Toward the Development of User-Centered Neurointegrated Lower Limb Prostheses

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(Clinical Application Review)

***Abstract*—The last few years witnessed radical improvements in lower-limb prostheses. Researchers have presented innovative solutions to overcome the limits of the first generation of prostheses, refining specific aspects which could be implemented in future prostheses designs. Each aspect of lower-limb prostheses has been upgraded, but despite these advances, a number of deficiencies remain and the most capable limb prostheses fall far short of the capabilities of the healthy limb. This article describes the current state of prosthesis technology; identifies a number of deficiencies across the spectrum of lower limb prosthetic components with respect to users' needs; and discusses research opportunities in design and control that would substantially improve functionality concerning each deficiency. In doing so, the authors present a roadmap of patients related issues that should be addressed in order to fulfill the vision of a next-generation, neurally-integrated, highly-functional lower limb prosthesis.**

***Index Terms*—Prosthesis, lower-limb, user's needs, comorbidities.**

I. Introduction

PROSTHESES were first developed to provide lower-limb amputees with stability and support, and for cosmetic purposes. Their optimization led to designs aiming at restoring not only basic locomotion tasks but also more advanced movements (e.g., running, cycling, swimming). In the developing world, the estimated number of amputees is 40 million, and up to 90% of amputations are performed in lower limbs [1].

Manuscript received 8 February 2023; revised 27 April 2023 and 30 June 2023; accepted 4 August 2023. Date of publication 28 August 2023; date of current version 15 January 2024. This work was supported in part by the Bertarelli Foundation, in part by INAIL (Centro Protesi, Vigorso di Budrio, Italy) under Project PR19-PAI-P2 MOTU++, and in part by the National Recovery and Resilience Plan - Italian Ministry of University and Research - European Union – NextGenerationEU through Projects MNESYS and THE. *(F. Barberi and E. Anselmino contributed equally to this work.) (Correspondence author: E. Anselmino.)*

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Digital Object Identifier 10.1109/RBME.2023.3309328

Designing the optimal prosthetic solution is a daunting task, and the process must take into account the users' needs, the presence of comorbidities, and the technological challenges. Previous reviews have addressed issues related mainly to the technological aspects ([2], [3], [4]), here we are going to focus on user-related matters. Lower-limb amputees present various issues related to their walking pattern, weight distribution, and perception of their prosthetic limbs (see Section II). These issues affect the usability and comfort of the devices, and prostheses design flaws might in turn aggravate them. On the prosthesis design side, the most known issues are related to the poor fitting and alignment of the socket system, the lack of sensorial inputs from the artificial limb, and the mechatronic design of the ankle-foot and knee components (e.g., reliability, weight, comfort) (see Section II and Section III).

Addressing these issues will enable a next generation of lower-limb prostheses (see Fig. 1), which will include improved socket and suspension systems, the ability to provide both powered and passive joint behaviors, improved integration between the knee and ankle-foot components, and bidirectional delivery of motor commands and sensory feedback.

In the following sections, we will review the state-of-the-art relative to these aspects, highlight the most promising perspectives and discuss how integrating them could lead to a novel generation of prostheses, more effective in addressing patients' needs.

II. Users' Needs, Comorbidities, and Technological Challenges

Amputees often present kinetic and kinematic asymmetries during gait [5] and implement compensation strategies [6] leading to higher metabolic movement cost [5], [7], [8], [9]. Most lower-limb amputees distribute their weight unevenly, leading to back pain and joint degeneration due to uneven bone growth. The presence of such conditions can cause the onset of comorbidities, that impact amputees' mobility and daily life [10], [11], [12] and influence the medical care and rehabilitation process.

Lower-limb amputees often suffer from comorbidities and related conditions [13], [14]: according to [15], less than 5% of amputees are free of comorbidities, whereas 60% present 3 or more. The most common are peripheral vascular disease, diabetes, lumbago and rheumatoid arthritis or osteoarthritis,

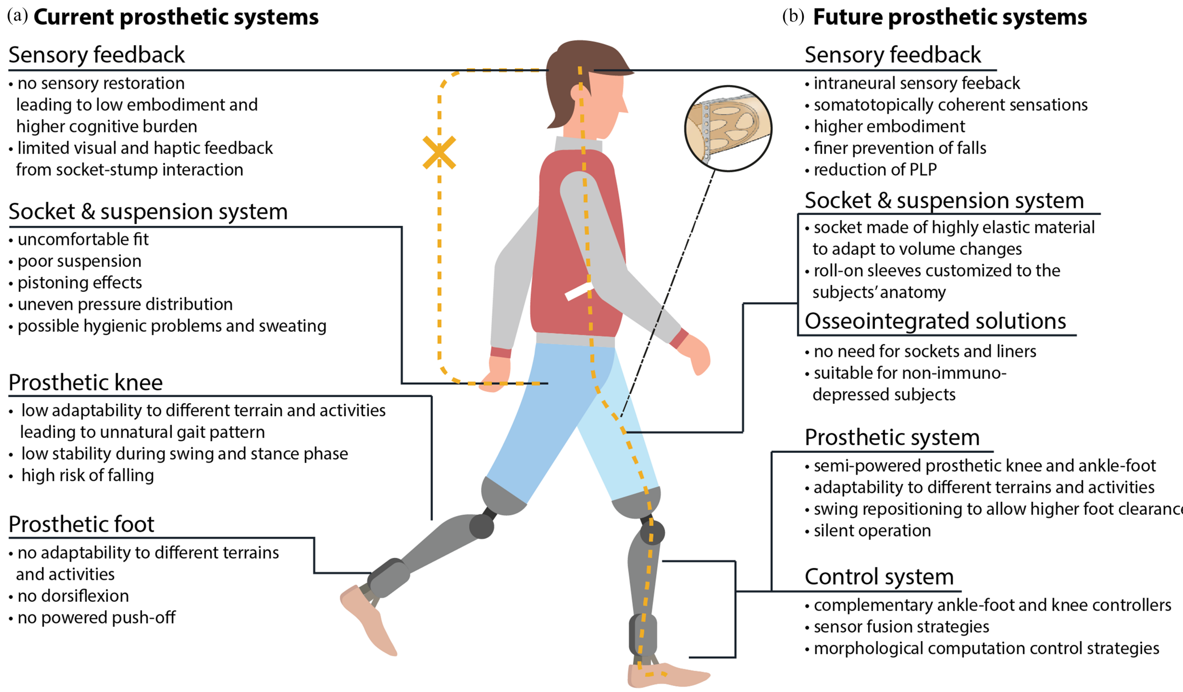

Fig. 1. Schematic representation of (a) issues and limitations of current prosthetic system; (b) novel technologies to overcome these issues and limitations to be included in future prosthetic system.

and their incidence is correlated to age, sex, cause of amputation, amputation level and presence of a bilateral amputation. Diabetes mellitus is one of the main causes of non-traumatic amputations, since it leads to neuropathy, soft tissue sepsis and peripheral arterial occlusive disease [16]. Pathologies connected to diabetes account for 82% of vascular-related amputations and patients suffering from them have an increased risk of limb loss: 30 times greater if compared to non-diabetic ones [17]. Patients with critical limb ischemia have a 12% probability of undergoing an amputation procedure during the first 6 months after the revascularization surgery [18]. Musculoskeletal comorbidities are a direct consequence of the biomechanical alterations of an amputee's gait and are exacerbated by the use of prostheses with poor fitting and weight distribution. Osteoarthritis, arthritis, osteoporosis, and osteopenia are the most common, but lower limb amputations often also lead to back pain and postural changes [19]. Osteoarthritis involves a degeneration of the cartilage, and generally affects the knee and hip of the healthy limb due to the increased stress to which these joints are subjected. Osteoporosis and osteopenia involve a decrease in the bone density and mass and tend to affect the amputated side. They are caused by the tendency of the amputees of limiting the weight put on the prostheses and by the subsequent insufficient loading of the lower limb bones.

User satisfaction plays a key role in amputees' rehabilitation process and help to avoid prosthesis rejection and lead to better prosthesis optimization [20], [21]. Several factors contribute to prosthesis acceptance: appearance, aspect of the residual limb, presence of pain, fit of the device, prosthesis properties and use of the prosthesis (see Table I). Prosthesis properties, fit and usability (i.e., locomotion task that are permitted and helped by the prostheses) improve the acceptability and embodiment of the prosthetic device, by allowing a better daily life use (e.g., easier donning and doffing, easier maintenance, etc.) and promoting user's independence and mobility. In addition, a better fit of the socket guarantees better control during movement and a healthier residual limb (e.g., less irritation, skin rashes, etc.). Prostheses' appearance plays a key role regarding the acceptability of the artificial limb, both from the point of view of the amputee and the society. It is therefore important to allow a deep customization of the prosthesis to meet the aesthetic taste of different demographic groups, avoiding early abandonment and limited use of the device. All the above-mentioned factors are not relevant for every amputee and are related to the level of amputation, gender, liner use and social conditions (e.g., employment, marital status). In addition, no single parameter significantly influences satisfaction on its own [22].

In order to accommodate the variable needs of amputees' gait, in addition to the presence of amputation-related pathologies and user satisfaction parameters, several deficiencies of currently available prostheses must be addressed. Table II reports an illustrative summary of the most common deficiencies of lower limb prostheses currently adopted by the majority of patients. The table was compiled based on the outcomes of the focus group meeting of MOTU++, held with a pool of amputee subjects, clinicians, and engineers; and on the personal experience of the researchers involved, backed up by the literature. In the following sections of the manuscript we are going to address state-of-the-art strategies to tackle each one of them. Designing an optimal interface between the prosthesis and residual limb can for instance help to overcome the biomechanical issues related to amputation: uneven weight distribution, gait asymmetries, atypical muscle activation and increased metabolic cost. In addition, a correctly designed socket system contributes to ensuring

TABLE I
PROSTHETIC SYSTEMS USERS' SATISFACTION FACTORS

PROSTHETIC SYSTEMS USERS' SATISFACTION FACTORS		
Appearance	• Aesthetic • Color	• Touch/Feel • Cosmetic
Residual limb	• Sweating/Transpiration • Wounds • Irritation • Blisters • Pimples	• Skin rashes • Swelling • Pain • Phantom pain
Prosthesis fit	• Comfort • Wearability • Ease of performing donning and doffing operations	• Presence of pistoning effects • Presence of rotations
Properties	• Weight • Noise • Durability • Reliability • Being waterproof	• Usefulness • Usability • Ease of cleaning • Interaction with clothing
Use of the prosthesis	• Ability to sit • Ability to walk	• Ability to walk on uneven terrains • Ability to walk on stairs

Summary of prosthetic systems users'satisfaction factors discussed in [22].

TABLE II
COMMON DEFICIENCIES IN CURRENT PROSTHETIC SYSTEMS

COMMON DEFICIENCIES IN CURRENT PROSTHETIC SYSTEMS	
Socket and suspension system [26], [28]	• Uncomfortable or poor fit which can affect the gait pattern and general stability • Poor suspension due to rigid (non-flexible) systems that do not adapt to volume changes • Possible pistoning effect • Uneven pressure distribution • Possible hygienic problems and sweating due to non-transpirancy • Possible skin issues, e.g., dermatitis, skin edema, rashes, etc.
Prosthetic knee [41], [58]	• Low adaptability to different terrains and activities • Unnatural gait patterns and compensation strategies commonly used • Step-to-step stairs climbing • Decreased ground clearance • Decreased stability during swing and stance • Decreased stability on sloped or uneven terrains • Increased tendency to scuff or stumble • Knee movements highly susceptible to perturbation • Inability to provide stance knee extension • Inability to restore perturbed knee motion
Prosthetic foot [48], [49], [51]	• Low adaptability to different terrains and activities • No dorsiflexion during swing phase • Decreased ground clearance • Increased tendency to scuff or stumble • Increased metabolic costs • Increased contralateral heel strike impact • No powered push-offs
Sensory feedback [147], [148], [150]	• No sensory feedback provided • Low embodiment • Higher cognitive burden • Few clinical trials on lower-limb amputees • Need to explore biomimetic approaches on lower-limb amputees • Need to explore intraneural stimulation paradigms to reduce phantom limb pain • Need to study the full range of sensations evoked to focus on the close-to-natural ones • Feedback only limited to haptic (socket-residual limb interaction) and visual feedback

Common deficiencies in current prosthetic systems.

stability and promotes the embodiment, reducing the risk of developing chronic conditions (e.g., arthritis and osteoarthritis) [23]. The ankle-foot and the knee prostheses design are of compelling importance: they need to be efficient, reliable, and able to restore locomotion functions, avoiding the introduction of harmful compensatory strategies and limiting the increase of the metabolic cost. Sensory feedback is another key aspect of a prosthesis, it helps in promoting usability, agency and embodiment restoring the missing afferent sensorial pathways, but to be effective it must be intuitive and easy to master to avoid increasing amputee's cognitive burden. Finally, the overall prosthetic system must be lightweight, comfortable and aesthetically pleasing, to avoid leading to limited use of the device or even abandonment [23], [24], [25], [26].

III. Prostheses: Components, Challenges, and Future Directions

A. Prostheses Sockets

The main physical human-machine interfaces in prosthetic legs are the socket and the suspension system [27], which are responsible for the mechanical coupling between the residual limb and the prosthesis. The socket design is critical both for prosthesis usability and acceptance (see Section II), since it often constitutes one of the main reasons for prosthesis abandonment, with a rate of around 25-57% [23], [24]. Socket design must take into account residual limb health (e.g., the presence of wounds, skin irritation, etc.), possible volume changes of the residual limb, the presence of comorbidities and the user needs in terms of mobility and activity. The perfect fit of the socket guarantees stability and good transmission of the weight to the prosthesis, essential for the execution of dynamic and natural movements and thus for prosthesis acceptance. Residual limb volume changes are more relevant in the period immediately after the amputation but persist in stabilized amputation as well [28], [29]. Such variations result in a compromised fit of the socket, which leads to relative movement between the socket and the residual limb and an uneven distribution of pressure on the tissue [28]. This can in turn cause dermatitis, skin edema, rashes, redness, and other skin problems [26], [30]. These conditions could be exacerbated by the sequence of swing and stance phases during ambulation, which produces a cyclic change in pressure on the residual limb [27], and by the presence of comorbidities, such as peripheral vascular disease and diabetes. Physical activity and changes in body weight also have a strong impact on the residual limb volume and socket fit [28].

Traditional rigid sockets and the skin can either be in direct contact, or have a prosthetic sock or liner interposed between them [8]. Alternatively, it is possible to use flexible inner sockets made of a silicone-based material that is coupled with an outer rigid frame and, where appropriate, with liners or prosthetic socks. Flexible inner sockets allow more residual limb volume variations, more dynamic movements and increase the proprioceptive feedback of the amputee. Efforts were made over the years to reduce localized stresses on the residual limb area, and evenly distribute the weight (e.g., with the Total Surface Bearing socket (TSB) [27]). However, many of the issues presented above, related to the socket and liner designs, are still open and need to be addressed.

A possible solution to these issues could be given by osseointegration, which is a direct connection between the prosthetic device and the residual limb via a metal implant inserted into the skeletal structure [23], [31]. Such an implant avoids the drawbacks brought by the socket interface, such as discomfort and pain, and enhances the transmission of the forces from the prosthesis to the limb, through "osseoperception" [25], [32], [33]. One of the major drawbacks of this method is associated with the percutaneous nature of osseointegration: with the pylon penetrating the skin, the risk of infection is increased [12]. In addition, safety measures to prevent excessive torque from being transmitted to the implant must be taken into account, since it can lead to fractures, implant loosening, or implant breakage [34]. Even though formal criteria for the inclusion of subjects for osseointegration do not exist, typical exclusion criteria include diabetes, vascular diseases, immunosuppressed subjects, a body mass index above 25 kg/m^2, and other situations that could lead to mechanical complications and insurgence of infections [25], [34], [35].

Another possible solution could be the use of highly elastic materials, pads and air or fluid chamber systems, allowing the implementation of adaptable sockets [36], that could therefore be better accepted, more comfortable and able to adapt to volume changes [29]. Despite compliant sockets being a promising solution, there is a lack of evidence in the literature regarding the specifications such systems must achieve due to the difficulty in evaluating both short and long-term volume changes of the stump. It is therefore necessary to implement technical solutions capable of accommodating large volume variations, such as fluid-filled socket inserts [37].

B. Powered Prostheses

As discussed in Section II, amputees present a different walking pattern if compared to non-disabled subjects, both in terms of kinetic and kinematic variables. Such differences lead to the adoption of compensation strategies [6] that generate gait asymmetries [5], an increase in the metabolic cost [5], [7], [8], [9] and joint degeneration, caused also by uneven weight distribution. Amputees' activity level is affected by the presence of movement difficulties: more than 60% are classified as "not sufficiently active" and more than 30% as "sedentary" [38]. Lower-limb amputees also present a significant increase in the risk of developing cardiovascular diseases [39], increasing the activity level can help mitigate this and other risks connected to a sedentary life [40].

The current standard of care in lower limb prostheses consists of a carbon-fiber ankle-foot in combination with a variable damping mechanism at the knee joint (see Fig. 2). The ankle generally provides a fixed stiffness about a nominally level ground slope, while the knee provides a low resistance to motion during the swing phase of gait, and a relatively high level of resistance during the stance phase. Both the knee and ankle are energetically passive, and therefore are unable to provide net power for movement.

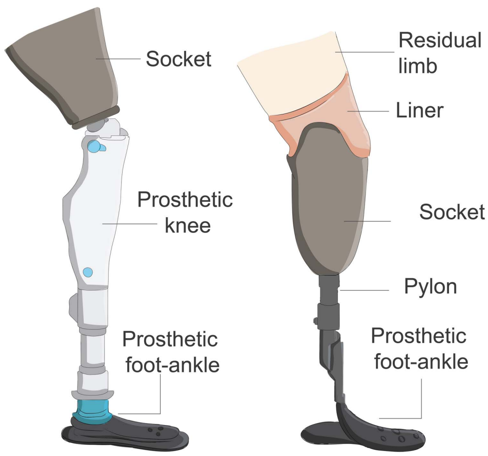

Fig. 2. Lower-limb prostheses for above-knee amputees (left) and below-knee amputees (right).

The healthy knee and ankle joints are, of course, able to provide both power dissipation and power generation behaviors, and in general, they do provide both during different locomotion activities (see, for example, [41]). Knee and ankle prostheses capable of power generation (in addition to power dissipation) would provide a better replication of the biomechanical functionality of the respective healthy joints [42], [43], [44], [45], [46], [47]. Although most readers would agree with the previous statement, it is informative to unpack it and discuss how power could specifically improve mobility, and what advances are necessary to fully implement power in knee and ankle prostheses. *In the case of the ankle*, the most salient deficiency of a passive prosthesis is the absence of powered push-off in the late stance phase. Powered push-off has been shown to: 1) provide propulsive power for locomotion; 2) set up the initial conditions for the swing phase; and 3) reduce the impact and corresponding loss of momentum during contralateral heel strike [48], [49], [50], [51], [52]. Restoring power to an ankle prosthesis is likely to lead to more energy-efficient locomotion, improved swing phase characteristics, and potentially reduced joint loading on the contralateral limb. In addition to powered push-off, power generation at the ankle would also have other important and perhaps less obvious benefits. Chief among these is the ability to adapt ankle behavior to varying terrain and activities. As previously shown, such adaptation requires modulation of the stiffness characteristics of the ankle, both in terms of the nominal equilibrium point (i.e., angle) and stiffness (e.g., [53], [54]). Although these characteristics can be varied without power for certain constrained movements, the general implementation of variable stiffness and equilibrium point requires power generation, as is exhibited by the healthy ankle during uneven and sloped terrain walking. In addition to the power generation needed for the stance phase, motive power is also required to reposition the ankle joint during the swing phase of gait in level walking, and to a much greater extent during slope and stair ascent and descent [55], [56]. In the latter case power generation is necessary during the swing phase to facilitate subsequent power dissipation during the stance phase [57], allowing the user to descend stairs in a controlled manner. One of the primary dissipation mechanisms occurs immediately after the toe strike when the ankle dissipates power under load while transitioning from a plantarflexed angle to a dorsiflexed angle [41]. In order to do so, the ankle must start at a plantarflexed angle, and must be positioned during the swing phase into that configuration, which in general requires power generation at the joint. Therefore, power generation is required to provide power dissipation. Further, power is required when responding to perturbations, such as stumble events during the swing phase. In such instances, particularly in the early swing phase, the healthy ankle generally responds with active dorsiflexion to clear the stumble obstacle. This type of "elevating" response is known to be an active (i.e., powered) response [58]. Finally, motive ankle power is necessary to restore healthy functionality for a large number of activities beyond basic mobility tasks, such as cycling, skiing, dancing, and other sport or recreational activities. Ideally, a prosthesis would restore volitional movement, which is only possible with a powered joint.

In the case of a knee prosthesis, powered movement offers several benefits for both the stance phase and swing phase (see [41]). A powered knee would enable stance-knee extension, which permits the reproduction of healthy knee joint function for stair and slope ascent, in addition to sit-to-stand and squat-to-stand movements. Less obviously, a powered knee can more easily replicate the non-dissipative behavior of the knee joint during the loading response, such as the stance-knee flexion and subsequent extension that occurs during normal walking. This behavior in general reduces impact forces during heel strikes, lessens the likelihood of slip, and reduces the vertical excursion of the center of mass of the body during locomotion. Although much of knee movement during the swing phase is passive (e.g., inertially coupling movement that results from the combination of ankle push-off and thigh acceleration, see [59]), several swing phase movements do require power: the swing phase during stair ascent, during slow walking, during backward walking, and when stepping over obstacles (see [41]). Additionally, stumble or scuff recovery movements, particularly during the early swing, are known to be active movements that require power at the knee [58]. Finally, as with the ankle, motive power is necessary to restore healthy functionality for a large number of activities beyond basic mobility tasks, such as sports or recreational ones. As also with the ankle, a prosthesis would ideally restore volitional movement, which is only possible with a powered joint.

Several advances have been recently made in the development and implementation of powered prostheses (e.g., [53], [56], [60], [61], [62], [63], [64], [65], [66], [67], [68], [69], [70], [71], [72], [73], [74], [75], [76], [77], [78], [79], [80]), although substantial work is required to fulfill the potential of powered artificial knees and ankles. Human muscle has a dynamic range of output impedance that has not yet been matched by robotic means of actuation, particularly at the low end of impedance. In addition, matching the torque and power output of biological joints, while also achieving the range of their movements and output impedances, remains an open issue [81]. Even if powered prostheses show encouraging results for some gait restoration metrics (e.g., preferred walking speed, metabolic cost, gait symmetry),performances are still distant from subjects without a disability, as in the case of Ottobock Empower [45]. Weight and noise are other key factors for the usability and acceptability of powered devices, that must guarantee adequate assistance limiting encumbrance and tedious sounds. For these reasons, the most adopted actuation principles are the electromechanical ones due to the controllability and power density of DC motors, especially if combined with compliant elements [3]. Improvements in the field of powered prostheses would lead to a novel generation of devices, able to restore not only volitional movements, but the complex motion patterns needed for performing sports and outdoor activities also, allowing amputees to regain an active lifestyle and independence.

C. Control Strategies

Commercial prosthetic legs are rather passive or rely on embedded sensors (e.g., inertial measurement units, encoders) to detect users' intentions and performed movements [82]. Sensor-based control presents a major limitation in not directly involving the user in the control loop, and this entails difficulties in performing challenging tasks without experiencing high cognitive fatigue and increased energy consumption [83]. Even if some high-end prostheses models (i.e., Genium X3 by Ottobock, Rheo Knee XC by Össur) provide a good level of adaptation to different terrains and activities, switching between them is mostly a manual operation. Consequently, a smooth transition is generally not possible, requiring additional effort from the user. As stated in Section II, inadequate controllability of the device affects the user's perception of usability, reducing the acceptance rate of lower limb prostheses and, consequently, possibly leading to abandonment [84], [85]. Lack of controllability, together with discomfort and poor mobility are the main causes of prosthesis rejection [86], [87], [88], [89]. To avoid the abandonment of the prosthetic device it is thus necessary to develop an efficient and reliable control strategy, capable of moving and adapting the artificial joints to accommodate each movement, locomotion task or gait phase of the user.

Volitional control can help improve the sense of ownership and agency [90]. In such a control scheme, the amputee directly or indirectly interacts with the prosthesis to change its state. It can be based on intent recognition algorithms, or it can refer to the use of manual switches [91]. EMG signals are typically used for direct control of prosthetic arms and legs. This strategy strongly depends on the level of disability of the users, increasing their cognitive burden and preventing smooth transitions, making it sometimes necessary to explore more automated approaches [92], [93]. Automated controllers for powered prosthetic devices are divided into three levels of control: high-level, mid-level, and low-level (Fig. 3). At a high-level, signals from the device, the environment, and the user are recorded [92] and the movement intention of the patient is decoded [92]. This information is then transmitted to the mid-level, which is responsible for the conversion of the decoded motion intention into the desired state of the prosthesis, and the transmission of the output to the low-level control [92]. The translated output can be a combination of joint position, angles, velocities, and/or torques [92], which depend on the design of the prosthetic actuator. Finally, at the low-level, the device is actively controlled by following the received input. At this level, there is a direct tracking of the references used at higher levels (e.g., position or torque) [94]. Proportional integral (PI) and proportional integral derivative (PID) systems are commonly used [94] to change emulated stiffness and damping values of the prosthetic joints to create desired joint behavior.

1) Control Schemes: Developing an efficient control scheme is extremely challenging due to the variability of the gait task, which includes several different locomotion modes (e.g., stairs and ramp negotiation, sit-to-stand, etc.) [60]. It is necessary to consider numerous aspects:

1) The number of activities to implement: a large number of motor tasks increase usability at the expense of complexity.
2) Training strategy: it impacts the effort asked to the user in terms of time and physical fatigue.
3) Input signals: they determine the setup burden and the maximum extractable information.
4) Critical time [95]: the time by which a classification decision must be delivered, it must consider the mechatronic response time of the prosthesis.

Other important aspects to be taken into account are the intrinsic variability of the human gait and the level of amputation. A prosthesis user can change gait parameters, such as the walking speed and the foot elevation, accordingly to the performed task and environmental conditions. Therefore, it is important to develop a controller capable to be robust to various walking speeds [96] and environment parameters, such as steps and slopes with different heights and inclinations [97], [98]. The amputation level can impact the control strategy selection due to the effect on muscles availability, subject mobility [99] and walking strategies choice.

The first distinction must be made between *echo control and non-echo control strategies* [60]. When the information is extracted from the amputated side, the strategy falls into the non-echo control group. With echo control, data are recorded through sensors placed on the healthy side of the amputee instead. This strategy tries to mirror, usually with gait pattern generator controllers, what happens on the sound side on the amputated side, with a delay of half a gait cycle [60]. Both echo and non-echo schemes can be used in combination with various types of signals (i.e., electromyographic, inertial, etc.). They can be time-dependent or based on different kinds of triggers (e.g., mechanical sensory interfaces (MSI)) [9], [100], [101], [102], [103]. Major drawbacks of the echo-control strategy is that it requires instrumentation of the sound limb, applies only to unilateral amputees, and it is not conducive to asymmetric behaviors [60]. Another major drawback is that echo-controlled prostheses require a high output joint impedance [104] to allow the device to determine the joint trajectory without the user freely moving the prosthesis [104]. In this way, the users cannot interact with the prosthesis but must follow its trajectory. Consequently, this type of control system leads to a low embodiment of the device, which is perceived as an external object, and it

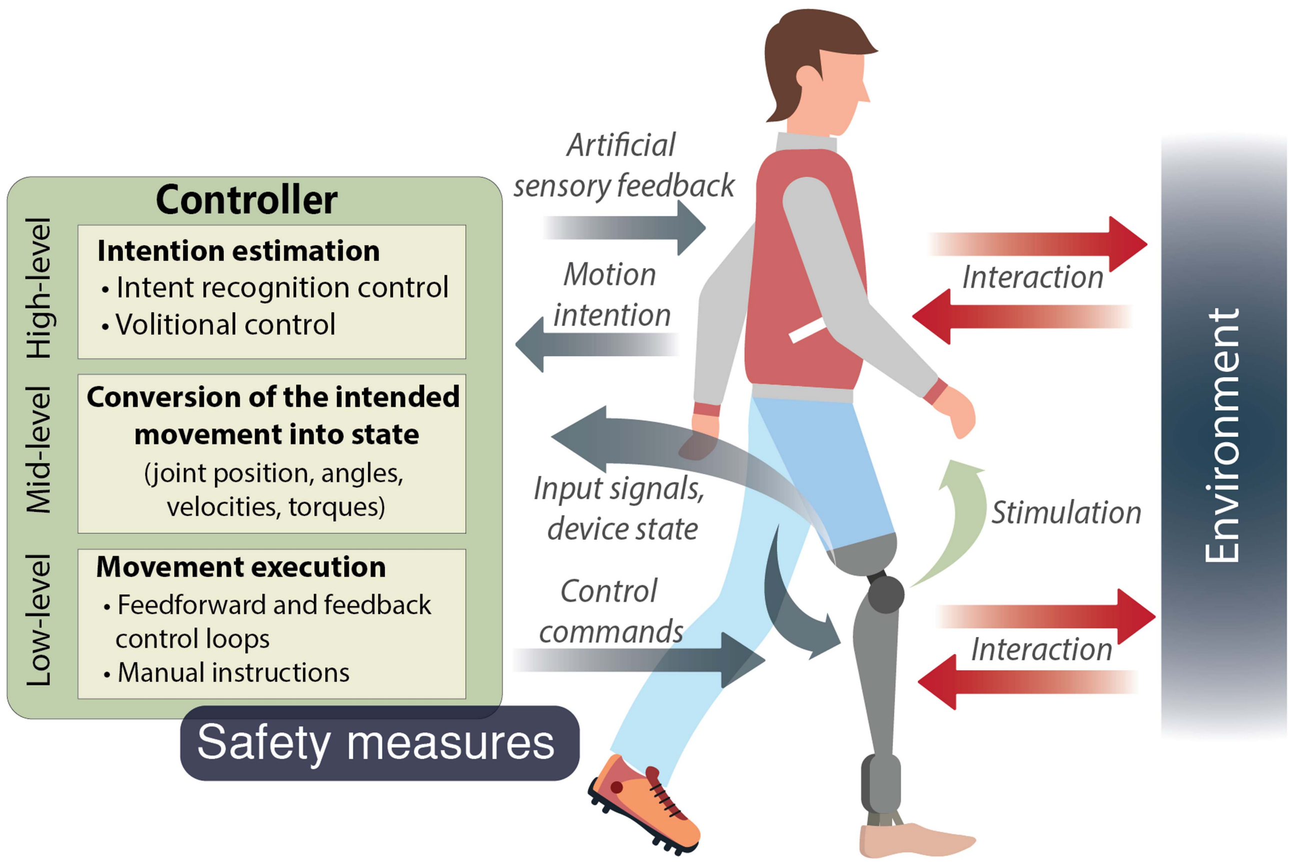

Fig. 3. Overview of a generalized control framework for powered lower-limb prostheses. Modified from [13]. Input signals coming from the user and the prosthesis must be decoded by the controller. The environmental state constrains the possible movements, and they can be read and decoded by the controller. Physical interactions are present between the environment and the user and the environment and the prosthesis. Sensory stimulation can be delivered from the prosthesis to the user. Finally, safety measures are necessary to avoid potential falls of the user.

is, therefore, less accepted by amputees [60], [104]. For the abovementioned reasons, echo control is not optimal for real-life prosthetic applications.

Secondly, *gait phase identification, motion intention recognition, and gait pattern recognition* algorithms [101] must be defined, and the relative differences discussed. With gait phase identification algorithms, the gait is divided into several sub-phases (e.g., stance phases and swing phases). Stiffness and damping parameters are adjusted based on the phase of the cycle of the prosthesis, which is identified through acceleration, angles, and other signals. Finite-state machines (FSM) are commonly used to switch from state to state [105]. Motion intention recognition is usually based on machine learning algorithms (e.g., neural networks, pattern recognition, etc.) that draw conclusions regarding the intention of movement [106], [107], [108], [109] or the prosthetic device impedance parameters [110] by processing the information extracted from the sensory apparatus on the prosthesis. Supervised learning, unsupervised learning, or reinforcement learning are usually implemented. Time-invariant classifiers, such as Linear Discriminant Analysis (LDA), Support Vector Machine (SVM), Artificial Neural Network (ANN), and nearest neighbor classifiers, are the most used approaches [93], [111], and have been widely tested in different input conditions such as, for example, varying input window length ([106], [107], Fig. 4(b)). Specifically, [106] tests different classification algorithms on five locomotion modalities, varying the length of the input window, to minimize classification error while maintaining real-time performances. To reduce classification errors in realistic scenarios, the algorithms can be tested by adding signals' noise, adopting data augmentation techniques [112] (see Fig. 4(c)), simulating sensors fault [108], [113], [106], [114], [112], [115] and implementing adaptive classifiers [111] able to adapt to slow variations of the input signals. For example, in [112] a deep generative model is used to reduce classification error both across different subjects and across different days for a five classes classification task (see Fig. 4(c)). Motion intention detection algorithms can also adopt non-machine learning approaches, leveraging neuromusculoskeletal models to compute the mechanical moment production around a joint [116], or directly modulating prosthesis parameters based on kinematic variables [97]. Pattern recognition algorithms rely on the periodicity of the gait, adapting pre-programmed walking patterns based on the stride time and other kinematic or kinetic information [101]. Pattern recognition is commonly used with mechanical sensory interfaces or electromyographic signals [109], [117], [118], [119], [120], allowing high accuracy,

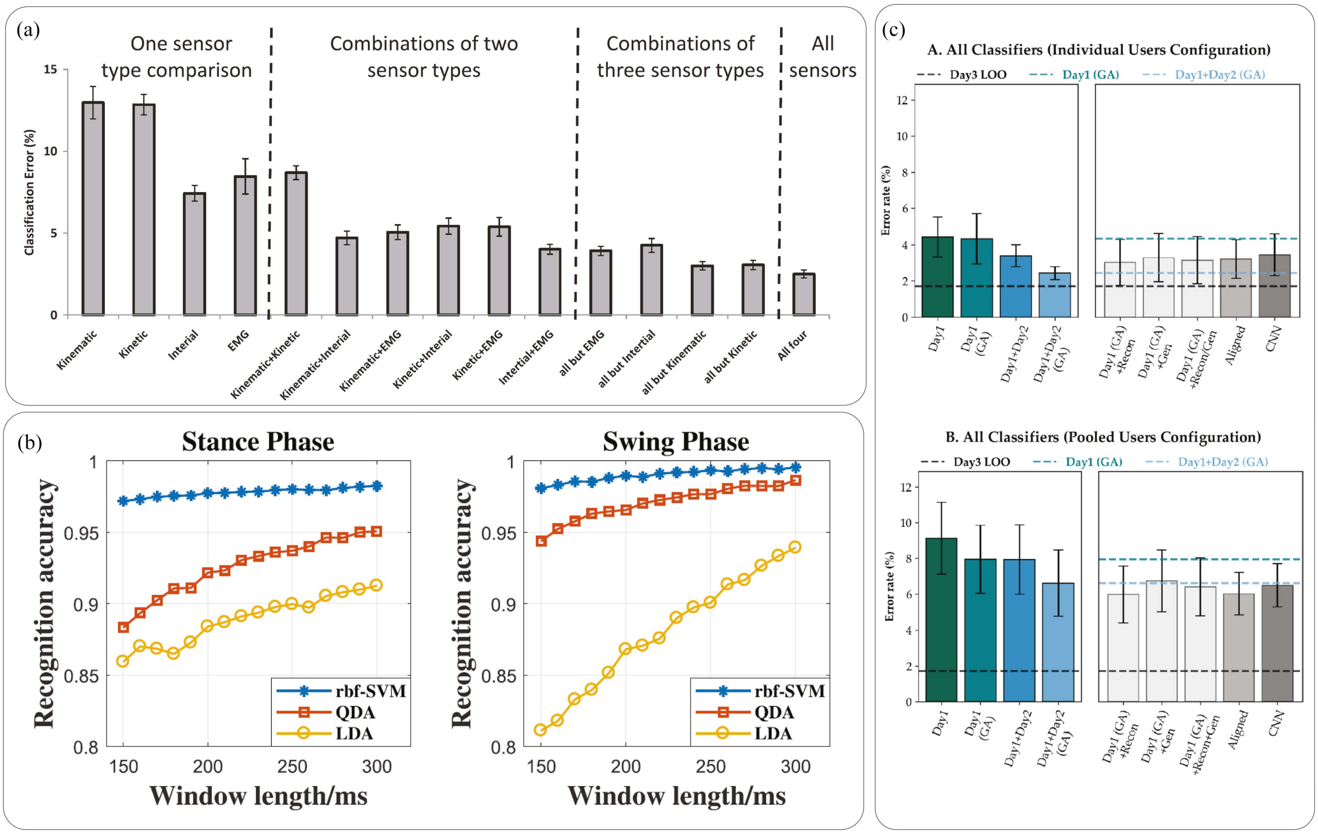

Fig. 4. Different approaches to classification algorithms for lower-limb prostheses presented. (a) Comparison of the performances of classifiers with different input signals and their combinations (i.e., kinematic, kinetic, inertial, EMG) [143]; (b) classification accuracy during stance phase and swing phase, when varying the length of the sliding window and the type of classifier used (i.e., linear discriminant analysis, support vector machine and quadratic discriminant analysis) (©1981 IEEE) [106]; (c) study of the classification performances with and without data augmentation through different strategies and with individual and pooled user configurations (©2019 IEEE) [112].

although in a controlled environment. Due to its versatility, the pattern recognition approach can be exploited for both gait phase and motion intention identification problems, as well as for the computation of gait cycle related features. Some shortcomings of the pattern recognition approach involve the necessity of a wide set of training data that must cover all the desired classes, and the pre-defined patterns created during training might be subject-dependent. With gait pattern recognition algorithms, the user inputs are also generally limited, not allowing significant variability to the predefined patterns [117].

Even though impressive progress has been made with the use of machine learning applied to prostheses, we are still in need of an efficient and 'faultless' control scheme. Classification performances above 90% can be reached, but the drawbacks of a classification error potentially leading to patient's fall regarding health and confidence in the prosthesis are so severe to render a 10% or even a 5% error probability not acceptable. Consequently, it is necessary to seek another candidate for controlling prosthetic legs. A potential solution could be brought by neuromorphic engineering approaches: prostheses would be implemented with tight interactions with the surrounding environment using sensor fusion and non-static signal acquisition techniques (i.e., "static frame decoding") [121]. The neuromorphic approach guarantees a high level of adaptability to different and changeable conditions, both from the point of view of the subject behavior and environment, while maintaining a high level of computational efficiency [121]. Sensor fusion approaches rely on different sensor inputs to improve the locomotion task separability and increase prediction accuracy. In particular, in addition to the canonical sensors (e.g., EMG, IMU and mechanical), these techniques implement sensors capable of acquiring environment-based data (i.e., cameras, depth sensors, lidars, etc.) that are less subject dependent and thus allow a better across-subjects generalization and a reduction in classification errors [122].

2) Control Signals: To decode the users' motor intention, several types of signals can be recorded through different types of interfaces, with various degrees of invasiveness [26]. It is possible to divide them into biomechanical sensory interfaces, (invasive) central nervous system (CNS) interfaces, (invasive) peripheral nervous systems (PNS) interfaces, and surface electromyographic (sEMG) interfaces [3], [123], [124]. The last three types all fall in the category of biological input-oriented signals [125].

Biomechanical signals interfaces, or mechanical sensory interfaces (MSI), use sensors (kinematic and/or kinetic [92], [125], often in combination with footswitches [93]) related to the biomechanics of gait, that extract forces, torques, angles, orientations, etc. [124]. The major advantage of such interfaces is the ease of implementation on the prosthesis since no direct contact with the amputee is needed, allowing for a self-contained device. On the other hand, the exclusion of the subject from the control loop does not allow the adoption of volitional control and limits the embodiment, adding complexity to the execution of challenging tasks [83].

CNS interfaces can be whether invasive or not invasive. Recording the activity at the cortical level is useful to collect information regarding volitional movements, and is generally done through intracortical electrodes or electrocorticography (ECoG) [124], [126]. However, the invasiveness of these techniques and the fact that many locomotion-related control loops happen through a reflex arc complicate the use of neural activity for the control of lower-limb prostheses [92]. Electroencephalography (EEG) is a non-implantable CNS interface alternative to record the electrical activity of the brain [92]. This type of interface is susceptible to movement artifacts and requires the user to specifically focus on the performed tasks [92]. Functional near-infrared spectroscopy (fNIRS) was also used in the rehabilitation of lower-limb impaired patients (i.e., stroke patients) and could be explored in amputation-related applications in the future [125], [127].

PNS signals interfaces are obtained invasively through percutaneous electrodes that reach the peripheral nerves, or implantable EMG electrodes that allow the recording of intramuscular EMG signals (iEMG) [124]. Various implantable EMG technologies are now commercially available, such as IMES electrodes [128], MIRA [129], iSens [130] and MyoPlant [131], [132]. Intramuscular electrodes pick up signals coming from single motor units, not providing the overall activation pattern of the target muscle. Therefore, a specific algorithm is needed to gather information about muscular activation and classify the movement of the users. Despite the invasiveness of the procedure, the electrode placement would be a one-time-only operation and would eliminate the need for calibration sessions at the beginning of each experiment. Furthermore, the signal is not subjected to motion artifacts, and the problems related to the electrodes being placed on the skin (e.g., comfort, possible detachment of the electrodes due to sweating, etc.) can be neglected [125]. However, due to the invasiveness and its related risks, this technique is less adopted than non-invasive ones [125]. When the amputation is too proximal, and the presence of functional muscles is rare, Targeted muscle reinnervation (TMR) represents a valid alternative solution [92]. TMR is a surgical operation in which the motor nerves of the residual limb are rerouted to reinnervate a proximal muscular region [133], [134], [135]. It improves the functioning of the prosthesis and reduces neuroma pain (i.e., growth of nerve tissue around the cut nerve) [4], [134], [136], [137], [138]. The rerouted nerves grow into the newly innervated muscles, gaining the capacity to excite them [4]. Alternatively, the user intent can also be inferred by decoding the electrical activity recorded from peripheral nerves through implanted neural electrodes. This technique is useful in case no residual functional muscles are present to apply EMG techniques and helps to overcome the typical drawbacks of surface EMG (e.g., electrode shifting, electrode detachment, etc.) [132]. The major drawback of this approach is its invasiveness, the risk of damaging the nerves [132] and the poor signal-to-noise ratio of the PNS neural signals [139].

Surface electromyography (sEMG) represents a less invasive technique to access informative signals from the PNS. sEMG control of active prostheses has been widely explored [135], [140], [141], [142], [143], both individually and in combination with mechanical sensors, such as in [143] (see Fig. 4(a)), in which the authors compared the performance of a dynamic Bayesian network in classifying five locomotion modeswith different sensor signals as input. This strategy provides intuitive control of the device, by processing sEMG signals recorded from the residual muscles of the users. EMG is, however, susceptible to signal variations due to noise and movement artefacts, changes in electrode-skin conductivity, fatigue, and cross-talk between muscles, making this approach more challenging [92], [144]. EMG signals have a wide inter-subject variability but present consistent patterns within the same subjects during the gait [144] if compared to iEMG, since they provide information related to the overall activation pattern of the target muscle. Especially for lower-limb applications, it is generally necessary to have multiple recording sites to exploit intention decoding algorithms' prediction capabilities [124]. EMG signals can be used alone or in combination with other sensors (e.g., mechanical sensors) within intention decoding algorithms or for direct control approaches [125], [126]. Sensor fusion also represent a viable strategy to improve the performances of classification algorithms, while still aiming at maintaining a light setup.

From the user's perspective, it is important to maintain good device performance while guaranteeing usability and comfort. Consequently, iEMG should be preferred when osseointegration represents a viable option. This would guarantee that the "wearable" setup is limited to the prosthesis only, avoiding surface electrodes covering the residual limb and limiting the related discomforts. When osseointegration is not a feasible approach, sEMG represents a less invasive solution, with proven efficacy when signals are used in an intention decoding framework. Commercial sEMG electrodes can be embedded in sockets, but more customizable sEMG electrodes could also be used (e.g., high density sEMG based on MXenes and other new materials [145]), which guarantee the coverage of a wide area together with better control of the recording sites' position. Such solutions must also take into consideration the breathability of the materials, to avoid sweating and hygienic problems.

D. Sensory Feedback

To fully restore the functionalities of the missing limb, prostheses should deliver sensorial inputs from the environment and proprioceptive inputs to the nervous system of the subject (See Section II). For instance, the lack of sensorial information has functional consequences on the embodiment of the prosthesis (a low embodiment level implies that the users perceive the prostheses as an external and foreign object, that doesn't belong to their body schema [146]). Low embodiment, in turn, might lead to a higher risk of falls, decreased mobility, and an increased

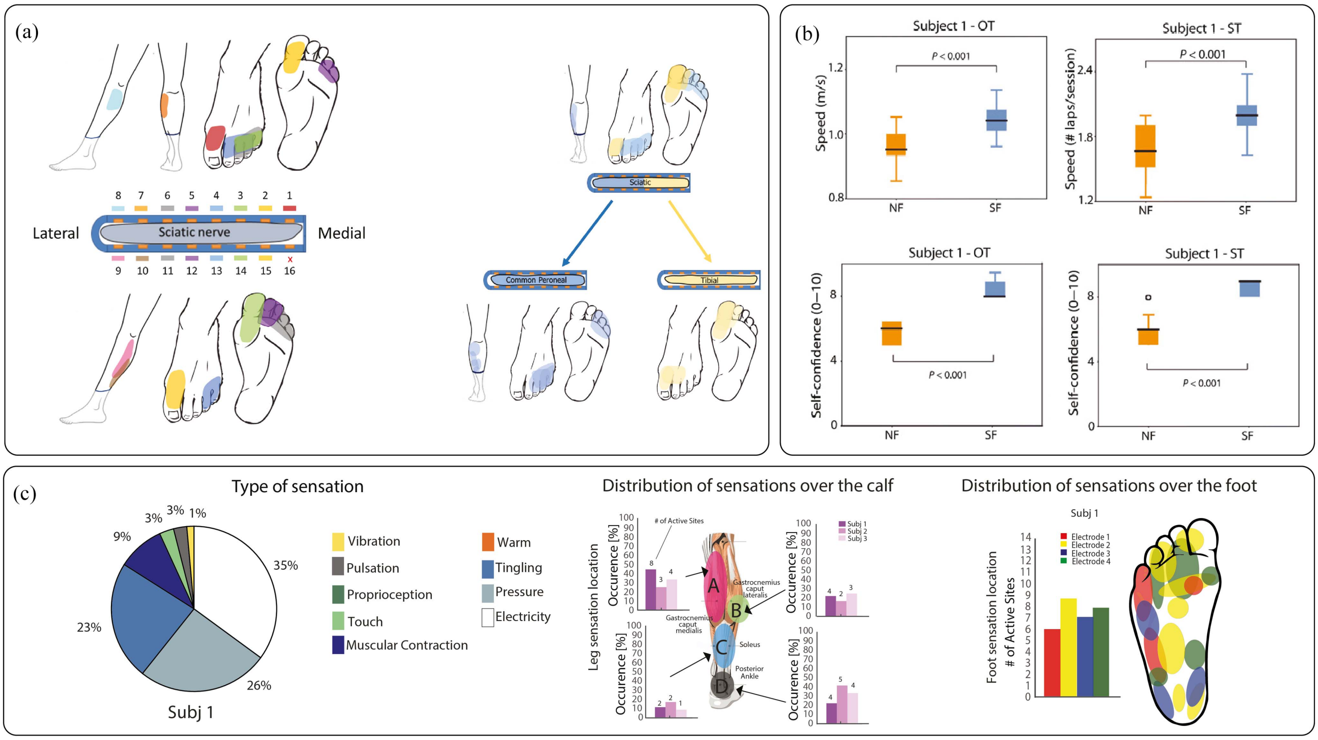

Fig. 5. Sensory feedback in lower limb prostheses. (a) Location of evoked sensation over the calf and foot with overlapping sensation when stimulating on the common peroneal branch or on the tibial branch of the sciatic nerve [170]; (b) comparison of the performances (speed and self-confidence) with (SF) and without (NF) sensory feedback, during walking (OT) and stair ascending and descending (ST) [151]; (c) type and location of the evoked sensation over the calf and foot through intraneural stimulation [147].

cognitive burden [147]. The general acceptance of prostheses is therefore reduced, and amputees tend to abandon them [89], [148]. Moreover, painful sensations coming from the missing limb (Phantom Limb Pain, PLP) or the residual limb (Residual Limb Pain, RLP) are often associated with alterations in the nervous system due to amputation [149]. The lack of sensation coming from the missing leg has been linked with PLP [150] and low embodiment [151].

Current commercially available prostheses do not restore the sensory feedback of amputees, who need to rely on visual and haptic feedback derived from the interaction between the socket and the residual limb [147].

Several approaches for providing sensory feedback to amputees have been presented, however, most of these studies focused on upper-limb amputees [152], [153], [154], [155], [156] and only a few efforts have been made for providing sensory feedback in lower-limb prostheses, especially in transfemoral amputations [148]. Neural stimulation and feedback restoration are exploitable through non-invasive (cutaneous) or invasive (direct nerve stimulation) techniques [157], [158].

Non-invasive sensory feedback can be delivered through vibration [159], electrotactile stimulation [160], mechanotactile pressure [161], and others. Such techniques have been proven effective in both reducing PLP and RLP and improving prosthetic device usability [149]. Despite the advantage of low invasivity and ease of implementation, the most relevant issue of non-invasive techniques is that the elicited sensation does not correspond to a homologous stimulation [162], [163]. Cutaneous stimulation techniques often require extensive training to provide complex stimuli and the elicited sensations are affected by variability [164], depending on the transducer position [132], and therefore the user usually engages in an intensive cognitive load to interpret the signals, as demonstrated for upper and lower limb applications in [164], [165], [166]. Some non-invasive techniques were also reported to be distracting for daily use [162].

Invasive sensory feedback is traditionally delivered through intraneural or extraneural electrodes, implanted through surgical operation (see Fig. 5). Extraneural (cuff) or epineural electrodes are wrapped around the nerves externally without penetrating them. They entail reduced risks of nerve damage [162] compared to intraneural electrodes and they are easier to implant and more robust [167]. On the other hand, they need a higher current to stimulate the neurons and stimulate a larger portion of the nerves, making this technique less selective compared to the intraneural counterparts [162]. Intraneural electrodes are implanted through the nerves (transversally (e.g., TIME electrodes [168]) or longitudinally (e.g., LIFE electrodes [169])) and potentially elicit a more natural and more selective sensation [162]. The technique is however more invasive, and can interfere with EMG recordings. The evoked sensation through intraneural stimulation results to be not only homologous (i.e., they match the quality of external stimulus [147], [150]) but also somatotopically coherent (i.e., they match the location on the phantom limb [147], [150], [170], Fig. 5(a), (c)). This entails the rapid and direct usability of such a technique, without the

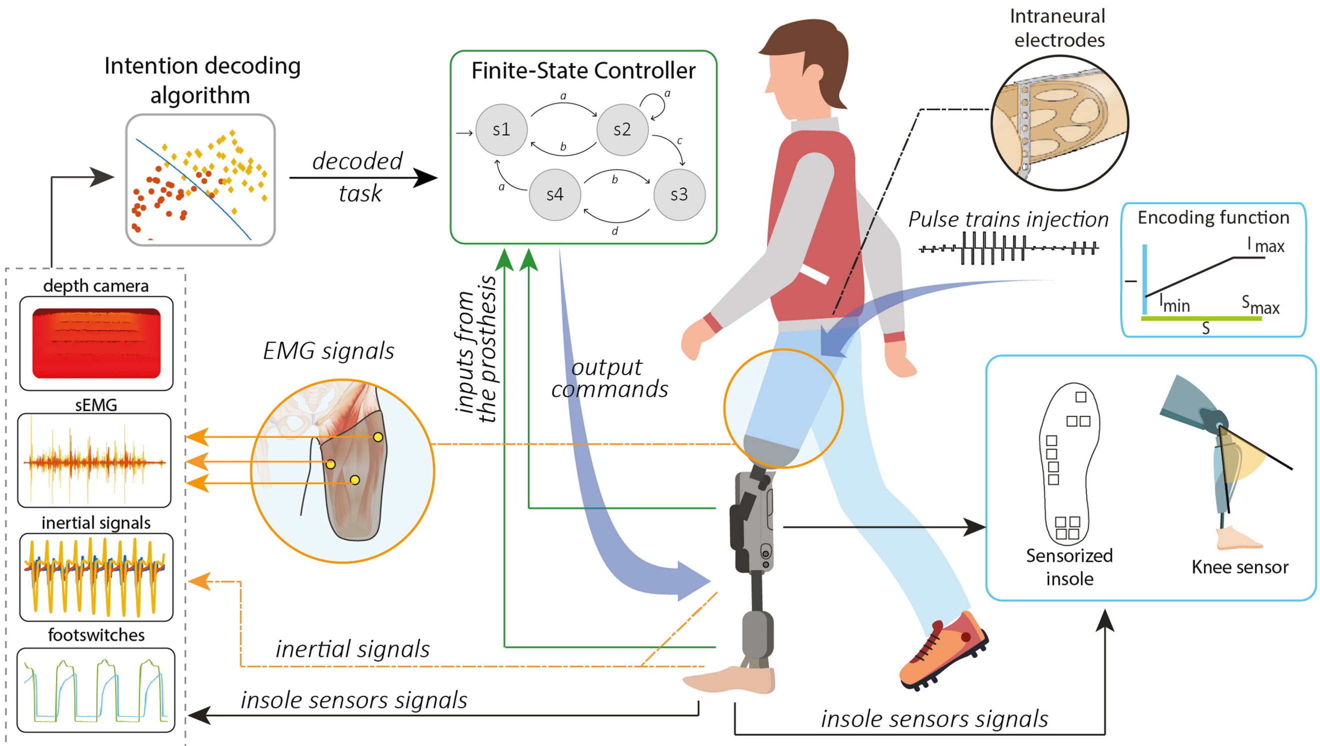

Fig. 6. Concept of a fully integrated lower limb neuroprosthesis.

TABLE III
TECHNOLOGY READINESS LEVEL (TRL) OF CURRENT PROSTHETIC TECHNOLOGIES

TECHNOLOGY READINESS LEVEL (TRL) OF CURRENT PROSTHETIC TECHNOLOGIES			
Prosthetic system	*Commercial*	*High TRL*	*Low TRL*
Socket and suspension system	• Rigid sockets • Flexible inner sockets with rigid frame • Harness suspension systems • Subatmospheric suspension systems	• Osseointegration • Electrodes embedded sockets	• Adaptable sockets
Prosthetic knee	• Passive knees • Semi-active knees • Powered knees • Microcontroller knees	• Pattern recognition controlled knees • Gait phase controlled knees • Motion intention controlled knees	• Volitionally controlled knees
Prosthetic foot	• Conventional feet • Energy returning feet • Powered feet	• Pattern recognition controlled feet • Gait phase controlled feet • Motion intention controlled feet	• Volitionally controlled feet
Sensory feedback		• Vibrotactile feedback • Mechanotactile feedback	• Intraneural feedback • Extraneural feedback

Technology Readiness Level (TRL) of the current prosthetic technologies.

need for a training session, to enable the users to benefit from the sensation return (see Fig. 5(b)). Furthermore, it was shown that restoring sensory feedback in upper-limb amputees through neural stimulation significantly decreased the PLP [152], [153], [171]. Sensory feedback was also successfully exploited through intraneural stimulation in lower-limb amputees performing various locomotion tasks [147], [148]. Besides the improvements in mobility [151] (see Fig. 5(b)), it also led to health and cognitive benefits [151], exhibiting a reduction in PLP [148], both in short and long-term periods after the stimulation was delivered [148]. Specifically, [151] quantifies the functional and cognitive benefits of intraneural sensory feedback, leveraging gait markers of the leg neuroprosthesis and confidence measures. More complex intraneural stimulation paradigms are yet to be tested to explore the effects on PLP and RLP in both the short and long term, and a limited number of in-depth studies have been conducted on this topic for lower limb amputees. The major limitation of neural stimulation techniques is their invasiveness and difficulty of implementation in long-term fully implantable systems [132]. The agonist-antagonist myoneural interface (AMI) [135], [172] is another invasive approach to reestablish proprioceptive feedback in amputees, by leveraging the spindle and Golgi tendon organs of the residual muscles. The AMI is created by surgically connecting the agonist-antagonist muscles pair, thus allowing the antagonist muscle spindle and Golgi tendon organs to be stretched by the activation of the agonist muscle, providing muscle-tendon proprioception. Despite the naturalness of the perceived sensations, the AMI is an invasive 2-stage surgical procedure and does not allow the connection of more than two muscles together, as for biological joints.

Despite the lack of extensive studies, intraneural sensory feedback represents the most promising and efficient way of pursuing sensory feedback restoration in lower-limb neuroprostheses for the reasons described above and its versatility in providing a wide range of somatosensory and proprioceptive sensations, especially with the use of biomimetic sensory encoding strategies (i.e., to evoke close-to-natural sensations [150]).

IV. Conclusion and Perspectives

Lower limb amputation is an impactful condition, which leads to reduced mobility and is associated with comorbidities that negatively affect amputees' daily life. While some of the comorbidities are among the causes of amputations (e.g., peripheral vascular disease, diabetes), some of them are consequences of the amputation (e.g., lumbago, arthritis) (see Section II). The complexity of the context reflects the complexity of the users' needs, which are various and depend also on both the medical and social conditions of the subject (see Section II). The non-compliance with one or more of such needs potentially leads to dissatisfaction, possibly worsening of comorbidities and, ultimately, to prosthesis abandonment. For these reasons, developing a functional and efficient user-centered prosthetic leg, capable of assisting the amputee in daily living tasks, is not trivial. Extensive at-home testing is still not a common practice, due to the setup complexity and home-monitoring challenges, but is crucial to avoid non-reproducible and impractical solutions. The encumbrance of the setup is a key factor for prosthesis acceptability: bulky acquisition devices, electrodes not embedded into the socket and solutions that extend to other parts of the body (e.g., TMR, EEG, etc.) are perceived as invasive and uncomfortable, and consequently abandoned. Similarly, noisy solutions are perceived as disturbing during daily activities. Treating PLP and RLP is equally essential for amputees' quality of life, but current treatments (e.g., medications, medical therapies, brain stimulation, etc.) are often time-consuming and present contraindications. Being able to mitigate the pain with intraneural stimulation allows for a better-integrated solution instead, capable of improving the user's quality of life effortlessly, concurrently restoring sensory functions and improving prosthesis usability.

In Section III we have identified a number of deficiencies in current prosthetic devices, both with respect to commercially available devices, and within the research field. We analyzed the key aspects to consider during the development of each module of a neurointegrated prosthesis, having as main objectives user experience, usability and functionalities restoration. In Fig. 6 the concept of a fully integrated neurally-controlled prosthesis is shown. The movement's intention is decoded through sensor fusion techniques, relying on EMG, IMUs and prosthesis' built-in sensors. The EMG signals can be acquired both with invasive techniques (i.e., iEMG) or with custom electrodes embedded inside the socket or the liner (i.e., sEMG). As explained in Section III, iEMG is preferable when osteointegration is possible, merging the benefits of a direct bone-prostheses connection to the better EMG signal quality of the implanted electrodes, concurrently reducing the setup burden by removing the socket. If contraindications for osteointegration are present (e.g., diabetes, vascular diseases, etc.), sEMG is a valuable substitute if the electrodes are designed to be integrated inside the socket structure, limiting the time required for the donning and doffing of the prosthesis. In the latter case, the comfort of the amputee can be enhanced by using adaptable sockets (i.e., sockets with air or fluid chambers) capable of accommodating slight residual limb volume variations. Once data from the different sensors have been acquired, the signals are preprocessed and interpreted by means of machine learning or neuromorphic approaches, relying on algorithms capable of adapting to the surrounding environment and the slow changes of the collected signals, such as in the case of EMG. After the movement intention is decoded at a high level, a finite-state machine is used to send commands to the powered prosthetic leg during specific gait phases. The use of a powered prosthesis allows the subject to perform dynamic movements decreasing the required metabolic cost, reducing the use of compensatory strategies and limiting the insurgence of related long-term comorbidities (see Section III). To close the control loop, intraneural electrodes are used to deliver electrical stimulation through the residual nerves of the subject. The stimulation is designed and delivered based on the information extracted from the knee encoder and sensors placed under the prosthetic foot, reestablishing the sensory and proprioceptive pathways lost during the amputation process.

The invasive approach can be also used in combination with non-invasive feedback, which can help in providing discrete information (e.g., state transitions), complementary to the more complex encoded by the intraneural electrodes. The choice of approach is dependent on both subject preferences and adopted prostheses. The combination of the presented technologies enhances prosthesis usability by allowing effective control of the device and restoring sensations coming from the missing limb, concurrently increasing the general embodiment of the prosthesis. Additionally, sensory feedback helps to mitigate PLP and RLP and enhance the awareness of the surrounding environment, decreasing the risk of falling events (see Section III-D). For the above-mentioned reasons, the development of a fully integrated powered neuroprosthesis would significantly improve the quality of life of lower limb amputees.

The neuroprosthesis we propose combines impactful solutions in a modular fashion, that can be fully integrated minimizing the setup burden, thus maximizing comfort, usability and acceptability. Therefore, it could represent the optimal compromise between a heavily research-oriented setup and an already commercially available prosthesis, solving most of the field's open issues with a user-centred approach and implementing innovations that directly address amputation-related problems.

How far are we from of achieving such a solution? Although excellent progress has been made in the implementation of an integrated device, the commercialization of a fully integrated powered neurally-controlled prosthesis is not close by (see Table III). The majority of ankle-foot and knee prostheses commercially available are passive or semi-passive and do not assist the user during force-demanding tasks. Additionally, the few powered models (e.g., Power Knee$^{\mathrm{TM}}$ by Össur and Empower by Ottobock) on the market do not involve the amputee in the control loop, relying on internal sensors only for the control and not providing sensory and proprioceptive feedback. Advanced prosthesis control still shows limitations regarding reliability and the setup burden, even in a research environment. Despite a fully integrated solution not being available already, most of the technologies discussed across this work present a high level of technology readiness. This entails the possibility of moving toward the final goal with an incremental approach, implementing, integrating and deploying the solutions when the technology of the single neuroprostheses module is mature enough to reach the market.

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