthetic control by an individual with tetraplegia. Lancet. 2013;381(9866):557–64.
72. Wodlinger B, Downey JE, Tyler-Kabara EC, Schwartz AB, Boninger ML, Collinger JL. Ten-dimensional anthropomorphic arm control in a human brain−machine interface: difficulties, solutions, and limitations. J Neural Eng. 2015;12(1):16011.
73. Hochberg LR, Bacher D, Jarosiewicz B, Masse NY, Simeral JD, Vogel J, Haddadin S, Liu J, Cash SS, van der Smagt P, Donoghue JP. Reach and grasp by people with tetraplegia using a neurally controlled robotic arm. Nature. 2012;485(7398):372–5.
74. Ajiboye AB, Willett FR, Young DR, Memberg WD, Murphy BA, Miller JP, Walter BL, Sweet JA, Hoyen HA, Keith MW, Peckham PH, Simeral JD, Donoghue JP, Hochberg LR, Kirsch RF. Restoration of reaching and grasping movements through brain-controlled muscle stimulation in a person with tetraplegia: a proof-of-concept demonstration. Lancet. 2017;389(10081):1821–30.
75. Bockbrader M, Annetta N, Friedenberg D, Schwemmer M, Skomrock N, Colachis S, Zhang M, Bouton C, Rezai A, Sharma G, Mysiw WJ. Clinically significant gains in skillful grasp coordination by an individual with tetraplegia using an implanted brain–computer interface with forearm transcutaneous muscle stimulation. Arch Phys Med Rehabil. 2019;100:1201–17.

76. Flesher SN, Collinger JL, Foldes ST, Weiss JM, Downey JE, Tyler-Kabara EC, Bensmaia SJ, Schwartz AB, Boninger ML, Gaunt RA. Intracortical microstimulation of human somatosensory cortex. Sci Transl Med. 2016;8(361):361ra141.
77. Kuiken TA, Li G, Lock BA, Lipschutz RD, Miller LA, Stubblefield KA, Englehart KB. Targeted muscle reinnervation for real-time myoelectric control of multifunction artificial arms. JAMA. 2009;301(6):619–28.
78. Hebert JS, Olson JL, Morhart MJ, Dawson MR, Marasco PD, Kuiken TA, Chan KM. Novel targeted sensory reinnervation technique to restore functional hand sensation after transhumeral amputation. IEEE Trans Neural Syst Rehabil Eng. 2014;22(4):765–73.
79. Serino A, Akselrod M, Salomon R, Martuzzi R, Blefari ML, Canzoneri E, Rognini G, Zwaag WVD, Iakova M, Luthi F, Amoresano A, Kuiken T, Blanke O. Upper limb cortical maps in amputees with targeted muscle and sensory reinnervation. Brain. 2017;140(11):2993–3011.
80. Frost CM, Ursu DC, Flattery SM, Nedic A, Hassett CA, Moon JD, Buchanan PJ, Gillespie RB, Kung TA, Kemp SWP, Cederna PS, Urbanchek MG. Regenerative peripheral nerve interfaces for real-time, proportional control of a Neuroprosthetic hand. J Neuroeng Rehabil. 2018;15(1):108.
81. Urbanchek MG, Sando IC, Irwin ZT, Vu PP, Woo SL, Chestek CA, Cederna PS. Abstract: validation of regenerative peripheral nerve interfaces for control of a myoelectric hand by macaques and human. Plast Reconstr Surg Glob Open. 2016;4:69.
82. Clites TR, Carty MJ, Ullauri JB, Carney ME, Mooney LM, Duval J-F, Srinivasan SS, Herr HM. Proprioception from a neurally controlled lower-extremity prosthesis. Sci Transl Med. 2018;10(443):eaap8373.
83. Phillip RD, Al MM, Kay AR, Kendrew JM. Osseointegration in bilateral above-knee amputees following blast: a review of the first five UK cases. In: Orthopaedic proceedings; 2018.
84. Resnik L, Benz H, Borgia M, Clark MA. Patient perspectives on osseointegration: a National Survey of Veterans with upper limb amputation. Pm&r; 2019.
85. Israel JS, Dingle AM, Sanchez RJ, Kapur SK, Brodnick S, Richner TJ, Ness JP, Novello J, Williams JC, Poore SO. Neuroma implantation into long bones: clinical foundation for a novel osseointegrated peripheral nerve interface. Plast Reconstr Surg Glob Open. 2018;6(5).
86. Mastinu E, Clemente F, Sassu P, Aszmann O, Branemark R, Hakansson B, Controzzi M, Cipriani C, Ortiz-Catalan M. Grip control and motor coordination with implanted and surface electrodes while grasping with an osseointegrated prosthetic hand. J Neuroeng Rehabil. 2019;16(1):49.
87. Spearman BS, Desai VH, Mobini S, McDermott MD, Graham JB, Otto KJ, Judy JW, Schmidt CE. Tissue-engineered peripheral nerve interfaces. Adv Func Mater. 2018;28(12):1701713.
88. Coker R, Zellmer E, Moran D. Micro-channel sieve electrode for concurrent bidirectional peripheral nerve interface. Part A: recording. J Neural Eng. 2019;16(2):26001.
89. Coker R, Zellmer E, Moran D. "Micro-channel sieve electrode for concurrent bidirectional peripheral nerve interface. Part B: stimulation. J Neural Eng. 2019;16(2):26002.