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PERSPECTIVE

# Bidirectional bionic limbs: a perspective bridging technology and physiology

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## Abstract

Precise control of bionic limbs relies on robust decoding of motor commands from nerves or muscles signals and sensory feedback from artificial limbs to the nervous system by interfacing the afferent nerve pathways. Implantable devices for bidirectional communication with bionic limbs have been developed in parallel with research on physiological alterations caused by an amputation. In this perspective article, we question whether increasing our effort on bridging these technologies with a deeper understanding of amputation pathophysiology and human motor control may help to overcome pressing stalls in the next generation of bionic limbs.

## 1. Introduction

The last decade has witnessed unprecedented progress toward the interfacing of prosthetic devices with the peripheral nervous system for the bidirectional control of robotic limbs [1–15]. Implantable myoelectric systems have been developed to read motor neural signals and decode user intentions as well as kinematic and kinetic information [4, 16–18]. Significant growth also occurred in the field of implantable devices that deliver sensory feedback from artificial limbs to the nervous system by interfacing the afferent nerve pathways [3, 5, 19–24]. Targeted muscle reinnervation [25], osseointegration [8], regenerative peripheral nerve interfaces [26] and agonist-antagonist myoneural interface (AMI) [27] are successful surgery interventions that have moved the field forward. Such remarkable progress emerged from concerted advances and close cooperation between emerging technologies, engineering, neurosciences, neurosurgery and orthopaedics.

While these highly refined prostheses fail to completely restore function and sensory feedback, they perform extremely well in clinical testing [28] and home-use trials [29–32]. Current bidirectional prostheses promote intuitive control [33], but they still cannot be controlled to produce human-like motion patterns and to delivery truly natural sensations [34]. One question is whether these technological advances have grown apart from our current understanding of the structural and neurophysiological alterations that occur post-amputation (figure 1), resulting in efforts to restore a disrupted system that we do not totally understand. An excellent review on the theory of human motor control and how it can help to improve sensory feedback in upper limb prostheses has been recently published by Sensinger and Dosen [35]. Sharing our concerns, the authors claim that even human motor control have been extensively studied in able-bodied individuals, it remains poorly explored in amputee populations. They propose a set of guidelines to incorporate motor control in future experiment design and assessment of artificial sensory feedback.

In this perspective article, we present the state-of-the-art in bidirectional prostheses and our

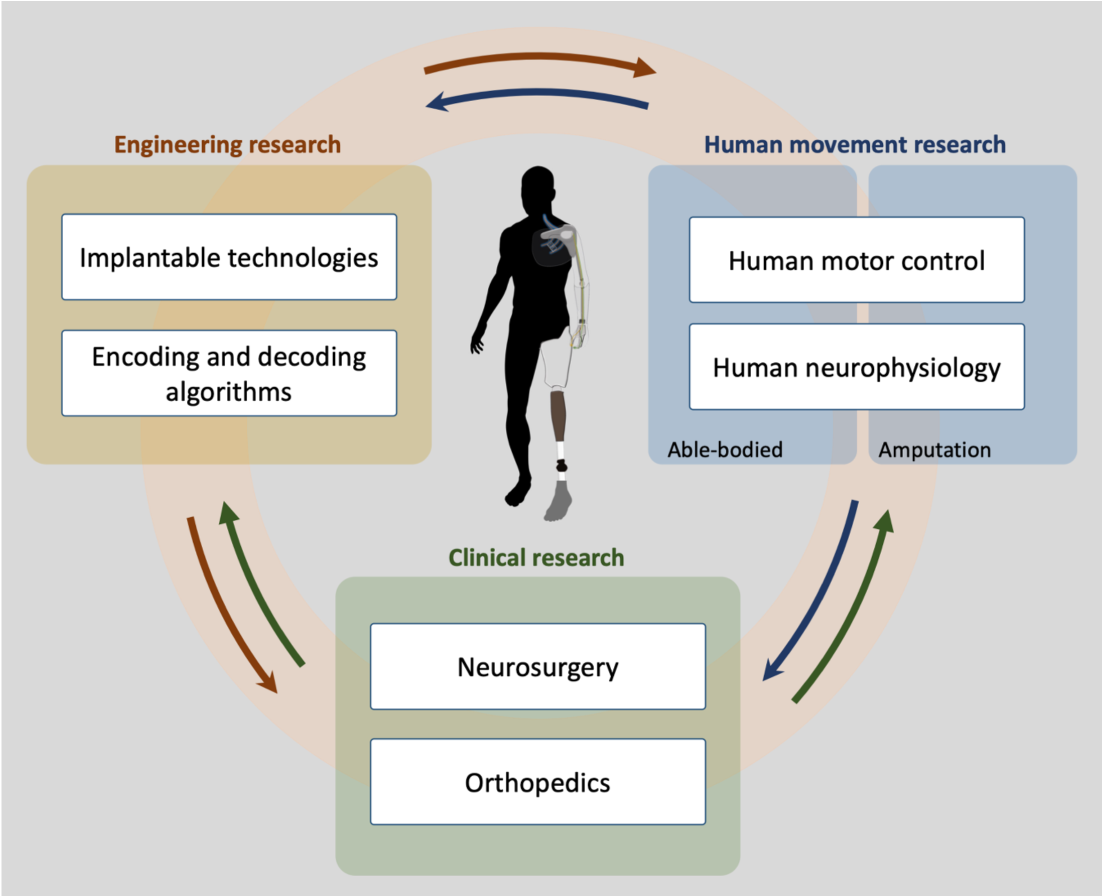


**Figure 1.** Merging engineering research with human movement science and clinical research is fundamental to further the development of bionics limbs with sensory feedback.

critical view on the historical divergences of engineering advancement and our knowledge of fundamental post-amputation physiology. We describe research foci that could help to overcome current stalls toward the next generation of bionic limbs.

## 2. Advanced neural interfaces

Controlling bidirectional prosthetic devices during activities of daily living requires the development of an intuitive and effortless neural interface. This challenging task can be split in the recording of efferent motor signal and their decoding (motor commands to the prosthesis), and the stimulation of afferent pathways to restore sensations (sensory feedback from the prosthesis). The success of both recording and stimulation depends on specialized hardware and software.

### 2.1. Accessing the nervous system with minimal damage

From the hardware side, optimal access to the nervous system requires invasive procedures interfacing the efferent and afferent nerve pathways. In this regard, the Cuff [36], FINE[7] [23], TIME[8] [3, 37, 38] (figure 2), LIFE[9] [39] and USEA[10] [40] are different types of epineural and intraneural nerve interfaces successfully developed to record electroneurography signals and stimulate sensory pathways [41]. The Cuff and FINE are similar neural interfaces that do not penetrate but surround the nerve, with the FINE gently flatting the nerve to improve accessibility to different fascicles. The TIME, LIFE and USEA are highly invasive neural interfaces that penetrate the nerve fascicles, with the advantage of greater stimulation selectivity. All of these neural interfaces have proven stability over long periods of time (from months to years), making them suitable for permanent implantation.

Recording of nerve signals to decipher motor commands is still challenging but feasible as preliminary results on extraction of relevant motor information show. For example, using recorded intraneural activity from four TIME neural interfaces implanted

[7] FINE: flat interface nerve electrodes.

[8] TIME: transversal intrafascicular multichannel electrodes.

[9] LIFE: longitudinal intrafascicular electrodes.

[10] USEA: Utah slanted electrode array.

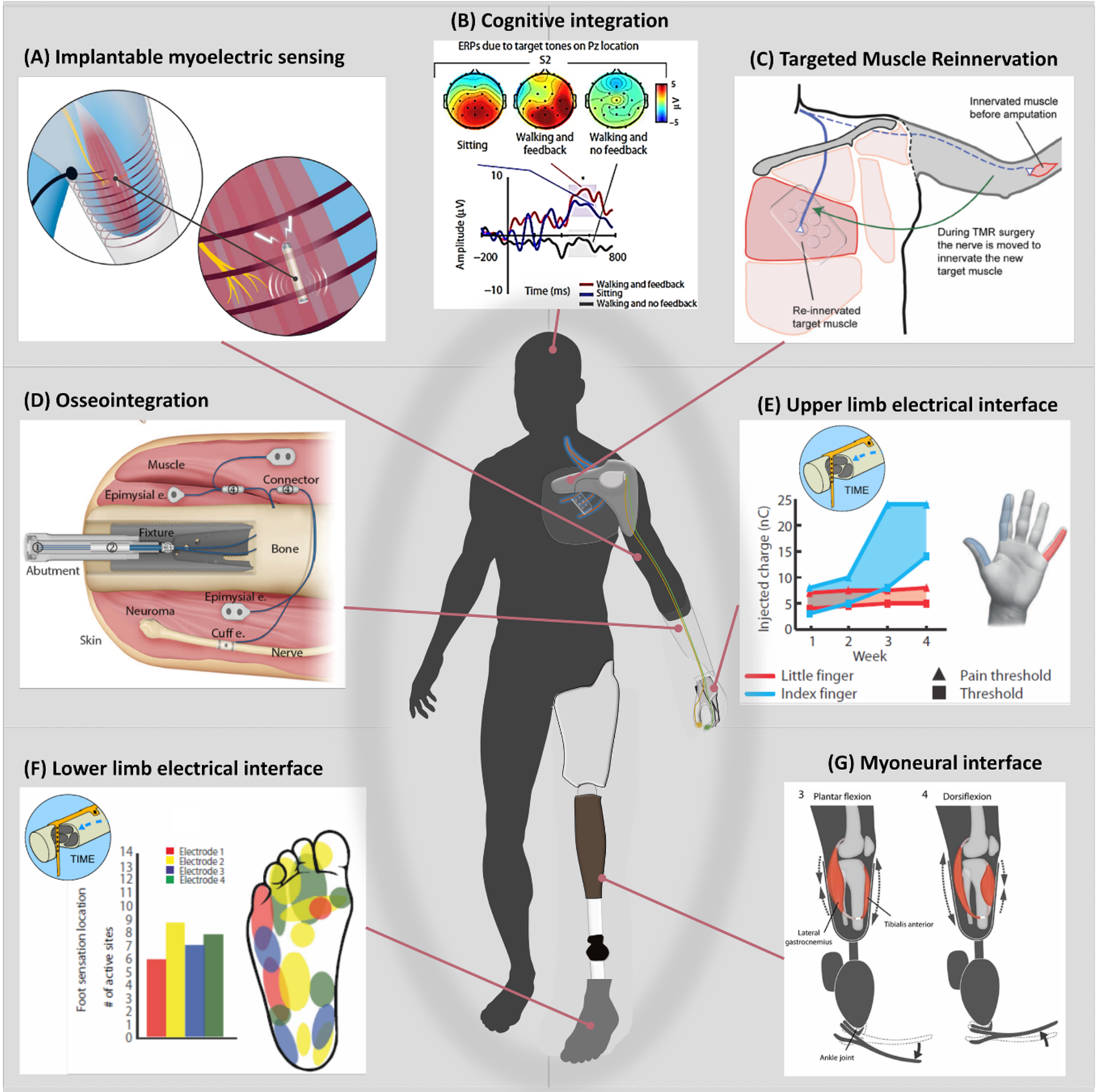


**Figure 2.** Current advances in bidirectional control of limb prostheses. The combined efforts of engineers, neurosurgeons and orthopedists are represented in the different approaches to restore the sensorimotor control of the missing limb. (A) The IMES technology. From [7]. Reprinted with permission from AAAS. (B) EEG signals showing cognitive integration after electrical stimulation of lower-limb nerve fibers. From [1]. Reprinted with permission from AAAS. (C) TMR advanced neurosurgery. Reprinted by permission from Springer Nature Customer Service Centre GmbH: Springer Nature, Current Surgery Reports [23] Control Strategies: A Clinical Perspective, Roche A D, Rehbaum H, Farina D and Aszmann O C, (c) 2014. (D) Osseointegration advanced orthopedic surgery. From [42]. Reprinted with permission from AAAS. (E) TIME interface to restore sensation in upper-limb prosthesis. From [5]. Reprinted with permission from AAAS. (F) TIME interface to restore sensations in lower-limb prosthesis. From [1]. Reprinted with permission from AAAS. (G) The myoneural interface as a novel neurosurgery to restore proprioception in lower-limb amputees. From [40]. Reprinted with permission from AAAS.

in the median and ulnar nerves of a transradial amputee, an outstanding offline decoding accuracy (of up to 83%) of 11 imaginary hand motor tasks was possible [42]. In addition, the combination of TMR with implantable multichannel electromyographic (EMG) sensors that transmits wirelessly to the prosthetic device (figures 2(A) and (C)) has proven viability as a chronically implanted myoelectric interface, leading to substantial functional improvement of the prosthesis [4, 16–18].

### 2.2. Decoding and encoding neural information

From the software side, and as important as the technology itself, mathematical modeling is required to decode neural information to produce motor outputs that accurately match the intention of the patient [41, 43–45]. Decoding single motor unit activity *in vivo* and in real time is one of the most challenging endeavors in human electrophysiology. Up to now, this has been successfully achieved by decomposing surface EMG signals into the activity of single motor units [46] (figure 3(C)), yet it presents the typical limitations of recording from the surface [15]. Current efforts are being directed to translate this modeling into intramuscular recordings [47, 48] (figure 3(A)).

In the afferent direction, biomimetic algorithms have been successfully used to encode artificial sensory information to improve the naturalness of

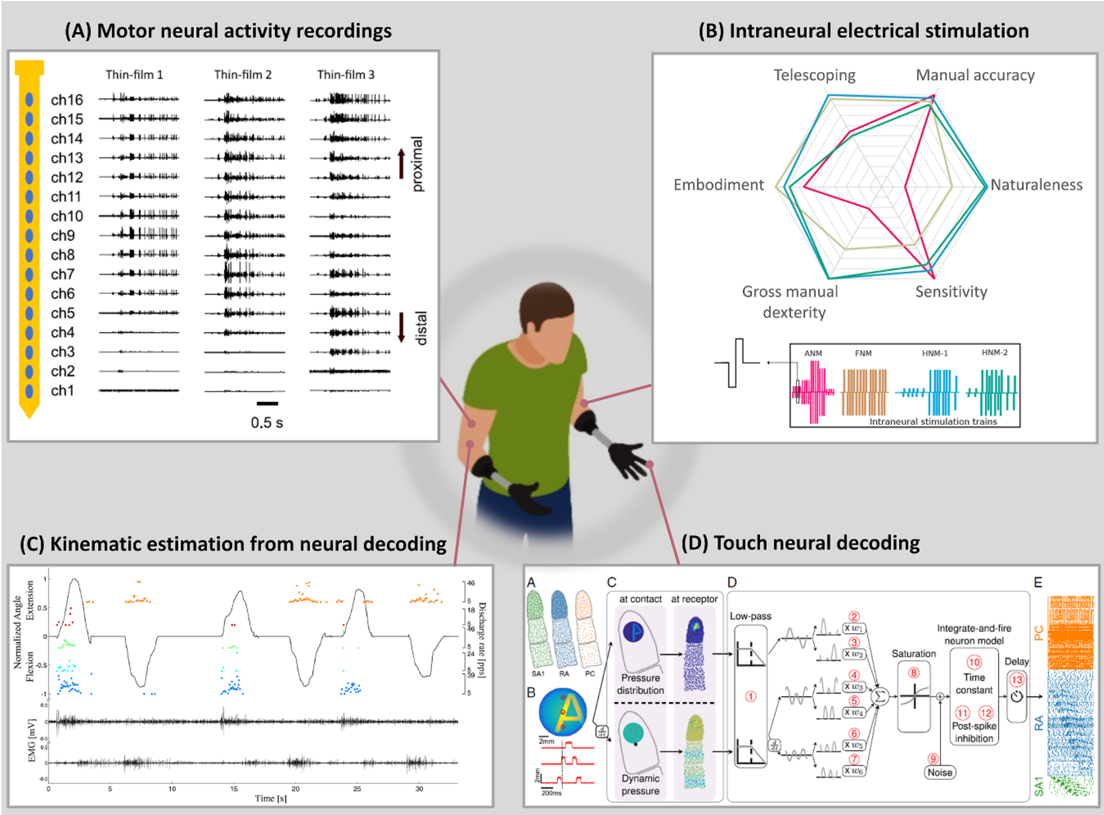


**Figure 3.** Decoding and encoding of neural signals. (A) Neural motor activity recorded from thin film electrodes. Reproduced from [28]. © IOP Publishing Ltd CC BY 3.0. (B) Different stimulation paradigms to restore sensory feedback via intraneural implants (ANM: amplitude neuromodulation, FNM: frequency neuromodulation, HNM: hybrid neuromodulation). Reprinted from [31], Copyright (2018), with permission from Elsevier. (C) Kinematic estimation using decoding neural signals from EMG recordings. Reprinted by permission from Springer Nature Customer Service Centre GmbH: Springer Nature, Journal of NeuroEngineering and Rehabilitation [26]. Predicting wrist kinematics from motor unit discharge timings for the control of active prostheses, Kapelner T, Vujaklija I, Jiang N, Negro F, Aszmann O C, Principe J and Farina D, (c) 2019. (D) Neural decoding of touch sensory feedback using a biomimetic mapping algorithm. Reproduced with permission from [34].

sensory feedback [7, 49–52] (figures 3(B) and (D)). For example, an algorithm was developed to mimic the aggregate activity of tactile fibers occurring during object manipulation in a natural hand [50]. In this model, the time-varying indentation depth, indentation rate, and acceleration were mapped to the naturally encoded time-varying firing rate and size of the recruited afferent fibers. This mapping may facilitate the translation of artificial sensory feedback from touch sensors placed on bionic hands into electrical stimulation pulses applied to nerve fibers.

## 3. Advanced neurosurgery and orthopedics

Further advances in neural interfacing technology incorporate neurosurgery procedures that exploit the anatomy and physiology of the remaining neural pathways to restore functions. This includes re-routing the remaining nerves after an amputation, anatomically linking remaining stump muscles to restore proprioception, and mechanically stimulating implanted skin graft.

### 3.1. Re-routing nerves for better recording and stimulation

Reinnervation of muscles by 'foreign' nerves during TMR amplifies the readout of neural signals and provides a new venue for neural stimulation [25, 53, 54] (figure 2(C)). It consists on re-routing the remaining peripheral nerves from the amputee's stump to a new target area, where afferent and efferent fibers reinnervate the hosting muscles, amplifying the signals from the efferent pathways and providing a more selective channel for activating afferent fibers. This approach has shown increased accuracy in decoding motor function using surface EMG signals recorded from the re-innervated area [55]. It further proved to be an excellent channel for mechanically stimulation of the re-innervated afferent pathways to deliver proprioceptive feedback in upper limb amputees [56].

### 3.2. Coupling agonist and antagonist muscles recreates natural proprioception

The recently introduced (AMI) restores proprioception by surgically connecting remaining agonist and antagonist muscles in transtibial amputees [27] (figure 2(G)). AMI aims to reestablish the functional dynamics that existed within the intact anatomy by mechanically linking this muscle group, recuperating the natural communication of the muscle mechanoreceptors with the central nervous system. This surgical technique has helped to recreate natural reflexive activities during stair climbing [27], to enhance motor control, and to improve EMG recording selectivity [57]. Thus, the AMI presents as a very promising surgical procedure to close the control loop in the lower limb after an amputation.

### 3.3. Direct anchoring of the prosthesis to the stump improves stability

Osseointegration presents a solution to anchor the prosthesis to the stump and replace the conventional socket, providing more stability and a port to route the cables of implantable devices [8, 58] (figure 2(D)). Osseointegration has proven stability in patients with transhumeral amputations lasting 3–7 years. Bidirectional communication is achieved by implanting neural cuff electrodes that deliver sensory feedback by electrical stimulation pulses, and by electrodes in the muscle epimysium that record muscle activity. The screw used to fix the prosthesis to the patient bone is utilized as a port to route the cables from the electrodes to the outside world. Remarkable outcomes of this technique include greater intuitiveness as no formal training was required to successfully control the prosthesis, improved sensory feedback, and ability to perform activities of daily life after daily use [8].

### 3.4. A mechano-neural interface to improve naturalness

A new mechano-neural interface aimed at restoring natural touch feedback without electrical stimulation of afferent nerves was recently reported [9]. It consists of implanting a skin flap in a cuff-like shape innervated by sensory fibers and surrounded by a muscle actuator that exerts pressure on the skin flap. The muscle actuator is controlled by electrical stimulation via an implanted electrode. While this technique has not yet reached human trials, it may shift current paradigms on how pressure sensation is delivered: the mechanoreceptors of the implanted skin remain intact and able to produce natural sensations, a physiologically relevant gain that is hard to attain by electrical stimulation.

## 4. Fundamental knowledge on post-amputation neurophysiology

Beside the past and current efforts, our fundamental understanding required to develop artificial limbs that can be intuitively controlled and felt as their human counterparts is still in its infancy (figure 4). Neuromuscular and cortical adaptations occur after an amputation to cope with a disrupted feedback system, loss of mechanical degrees of freedom and psychophysical alterations. Thus, it is not only a matter of restoring function and sensory feedback, but also of understanding how this would affect an already altered complex system.

### 4.1. Do the cortical representations of the missing limb remain intact?

Reorganization of central motor pathways has been observed in patients with lower limb amputation, including an increased number of recruited motoneurons during stimulation of the motor cortex, a decreased latency of the onset of motor evoked potentials on the same side of the amputation, and an increased size of motor areas representing the muscles near the amputation site [59]. After an amputation, there is an extension of the somatosensory representations of the face and upper body towards the areas of the arm and hand in upper limb amputees, with the extent of the shift being correlated with the level of phantom [60]. The motor reorganizations seem to occurs mainly at the cortex level since excitability to transcranial magnetic stimulation of the motor system on the amputation side increased after an amputation without observing changes in the excitability of subcortical and spinal structures [60].

Patients with lower limb amputation also present changes in functional connectivity between cortical and subcortical areas, reduced gray matter volume and loss of integrity of white matter. These changes occur even without experiencing pain and they are not related to the use of the prosthesis [61]. A reduction of functional connectivity between hemispheric somatosensory areas and motor areas were also observed in patients with long-term lower limb traumatic amputations with phantom sensation that do not present pain. Further, increased functional connectivity within hemispheres were observed between somatosensory areas, and between the primary and premotor areas, contralateral to the amputation side. Taken these findings together, it seems that pain is not critical for sensorimotor network changes after an amputation [62]. Further, cortical reorganization has been observed beyond the sensorimotor network following lower-limb amputation [63]. Amputees present impaired use of internal models when picking up objects with their prosthesis with poor grip force regulation [64]. Incorporating tactile feedback improves performance during grasping and lifting while using feedforward control under uncertainty conditions [65].

### 4.2. Can cortical representations of the missing limb be restored?

Aside from neuromuscular compensatory adaptations and cortical reorganization that occur upon loss of sensation or loss of a limb, there are other factors arising from interfacing the nervous system

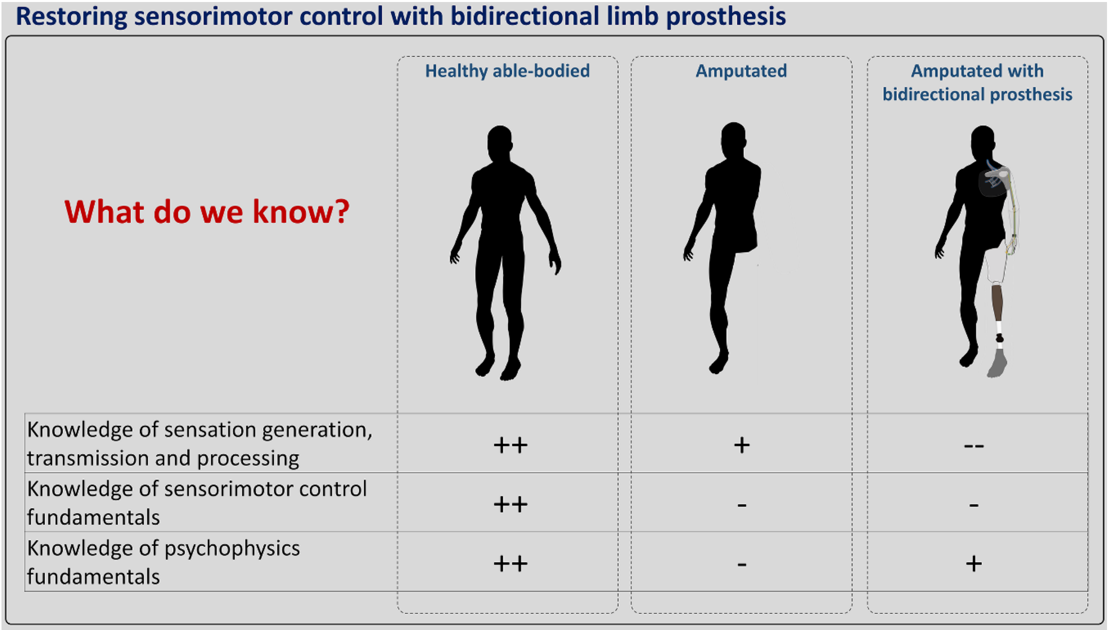


**Figure 4.** General overview of what is our current knowledge regarding the human pathophysiology of a limb amputation.

with artificial stimulation and neural recording that are largely unexplored. For example, little is known about the control strategies for postural balance before and after a lower-limb amputation, and even less is known about adjustments after the restoral of sensory feedback [66]. It has been observed that balance adjustments during quiet standing in unilateral transfemoral amputees are mainly controlled by the intact limb and that these patients may rely more on proprioception from the intact limb [67]. Comparable postural responses to electrically-elicited tactile sensations via implanted cuff electrodes and responses from vibrotactile stimulation in the intact foot of transtibial amputees have been recently reported [68]. This implies that the human sensorimotor control system seems to assimilate artificial sensory feedback in the same way it does natural tactile feedback. The use of the AMI appears to increase functional connectivity in areas of the brain associated with motor coordination and error correction and reduce visual dependency in the control of movement in lower limb amputees [69]. Further, electrical stimulation of peripheral nerves via TIME interfaces made it possible to shift the commonly reported misperception of the weight of the prosthesis in lower limb amputees [70]. This indicates enhanced cognitive integration of artificial sensory feedback and an increased embodiment of the prosthetic limb.

A few studies evaluated sensorimotor integration after TMR or after restoring sensory feedback in the upper limb [32, 44]. Long-term use of upper-limb bidirectional prosthesis after TMR may induce cognitive changes [32]. Recently, Marasco and colleagues demonstrated that providing touch, kinesthesia, and movement feedback to upper limb amputees via TMR and a non-invasive robotic technology restored brain behaviors similar to able-bodied individuals [33]. Optimal integration of somatosensory information delivered by intraneural interfaces with visual information has been observed in transradial amputees [71]. Further, functional changes in both hemispheres of the brain and in the contralateral hemisphere of the amputation side were observed after chronic use (5 amputees, implantation duration between 4 and 36 weeks) of an artificial hand [72]. Intensive use of myoelectric prosthesis reduced phantom pain and cortical reorganization [73]. However, long-term use (up to three years) of a bidirectional prosthesis with a mismatch between sensor location and the resulting tactile perception did not change perceived touch location [74]. The authors posited that sensory maps in the adult brain might be unmodifiable. Visuotactile synchrony has also been studied in transtibial and transradial amputees while stimulating afferent nerves with non-penetrating cuff-type interfaces [24]. Results from electrically-evoked sensations showed no significant differences in processing time and temporal sensitivity compared to natural touch [24].

### 4.3. Does artificial feedback control produce new neuromuscular adaptations?

The study of how neurophysiology changes after restoring sensory feedback or while providing a more intuitive functional control of the artificial limb is a challenge in its own right. Perhaps, while trying to restore the missing sensorimotor pathways, we end up altering an already disrupted system. Nevertheless, this physiological challenge shall not deter further progress; it was precisely through this trial-and-error strategy that we now know that restoring sensory feedback possibly induces neural adaptations at the cortical level [1] (figure 2(B)). Further, certain adaptations can be self-reliant. For example, just as it occurs with natural touch, artificial touch delivered through electrical stimulation of peripheral nerves naturally experiences adaptation-induced adjustments of sensations without requiring the adaptation process to happen at the transducer level [75]. Our knowledge of neuromuscular adaptations that occur in response to artificial feedback control is still limited.

## 5. Future direction

We believe that the incomplete link between technology, our understanding of the pathophysiology of limb amputations and human motor control hampers efforts toward restoral of function and sensory feedback. On the solid grounds of current progress, neurosurgeons, engineers, neuroscientists and orthopedists have great prospects to improve patient's quality of life, and the next approaches can take more than one direction. Should the field of bionic limbs invest more on integrating our understanding of the pathophysiology of an amputation in the design of artificial sensory feedback? We argue that this trans-disciplinary approach is highly desirable and that further efforts should be dedicated to the understanding of the disrupted mechanisms resulting from a limb amputation and its consequences in the neuromuscular system. We believe that this direction may bring us closer to reproduce and restore the sensorimotor system of the missing limb, having a real and sustained impact on the quality of life of patients, especially if we include them as experts in patient-centered care after the amputation [76].

## Data availability statement

No new data were created or analysed in this study.

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