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## **Active Upper Limb Prostheses: A Review on Current State and Upcoming Breakthroughs**

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#### Abstract

The journey of a prosthetic user is characterized by the opportunities and the limitations of a device that should enable activities of daily living (ADL). In particular, experiencing a bionic hand as a functional (and, advantageously, embodied) limb constitutes the premise for promoting the practice in using the device, mitigating the risk of its abandonment. In order to achieve such a result, different aspects need to be considered for making the artificial limb an effective solution to accomplish activities of daily living. According to such a perspective, this review aims at presenting the current issues and at envisioning the upcoming breakthroughs in upper limb prosthetic devices. We first define the sources of input and feedback involved in the system control (at user-level and device-level), alongside the related algorithms used in signal analysis. Moreover, the paper focuses on the user-centered design challenges and strategies that guide the implementation of novel solutions in this area in terms of technology acceptance, embodiment, and, in general, human-machine integration based on co-adaptive processes. We here provide the readers (belonging to the target communities of researchers, designers, developers, clinicians, industrial stakeholders, and end-users) with an overview of the state-ofthe-art and the potential innovations in bionic hands features, hopefully promoting interdisciplinary efforts for solving current issues of ULPs. The integration of different perspectives should be the premise to a transdisciplinary intertwining leading to a truly holistic comprehension and improvement of the bionic hands design. Overall, this paper aims to move the boundaries in prosthetic innovation beyond the development of a tool and towards the engineering of human-centered artificial limbs.

Keywords: bionics, biosignals, closed-loop, embodiment, feedback, prosthetic hand, user experience

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Figure 1. Graphical representation of a ULP system and its elements. The user level (left panel) includes: input data sent from subject to the prosthesis (Input Signals), artificial sensory feedback information delivered from the prosthesis to the user (Sensory Feedback), and external sources of interaction (External Factors), such as actuation coming from the unimpaired limb or environmental/accidental sources of feedback such as vision and sound. The device-level (right panel) includes the control commands used to drive the prosthesis and the feedback information collected by the end-effector. The user-device interface is characterized by a bidirectional exchange of information (overlap of the two panels).

#### 45 1. Introduction

 Over the past twenty years, poly-articulated upper limb prostheses (ULPs) have undertaken several technological and scientific developments to satisfy the different needs of the upper limb amputee community. Nonetheless, in a recent study, Salminger et al. (2020) observed overall abandonment rates of ULPs of about 44% in a population of mainly (92%) myoelectric prostheses users. They also highlighted how the past decade of developments still presents technological limiting factors that did not permit the restoration of the full functionalities of a missing limb, hence leading to a substantial increased rate of prosthesis abandonment. The main cause of such ineffectiveness mainly resides in a non-sufficiently patient-tailored design process (Salminger et al., 2020).

According to the American Orthotic & Prosthetic Association (AOPA, 2016), partial amputations, i.e. finger amputations, represent the majority of upper-limb losses (75.6%), while trans-radial and trans-humeral amputations constitute a percentage oscillating between 5 and 6%. Despite this, the level of impairment caused by trans-radial and trans-humeral amputations is greater than for partial amputations.

68 Without tracing back all the evolution of upper limb 69 prostheses – the reader might find useful the reviews of 70 Trent et al. (2019) and Ribeiro et al. (2019)). Trent et al. 71 (2019) work focuses on a classification of the upper-limb 72 prostheses architectures based on the type of adopted 73 actuation, e.g., passive, body-powered or active. On the 74 other hand, Ribeiro et al. (2019)'s research investigates the 75 most relevant control signals used for the man-machine 76 interface.

This work focuses on trans-radial and trans-humeral devices, excluding partial amputations, and it details the latest and most technologically advanced solutions, namely poly-articulated myoelectric prostheses. Moreover, this review aims at presenting and analyzing the key elements of state-of-the-art upper limb prostheses in a user-centered and human-in-the-loop fashion and to provide guidelines for the development of such prostheses and the relative control algorithms, to possibly achieve solutions capable of promoting the systems use and overcoming the elevated abandonment rates observed so far. Overall, the reader could take advantage of this review as an analytical collection of solutions constituting a premise to provide the user with a seamless control experience.

## 91 2. Upper limb Prosthetics classification: a twofold92 perspective

An ULP system can be observed from two main points of views: its mechatronics, namely the combination of the mechanical and electronic components necessary for its operation, and the control strategies and algorithms implemented to orchestrate its functions. Research groups have therefore attempted to solve the prostheses abandonment problem by addressing different technological and scientific challenges, either focusing on mechatronic design, or on control strategies aimed at increasing the human-machine interaction and, in some cases, introducing feedback sources, as detailed in the next sections.

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Figure 2. Graphical representation of information flow of a possible ULP architecture. Input flow (top panel): from user (input signals i.e., from EMG sensors) to prosthesis (control commands i.e., through power train). Feedback flow (bottom panel): from prosthesis (end-effector feedback i.e., from tactile force sensors) to user (sensory feedback i.e., through vibrotactile motors).

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<sup>18</sup>105 ULP control can be divided into two synergistically 143 <sup>19</sup>106 interacting sub-systems: the user-level and the device-20 107 level, as depicted in Figure 1. The user-level includes the 21 108 patients and the most proximal device component 22 109 interacting with the user (i.e., the socket), while the device-23 110 level extends from the socket to the ULP device. These two 148 24 111 149 sub-systems overlap at the socket level, which is involved 25 26112 150 in a bidirectional flow of information. On one hand, it 27113 receives inputs from the user (i.e. movement intentions) 28<sup>114</sup> and translates them into movement commands for the <sub>29</sub>115 153 device; on the other hand, it receives information (both 30116 from the device and the environment) and communicates it 154 31117 the user through sensory feedback (Figure 1). to 32118 Importantly, the socket itself severely limits the user 33119 157 comfort, and together with the prosthetic weight highly 34120 contributes to the prosthetic abandonment.

35121 Even if the state-of-the-art in prosthetic research 36122 encompasses studies based on psychological processes too, commercial ULP systems have focused on restoring 37123 38124 functional capabilities by capitalizing on the device-level 39125 only, therefore on mechatronic, and several solutions can 40126 be found on the market for trans-radial level of 41127 amputations. Commercially available systems merge basic 42128 functionalities and aesthetic requirements, targeting the 43129 clinical needs given by a certain kind of amputation, rather 44130 than focusing on each patient's specific needs.

45131 Commercial solutions range from tri-digital hands, e.g., 46132 VaryPlus Speed, SensorHand Speed by Ottobock <sup>47</sup>133 (Ottobock, 2020c) and Motion Control (MC) Hand by <sup>48</sup>134 Fillauer (Fillauer, 2021); through polyarticulated hand <sup>49</sup>135 e.g., Michelangelo under-actuated, by Ottobock <sup>50</sup>136 (Ottobock, 2020b); to fully actuated polyarticulated hand, <sup>51</sup>137 e.g., BeBionic by Ottobock (Ottobock, 2020a), i-Limb by 138 Ossur (Ossur, 2020b), Vincent Hand by Vincent Systems 139 (Systems, 2020), TASKA hand by Taska Prosthetics 140 (Taska, 2022), BrainRobotics Hand by BrainRobotics 56<sup>141</sup> (BrainRobotics, 2022) and Ability Hand by Psyonic 57<sup>142</sup> (Psyonic, 2022).

In the last decades, many research groups have focused on the mechatronic development of ULP devices, entrusting the intelligence of the device to the embedded mechanics in a very thorough design, structuring the development of the concept of under-actuation, such as the Vanderbilt Multigrasp Hand (Bennett et al., 2014), the MIA Hand (Controzzi et al., 2016), the SoftHand Pro (Godfrey et al., 2018), the KIT Hand (Weiner et al., 2018), and the Hannes Hand (Laffranchi et al., 2020).

On the other hand, there is a family of very dexterous devices, not yet market-ready, that mimic the complexity of the human hand, implementing a fully-actuated multidegrees of freedom mechatronics, e.g. the University of Bologna Hand (Meattini et al., 2019) or the Shadow Hand (Company, 2020).

High level of amputations, as the trans-humeral ones, require prosthetic elbows, such as the Dynamic Arm (Ottobock, 2022a), the Dynamic Arm Plus (Ottobock, 2022b), and the ErgoArm (Ottobock, 2022c) from Ottobock; the Espire Elbow (Classic, Classic Plus, Pro and Hybrid,) from Steeper Inc. (Steeper, 2022); and the Fillauer Motion E2 Elbow (Fillauer, 2022a) and the Utah Arm 3 (Fillauer, 2022b) from Fillauer. In the research context, full robotic arms include the DLR hand system (Grebenstein et al., 2011), the APL modular prosthetic limb (Johannes et al., 2011), the LUKE Arm (Bionics, 2022), the Rehabilitation Institute of Chicago arm (Lenzi et al., 2016), and Edinburgh Modular Arm System (Gow et al., 2001).

However, this great variety of products does not match with the elevated abandonment rates, demonstrating the lack of satisfaction of the patients' needs from a mechatronic perspective. In particular, structural and supporting part lack of adjustability of user size, allow limited kinematic and motion possibilities and more advanced systems present limited operational time (Harte et al., 2017). This leads to limited satisfaction and feeling of security. Moreover, these systems generally present poor personal and social acceptance because of limited

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3 182 anthropomorphism, high weight and presence of acoustic 4 183 disturbances during use (Harte et al., 2017), This suggests 184 that ULP development should not only focus on the device 185 level, but improvements at the user level could play a key 7 186 role for truly meeting the user requirements and 187 consequently obtain device acceptance. Motivated by this, 188 in this review, we analyse all the possible approaches that <sup>10</sup>189 could potentially address the user needs in terms of device <sup>11</sup>190 controllability, robustness and hence embodiment and user 12 191 experience. To this end, it is fundamental not only to focus <sup>13</sup>192 on the functionality restoration but also on the sensory 14 193 information recovery, which are fundamental to effectively 15 194 control the device. All the described approaches range from 17<sup>195</sup> improvements in decoding user intentions, hence analysing <sub>18</sub>196 all possible input sources and their related control 19<sup>197</sup> strategies, to inclusion of additional sources of feedback 20<sup>198</sup> capable to restore the sensory information. These 21199 approaches tackle the issues related to poor device control 22200 because of lack of intuitiveness and sensory feedback.

23201 Therefore, in this review we present current and 24202 emerging methods in ULP development, detailing various 25203 sources of input and feedback signals, as well as control 26204 strategies. We also highlight current challenges and open 27205 issues in the field, specifically focusing on the importance 28206 of user experience and involvement in the design and

207 development process. This is fundamental to promote 208 patient-tailored approaches leading to the development of 209 truly personalized devices, which are currently lacking. We 210 finally provide an overview of the most promising 211 approaches that if followed, may one day provide upper 212 limb amputees with a true substitute of their missing arm.

#### 213 3. Input and Feedback Signals for Prosthetic 214 Control

Prosthetic control is regulated by a flow of signals, as depicted in Figure 2. Input signal runs from the user to the device and they are often of biological or electrophysiological nature, in which case are called biosignals. Signals flowing in the opposite direction convey information from the device to the user and are therefore defined as sensory feedback signals. Moreover, some external factors convey to the user additional source of feedback (i.e., incidental feedback), such as visual or auditory information that can be used to estimate the prosthesis state (Wilke et al., 2019, Sensinger and Dosen, 2020, Gonzalez et al., 2021).

Input signals include all the sources of information that can be taken from the amputee and translated into motor commands for driving the prosthesis (e.g.,



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3 230 electromyography - EMG), see section 3.1. Instead, 4 231 sensory feedback information encompasses different prosthetic sensing solutions acquired either from the prosthetic device or from the environment, see section 3.2 that can be translated into sensory stimuli for the amputee 8 235 (e.g., vibrotactile stimulation, see section 3.3). All types of signals can be classified according to their level of <sup>10</sup>237 invasiveness, with consequent advantages and drawbacks. 

#### <sup>12</sup>238 3.1. Input Signals

In recent years, many research activities have focused on the extraction of useful information from the biological signals in order to suitably control upper limb prostheses. Traditionally, the surface EMG (sEMG) is the most widespread signal for prosthesis control but its use still faces many drawbacks (Kyranou et al., 2018). In the following, we describe various methods to employ EMG as input signal for ULP control and we also explain how other input sources can be exploited to obtain more dexterous prosthetic behavior, overcoming the limitations of current ULP systems. 

Figure 3 collects input signals for ULP control that will be described in the following subsections, ranging from those used by commercial systems, up to those currently under investigation.

#### 3.1.1. Biosignals



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The term *biosignal* indicates every possible signal that can be detected and measured from biological beings, humans - in our case. Usually, the term is used for signals of electric nature (i.e., EMG), but actually every signal collected from the activity of different tissues or organs belonging to the human body, can be considered as a biosignal.

We here adopt this latter definition to group input sources that are described next. Given its large use both in research and commercial ULP devices, electromyography deserves a dedicated subsection, while other biosignals are grouped together. We also dedicate a whole subsection to brain-derived signals, which are especially used in brain-machine and brain-computer interfaces (BMIs, BCIs), but that are also showing potential use for ULP applications. Table I summarizes biosignals for ULP control that will be described in the following subsections.

Table I: biosignals	used as	input	sources	ın pı	osthetic a	appl	ications.	
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		Measured Property	Sensors' placement	PROs	CONs	Sensor Fusion	Examples
ography G)	Surface EMG	Muscle Electric	On the skin over targeted muscles 2–32, up to 192 sensors	Non-invasive, long-term use, a large number of people	Sweating, electrodes shift, Muscle fatigue, Electromagnetic noise	NIRS, IMU,	(Merletti et al., 2010) up to 27 gestures
Electrom; (EN	Invasive EMG	Potentials	Underneath the skin, on or inside targeted muscles 4-8 sensors	High signal/noise ratio, directly on the nerve, no shift with respect to the source	Invasive, infections	FMG, SMG, MMG	(Cipriani et al., 2014, Ortiz-Catalan et al., 2020)
Force-	myograpny (FMG)	Change of muscle morphology measured on the skin surface	Over targeted muscle, over related tendons 8, up to 126 sensors	Physiologic, small size, high signal/noise ratio, flexible	Muscle fatigue, sensors shift, pre- load force, small spatial resolution, crosstalk	EMG	(Xiao and Menon, 2019) up to 8 gestures
Mechano-	myograpny (MMG)	Muscle fiber oscillations using microphone or accelerometers	Over targeted muscle 6-20 sensors	low cost, no pre- amplification, no precise positioning, no skin impedance or sweat influence	Ambient acoustic noise, Adjacent muscle crosstalk, Sensor displacement	EMG, IMU	(Wilson and Vaidyanathan, 2017, Guo et al., 2017a, Castillo et al., 2020) up to 5 gestures
Sono-	myograpny (SMG)	Change of muscle morphology	Over targeted muscle, over related tendons transducers of different shapes	Deep and superficial muscles, some models are cheap and energy- efficient	Probe shift, tissue impedance, no wireless, some models expensive and bulky	EMG	(Dhawan et al., 2019) up to 15 gestures

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Near- Infrared Spectroscopy (NIRS)	Tissue oxygenation through the amount of scattered light	Over targeted muscle 2-4 sensors	Deep and superficial muscles, high spatial resolution, no electronic interference	Ambient light, Muscle fatigue, tissues heating	EMG, IMU	(Paleari et al., 2017) up to 9 gestures	
Electrical Impedance Tomography (EIT)	Tissue impedance	Over targeted muscle, over related tendons 8, up to 64 sensors	No need precise positioning	Low time resolution, sweating, Electromagnetic noise, high consumption	- •	(Zhang et al., 2016, Wu et al., 2018) up to 8 gestures	
Capacitance sensing	Tissue capacitance	Over targeted muscle, over related tendons 3 receiver sensors	Non-invasive, low cost, deep and superficial muscles	Sweating, Electromagnetic noise, displacement, ambient temperature	Ĉ	(Cheng et al., 2013, Truong et al., 2018) up to 2 gestures	
Magneto- myography	Magnetic fields generated by muscle	Over/inside targeted muscle 7 sensors	Not sensitive to sensor's shift and sweat	Magnetic interference, can be invasive, movement artifacts	2	(Zuo et al., 2020) concept	
Peripheral Neural Interfaces (PNIs)	Electrical activity of the nerves	Microelectrode arrays placed on different fascicles within the median and ulnar nerves	Intuitive, direct maps of complex movements, high accuracy, robust	Invasive, difficult to separate EMG and PNI components, recording channels really closed each other	_	(Nguyen et al., 2020) up to 15 DoFs	
Intracortical neural signals	Intracortical neural signals from the brain, action potentials of individual neuron	16-192 high-density channels electrodes inserted into the motor cortex tissue	Accurate and capable of collecting the most information-rich data, high spatial resolution	Very invasive, influenced by tissue reactions	-	(Hochberg et al., 2006, Hochberg et al., 2012, Collinger et al., 2013, Wodlinger et al., 2014) 7-10 DoFs	
Electrocorticography (ECoG)	Electrical activity of brain's surface	32-128 high-density channels on sensorimotor regions	Less attenuated than EEG, good spatial resolution and wide frequency content	Surgical procedure and lack to measure single cell activity	-	(Wang et al., 2013, Fifer et al., 2013, Bleichner et al., 2016, Hotson et al., 2016) 4 gesture recognition and wrist movements	
Electroencep halography (EEG)	Electrical activity of the brain	6-32 channels headsets	Not invasive, low cost, portable, stable, and very easy to use	Signal attenuated by the dura, the skull, and the scalp, loss of important information	-	(McFarland et al., 2010, Yang et al., 2012, Edelman et al., 2019, Fuentes- Gonzalez et al., 2021) single DoF	
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#### 15274 3.1.1.1. Electromyography

16275 While cosmetics, electronic components and 17276 computational efforts have undergone a significant <sup>18</sup>277 improvement, the control strategies currently used in <sup>19</sup>278 prosthetic applications have not changed since their first <sup>20</sup>279 appearance in the 1960s (Schmidl, 1965). The EMG has 21280been one of the major sources to control upper limb <sup>22</sup>281 prostheses (Merletti and Farina, 2016). These signals carry 23282 24282 25283 25284 26285 28286 29287 30288 31289 information about neuromuscular activity, and they are used to retrieve human intention. EMG is indeed a technique for studying the activation of the skeletal muscles through the recording of electrical potentials produced by muscle contraction (Hudgins et al., 1993). The theory behind the sEMG electrodes is that they form a chemical equilibrium between the detecting surface of the 314 electrode and the skin of the body through electrolytic 32<sup>290</sup> conduction, so that the current can flow into the electrode.

33291 Multiple methods have been used to obtain the intended 34292 318 gesture from the processed EMG signals, all of which 35293 exploit the fact that the amputees can still generate different 36294 and repeatable muscular patterns related to each forearm 37295 movement with residual muscles of the stump. Low-38296 density EMG is commonly used in prosthetic application, 39297 both in research and commercial context. Noteworthy, 40298 EMG signals can also be collected with invasive methods. 41299 The sEMG can be thus classified according to the level of



Figure 4. sEMG electrodes. A: bipolar dry sensors, Ottobock and IIT/INAIL (Marinelli et al., 2021) respectively. B: high-density wet sensors (OT Bioelettronica).

300 resolution and density of the sensors. In the following, we 301 provide an overview of the different types of EMG-based 302 biosignals.

### Surface EMG

The sEMG can be classified according to the number of electrodes used (Figure 4). Low-density EMG generally refers to the use of a small (<10) number of EMG bipolar sensors, that can be either wet, i.e. contain an electrolytic substance that serves as interface between skin and electrodes, or dry (Jamal, 2012). Conversely, high-density EMG is typically composed by wet monopolar sensors spread on a planar patch, around 1cm apart, and with the ground reference generally placed on the wrist or on the elbow (Drost et al., 2006). Importantly, sEMG electrodes also differ in their electronic configuration, as they can be either preamplified or not (Zheng et al., 2021). Merletti and Muceli (2019) provided a guide with the best practice to acquire and manipulate EMG data according with the different aims, from signal analysis to motion prediction.

Prosthetic control with low-density EMG is generally obtained by using two bipolar electrodes placed on antagonist muscles. This configuration allows the control of the prosthetic system in a robust and simple way (Hudgins et al., 1993). However, the detection of complex and simultaneous movements of the phantom limb can be improved by using an array of EMG electrodes placed on the superficial skin of the residual forearm (COAPT, 2017, Dellacasa Bellingegni et al., 2017, Ottobock, 2019, Marinelli et al., 2020), The use of sEMG in prosthetic applications has become the most widespread source of information about voluntary movement (Schmidl, 1965) because of the direct correlation between EMG activity and subjects' intentions.

333 Differently from the low-density, the high-density 334 sEMG (HD-sEMG) is based on a higher number of 335 electrodes placed on a small portion of the body. Recently, 336 a growing number of researchers has focused on the use of 337 these electrodes aiming to increase the amount of collected 338 data, although at the cost of a greater computational 339 burden. HD-sEMG sensors have been used to discriminate 340 muscular patterns related to different gestures. Their 341 signals can be handled in various ways to retrieve unique

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342 and repeatable information, as described in section 4. 4 343 These sensors have to be positioned according to the 344 distribution of the underlining muscle fibers and this 345 configuration provides a low resolution map of the 346 synergistic activation of the muscles during movement 347 production (Winters, 1990, Sartori et al., 2018). For 348 example, from contraction of the muscles under the <sup>10</sup>349 acquisition grids, it is possible to extract bi-dimensional 11350 12351 13352 14353 15354 16354 17355 17356 18356 19357 20358 images, in which the EMG amplitude is mapped to a color scale. These maps can be thus handled by complex algorithms, as the ones used for objects detection in robotic navigation (Chen et al., 2020). The main limitation of the HD-sEMG, which currently bounds its application to a laboratory scenario, is the skin-electrode contact since it requires conductive gel to reduce the interface impedance. The wet area is mainly needed to reduce artifacts in the EMG signals since it is generally acquired in monopolar 20350 21359 22360 23361 configuration. Another disadvantage of this technique consists in the fact that computation is time-consuming.

414 Overall, the main drawback of sEMG-based approaches 24362 415 is constituted by the influence that skin impedance, sweat, 25363 and electrode shift have on the stability of the input signals 416 26364 417 (De Luca, 1997). Additionally, muscle crosstalk and the 27365 418 difficulty to reach deep muscles further limit the quality of 28366 419 the collected signal. In the context of ULP, the use of 29367 sEMG can be further complicated by the fact that the 420 30368 421 amputation strongly affects muscles strength and 422 31369 organization and therefore signal quality, as discussed in 32370 423 section 6.4. 33 424

#### 34371 Invasive EMG and Surgical Procedures

35372 426 The invasive approach has been exploited to explore the 36373 activity related to the production of movement for many 37374 428 years (Adrian and Bronk, 1929) and it is still investigated 38375 by many groups. However, the main drawback of this 429 39376 40377 41378 42379 43380 44381 45382 46383 47383 48384 48385 49386 50386 51387 52388 53389 430 approach is constituted by the surgery and by the 431 barriers still faced by the available technological equipment. the other invasive 432 On hand, electromyography (iEMG) allows to measure single 433 motor unit action potentials, enabling a higher selectivity 434 and a better accuracy of the input signal, overcoming the 435 436 limitations imposed by sEMG. There are several examples 437 of iEMG, which vary in the type of electrodes and level of 438 invasiveness, as detailed hereafter.

EMG can be invasively detected by inserting electrodes into the internal surface of muscles (Merletti and Farina, 2009). This invasive technique exploits two different percutaneous electrodes: needles and fine wires (Jamal, 2012, Rubin, 2019). The most used are needle electrodes. <sub>54</sub>390 These electrodes are concentric, and their bare hollow 55391 needles contain an insulated fine wire into their cannula, 56392 which is exposed on the beveled tip, which is the active 57393 recording site. Wire electrodes are typically made of non-58394 oxidizing and stiff materials with insulation, they can be

implanted more easily and are usually less painful than 396 needle electrodes.

Since both these sensors are percutaneous, i.e., passing through unbroken skin and leaving an open passage between the internal structures of the body and the external world, the risk of infection is quite probable. For this reason, and because of their intrinsic discomfort due to the percutaneous wire that can easily break, their usage is limited to laboratory research (Hargrove et al., 2007, Cloutier and Yang, 2013a). A detailed description of invasive electrodes both to record biological signals and to deliver electrical stimulation can be found in Raspopovic et al. (2021a).

In the last decades, growing attention has been paid to the development of intramuscular electrodes that could be implanted under the skin of the subject to achieve the advantages of invasive sensors and simultaneously avoid the risks and inconvenience of percutaneous instruments. For example, Weir et al. (2008) developed an implantable myoelectric sensor (IMES), a system able to receive and process up to 32 implanted sensors with wireless telemetry. A transcutaneous magnetic link between the implanted electrodes and the external coil allows reverse telemetry, which transfer data from the sensors to the controller, commanding the control of the prosthesis, and forward telemetry to supply power and configuration settings to the electrodes. These sensors are designed for permanent longterm implantation without any kind of servicing requirement and have been tested on animals. Four months after the implantation of IMESs in the legs of three cats, the sensors were still functioning (Weir et al., 2008). Intramuscular electrodes have been used in prosthetic application to decode 12 different hand gestures from 4 healthy subjects (Cipriani et al., 2014). Moreover, it has been shown that the application of this invasive approach enhances the simultaneous control of multi-DoFs system (Smith et al., 2014).

Recently, the group of Ortiz-Catalan showed an invasive procedure for ULP control. They positioned EMG electrodes under the skin of amputated subjects and sutured them directly on the external surface of the muscles (Ortiz-Catalan et al., 2020). More precisely, sensors were sewn onto the epimysium of the two heads of the biceps' muscles and the long and lateral heads of the triceps muscles. These invasive electrodes were used in combination with an osseointegrated prosthesis, i.e. a system obtained following a very invasive surgical procedure, which allows to anchor the prosthesis to the remaining limb's bone (Ortiz-Catalan et al., 2020). In the context of ULP, osseointegration is offered for trans-humeral amputees, and the prosthesis is anchored to the humerus with two mechanical elements: the fixture, a screw made of titanium placed inside a hole made in the bone that becomes osseointegrated, and the

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3 448 501 abutment, placed within the fixture and extending outside 4 4 4 9 of the body in a percutaneous way, onto which the 502 5 450 503 prosthesis is connected. This technique was tested on four 6 451 osseointegrated patients.

7 452 505 This latter example indicates that also surgical 8 453 506 approaches can be taken to improve the quality of the <sup>9</sup> 454 collected EMG. A promising surgical technique that is 507 <sup>10</sup>455 performed in case of high-level amputation is Targeted <sup>11</sup>456 Muscle Reinnervation (TMR). This method was developed 12457 13458 14459 15460 16461 17461 18462 19463 509 by the group of Kuiken in the early 2000s and consists in transferring residual arm nerves to alternative muscle sites. 510 Following reinnervation, these target muscles are able to 511 512 produce EMG that can be collected and used to control 513 prosthetic arms (Kuiken et al., 2009). This strategy works at the condition that each reinnervated muscle produces an 514 515 EMG signal in response to only one transferred nerve, with 20464 516 the consequence that native nerves innervating the target 21<sup>465</sup> 517 muscle has to be cut during the surgical procedure to avoid 27466 unwanted EMG signals (Kuiken et al., 2017). In the last 15 518 23467 519 years, TMR has allowed intuitive control of ULP to several 24468 520 subjects with high-level amputation for whom standard 25469 ULP devices allowed a poor restoration of motor functions 521 26470 522 (Kuiken et al., 2017). Importantly, given that it is 27471 523 performed on complex amputations, this technique is 28472 524 strongly tailored to each patient's physical and clinical 29473 status (Cheesborough et al., 2015, Mereu et al., 2021).

30474 526 Recently, a new surgical method for improving EMG-31475 based control has emerged: the *regenerative peripheral* 32476 nerve interface (RNPI) (Vu et al., 2020a). Just as TMR, its 33477 goal is to turn a muscle into a biological amplifier of the 34478 motor command, in order to improve the quality of the 35479 EMG signal recorded, processed and used to drive the 36480 prosthesis. To this end, RNPI exploits the regeneration 37481 capabilities of nerves and muscles, to implant a transected 38482 nerve into a free muscle graft. Following regeneration, <sup>39</sup>483 revascularization and reinnervation by the transected 40484 nerve, the muscle graft effectively becomes a stable <sup>41</sup>485 peripheral nerve bioamplifier, able to produce high-4485 42486 43487 44488 45489 46490 47490 48491 48491 48492 49492 amplitude EMG signals (Urbanchek et al., 2012). The potential of this novel interface has been tested by Vu et al. (2020b): they used EMG signals collected by intramuscular bipolar electrodes implanted into RNPIs obtained in amputated individuals, who could successfully perform real-time control of an artificial hand. Surprisingly, subjects were able to control the device with a high level of 49 50 493 50 493 51 494 52 495 accuracy even 300 days post-implantation, without recalibration of the control algorithm.

Another surgical technique, not directly related to EMG 5<u>3</u>496 signals but worth mentioning, is *cineplasty*, an old method 54497 revived in the last years with a new and more modern 55498 approach. This method was introduced for the first time by 56499 Vanghetti in 1899 and then replicated by Sauerbruch ten 57500 years later (Tropea et al., 2017). It consisted of the direct

mechanical linking of residual muscles and/or residual tendons of the affected limb to the prosthesis through external cables (i.e., Bowden cables). In 2001. 504 Heckathorne and Childress (2001) implemented an evolution of this surgical solution for the control of 1 DOF ULP by exploiting exteriorized tendons directly linked to a force sensor.

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#### 508 3.1.1.2. Other biosignals

The limitations imposed by the use of EMG (either invasive or non-invasive), have led researchers to study new approaches, aiming at increasing algorithms robustness and accuracy. Some may be soon used in commercial prosthetic systems, while others represent promising research scenarios, but still far from real-life applications. We here describe some of these peripheral signals, both non-invasive and invasive.

For example, forcemyography (FMG) has been widely investigated in the past 20 years (Xiao and Menon, 2019) (Table I). This approach is based on force sensors able to record muscle stiffness around the forearm during different movements. The muscle deformation of the stump can be measured with various types of sensors, such as: force sensing resistors (Prakash et al., 2020), optical fiber transducers (Fujiwara et al., 2018), capacitance-based deformation sensors (Truong et al., 2018), Hall-effect based deformation sensors (Kenney et al., 1999), barometric sensors (Shull et al., 2019), thin arrays of adhesive stretchable deformation sensors (Jiang et al., 2019), or high density myo-pneumatic sensors for topographic maps of pressures and residual kinetic images of the stump (Phillips and Craelius, 2005, Radmand et al., 2016). The accuracy of the sensors may limit the robustness of FMG-based control. Therefore, FMG is often fused with other input sources, such as IMU (Ferigo et al., 2017) or EMG (Nowak et al., 2020). FMG is indeed complementary to EMG due to its capability to get information about extrinsic hand muscles placed in several layers underneath the skin, and therefore difficult to be detected with the EMG sensors. Moreover, with respect to EMG-based control strategies, FMG is not influenced by electrode shifting.

Another technique is mechanomyography (MMG), which measures the lateral oscillations, detected as lowfrequency vibrations (in the range of 1-100 Hz), generated by deformation in muscle fibers actively involved in the contraction (Table I). This approach can be considered as the mechanical counterpart of EMG and it is also known as acousticmyography, phonomyography or vibromyography, depending on the type of sensor used. It can actually be based on different types of sensors, such as: low mass accelerometers (Farina et al., 2008, Youn and Kim, 2010), microphones (Meagher et al., 2020, Castillo et al., 2020), piezoelectric contact (Orizio et al., 2008, Tanaka

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3 554 et al., 2011), force sensing resistors (Esposito et al., 2018), 4 555 and laser distance sensors (Scalise et al., 2013). With 556 respect to EMG, this technique shows some advantages: it 557 is low cost, it does not require pre-amplification or precise 558 positioning, and signals are not influenced by skin 8 559 impedance or sweat. However, it is very susceptible to <sup>9</sup> 560 environmental noise and motion. Artifact removal can be <sup>10</sup>561 implemented with the integration of an IMU, as proposed by (Wilson and Vaidyanathan, 2017) and (Woodward et al., 2017). MMG has also been used in combination with EMG signals (Guo et al., 2017a), achieving better control performance and robustness.

11562 12563 13564 14565 15566 16567 17567 18568 19569 20570 21571 22572 23573 24574 619 The sonomyography (SMG) measures muscle volume changes and thickness using reflected ultrasound waves 620 (Table I). Wave amplitude depends on the acoustic 621 622 impedance of the tissue, and it can be detected using 623 ultrasound transducers. Currently, no portable prosthetic systems based on SMG have been developed, but the 624 results obtained using this technique are very promising. 625 626 For example, Dhawan et al. (2019) were able to detect 627 eleven different movements in real-time placing the sensor 25575 on the stump of a trans-radial amputee, obtaining better 628 26576 629 results than using EMG signals alone. This non-invasive 27577 630 approach allows a faster user training and the detection of 28578 631 both superficial and deep muscles, but even a small shift of 29579 the sensor can change the cross-section view and bring to 632 30580 the failure of the control algorithm. SMG signals have been 633 634 31581 used in combination with EMG signals, leading, to 32582 635 improved performances with respect to EMG alone (Xia et 33583 636 al., 2019, Engdahl et al., 2020a).

34584 Near-Infrared Spectroscopy (NIRS) is a non-invasive 637 35585 638 technique measuring the level of oxygenation of active 36586 muscles under contraction (Table I). The detection unit 639 37587 640 consists of a near-infrared led emitter and a photodetector, <sup>38</sup>588 641 placed on the skin surface. The emitted IR light is partly 39589 40590 41591 42592 43593 44594 45595 46595 46595 46597 48597 48597 49598 absorbed by the tissue, mostly by hemoglobin, and partly 642 643 scattered back to the skin surface and detected by the photodetector. NIRS thus detects changes in the amount of 644 645 IR light scattered back due to muscle contraction 646 (Schneider et al., 2003). This technique has a high spatial resolution and is immune to electronic interference. 647 648 However, tissue heating may take place after prolonged use. Recently, Paleari et al. (2017) developed a wireless 649 NIRS unit for hand gesture recognition, indicating the 650 potentiality of this technique for ULP control. NIRS has 651 <sup>49</sup>50599 51600 indeed been used in this context in conjunction with EMG 652 (Guo et al., 2017b) and IMU (Zhao et al., 2019). 653 654

52<sup>601</sup> The electrical impedance tomography (EIT) measures 53602 the internal electrical impedance of the tissues in the cross-54603 section plane covered by specific surface electrodes (Table 55604 I), which may range from 8 to 64 (Padilha Leitzke and 56605 Zangl, 2020). The measurement is executed by exciting a 57606 sine wave of electrical current (amplitudes ranging from 10 µA to 10 mA and frequencies from 10 kHz to 1 MHz (Grushko et al., 2020)) and by recording the voltages collected by surface electrodes. The detected changes in phase and amplitude represent the distribution changes of internal conductivity within the affected area, identifying patterns of movement. Wearable systems for ULP control have been developed, such as the ones proposed by Zhang et al. (2016) capable to recognize hand gestures, and by Wu et al. (2018), who also tested an EIT-based hand prosthesis control system on healthy people, achieving an accuracy of 98.5% with a grouping of three gestures and an accuracy of 94.4% with two sets of five gestures. This non-invasive method does not require a precise positioning of the electrodes, it only needs changes in impedance to be large enough. On the other hand, the current available systems have slow measurement and long processing time, leading to a high-power consumption. Moreover, the technique is affected by surface electrodes issues, namely skin contact conditions, electromagnetic interference, etc.

Capacitance sensing measures capacitance variations between two or more conductors (Table I). A capacitance exists when the two conductors are separated by a given distance d. In ULP context, electrodes may be placed on the prosthetic fingers, which work as capacitor plates. When a user performs a gesture, the skin deformation will cause a change in distance (d) between the conductors. This technique was used for hand gesture prediction in (Cheng et al., 2013) and in (Truong et al., 2018), using wearable systems. This technique is low cost, non-invasive, and it is capable to detect deep and complex signals, but it owns the standard disadvantages affecting surface electrodes, and it is susceptible to ambient temperature changes.

Magnetomyography is a promising approach aimed at measuring the magnetic fields produced by electrical currents propagating through muscles during contraction (Table I). This technique foresees the placement of magnetometers on the muscle, either non-invasively or beneath the skin, following a surgical procedure. The magnetometers convert the magnetic fields into measurable quantities, such as currents or voltages that can be used for the control of the prosthesis. Small implantable magnetometers have been proposed in Zuo et al. (2020), but they still need to be clinically tested. This technique is less sensitive to sensors' shift or sweat but may be strongly influenced by the environmental magnetic noise and the magnetic field of the Earth.

Peripheral neural interfaces (PNIs) measure the electrical activity of the motor peripheral with an invasive approach (Table I). There are three types of electrodes: extraneural, like CUFF or FINE, which embrace the nerve; intraneural, which run longitudinally (LIFE) or transversally (TIME or USEA) through the nerve; and regenerative, such as SIEVE or Microchannel, attached

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#### <sup>11</sup>667 3.1.1.3. Brain signals

12668 13669 14670 15671 16671 17672 18673 19674 722 The first neuroprosthetic application on humans was reported by the group of Donoghue, who demonstrated that 723 tetraplegic individuals implanted with arrays of 724 725 microelectrodes over the motor cortex were able to 726 remotely control the movement of a cursor on a screen (Hochberg et al., 2006). This clinical trial was soon 727 728 followed by another from the same group reporting the 20<sup>675</sup> control of reaching and grasping actions of a robotic arm 729 21676 (Hochberg et al., 2012). The group of Schwartz also 730 22677 showed similar results of an individual with tetraplegia 731 23678 successfully controlling a 7 DoF robotic arm (Collinger et 732 24679 733 al.. 2013). In all these examples, intracortical brain 25680 signals were used, i.e., action potentials of individual 734 26681 neurons were detected with an array of electrodes inserted 735 27682 into the brain, usually in the motor cortex (Table I).

28683 736 Less invasive measurements of cortical currents using 29684 electrocorticography (ECoG) have been widely used for 738 30685 neuroprosthetic control in the lab. ECoG detects the 739 31686 electrical activity of the brain with strips of electrodes laid 32687 on the brain's surface, usually in the motor cortex area. 33688 741 ECoG signals have been used for hand gesture recognition 34689 (Bleichner et al., 2016), for the control of a virtual 35690 prosthesis (Wang et al., 2013) and of a robotic limb (Fifer 36691 et al., 2013), and also with a detached prosthesis with active 37692 745 digits (Hotson et al., 2016). 746

<sup>38</sup>693 ECoG provides an ideal trade-off between the <sup>39</sup>694 invasiveness of intracortical recordings and the poor spatial <sup>40</sup>695 resolution of electroencephalography (EEG) (Thakor et <sup>41</sup>696 al., 2014). However, whether non-invasively collected <sup>42</sup>697 signals convey enough motor information to control a neuroprosthetic hand is still debated (Fukuma et al., 2016).

43699 44699 45700 46701 47702 48702 49703 50704 51705 52706 53707 54708 EEG measures the electrical activity of the brain with an 752 753 external helmet made of electrodes (Table I). In a ULP application, a motor imagery task is typically used, and the 754 subject only needs to think about the movement. EEG 755 756 signals corresponding to the intention of the movement are therefore used to drive the end-effector. Recently, 757 McDermott and coworkers were able to extract from EEG 758 759 recordings relevant brain states in real-time and indicated 760 such states as prospective therapeutic targets for motor neurorehabilitation (McDermott et al.). Similarly, the 761 55709 group of Wolpaw showed that paralyzed patients could use 762 56710 763 EEG signals to control a cursor in 3-dimensional space 57711 (McFarland et al., 2010), suggesting that noninvasive 764 58712 EEG-based BCIs can be exploited for control of robotic 765 59

devices or neuroprostheses. EEG-based neuroimaging is indeed emerging as a useful tool for robotic device control, as demonstrated by Edelman et al. (2019).

Another promising technique is the functional Near-Infrared Spectroscopy (fNIRS), which detects activityrelated brain oxygenation. The instrumentation is the same used for NIRS, i.e., a near-infrared led, and a photodetector are used to measure the amount of scattered back light and, therefore, the amount of IR light absorbed by the hemoglobin in the brain, which increases during brain activity. In 2020, Syed et al. (2020) used these hemodynamic brain responses to control a ULP for transhumeral amputees with 3 DOFs, gaining eight out of ten classified movements in real-time.

These examples demonstrate that groundwork for brain control of motor prosthetics has been laid. However, it has been limited to the lab and mostly addresses paralyzed patients. Nevertheless, there is a growing interest in brainderived measures for prosthetic applications and different recording techniques have been investigated for ULP control.

## 3.1.2. Other techniques under investigation

Besides the detection of physiological changes in residual muscles of the stump or in the brain during movements, described above, there are many other input sources and techniques capable or with the potentiality to control an upper limb prosthesis. Some of these are mainly used in the research field and since they lack usability, they do not find a real application in everyday life of amputees, or they are conceived for patients without the possibility to exploit other more convenient and intuitive sources (i.e., tetraplegic people). Some of them, instead, have been still only proposed as proof-of-concept.

The most studied approach is based on the use of inertial measurement units (IMUs). IMU sensors are cheap, small and can therefore by easily embedded in the prosthesis. They can increase the amount of data useful to successfully discriminate between different gestures of ULP during distinct phases of the reaching movement. These devices exploit accelerometers, gyroscopes and magnetometers to understand which is the actual altitude, position and orientation of the prosthesis. These sensors deliver information through quaternions and they are often used together with EMG to improve the classifier robustness (Georgi et al., 2015). Zhang et al. (2011) depicted the possibility to manipulate objects and perform complex tasks using both inertial measurement unit (IMU) and EMG sensors. As a matter of fact, the accelerometers can capture information that sEMG sensors cannot easily detect, such as hand withdrawal or rotation (Chen et al., 2007). It has been shown that the use of IMU sensor coupled to EMG is more advantageous than increasing the number of EMG sensors (Fougner et al., 2011). Similar

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3 766 results have been achieved by Krasoulis et al. (2017), who 4 767 have combined EMG and IMU to feed pattern recognition systems (see section 4.3.1). They demonstrated that this combination could significantly improve the real-time 7 770 completion rates compared to the traditional methods, 8 771 exclusively based on sEMG signals. Moreover, the data coming from IMU can be used alone to control a single <sup>10</sup>773 module, usually the wrist or the elbow (Merad et al., 2018) <sup>11</sup>774 or to realize other types of control for rehabilitation purposes, such as shadow control, in which the control <sup>13</sup>776 policy consists in replicating the movement captured by the 15<sup>1</sup>777 IMU sensors (Rapetti et al., 2020). These devices were also

placed on feet to directly control an ULP by implementing precise foot movements (Resnik et al., 2014). The adoption of IMU sensors is specifically promising in sensor fusion approaches, as discussed in section 3.1.3. Besides EMG signals, IMU data have been also combined with NIRS (Zhao et al., 2019) and MMG (Wilson and Vaidyanathan, 2017, Woodward et al., 2017).

Table II summarizes the use of IMU and other input sources investigated for the control of ULP, many of which are described in (Grushko et al., 2020).

Input source	Measured property	Sensors' placement	PROs	CONs	Sensor Fusion	Examples	
IMU	Specific force, angular rate, orientation of the body	Up to 8 IMU sensors located on feet	Non-invasive, simple, low cost,	Problems during walking, not intuitive, unnatural	EMG, NIRS, MMG	(Resnik et al., 2014) DEKA Arm control	
Myokinetic control	Change of muscle morphology trough magnetic fields	Permanent magnet markers implanted over targeted muscles and external three-axis magnetic field sensors placed in the socket	Intuitive control, force and position feedback	Magnetic interferences, misalignments between socket and initial position, invasive	-	(Tarantino et al., 2017, Clemente et al., 2019)	
ice	Throat vibration	Piezoelectric sensor on the throat	Ease of use sequence of movements	Ease of use	use External noise,	EMG	(Mainardi and Davalli, 2007)
Vo	Voice commands	Microphone near mouth		unintuitive control	IMU	(Alkhafaf et al., 2020)	
Tongue	Pressures made by the tongue	Board of coils on the palate and activation unit on the tip of the tongue	Mobile, wireless, invisible	Unintuitive control, uncomfortable	EMG	(Johansen et al., 2016, Johansen et al., 2021)	
Feet	Pressures made by the feet	Insole made of force sensing resistors	Simple Low cost	Unintuitive control, problem during walking, need of accurate calibration	IMU EMG	(Carrozza et al., 2007)	
Optical myography (OMG)	Skin surface deformations caused by underlying muscle contraction	Single low-resolution camera and marker- based tracking methods	Simple Low cost	No space for camera in the socket, low robustness	-	(Nissler et al., 2016, Wu et al., 2019)	

Table II: Alternative input sources investigated for the control multi-DoF prosthesis devices

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Table III: integrative sources of information used to improve prosthesis control.

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## 3.1.3. Integrative sources

An integrative input source is not used as the main 6 794 responsible for the actual command of the prosthesis, but it 7 795 is used to help and to facilitate its control, which usually 8 796 depends on EMG signals. The integrative input sources

797 work in parallel and together with the main ones, 798 integrating their information and implementing the so-799 called data-fusion or sensor-fusion methods, see also 800 section 4.3.3. Table III summarizes integrative sources 801 found in the literature that have been used for ULP control. 802

11 12 13 14 15 16	Integrative input source	Instruments and measured information	Application	PROs	CONs	Fusion	Examples
17 18 19 20 21	ter vision	Two cameras used to collect images and estimate depth	Estimation of size, distance and grasp type for a semi-	Ease of use fixing of errors without looking at the prosthesis	Expensive, cumbersome and	EMG	(Markovic et al., 2014) Stereovision (depth?)
22 23 24 25 26	Compu	Depth estimated by the colour intensity of the pixel collected by the camera	autonomous control of the prosthesis	automatic help in controlling the prosthesis	uncomfortable	IMU	(Mouchoux et al., 2021) Depth and colour camera RGB
27 28 29 30 31 32 33	novements	4 Superficial electrodes for the measuring of the corneo-retinal standing potentials between the front and the back of the human eye	Estimation of the position/length/ width/orientatio n of a final target and	Ease of use automatic help in controlling the	Distinction with random eye movements,	EMG	(Hao et al., 2013) Electro-oculography
34 35 36 37 38 39	Eyen	Camera mounted on a pair of glasses measuring the reflection of infra- red (IR) light from the eyeball	preparation of the preshape and direction of the hand	prosthesis	cumbersome and uncomfortable		(Krausz et al., 2020) Eye tracking glasses
40 41 42	ų	Led-based optical sensor mounted on fingertips		3			(Sani and Meek, 2011) LED motion detection sensor
43 44 45 46 47 48 40	Optical senso	miniature reflective optic sensor that combines an Infrared LED and a phototransistor in the same package.	Slip detection and eventual automatic suppression	Accurate, robust simple, low cost and power consumption	Poor detection with transparent EM surfaces	EMG	(Nakagawa-Silva et al., 2018) Reflective optic sensor
50 51 52 53 54	IMU	Accelerometers, Gyroscopes, Magnetometers	Decreased #sensors, better controllability, artifact detection	Non-invasive, simple, low cost, motion artifact deletion	Prone to error cumulate over time	EMG, NIRS, MMG	(Krasoulis et al., 2017, Krasoulis et al., 2019b) up to 6 gestures
\$04 56 57 <sup>805</sup>	3.2. Prosthet	ic Sensing		806 807 r	Natural moveme neural information,	nts occur w i.e., motor o	with a bidirectional flow of commands on one direction

Natural movements occur with a bidirectional flow of 806 807 neural information, i.e., motor commands on one direction 808 and sensory feedback on the other. In prosthetic

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3 809 applications, while many efforts have been spent to provide 4 810 signals carrying motor intentions, a less explored path is 859 811 the integration of sense of touch into the prosthesis 812 (Clemente et al., 2015). This lack is highly responsible for 7 813 the missing perception of the prosthesis as part of one's 861 8 814 own body and is also precluding a closed-loop control of 862 <sup>9</sup> 815 the prosthesis.

863 10816 11817 12818 13819 14820 15821 16822 17823 18823 19824 More recently, the scientific community has started exploring different methods to equip prosthetic devices 865 with perception of tactile and pressure information 866 (Schmitz et al., 2008, Tee et al., 2012, Lucarotti et al., 2013, 867 Hammock et al., 2013, Taunyazov et al., 2021), although 868 often resulting in very complex, unreliable, or unpractically 869 cumbersome solutions. The few solutions tested on real 870 prosthetic setups impacted on their anthropomorphism and 871 dexterity. 872

20825 To integrate touch sensors into robotic and prosthetic 873 21826 devices (Figure 2, end-effector feedback) (Lucarotti et al., 874 22827 2013, Iskarous and Thakor, 2019, Dimante et al., 2020), 875 23828 different technologies have been investigated and 876 24829 employed (Ciancio et al., 2016), namely capacitive 877 25830 (Maiolino et al., 2013, Jamali et al., 2015), resistive 878 26831 (Beccai et al., 2005, Tee et al., 2012, Zainuddin et al., 879 27832 2015), piezoelectric (screen printed piezoelectric polymer, 880 28833 PVDF) (Alameh et al., 2018), and magnetic sensors 881 29834 (Ahmadi et al., 2011). Other examples include 882 30835 technologies based on electrical impedance (Zainuddin et 883 31836 al., 2015, Wu et al., 2018), pressure and electrical 32837 impedance (Lin et al., 2009), optical fibers (Bragg fiber 885 33838 (Massari et al., 2019)), Micro-electro-mechanical 34839 Systems (MEMS, texture sensing (Mazzoni et al., 2020)) 887 35840 combined with Spiking based on Izhikevich neuron model 888 36841 (Gunasekaran et al., 2019)) and Optoelectronic (Alfadhel 889 37842 and Kosel, 2015). 890

<sup>38</sup>843 Examples of the application of these sensors into <sup>39</sup>844 prosthetic devices include the E-dermis (piezoelectric 40845 41846 42847 43848 44849 45850 46851 47852 48852 sensors integrated on the Bebionic's fingertips) (Osborn et al., 2018), E-skin (integrating different types of sensors) (Iskarous and Thakor, 2019), and BioTac (impedance sensor integrated on the Shadow Hand (Robot, 2022)) (Fishel and Loeb, 2012).

Among commercial devices, the SensorHand Speed (Ottobock, 2021) made by Ottobock is the only one including tactile sensors based on resistive technology 49<sup>853</sup> (Ottobock, 2021).

50<sup>854</sup> Therefore, tactile sensation is the first step towards 51855 novel and more efficient control strategies that do make use 52<sup>856</sup> of feedback information (Raspopovic et al., 2014). To this <sub>53</sub>857 end, artificial intelligence can be exploited to detect the

858 grasp of different objects from sensor data (Alameh et al., 2020).

#### 860 3.3. Sensory Feedback

Sensory feedback patterns are designed to enrich the perceived responsiveness of the device and the subjective experience of its use as a limb (Antfolk et al., 2013b, 864 Svensson et al., 2017, Raspopovic et al., 2021a). Such a result derives from the elicitation of physiological and psychological reactions that promote embodiment processes (described in paragraph 5.1). Furthermore, such stimulations (haptic feedback in many cutting-edge devices) are designed as a fundamental component of bidirectional human-machine interfaces empowering prosthetic control (Navaraj et al., 2019). Establishing such a closed-loop can trigger learning processes even for artificial sensations (Cuberovic et al., 2019), pointing at somatosensory plasticity processes. These phenomena provide the user with an engaging guidance within a natural interaction, facilitating the execution of prosthetic maneuvers during calibration, training, and daily use. Importantly, such an enhanced practice will ease the production of consistent biosignals that will progressively become easier to interpret as user commands.

However, current commercial prostheses generally do not incorporate an explicit haptic feedback but the incidental feedback, like visual and the sound cues, could be exploited by the user to estimate the prosthesis state (Wilke et al., 2019). For example, the acoustic feedback provides a guidance on how to reach target during the rehabilitation session, in this way the rehabilitation step can be more interactive and engaging if appropriately designed (never obnoxious, possibly plausible). Overall, the next sub-sections will discuss the design of sensory feedback in prosthetics, distinguishing invasive and non-invasive stimulation modalities.

#### 893 3.3.1. Non-invasive methods

Non-invasive feedback restoration for upper limb amputees is a hot topic in the research community, and yet it has not achieved broad clinical application (Sensinger and Dosen, 2020). Many solutions have been proposed, but the main problem lays in their poor robustness. (Ribeiro et al., 2019) highlighted the most widespread types of noninvasive feedback, described in Table IV.

Table IV Non-invasive methods for sensory feedback in ULP.

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Fee	Feedback sense		Instruments and feedback information	Application	PROs	CONs	Examples
		Vibrational	Eccentric rotating motors, proprioception, force	Array over the forearm or over the arm	Non-invasive, robustness control, brief training period, intuitive, cheap, small	(Bark et al., 2014, Markovic et al., 2019) up to 3 DoFs or different force levels	Non-physiological, need calibration, coupled intensity and rotation frequency, position displacement
Touch		Mechanotactile	Linear actuator, pressure sensation, spatial touch sensation	Detected areas to reproduce real touch sensation, array over the arm	Non-invasive, intuitive, brief training period, decoupled intensity and frequency	(Antfolk et al., 2013a, Svensson et al., 2017, Tchimino et al., 2021) different pression level, touch sensation	Need spatial and intensity calibration, bulky, position displacement
(wite		Electrical	Transcutaneous stimulation using bipolar electrodes, pressure, slip, proprioception	Array over the forearm or arm	No electrode displacement, low power consuming, high sensor skin contact, intensity or frequency modulation	(Jorgovanovic et al., 2014, Xu et al., 2015, Garenfeld et al., 2020) touch location, pression, proprioception	Noise during acquisition, long calibration, not localized sensation
-	Vision Sound (Visual) (Acoustic)		Acoustic speaker, proprioceptive movements	Laptop speaker to guide the training acquisition and improve the pattern recognition strategy	Low cost, no calibration, intuitive	-	(Gigli et al., 2020) multiple arm positions
• • • • • •			Camera on board, external camera	head-mounted displays, laptop displays, virtual reality, augmented reality	Increase perceptual experience, engagement, intuitive, promote training	Bulky, not portable, uncomfortable	(Clemente et al., 2016, Markovic et al., 2017, Sharma et al., 2018, Hazubski et al., 2020, Sun et al., 2021b) trajectory, force

The most investigated feedback relies on the sense of touch and therefore consists of cutaneous stimulation. This can be performed with different modalities namely, vibrational, mechanotactile or electrical stimulation. 48<sup>909</sup> The vibrational feedback is generally implemented with 923

the addition of eccentric rotating motors placed in contact with the skin surface of the stump (Ribeiro et al., 2019). This method is generally employed to augment the robustness of the control system by providing the user with additional information regarding the position of the prosthetic device but it lacks intuitiveness, as the association between perceived sensation and the corresponding information has to be learned by the user. For example, in Bark et al. (2014), the motors were placed 

in 4 distinct areas of the stump to guide the user through the desired trajectory while grasping object and the results showed a significant decrease in the root mean square angle error of their limb during the learning process. More recently, Markovic et al. (2019) proposed a joint-oriented feedback criterion consisting of three vibromotors placed on the arm to provide the information on which joint is currently activated by the user, thus restoring proprioceptive sensation. The experiment was performed by 12 able-body subjects and 2 amputees controlling 3 DoF prosthesis, and it was found that the myoelectric multiamplitude control outperformed the pattern recognition method when the feedback was applied.

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3 932 985 Differently from the vibrational, the mechanotactile 4 933 986 feedback is based on the application of linear actuators on 5 934 987 the skin and provides pressure sensation. Antfolk et al. 6 935 988 (2013a) exploited this technique and proposed a multisite 7 936 mechanotactile system to investigate the localization and 989 8 937 990 discrimination threshold of pressure stimuli on the residual <sup>9</sup> 938 991 limbs of trans-radial amputees. They demonstrated that 10939 992 subjects were able to discriminate between different <sup>11</sup>940 993 location of sensation and to differentiate between three <sup>12</sup>941 994 different levels of pressure. This study demonstrated that it 13941 14942 15944 15944 16945 17946 19947 20948 21949 22950 23951 24952 is possible to transfer tactile input from an artificial hand to 995 996 the forearm skin after a brief training period. Recently, 997 Svensson et al. (2017) used it to translate the interaction 998 between a virtual reality environment and a virtual hand 999 into user sensation. The authors showed that by placing the tactile actuators in correspondence with the areas of the 1000 skin involved in object manipulation, subjects were able to 1001 feel a real touch sensation that increased their sense of body 1002 ownership. For example, pressure applied to the prosthetic 1003 fingers was perceived as a tactile sensation on the skin 1004 (Svensson et al., 2017). 1005 25953 The electrical feedback is based on transcutaneous 1006

stimulation. The elicited sensations range from perception 1007 of pressure (Jorgovanovic et al., 2014) to slip sensations 1008 (Xu et al., 2015), depending on the electrical parameters 1009 (i.e., current amplitude, pulse frequency, pulse width). One 1010 advantage of this approach with respect to the vibrotactile 1011 and mechanotactile ones is the lack of moving components 1012 avoiding problems of electrode displacement and, thus,

33961 improving the sensors-skin contact. Nevertheless, it is 1013 34962 important to take into account that the noise introduced by 1014 35963 the electric stimulation can corrupt the acquisition of 1015 36964 muscular activity, causing errors if the ULP is 1016 37965 myoelectrically controlled. Moreover, the perceptions are 1017 <sup>38</sup>966 not strictly confined to the zone under the stimulating 1018 <sup>39</sup>967 device but they can spread in a wider region if the area 1019 40968 1020 above a nerve is considered.

<sup>41</sup>969 Another sensory modality exploited for feedback 1021 <sup>42</sup>970 delivery is the acoustic one. Gigli et al. (2020) recently 1022 43971 44972 45973 46974 47974 48975 49976 49976 50977 51978 52979 53980 tested a novel acquisition protocol with additional acoustic 1023 feedback in 18 able-body participants to improve 1024 myoelectric control. The protocol consisted in dynamically 1025 acquiring EMG data in multiple arm positions while 1026 returning an acoustic signal to urge the participants to 1027 hover with the arm in specific regions of their peri-personal 1028 space. The results showed that the interaction between user 1029and prosthesis during the data acquisition step was able to 1030significantly improve myoelectric control. Auditory 1031 feedback has also been employed to convey artificial 1032 54981 proprioceptive and exteroceptive information. Lundborg et 1033 55982 al. (1999) and Gonzalez et al. (2012) employed auditory 1034 56983 feedback by encoding the movement of different fingers 1035 57984 into different sounds. The method demonstrated that the 1036 1037 58

inclusion of auditory feedback reduces the mental effort and increase the human-machine interaction; furthermore, better temporal performance and better grasping performance were obtained.

In the last years, there have been some examples exploiting vision to deliver sensory feedback. Indeed, visual stimulation can be provided as explicit feedback through screens during game-like exercises, helping the prosthetic user to learn how to control the device (e.g., adjusting trajectory or grasping force) (Markovic et al., 2018). However, adding sensory information to the prosthetic user's perceptual experience in real contexts requires solutions like Augmented Reality (AR, occurring when computer-generated items overlay a real setting) or Mixed Reality (MR, a term that represented different combinations of real and virtual items) (Milgram and Kishino, 1994, Speicher et al., 2019). AR and MR environments, implemented through wearable solutions like head-mounted displays, can support the actual control of a prosthetic device through visual feedback that does not occlude the real context (Clemente et al., 2016, Markovic et al., 2017, Hazubski et al., 2020). However, they can also be used for prosthetic use training (Anderson and Bischof, 2014, Sharma et al., 2018) - in such a case, Virtual Reality (VR, a fully computer-generated setting) can offer visual feedback too (Lamounier et al., 2010, Sun et al., 2021b), especially within game-based frameworks (Nissler et al., 2019) for engaging the users and motivating their activity.

#### 3.3.2. Invasive methods

There are different technologies that can be employed to provide a sensation directly to the nerve (Cutrone and Micera, 2019, Raspopovic et al., 2021a). The most used employ **intrafascicular electrodes**, such as **transverse intrafascicular multichannel electrodes** (TIME) and **wire** and **thin-film longitudinal intrafascicular electrodes** (LIFE), which can both record muscle activity (e.g., iEMG) and stimulate nerves. Other solutions are characterized by the fact that the electrodes are placed around the nerves, such as **cuff electrodes** and **flat interface nerve electrodes** (FINE).

The first example of ULP with sensory stimulation dates back to 1979 and it was based on the remapping between pressure signals acquired by prosthesis sensors to an amplitude-frequency modulation. This consisted of a series of pulses delivered with a pulse rate proportional to the increment of the pinch force and provided through dry electrodes placed over the skin in correspondence of the median nerve, as described in Shannon (1979). Later, the group of Micera employed thin-film intrafascicular electrodes longitudinally implanted in peripheral nerves (tf-LIFE4) to deliver electrical stimulation. With this method, they were able to elicit sensation of missing hand in the fascicular projection territories of the corresponding

31038 nerves and to modulate the sensation by varying the pulse 1090 41039 width and pulse frequency (Benvenuto et al., 2010). 1091 51040 Importantly, this method avoids muscle crosstalk, 1092 61041 fundamental for guaranteeing myoelectric control. More 1093 71042 recently, new bioinspired paradigms have been suggested 1094 <sup>8</sup>1043 to better induce natural sensations (Raspopovic et al., 1095 <sup>9</sup>1044 2021a). In particular, the study of Oddo et al. (2016) 1096 <sup>1</sup>045 showed that it is possible to restore textural features 1097 11046 recorded by an artificial fingertip. This device embedded a 1098 **f**047 neuromorphic real-time mechano-neuro-transductor, 1099 **≹**048 which emulated the firing dynamics of SA1 cutaneous 1100 **1**049 afferents. The emulated firing rate was converted into 1101 2050 temporal pattern of electrical spikes that were delivered to 1102 **1**051 the human median nerve via percutaneous 1103 **1**052 microstimulation in one trans-radial amputee. 1104

**L**053 Valle et al. (2018) suggested a 'hybrid'' encoding 1105 26054 strategy based on simultaneous biomimetic frequency and 1106 2<sup>1</sup>055 amplitude modulation. This kind of stimulation was 1107 2,056 perceived more natural with respect to classical stimulation 1108 21057 protocol, enabling better performance in tasks requiring 1109 21058 fine identification of the applied force. This paradigm was 1110 2**1**059 tested and validated during a virtual egg test (Valle et al., 1111 26060 2018), where the subject needed to modulate the force 111227061 applied to move sensorized blocks. This encoding strategy 1113 2**8**062 not only improves gross manual dexterity in functional task 1114 29063 but also improved the prosthesis embodiment, reducing 1115 30064 1116 abnormal phantom limb perceptions.

31065 Similarly, Osborn et al. (2018) implemented a 1117 32066 neuromorphic feedback paradigm based on Izikevich 1118 33067 neuron model to generate the current spike train to inject 1119 34068 directly in the median and ulnar nerves, using beryllium 1120 3\$069 copper (BeCu) probes. Their prosthesis proposes a 1121 36070 neuromorphic multilayered artificial skin to perceive touch 1122 37071 and pain. Their transcutaneous electrical nerve stimulation 1123 <sup>38</sup>072 (TENS) allows to elicit innocuous and noxious tactile 1124 <sup>3</sup>9073 perceptions in the phantom hand. The multilayered 1125 49074 electronic dermis (e-dermis) produces receptor-like spiking 1126 <sup>4</sup>1075 neural activity that allows to discriminate object curvature, 1127 <sup>4</sup>1076 including sharpness in a more natural sensation spanning a 1128 <sup>43</sup>1077 range of tactile stimuli for prosthetic hands. The authors 1129 4**1**078 were able not only to restore finger touch discrimination 1130 2079 and objects recognition, but also to provide a pain sensation 1131 46 1080 when the prosthesis touched sharp objects. In particular, 1132 47 48 48 082 they found that pain sensation is generated by a stimulation 1133 49082 1134 of 15-20Hz.

Tan et al. (2014) suggested that simple electronic cuff 1135 placed around nerves in the upper arm can directly activate 1136 placed around nerves in the upper arm can directly activate 1136 the neural pathways responsible for hand sensations. This 1137 neural interface enabled the restoration of different 1138 sensations at many locations on the neuroprosthetic hand. 1139 Different stimulation patterns could transform the typical 1140 tingling sensation" of electrical stimulation into multiple 1141

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59 60 different natural sensations, enabling the amputees to

perform fine motor tasks and improving the embodiment. In George et al. (2019a) a biomimetic method was described to restore both force and haptic sensation. The sensory feedback was implemented to restore the force sensation and promote objects recognition: Utah Slanted Electrode Array (USEA) electrodes were used to deliver stimulation proportional to the variation of contact force exchanged between the prosthesis and the object during manipulation. Instead, the haptic sensation was based on the distribution of stimulation delivered during contact with the object with a fixed frequency and amplitude. The characteristic of this encoding scheme is based on electrical biphasic, charge – balanced of 200- or 320-us phase durations. The biomimetic model describes the instantaneous firing rate of the afferent population using the contact stimulus position, velocity, and acceleration simulating all tactile fibers to any spatiotemporal deformation of the skin and hand. This strategy allows the amputee to augment the active exploration experience and to discriminate object size and stiffness.

Liu et al. (2021b) have shown that primary afferents encode different stimulus features in distinct yet overlapping ways: scanning speed and contact force are encoded primarily in firing rates, whereas texture is encoded in the spatial distribution of the activated fibers, and in precisely timed spiking sequences. When multiple aspects of tactile stimuli vary at the same time, these different neural codes allow for information to be multiplexed in the responses of single neuron and populations of neurons. Exploiting this sensory architecture with invasive methods may lead to the development of prosthetic devices able to truly evoke natural sensations.

Another promising approach is **targeted sensory reinnervation** (**TSR**), i.e. the sensory version of TMR, which consists in coupling a pressure sensor placed on the prosthetic device to surgically redirected cutaneous sensory nerves (Marasco et al., 2011). This technique strongly helps discrimination of objects size and stiffness during active exploration, especially if the tactile feedback is biomimetic (George et al., 2019b). Recently, Marasco et al. (2021) have developed a prosthetic system based on both targeted sensory and motor reinnervation. TSR was used to deliver both touch and kinesthetic feedback. The authors showed that the system was able to significantly improve device control and promote embodiment.

These results indicate that, in order to close the loop on user and provide useful sensation (regardless the specific feedback modality), an optimal feedback control policy is necessary (Sensinger and Dosen, 2020), as discussed in section 4.4.

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environment (E) are also processed in the embedded processing unit (C) to deliver sensory feedback (B). The embedded processing unit (C) can be set up 42 by different layers: layer 1 (intention detection, yellow panel) is the software turning the input signals (A) sampled by master board into detected movement 43 intentions, by means of specific control algorithms (e.g., machine learning or deep learning algorithms); layer 2 (human-robot interaction, green panel) is 44 the software responsible of processing prosthesis position (joint and cartesian space control) and external information (tactile identification, E); layer 3 (encoding haptic feedback, blue panel) is the software responsible for encoding the information processed in layer 2 into sensory feedback. The output 45 of the embedded processing unit are control commands (mediated by actuator drivers) both to move the device and to provide sensory feedback. This has 46 a direct impact on the user experience (F) in terms of learning how to use the device (training) and of user-prosthesis integration (embodiment).

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154 of input signal and the sensors density. 1173 <sub>5</sub>]155 In general, prosthetic control is performed at different 1174 <sub>5</sub>],156 levels. The low level refers to motor actuation (Figure 5 1175 5<u>3</u>157 D) and, more in general, to the control of the active degrees 1176 5**1**158 of freedom of the device; the medium level consists of the 1177 5**§**159 translation of movement intentions into joint references 1178 56160 and gestures (Figure 5 C); the high-level control translates 1179 57161 input signals collected from the user (Figure 5 A) into 1180

disparate solutions for ULP control depending on the type 1172

these control architectures. However, if the readers are curious, a more complete and detailed analysis of robot lower-level control is provided by the comprehensive work of Siciliano et al. (2010).

In brief, at the base of these controls, there is always an active and controllable actuator, that for upper limb prosthetic solutions coincides - most of the times - with an electrical motor (either brushed or brushless) often coupled to a dedicated transmission system (e.g., a planetary gear)

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31181to reach the desired torque-speed characteristic. It is 123241182possible to present the low-level control of upper limb 123351183prostheses as the combination of three possible nested 123461184controllers: the current, the speed and the position control 123571185loops (Figure 5 D).81186The current control loop takes care of reliably tracking 1237

The current control loop takes care of reliably tracking 1237 <sup>9</sup>1187 desired current trajectories. To be implemented, it requires 1238 10188 the presence of reliable and precise current measurement 1239 <sup>1</sup>1189 sensors. The current control also provides a relatively good 1240 **1**190 force/torque control of the system, being the current 1241 <sup>1</sup>,191 absorbed by the actuator directly proportional to the 1242 1191 14192 15193 16193 16194 1194 generated output torque. On top of the current controller, it 1243 is usually found a speed control loop to regulate the 1244 rotational speed of the motor and, thus, the speed of the 1245 18195 actuated system. The combination of an external speed 1246 ¦19196 controller with an internal current control guarantees the 1247 20197 possibility of safely operate the actuating unit in terms of 1248 21198 desired speeds and torques. Sometimes, on top or in 1249 -2 199 substitution to the speed controller, systems also 1250 21200 implement a *position control loop*. The position controller 1251 24201 guarantees the tracking of desired angular trajectories. It is 1252 2\$202 therefore preferable to use the speed controller if the goal 1253 26203 is to precisely track given trajectories in specific time 1254 27204 intervals. The implementation and application of speed and 1255 28205 position controllers can be performed either before (fast 1256 29206 shaft) or after (slow shaft) of the transmission system. The 125730207 decision depends on the availability of sensing devices 1258 31208 (e.g., angular sensors such as encoders or resolvers) to 1259 32209 measure the required physical quantities. 1260

33210 All these controllers are implemented in a negative 1261 34211 feedback architecture and typically controlled by means of 1262 3≸212 **PID** controllers, whose proportional (P), integrative (I) 1263 **3∮**213 and *derivative* (D) parameters are tuned to reach the desired 1264 <sup>37</sup>214 <sup>38</sup>215 system response in terms of control reactivity (rise time and 1265 settling time), precision (steady-state error and overshoot) 1266 <sup>3</sup><sup>1</sup>216 <sup>4</sup><sup>1</sup>217 and stability. It is worth mentioning that a negative 1267 feedback architecture is typically only bounded to the low- 1268 <sup>41</sup>218 <sup>4</sup>219 <sup>43</sup>220 level control of the prosthesis, while higher level 1269 controllers and especially high-level control (see Section 1270 4.3) are often treated in an open-loop fashion, where the 1271 44221 45221 45222 user directly generates the reference control signal without 1272 any feedback verification. The generated reference 1273 45-1223 commands will then be directly sent to the low-level 1274 **†**{224 controller. 1275

## 1277 4.2. Mid-level control: from movement intention to 1277 51226 control commands 1278

The mid-level techniques (Figure 5 C, yellow panel – 1279 1280 1228 *layer 1*) aim to synthetize the **control commands** to 1281 1229 suitably activate the electric motors of the multiple DoFs 1282 1230 ULP (actuation drivers in Figure 5 C). These signals are the 1281 1282 input of the aforementioned low-level control.

A major classification of the mid-level control strategies for multi-DoFs robots divides them in two categories: joint-space and task-space (Cartesian) controllers (Siciliano et al., 2008, Corke and Khatib, 2011).

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**Joint-space control strategies** directly feed the commands to each of the actuated joints, namely DoFs, of the upper-limb robotic device. It is a direct approach that does not require any particular mathematical manipulation. In such a scenario, the mid-level control receives information from the high-level (see Section 4.3), then it assigns specific commands to each low-level controller (see Section 4.1). The logic used to assign the control commands is strongly based on the kind of information coming from the high-level side. Nonetheless, it will most likely reduce to a set of independent commands for each of the actuated joints.

On the other side of the spectrum, we have task-space based control strategies. In this case, the control commands for each of the joints are the results of a mathematical manipulation that involves the transformation from the *Cartesian space* to the *joint space*. If the aim is to regulate the Cartesian trajectory, the controller will need to translate the Cartesian trajectories into joint angles, by means of a process known as inverse kinematics. If instead the aim is to regulate the Cartesian force, the controller will transform the Cartesian forces into joint forces (or torques) utilizing the process of inverse dynamics.

Both these approaches are well known to robotic applications and will not be treated in detail in this review. Nonetheless, the authors suggest the comprehensive works of Corke and Khatib (2011) and Siciliano et al. (2008) to get the fundamentals of the aforementioned approaches.

In general, Cartesian based controls are more intuitive for the external user, namely any subject interacting with the robot as an external tool. In fact, the robot behavior can be more naturally interpreted being the forces or the trajectories referred to the three-dimensional space we are used to deal with. However, from a computational and complexity point of view, task-space controllers require a bigger effort and introduce limitations to their application, e.g., singularities, redundancies. On the other hand, joint space control behavior is less intuitive to predict but it is easier and less complex to implement.

Which approach is better for upper-limb prosthetic devices is still unclear. However, it is important to notice that, even if Cartesian controls are more intuitive from an external perspective, they might appear more complex from an internal perspective, such as the one of a prosthesis user, where the motion of the arm is more likely imagined in terms of joint motions and not Cartesian ones.

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# <sup>3</sup>1283 4.3. High-level control: from input signals to <sup>4</sup>1284 movement intentions

1321 61285 This section summarizes the most assessed techniques 1322 71286 for ULP control. Considering the prostheses available on 1323 81287 the market but also the research activities, the main input 1324 91288 source exploited to control such devices is the EMG. On 1325 10289 the basis of the EMG type multiple control strategies can 1326 11290 be employed, and the last decades of studies on active 1327 12291 prostheses mainly focused on the control strategy design 1328 13292 and development. 1329

1**†**293 The most common control strategy is based on dual site 1330 <sup>1</sup>₹294 control which consist in two electrodes placed in two 1331 <sup>1</sup>¶295 antagonist muscles (Scott and Parker, 1988). This solution 1332 17296 allows the control of the motor in two directions according 1333 **§**297 to the muscle amplitude of the selected electrodes. The 1334 1297 1298 20299 21299 21300 22201 synthetized reference usually is proportional to the 1335 amplitude of the muscle signal in term of speed or force. 1336 With the introduction of multiple DoFs, a co-contraction 1337 21301 strategy has been implemented to switch between 1338 -**1**302 controlled joints (Resnik et al., 2018). This allows the 2<u>1</u>303 control of a single DoF at a time using two electrodes as in 1339 2¢304 dual-site control. When both muscles are simultaneously 1340 2<sup>1</sup>/<sub>2</sub>305 contracted the control signal switches the joint to be 1341 21306 controlled. This is a simple solution yet unnatural and 1342 2**j**307 lacking intuitiveness. 1343

Another diffused strategy to control prosthesis with 1344 3**b**308 multiple active DoF is the finite state machine (FSM) 1345 31309 31310 (Moon et al., 2005). Commercially available ULPs 1346 31311 implement this strategy to switch the position of the thumb 1347 34312 to reproduce different types of grasp (Ottobock, 2020b, 1348 3**\$**313 Ottobock, 2020a, Ossur, 2020b). For example, the 1349 36314 Michelangelo hand allows to switch the thumb position 1350 37315 when a signal of opening is triggered with the hand in a 13513**\$**316 fully opened configuration (Ottobock, 2020b). 1352 39317

muscle synergies, feature extraction (FE), multiamplitude threshold control and machine learning methods. Muscle synergies capture muscle activation invariance during motor production and can be exploited as control variables for ULP, with aim of obtaining a biomimetic human-like behavior (d'Avella and Bizzi, 2005). The main idea is to extract motion primitives from muscle synergies and combine them to generate complex arm movements (Jiang et al., 2013, Liu et al., 2021a). Furui et al. (2019) propose a biomimetic control based on muscle synergies to extract motion primitives and combine them to generate complex movements. Feature extraction methods foresee the computation of some EMG-based metrics that reflect movement intentions (Guo et al., 2015). Multi-amplitude threshold methods work as dual-site control, but they associate different amplitudes of the input signal to different DoFs (Markovic et al., 2019). Although robust, these techniques are poorly used because they lack intuitiveness (Markovic et al., 2019). Machine learning methods will be described in the following paragraph.

#### 4.3.1. Machine Learning Algorithms

Figure 6 illustrates the main machine learning methods employed for ULP control These methods generally solve a pattern recognition problem in which, given the input signal, an output movement have to be identified.

The first PR-based control schemes arose around the second half of 1960s (Scheme and Englehart, 2011). In this configuration, the acquired EMG signals are elaborated by the controller to determine the action to be performed by the prosthesis. The five pillars of this computation process are: *pre-processing, data segmentation, feature extraction, classification,* and *post-processing.* Each step is briefly described in Table V.

**39317** With the aim of increasing the number of controlled 1353 **40318** DoFs, many different methods were proposed, such as

Pre-processing	During this phase, the incoming signals are firstly filtered to delete the interferences, such as acquisition noise and artifacts.
Data segmentation	This process divides the signals into time-windows, overlapping or adjacent (Parajuli et al., 2019).
Features extraction	It reduces the signal information into a set of representative features in time domain (e.g., variance, zero crossing, etc.), frequency domain (e.g., mean frequency, spectral properties, etc.) or time-frequency domain (e.g., the wavelength transform, an alternative to the traditional Fourier Transform useful for noise-removal and data compression (Hartwell et al., 2018)), as described in Boostani and Moradi (2003). Importantly, this part can greatly affect the computational costs.

Table V: Pattern recognition steps.

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3 4 5 6	Classification	This is the crucial step for the classifier, where the controllers recognize and classify the signals input information and generate an output for the actuators.
7 8 9 10 11 12	Post-processing	It has the main goal to reduce as much as possible the misclassification. An example is the majority vote strategy, in which the current output is calculated on the previously most recognized class. The majority vote scheme is used for eliminating spurious misclassifications caused by too short windows on which the most recurrent class is selected; it employs the previous classification results and evaluates the current output on the basis of the previously most recognized class (Englehart et al., 2003).
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1**f**356 EMG-based pattern recognition controllers are now 1384 <sup>1</sup>¥357 investigated by many groups and are even available in 1385 <sup>1</sup>¶358 commercial prostheses (COAPT, 2017, Ottobock, 2019, i- 1386 <sup>1</sup>7359 biomed, 2021). 1387

<sup>18</sup>360 The PR-based controllers apply linear and non-linear 1388 361 methods to classify the EMG signal into a possible large 1389 <sup>2</sup>0362 number of movements. The two main families of 1390 363 classification methods used in this context are regression 1391 23364 (Hahne et al., 2014) and classification techniques 1392 24365 (Hudgins et al., 1993). While the former is usually simple 1393 2<u>1</u>366 to implement and train, the latter are generally more 1394 26367 difficult to employ. The embedding of neural networks 1395 2<sup>1</sup>/<sub>2</sub>368 (NN) in an ULP strictly depends on the structure of the 1396 28369 algorithm (number of layers and neurons), since complex 1397 2**b**370 architecture requires high computational effort (Hagan et 1398) 30371 al., 1997). 1399

Statistical regression models usually produce good 1400 31372 **3½**373 results in terms of high accuracy percentages. However, the 1401 31374 out-of-laboratory results are particularly poor, because 1402 34375 these techniques are extremely sensitive to changes of the 1403 3\$376 input signals (Parajuli et al., 2019). Motivated by this issue, 1404 36377 in the last decade, many groups focused on classification- 1405. 31378 based techniques to implement more reliable decoders. 1406 38379 Importantly, training classifiers requires longer than 1407 39380 training linear models, however, the formers can achieve 1408 40381 better results during real-time execution. Different 1409 41382 classifiers have been exploited in ULP control such as 14104**2**383 Support Vector Machine, Regularized Least Squares, 1411



Figure 6: Division of machine learning approaches for ULP control.

whereas the gold-standard is the Linear Discriminant Analysis (Scheme and Englehart, 2011, Cloutier and Yang, 2013b, Di Domenico et al., 2021). Among NN, the most common architecture is the Multi-Layer Perceptron (MLP) (Amrani et al., 2017, Shahzaib and Shakil, 2018). The MLP is a supervised ML technique, which exploits labeled data to train the algorithm. It is characterized by three types of layers: input, hidden and output layer. The first one contains the same number of neurons as the input signals (for example, features extracted from EMG signals), the second stage can have one or more layers where there are all the trainable neurons, while the last layer comprises all the output nodes representing the results (for example, classification likelihood of each class of movement). Neurons of a certain layer are fully connected to the neurons in the next layer via nonlinear activation functions. However, as for the regression algorithms, the performance results obtained in the lab are not easily replicated in the real-life scenario. Moreover, the complexity of the controlled prosthesis (e.g., the number of DoFs) corresponds to a higher number of neurons in the NN, with important consequence not only on the computational burden, but also on the memory consumption.

When considering an increase in the number of controllable DoFs, current pattern recognition approaches demonstrated poor performance (Piazza et al., 2020). As a matter of fact, to enhance the classification rate (i.e., number of correctly recognized movement) a greater content of information should be handled. The higher the amount of input data, the more complex would the ML algorithm be.

Therefore, HD-sEMG can be exploited to increase the amount of muscular information but this comes at the cost of higher computational burden. It has been proven that the use of this type of data can be helpful in increasing the robustness against electrode shift (Pan et al., 2015), allowing an improvement of the classification by exploiting spatial images of the muscular contractions (Geng et al., 2016), and for retrieving measures of motor unit potentials, which can be difficult to assess without invasive techniques (Merletti et al., 2008).

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31426 Different techniques can be exploited to extract motor 1478 41427 units' activity from the HD-sEMGs. The main used 1479 51428 decomposition algorithm is the blind source separation 1480 61429 (with the Convolution Kernel Compensation described by 1481 71430 Holobar and Zazula (2007)) which seems to be the most 1482 <sup>8</sup>1431 suitable since it does not make any prior assumptions on 1483 <sup>9</sup>1432 the action potential shapes. The main problems related to 1484<sup>1</sup>9433 this technique is the lack of a useful output for the 1485 <sup>1</sup><u>1</u>434 prosthesis control, since the decomposition provides an 1486 **1**435 extraction of principal features of the EMG signals. On the 1487 **1**436 one hand, the algorithm returns reliable information about 1488 1437 neural activity, but, on the other hand, it increases the 1489 **र्**438 computational burden required to the system. Indeed, the 1490 1439 Holobar algorithm has been used together with ML 1491 **j**440 real-time 1492 algorithms to control robotic arm in **j**441 1493 (Barsakcioglu and Farina, 2018).

21442 Another approach includes the exploitation of ML 1494 algorithms where the input EMG signals are considered as 1495 21444 numeric values and the definition of the output is based on 1496 23445 a Black Box technique. Therefore, the mathematical tools 21446 contained in the Black Box do not take into account the 1497 2\$447 biomechanics of the amputated limb and they are not 1498

26448 1499 specific for prosthetic applications. 27449 It is relevant to feed the ML algorithm via a set of EMG 1500 28450 signals (muscular patterns) specific for different prosthesis 1501 29451 movements in such a way that the classifier does not 1502 30452 misclassify. However, it is not always feasible to acquire 1503 31453 the same signals for each movement due to different 1504 32454 sources of errors (i.e., muscle fatigue, sweating, electrode 1505 33455 classifiers 1506 misalignment). Indeed, more complex 34456 belonging to the **Deep Learning** (DL) field are exploited 1507 3\$457 to make the control more robust. A possible application can 1508 36458 be the use of Convolutional Neural Network (CNN), 1509 37459 which exploits dimensionality reduction to extract complex 1510 <sup>38</sup>460 features from the activation maps of the HD-sEMG without 1511 <sup>39</sup>461 dramatically increasing the computation time (Olsson et 1512 <sup>4</sup>9462 al., 2019). This type of algorithm is also ideal for increasing 1513 <sup>4</sup>1463 the number of DoFs (and therefore the number of classes 1514 <sup>4</sup>1464 to be recognized) while keeping a quite high accuracy rate 1515 <sup>4</sup>1465 (Hartwell et al., 2018). Moreover, Zhai et al. (2017) has 1516 44 1466 45 1467 proved that the exploitation of CNN can help in removing 1517 issues of daily life noise, updating its feature map to 1518 46<sup>-101</sup> include this new information, avoiding the need of 1519 41469 48470 periodical readjustment. 1520

Adaptive technique based on reinforcement learning 1521 50471 (Vasan and Pilarski, 2017, Wu et al., 2022) has been 51472 recently investigated, with the aim of facilitating the 1522 <sub>5</sub>]473 learning process of prosthetic use. This approach is 1523 5<u>1</u>474 promising as it points towards the development of a 1524 5**1**475 "human-prosthesis symbiosis in which human motor 1525 5**§**476 control and intelligent prosthesis control function as one 1526 5**6**477 system", as defined by the group of Huang et al. (2021). 1527 1528

Other DL algorithms take into account time series with feedback loops with prior hidden layers (Sun et al., 2021a). This architecture allows storing the history of the input signals by considering the information of previous time instants, also resulting in performance improvements with respect to simpler DL architectures (Amado Laezza, 2018).

Recently, novel DL strategies have also been proposed for ULP: Recurrent Neural Networks process temporal or sequential information; Temporal Convolutional Networks take advantage of a one-dimensional convolution layer running along the time dimension to learn the time dependence of a given input signal (Li et al., 2021); Transformers are attention-based architectures applied to HD-sEMG data (Montazerin et al., 2022, Burrello et al., 2022).

Overall, the main problem related to ML applied to the bionic field is the evident gap between the results observed in a closed safe environment, such as a laboratory, and in real daily life (Resnik, 2011).

#### 4.3.2. Model-based approaches

To overcome the limitations of ML algorithms for ULP control, some groups investigated the model-based approach, which consists of an accurate description of the muscles and bones involved in the movements starting from the Hill model of muscle fiber (Winters, 1990). For example, the neuromusculoskeletal model extracts from the residual EMGs the activation dynamics of the limb (Pan et al., 2018, Zhao et al., 2022). The activation dynamics combined with the kinematics of the limb produces the contraction dynamics. This consists of the modification of fiber length involved in the motion along the specific DoFs. In particular, Sartori et al. (2018) implemented a control strategy based on the physiology and kinematics of a real hand and tested it with an amputated subject performing some complex grasping tasks. This approach needs a calibration step to scale the model to the subject specific activation EMGs. Results showed great stability over the noise introduced by sensors or movements artifacts. Moreover, the amputee was able to reproduce simultaneous multi-DoF gestures. The limitation of this approach is its susceptibility to electrode shift and fatigue condition that affects the EMG acquisition. The real-life scenario is yet to be tested, but preliminary results appear very promising (Sartori et al., 2018).

#### 4.3.3. Sensor/Data-fusion and other techniques

For ULP control using different input sources together with or without EMG signals, other methods can be adopted. In case of force myography, the same algorithms used for EMG input can be applied. For example, machine learning techniques can be used to analyze and synthetize output starting from FMG input (Cho et al., 2016). The adoption of other input signals different from EMG clearly

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31530requires the implementation of ad-hoc methods for their 158241531processing. For example, voice control introduces audio 158351532analysis method to detect and translate command into 158461533prosthetic movements (Mainardi and Davalli, 2007, 158571534Alkhafaf et al., 2020). Further, tongue control allows the 158681535motion of the prosthesis using a wireless controller 158791536resembling a dental retainer and providing the functionality 158819537The high complexity of ULP control has led to the 1590

1538The high complexity of ULP control has led to the 15901539development of sensor fusion approaches, in which input 15911540signals of different nature are simultaneously collected and 15921541then processed to estimate the intended movement more 15931542reliably and accurately.

 $16^{342}_{17}$ On low-density sEMG, we can find robust and semi- 1595 18544 18545 19545 autonomous control solutions based on custom multi-1596 amplitude algorithms, as those implemented on the 1597 20546 Michelangelo hand with CMAC control (Markovic et al., 1598 -2**1**547 2019, Mouchoux et al., 2021). The adoption of IMU 1599 2,548 sensors may lead to further improvements, such as the 1600 21549 automatic adaptation to unexpected external factors, 1601 24550 including sweat, muscle fatigue, mental stress, electrode 1602 2\$551 re-positioning and weather conditions. The state-of-the-art 1603 26552 algorithms have to cope with these challenging issues. 1604 27553 Therefore, the combination of EMG and IMU as input to a 1605 2\$554 classifier could provide useful localization information of 1606 29555 the hand position, which could delete possible false 1607 30556 positives, actively improving the obtained accuracy 1608 31557 (Krasoulis et al., 2017, Krasoulis et al., 2019b). Moreover, 1609 32558 it has been observed that integrating EMG, IMU and 161033559 artificial vision sensors could benefit both the classifier 1611 34560 accuracy and the increment of available DoFs (Mouchoux 1612) 3₽561 et al., 2021). Other promising research advancements 1613 **3∮**562 demonstrated that mixing EMG with FMG could lead to an 1614 37563 improved multi-DoFs control as proposed by (Nowak et 1615 <sup>38</sup>564 al., 2020). Similarly, Jiang et al. (2020) proposed a sensor 1616 <sup>3</sup><sup>9</sup>565 fusion approach among EMG and FMG. Moreover, by 1617 49566 fusing FMG and IMU, other interesting results were 1618 <sup>4</sup>1567 presented by (Ferigo et al., 2017). In addition, other 1619 <sup>4</sup>1568 research activities treated NIRS fused with EMG (Guo et 1620 <sup>43</sup>1569 <sup>44</sup>1570 <sup>45</sup>1571 al., 2017b) and IMU respectively (Zhao et al., 2019). 1621

41570In conclusion, a data fusion aims at compensating some 162245571of the main limiting factors of single input approaches 16234572(such as EMG-based or others) as these latter suffer from 16244573artifacts, electrodes shift, etc.16251626

## 49<br/>504.4. Control strategies for the Sensory Feedback and 1627<br/>51515755157561628

57576Recent developments in the prosthetic field have162957577focused attention on sensory feedback restoration. In163154578particular, many groups began studying how to provide the163254579user with information about the interaction between the163354580prosthetic system and the physical world. This information163354581needs to be collected (Figure 5 E), processed (Figure 5 C,

green panel - layer 2) and encoded into control signals (Figure 5 C, blue panel - layer 3) for the feedback system (Figure 5 B, e.g., vibromotors, electrostimulation, etc.).

The control strategy implemented to encode this information depends on the type of sensation to restore as, for instance, tactile feedback (pressure, temperature, pain) or proprioception feedback (gestures, joint movements). o this aim, different solutions have been developed.

Mamidanna et al. (2021) focused their research activity on the force feedback that the prosthesis applies to the grasped objects by using vibromotors attached to the forearm skin. To do that, an encoding scheme of the current absorbed by the prosthetic motor was translated into vibromotors amplitude. Other sensorized solutions have been developed to directly translate the prosthesis interaction to user sensation like artificial skin able to translate the distribution of pressure and intensity to tactile and pain sensations on users with invasive interfaces (Jiang et al., 2019). Similarly, Markovic et al. (2019) implemented a proprioceptive feedback translating prosthesis movements into vibration orientation and shape to be intuitively interpreted by users.

In addition to prosthetic feedback, some groups are working on user feedback in terms of providing information about how the prosthesis is controlled by means of closed-loop approaches. For example, Schweisfurth et al. (2016) have tested on amputees a ULP system in which EMG input used to drive the prosthesis was translated into intensity of vibromotors activation. In this configuration, the amount of EMG activity detected is directly proportional to prosthesis grasping strength and to intensity of vibration amplitude. In another work, the control commands generated by the user and translated into joint angles were encoded as proprioceptive information delivered through electrical stimulation (Garenfeld et al., 2020). This allowed user to understand if the intended control command was correctly detected by the algorithms.

Similarly, Tecnalia developed a ULP system with sensory feedback by merging into a unique device EMG acquisition and electrical stimulation (Štrbac et al., 2016). Although this solution significantly reduced the problem of encumbrance, it still faces some issues mainly related to the artifacts that the stimulation produces on the EMG signal and that cannot be removed using standard signal processing algorithms (Li et al., 2019).

As for decoding of movement intention from input signals, the interpretation of feedback information needs a calibration procedure aimed at familiarizing the user with the ULP device. In this context, it is fundamental to guide the user to: (i) produce the correct input signal to perform the desired movement, and (ii) to intuitively convert the feedback signal into useful information for motor planning.

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31634 A user-centered approach can maximize and speed-up the 1686 41635 learning process, as detailed in next section. 1687

#### 61636 5. User-Centered Solutions in Upper Limb

#### <sup>7</sup>1637 **Prosthetics** 8

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91638 As observed in previous sections, multiple efforts in heterogeneous 1691 10639 research and development offer technological solutions to enable a proficient control of an 1692 11640 ULP device. However, selecting a sub-set of these 1693 12641 solutions is compulsory for implementing and validating 1694 13642 them. Accordingly, this section will discuss user-centered 1695 14643 1\$644 solutions based on the technologies described in the 1696 1¢645 previous paragraphs, highlighting the opportunity of 1697 overcoming a separation (often, an opposition) between 1698 <sup>1</sup>**1**646 <sup>1</sup>**8**647 (for instance) user-centered features and technical ones, or 1699 <sup>1</sup>9648 between ADL-related performance and biomimetic one. 1700 <sup>2</sup>9649 Nevertheless, we decided to proceed in the selection of 1701 <sup>2</sup>1650 one 1702 each solution by pragmatically moving from <sup>2</sup><del>1</del>651 <sup>2</sup>1652 1703 perspective towards the other.

Fundamentally important criteria for performing such a 1704 <sup>2</sup><sup>1</sup>653 selection should come from the analysis of the prosthetic 1705 **1**654 user experience (Figure 5 F). Indeed, special attention 1706 26 1,655 should be paid to the user needs in order to promote the 1707 -1656 28 daily use of prosthetic devices, a prerequisite for checking 1708 29657 the validity of any technological solution presented in 1709 \_1658 1710 previous sections.

31659 In particular, the prosthetic technology acceptance 1711 constitutes a dramatic issue in this domain. Overall, ULP 1712 3,1660 technology acceptance (Longfellow, 2014) is tied to 1713 34661 34662 several interdependent functional factors related to ease of 1714 use (sensory feedback, control), dexterity (motion 1715 3\$663 complexity, force output, actuation speed, manipulation), 1716 36664 body integration (anthropomorphism, autonomy, weight), 1717 37665 technology transfer (cost, reliability). Further factors 1718 3\$666 embrace several domains, namely clinical (age, level of 1719 3∮667 amputation, fitting timespan), cultural (education, social 1720 40668 conditions, living environment, country development), and 1721 41669 personal (psychological attitudes, subjective expectations, 1722 42670 1723 43671 occupation, activity, environment).

Low acceptance can contribute to the abandonment of a 1724 44672 prosthetic hand, erasing any chance of improvement in the 1725 4\$673 control skills of the users (Castellini, 2020). Thus, it is 1726 **4§**674 47675 important to promote an intrinsically motivated and 1727 <sup>4</sup>**§**676 continuous ULP practice, which must be experienced by 1728 49677 the users as immediate and rewarding in order to achieve 1729 <sup>5</sup>9678 high degrees of technology acceptance (Rodgers et al., 1730 <sup>5</sup>1679 2019) and integration (Shaw et al., 2018). The users must 1731 <sup>5</sup>7680 also feel engaged enough to surpass the impact of feeling 1732 <sup>5</sup>1681 social stigma or the doubts on the functional impact of the 1733 <sup>54</sup>682 system on daily life. Intuitive patterns of system control 1734 <sup>5</sup>1683 play a critical role in this context to facilitate a spontaneous 1735 56 -1684 use of the system and to improve the user experience 1736 58<sup>1685</sup> 1737 (Krasoulis et al., 2019a).

Obviously, the absence of appropriate acceptance, usability, and user engagement creates a barrier for the introduction (and the further development) of any technological improvement in prosthetics.

#### 1690 5.1. Towards User-Centered Upper Limb Prosthetics

In order to improve the ULP acceptance, different approaches can be adopted, especially in terms of user research (Figliolia et al., 2019). A review of Cordella et al. (2016) provided a rich set of guidelines for enhancing the prosthetic hand technology acceptance through the analysis of the user requirements, considering literature and case studies like Luchetti et al. (2015). Among these requirements: the capability to accomplish basic grasping actions during activities of daily living with minimal visuoattentional focus, high dexterity, appropriate strength control; biomimetic features of sensory feedback and anthropomorphism; duration and reliability of the device and its component; technical features with impact on comfort like heat dissipation and motor noise reduction.

All features must be designed according to individual preferences can preferences. These depend on demographic factors, type and level of amputation, pain symptoms, and type of prosthesis (e.g., body-powered or myoelectric) (Biddiss and Chau, 2007, Biddiss et al., 2007, Davis and Onge, 2017, Uellendahl, 2017, Smail et al., 2020, Kerver et al., 2020). The amputees' preferences must also be investigated to design virtual and augmented environments for prosthetic use training (Garske et al., 2021b). If appropriately devised, game-like engaging exercises can motivate the user to train, feeding the prosthetic with consistent biosignals that efficiently represent different types of grasps, an advantageous condition for ML based control (Tabor et al., 2017). This can possibly happen with a successful generalization if the training is adequately designed with solutions like task switching (Heerschop et al., 2021). Overall, the training designers should focus not only on playfully engaging the user to train the muscles, but also on accurately representing prosthetic use tasks to enable the related skills transfer (Garske et al., 2021a). Furthermore, the parameters of meaningful and, possibly, ecological interactive settings can be experimentally controlled by the clinician or the researcher (Resnik et al., 2011, Bouwsema et al., 2014, Paljic, 2017, Markovic et al., 2017, Nissler et al., 2019, Phelan et al., 2021, Boschmann et al., 2021). In addition, interactive settings can be adjusted to the individual needs and reactions. To understand the individual needs in prosthetic use (training and daily activities), the improvement of user research methodologies themselves becomes a priority to promote effective co-creation frameworks. Recent works (Jones et al., 2021) described surveys and workshops to investigate the point of view of

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31738 amputees and all stakeholders (clinicians, academics, 1791 41739 experts and managers in industry and charity), observing a 1792 51740 gap between laboratories and the real life of prosthetic 1793 61741 users (whose issues are typically misrepresented by media 1794 71742 too). Interestingly, initiatives like the Cybathlon 1795 <sup>8</sup>1743 competitions for assistive and prosthetic technology users 1796 <sup>9</sup>1744 are also devised for overcoming such a gap (Riener, 2016). 1797

<sup>1</sup>9745 The users' involvement in iterative activities of design 1798 <sup>1</sup>1746 and evaluation of products and of product services is highly 1799 **f**747 important (O'Sullivan et al., 2017). Such activities must 1800 ₹748 be planned for checking and improving the usability of 1801 1749 prostheses as medical devices according to the 1802 1750 international standards (Pelayo et al., 2021) and for 1803  $^{16}_{17}$ estimating the impact of user experience on the technology 1804 **၌**752 acceptance (Longo, 2018, Lah et al., 2020). Obviously, 1805 ไส753 user-centered evaluation methodologies and metrics must 1806 20754 be adjusted to the specific case of ULPs (Resnik, 2011, 1807) 2<sup>1</sup>755 Zahabi et al., 2019), especially considering how their user 1808 21,756 interface is not based just on buttons, plugs, and LEDS and 1809 21757 their behavior and feedback are eminently biomimetic in 1810 21758 1811 hand-like manipulation tasks.

2\$759 The functional resemblance of the ULP design to a real 1812 26760 hand is a wise strategy for promoting a positive interaction 1813 27761 between user and prosthesis. Such an approach (implicitly 1814) 28762 and explicitly) aims at building artificial limbs that are 1815 29763 spontaneously used by the amputees as their own. Such a 1816 30764 "prosthetic ownership" experience is deeply investigated 1817 31765 within the domain of the embodiment research, crossing 1818 32766 disciplines like cognitive psychology and robotics 1819 33767 according to the roadmap in Beckerle et al. (2018).

34768 The embodiment phenomenon can be constituted across 1820 its components, i.e., self-location, ownership, and agency, 1821 3§769 3\$770 by the sensation that an artifact is integrated in one's body 1822 37771 scheme (Kilteni et al., 2012, Maimon Mor and Makin, 1823 <sup>3</sup>§772 2020, Toet et al., 2020). Overall, the technology 1824 <sup>3</sup>**9**773 embodiment promotes intuitive control with improved user 1825 4**9**774 experience and acceptance (Makin et al., 2017, Nelson et 1826 1775 al., 2020, Toet et al., 2020). About ULPs, the embodiment 1827 1776 improves: (i) movement control (Grechuta et al., 2017), (ii) 1828 <sup>4</sup>1777 object discrimination and manipulation (Tan et al., 2014), 14778 1829 (iii) manual accuracy and sensitivity. Furthermore these 1830 2779 processes contribute to: (iv) the reduction of the phantom-1831 **Ç**780 limb pain (Page et al., 2018) and (v) the mitigation of the †1781 48781 1832 risk of prosthesis abandonment (McDonnell et al., 1989, 1833 4**1**782 Beckerle et al., 2019).

50783 1834 Obviously, we must ponder how to measure and to 5**1**784 1835 stimulate the prosthetic embodiment. Overall, the 1836 <sub>5</sub>1785 embodiment evaluation is typically entrusted to methods 1837 5**1**3786 (questionnaires, biosignal analysis, proprioceptive drift) 1838 5**1**787 based on the Rubber Hand Illusion (RHI) studies 1839 5**§**788 (Botvinick and Cohen, 1998, Tsakiris and Haggard, 2005, 1840 5\$789 Ehrsson et al., 2008, Romano et al., 2021). RHI can be also 1841 52790 implemented on its different versions - e.g., Virtual Hand 15842

Illusion (Pyasik et al., 2020, Beckerle, 2021) and Robotic Hand Illusion (Romano et al., 2015, Huynh et al., 2019). However, these methodologies are still debated in cognitive studies (Gallagher et al., 2021) which show the complexity of the processes underlying the embodiment itself.

Understanding such processes is required for designing appropriate strategies to enhance the embodiment of an artificial limb. First of all, it must be said that daily prosthetic practice, individual characteristics (like the cause of limb absence), and multisensory feedback congruency play fundamental roles in this process, which does not necessarily require cosmetic improvements or specific control patterns (body-powered or myoelectric) (Dornfeld et al., 2016, Engdahl et al., 2020b, Zbinden et al., 2021, Moore et al., 2021). Embodiment training strategies can also be explored in virtual and augmented settings (Barresi et al., 2021), even if the generalization of their effects to actual prostheses must be investigated. Importantly, establishing optimal techniques to promote the embodiment of an artificial limb is a way to fully engage the user in exploring the prosthetic device and its potential, further improving its embodiment too within a virtuous circle.

However, it is necessary to consider what technological challenges must be faced for achieving a truly "biomimetic" experience as the prosthetic embodiment to improve the use and the acceptance of an artificial limb.

## 5.2. Promoting Prosthetic Use and Acceptance through Improved Mechatronics and Control

To improve ULPs, two main classes of approaches can be taken: one focusing on mechatronic development and the other on control implementation. From the mechatronic side we suggest optimized actuation, anthropomorphism, human-like grasping behaviour, and biomimetic performance as key factors to take into account for promoting ULP use and acceptance, while from the control perspective we identify robust control strategies and use of smart prostheses. Moreover, we believe the inclusion of multimodal sensory feedback a fundamental prerequisite of next generation prostheses. Each approach contributes to approximate the prosthetic user experience and the userprosthesis system performance to, respectively, the sensations provided by a natural limb and its spontaneous and effective usage. However, all approaches face issues that must be solved in order to obtain a robustly controlled prosthetic system easily accepted by the user. These approaches thus constitute research challenges, summarized in Table VI with their actual potential solutions.

Table VI: Current issues affecting ULP mechatronics and control.

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#### **Challenge Description**

#### **Current and Possible Solutions**

Optimized Actuation	
<ul> <li>The actuation architecture (i.e., the number of actuators employed) influences the overall performance of the device in terms of:</li> <li>amount of possible gestures/configurations (therefore controllability and dexterity);</li> <li>contribution to ULP weight;</li> <li>grasping strength;</li> <li>acoustic noise during actuation (i.e., reduction stage).</li> </ul>	<ul> <li>There are two possible strategies to optimize the actuation of ULPs.</li> <li>From a qualitative point of view, a fully actuated system might lead to independent control of each single joint thus allowing to replicate the full amount of gestures of a real hand. However, this solution is typically characterized by a heavier and bulkier or poorly performing system. Moreover, this configuration prevents the use of power motors to generate human-like grasping strength.</li> <li>On the other hand, an underactuated device might guarantee compactness, light weightiness and the possibility to achieve more efficient actuation and therefore higher performance, at the cost of passive uncontrolled degrees of freedom.</li> <li>Both actuation solutions are still affected by acoustic noise during prosthetic movements and this constitutes room for improvement for future development.</li> </ul>
Anthropomorphism	
Anthropomorphism also represents a key design feature for an ULP. In fact, users are more prone to adopt and utilize anthropomorphic devices that anatomically and functionally resemble their missing limb as much as possible (Varol et al., 2014).	In two useful reviews on mechanical and anthropomorphic aspects of prosthetic hands, Belter and colleagues proposed a list of guidelines to achieve, by mechanical and mechatronic means, the desired hand anthropomorphism in terms of size, weight, shape and kinematic capabilities (Belter and Dollar, 2011, Belter et al., 2013). The group of Metta proposed a systematic approach to benchmark different robotic and prosthetic hands in terms of shape, feature and performance, observing a continuous need for weight, payload and generic grasps improvement while maintaining an anthropomorphic appearance (Vazhapilli Suraekhabu et al. 2019)

However, it should be mentioned that a minority of ULP users do not recognize anthropomorphism as priority, focusing their needs on functionality. In some cases, the ULP is deliberately unconventional and worn as a fashion gadget or stylized wearable art pieces (De Oliveira Barata, 2021).

## Human-like grasping behavior

grasping tasks.

Human-like grasping behavior represents the aesthetic Underactuated solutions greatly simplify the accomplishment of capability of the ULP to synergistically operate and adapt its this due to their intrinsic capability of conforming to the object to configuration and to robustly perform different sets of be manipulated during grasp (Catalano et al., 2014, Weiner et al., 2018, Laffranchi et al., 2020). On the other hand, in systems with

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feedback-to-prosthesis. This can be obtained by sensors embedded on the prosthesis, which can measure the interactions between the device and the external world. This can be done exploiting different measurements ranging from the motor current (Ajoudani et al., 2013, Laffranchi et al., 2020, Deng et al., 2020), to tactile/pressure sensors (Tomo et al., 2018), Inertial measurement units (IMU) to understand the actual pose of the prosthesis (Krasoulis et al., 2019b), or artificial vision (Mouchoux et al., 2021) to understand which is the shape and orientation of the nearby objects. 

#### Multimodal sensory feedback

The sensory feedback, namely the possibility to restore the Many groups are now exploring novel solution, both invasive and complexity of the human-machine-environment interactions. controlled device. Multimodal sensory feedback is necessary to empower the prosthetic control training and to trigger the embodiment The feedback-to-user can also be adjusted to the user through processes.

29844 These technological approaches constitute the premise 1871 30845 for many kinds of breakthrough in prosthetics. Obviously, 1872 31846 we need to consider that tradeoff calculations must be made 1873 32847 for selecting the most rational set of features that can be 1874 33848 combined for providing a satisfying (without creating 1875 34849 excessive expectations in users and any stakeholder) and 1876 3\$850 (also economically) sustainable design of the devices. 1877 36851 However, the features we described, and their user-1878 37852 centered synergies, can make us foresee the perspectives 38853 on bionic hands innovation that will be discussed in next 1879 39854 section. 1880

#### 41855 6. Perspectives on Tomorrow's Upper Limb <sup>4</sup>1856 **Prosthetics**

44857 By analyzing the state-of-the-art techniques for ULP 1884 input (section 3.1) and feedback (section 3.2) signals, it 1885 4**\$**858 46859 emerges that there exist two parallel directions for future 1886 development, namely the non-invasive and invasive 1887 47860 **48**861 approaches. This is due to different reasons: first of all, 1888 49862 because non-invasive solutions may provide the amputees 1889 59863 with a plug and play device ready to be used for ADLs, 1890 51864 while invasive solutions still need to overcome 1891 <sup>5</sup><del>1</del>865 technological barriers before they can be routinely adopted 1892 <sup>5</sup>866 by the majority of amputee population. Moreover, the 1893 <sup>5</sup>1867 specific choice of non-invasive vs invasive strategy is 1894 <sup>55</sup>1868 highly dependent on the level of amputation. For example, 1895 56 -1869 for trans-humeral amputees, TMR represents the most 1896 57809 57870 58 promising opportunity for restoration of lost functionality, 1897

feel of interaction with the external world, represents the last non-invasive, to provide sensory information about prosthetic key element of ULPs. Current ULP systems rely solely on movement. Regardless the specific methodology used, it is vision as feedback information. However, we cannot fundamental to achieve an intuitive or easily learnable strategy to consider just visual (unimodal) feedback to catch the associate the perceived feeling with a specific posture of the

> intelligent solutions, for instance through EMG biofeedback strategies based on the individual monitoring of the physiological input (Dosen et al., 2015).

which could not be achieved with non-invasive approaches. In the following, we describe possible direction for future prosthetics. In particular, for noninvasive solution we suggest the use of multiple input sources and of sensory feedback. For invasive solution, we recommend strategies promoting a direct translation of user intentions into prosthetic movements. These directions are also outlined in Table VII.

#### 6.1. Short-term non-invasive solutions

The most widespread technique for non-invasive control is based on sEMG. This technique has lots of advantages, such as low cost, direct correlation between muscle activation and movements, and intuitive control, as described in sections 3.1.1.1.Surface EMG and 4.3. Nevertheless, EMG-based systems lack of robustness, due to EMG susceptibility to artifacts of biological nature (sweating, hair, muscle fatigue), instrumental source (electromagnetic disturbances), intrinsic to the device (movement artifacts, electrode shift, variations in contraction depending on the orientation of the arm), or intrinsic to the control algorithm (optimization of the classifier).

For this reason, there is ample room for improvement in non-invasive approaches for ULP control. One research direction points towards the use of sensors fusion techniques, in which multiple input data is taken into account to estimate the movement intentions, as described

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31898 in section 4.3.3. However, the use of great number of 1916 41899 sensors may be impractical for creating an embedded 1917 51900 system for everyday applications. Future ULP should be 1918 61901 equipped with multi-modal control based on minimal 1919 71902 number of sensors (Jiang et al., 2012, Di Domenico et al., 1920 <sup>8</sup>1903 2021). Moreover, recent studies are investigating the 1921 <sup>9</sup>1904 miniature technology to limit the encumbrance within the 1922 10905 socket (Marinelli et al., 2021). 1923 <sup>1</sup>1906

With the aim of improving ULP control, we pose that a 1924 <del>2</del>907 fundamental element is the feedback. This will allow a 1925 **1**908 closed-loop interaction between user and prosthesis, a 1926 **1**909 essential prerequisite for promoting the integration of the 1927 2910 prosthesis into the body scheme and for facilitating the 1928 **1**911 controllability of the entire system. In this direction, many 1929 912 studies have pointed out the usefulness of vibrotactile 1930 913 stimulation for providing sensory feedback information 1931 914 (Sensinger and Dosen, 2020). This technique is cheap, 1932 915 easily integrated into a socket, and its modulation in

frequency and intensity allows to provide various information.

In the last years, wearable technology has largely expanded in many fields, influencing also prosthetics. For example, the CTRL Labs have realized a wearable wristband, which reads EMG signals and translates them into finger movements (Melcer et al., 2018), later improved by the Facebook Reality Labs by means of advanced ML algorithms (Basu, 2021). This technology could be exploited for prosthetic applications with a strong impact for ADLs usage.

Another promising approach consists in providing sensory information by stretching the skin of the stump. This can be done with a wearable haptic device producing rotational skin stretch according to the movement of the controlled device (Kayhan et al., 2018, Battaglia et al., 2019).

considerable improvements in

usability, and embodiment.

device functionality,

Table VII: Perspectives on Tomorro	ow's Upper Limb Prosthet	ics
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23	Future		
24	nerspectives	Short-term non-invasive solutions	Long-term invasive solutions
25	perspectives		
26	Increase of input	Multiple input data to estimate the movement	Increase the number of myoelectric input sites;
27	sources	intentions; data fusion.	neuroprosthetics.
28			
29	<b>Restoration of</b>	Build artificial feedback, i.e., proprioception and	Restore natural sensation, i.e., proprioception (by
30	sensory feedback	tactile sensations by use of vibrotactile feedback	kinesthetic illusion), spatial sensation and phantom limb
31		or skin stretching.	contear representation (by refer touch strategies).
32	Classed laser	Implementation of a bidirectional communication l	between user and prosthesis to restore a link between motor
33	Closed-loop	and sens	ory counterparts.
34			
35		Promote learning with engaging/immersive train	ing and rehabilitation protocols (from user to prosthesis).
36	User-prosthesis		
3/	co-adaptation	Adaptive control, advanced Pl	k algorithms (from prostnesis to user).
38		Co-adaptive feedback (feedback	ck-to-user and feedback-to-prosthesis).
39			
40 41	Miniaturization	Miniature technology to limi	it the encumbrance within the socket.
41 42			
4Z 12	Modular	Modular prosthetic system enabling the progress	sive replacement of the non-invasive input and feedback
45 44	architecture	sources wi	ith implanted ones.
44 15			
45	Standardization of	Standardization of level of amputation to help	designing sockets that are simultaneously comfortable,
40	amputation and	anunoponiorpine, and spacious (to i	integrate the chednity and the power system).
47	surgery		Chronic and reliable implants
40 70	procedures		Chrome and remaine implants.
19634			
51935	These examples sho	w that innovative ULP solutions can 1941 at t	he cost of several issue related to the surgical procedure
5936	be adopted for restoring	plost functionality in the short-term 1942 Ne	vertheless, there are some promising approaches whose
51937	using non-invasive app	proaches. 1943 inv	vasiveness drawbacks are counterbalanced by

54 6.2. Long-term invasive solutions 5**\$**938

56 -1939 The great advantage of invasive approaches is a direct 57939 1940 58 bidirectional contact with the nervous system. This comes

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31946Moreover, although still far from clinical usage due to 199841947technological barriers, brain-based approaches seem a 199951948promising solution for prostheses of the future.2000

## 71949 6.2.1. Peripheral bionics implants

<sup>8</sup>1950 Among the invasive approaches, surgical procedures 2003 <sup>9</sup>1951 aimed at augmenting the signal containing the motor 2004 10952 commands have gained popularity in the last decades. 2005 <sup>1</sup>1953 Indeed, TMR is now routinely adopted in case of trans- 2006  $^{12}_{17954}$ humeral amputation, and it allows to increase the number 2007 **1**955 of myoelectric input sites, which can be exploited for 2008 **1**956 multi-DoFs control. Differently from invasive procedures 2009 रे957 for electrodes implantation, TMR is permanent, turning the 20101958 reinnervated muscles into natural bioamplifiers of motor 2011 959 commands. It is also adopted for phantom limb pain 2012 **J**960 reduction (Mereu et al., 2021). 2013

2\$966 As for delivery of feedback information, invasive 2019 26967 approaches represent the more intuitive and natural 2020 27968 solution towards the retrieval of sensations, as 2021 28969 demonstrated in (Osborn et al., 2018, Nguyen et al., 2021). 2022 29970 However, the main limitation towards the diffusion of these 2023 30971 techniques is represented by their invasiveness, i.e., poor 2024 31972 compatibility of electrodes, risk of infection due to external 2025 32973 2026 cables, scar tissue formation on the nerve, etc. 33 2027

#### 34974 6.2.2. Neuroprostheses

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3\$975 Ideally, a prosthetic limb should be a perfect replication 2029 36976 of the natural limb, both in terms of control and perception, 2030 37977 such as Luke Skywalker's arm in the Star Wars saga. In 2031 38978 this scenario, control signals should directly derive from 2032 39979 the brain and communicate the intended movement to the 203340980 robotic device, while sensory information should be 2034 <sup>4</sup>1981 encoded into stimulation patterns delivered to the brain. 2035 <sup>4</sup>7982 The field of Neuroprosthetics, among other things, aims at 2036 <sup>4</sup><sup>3</sup>983 addressing these fascinating goals and in the last 50 years 2037 <sup>44</sup>1984 several progresses have been made, indicating that these 2038 4<sup>4</sup>1985 visionary scenarios might one day become true. 2039

46 1986 Fetz (1969) demonstrated that monkeys could 2040 47987 voluntarily modulate the firing rates of neurons in the 2041 primary motor cortex, in the absence of movement. At the 2042 same time, Humphrey et al. (1970) were able to predict arm 2043 displacement from the activity recorded from small 2044 51991 populations of neurons in the motor cortex. These exciting 5**1**992 and pioneering works thus proved the possibility of 2045 controlling artificial devices with the mind and eventually 20465**1**993 led to a rapid flourishing of investigations aimed at 20405**1**994 interfacing the brain with machines. These studies 204851995 57996 culminated with the first demonstration by the group of ; 2049 5**8**997 Nicolelis, of a robotic arm controlled with signals produced

by an ensemble of neurons recorded from the motor cortex of a rat (Chapin et al., 1999). At the beginning of this century, brain-machine interfaces (BMIs) were thus born and scientists were therefore hoping that in few decades, fully functional bionic limbs would have been routinely adopted by amputees and paralyzed individuals (Nicolelis and Chapin, 2002). Sadly, this is not at all how the story ended. Indeed, more than 20 years after the first demonstrations of brain-controlled devices, we still do not have the technology nor the computational capabilities to effectively control artificial devices with cortical brain signals.

However, in the last few years, some groups have presented promising examples of paralyzed individuals with neural implants in the motor and premotor cortices controlling artificial limbs for several months/year, while other groups worked on non-invasive applications on neurological populations, as detailed in section 3.1.1.3. Although the target population of these studies is mostly composed by stroke or paralyzed patients, exploitation of results for prosthetics applications clearly emerges, i.e., the possibility to perform device control by reliably and timely accessing to the subject's motor intentions. These examples indeed demonstrate that groundwork for brain control of motor prosthetics has been laid. However, it has been limited to the lab and mostly addressing paralyzed patients, for whom there are currently not viable solutions to enable dexterous device control as for amputees, whose residual motor functions can be successfully leveraged for prosthetic control signals.

In sum, brain control approaches are still far from clinical and personal applications, not only because of the poor controllability that they exert over the prosthetic device, but mainly because of the cumbersome apparatus they need for their collection and processing. However, the dream of brain-controlled devices has spread outside the academic labs and has contaminated also visionary entrepreneurs from venture capitals and tech giants, with the consequent birth of some important companies interested in brain-interfacing technology, such as Neuralink (Musk, 2021), Facebook Reality Labs (Zuckerberg, 2021), and Google DeepMind (Deepmind, 2021). In conclusion, cutting edge research that we are currently witnessing both in academic and non-academic contexts may thus soon push the envelope of Neuroprosthetics up to its diffusion in our everyday life, with important consequences also for amputees.

#### 6.3. User-Prosthesis Co-Adaptation

Designing user-centered prosthetic devices and usercentered prosthetic trainings is necessary to guide an appropriate learning of the system, as explained in section 5.1. Indeed, motivating the user to exercise and to get

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32050practice in using the bionic hand constitute the main way 210342051to improve the prosthetic control. Such approach can 210452052facilitate and accelerate the co-adaptation between humans 210562053and machines, as described in the following.2106

72054 Humans implicitly learn how to control devices, even if 2107 <sup>8</sup>2055 initially they must adopt explicit strategies. Indeed, it must 2108 <sup>9</sup>2056 be underlined that ULP control training is an important step 2109 $1\bar{2}057$ of rehabilitation. In particular, the ability of generating 2110 1205712058120581205913059distinct muscle contractions increase with time and 2111 exercise. The use of functional tasks, like Target 2112 <sup>1</sup>3060 Achievement Test (Simon et al., 2011) or activities of daily 2113 1<u>2</u>061 living, allows users to learn how to produce repeatable 2114 1<u>5</u>062 patterns of contraction to better control the prosthesis. 2115 12062 12063 12064 12064 12065 12065However, the learning process can be long and sometimes 2116 stressful, as described in (Zecca et al., 2002). The 2117 development of more engaging training tasks and of a more 2118 2<del>0</del>066 immersive rehabilitation protocol could promote the 2119 24067 learning process by increasing the engagement of the users 2120 23068 (Roche et al., 2019). In this context, user-centered design 2121 22069 can truly make a difference in the effectiveness of a training 2122 2123 22070 procedure, as better discuss in paragraph 5.

2**2**071 While humans have to learn ULP control, machines 2124 22072 need to be trained with growing datasets for classifying the 2125 22073 signals in terms of user's commands. For effective ULP 2126 22074 control, PR-based algorithms currently represent the most 2127 22075 effective solution, as they are able to recognize the human 2128 30076 intentions on the basis of training data. An important aspect 2129 32077 that can affect the accuracy of the classifiers is thus the way 213032078 in which these data are collected. Indeed, the prosthesis 2131 32079 control might not ensure good performances under 2132 324080 different arm positions and several studies have been 2133 32081 conducted on the evaluation of the impact of upper limb 2134 36082 position during the data acquisition on classifier 2135 372083 performance (Geng et al., 2017). For example, as far as 2136 <sup>38</sup>2084 EMG is concerned, muscle activation is not completely the 2137 <sup>3</sup>2085 same when performing a given movement under different 2138 42086 elbow and shoulder configurations. The signals on which 2139 4<u>2</u>087 4<u>2</u>087 the algorithm is trained are thus different from the ones 2140 obtained in a daily living scenario. Indeed, the 2141 <sup>4</sup>2089 classification performances strictly depend on the labeled 2142 442090 42090 42091 data assigned to the specific movement. Moreover, because the method used for the acquisition strongly affects the 2143 45091 42092 42093 42093 42094 5095 5095 classification accuracy, it is important to collect data under 2144 the same conditions of ADLs, i.e. by wearing the 2145 prosthesis, in order to have the training signals as similar 2146 as possible to the online ones. Cipriani et al. (2011) 2147 5<del>2</del>096 highlighted that indeed EMG signals do not carry just 2148 5<u>2</u>097 information about the desired arm movement, but they also 2149 52098 contain the muscular contribution to sustain the prosthesis 2150 52099 weight. This aspect has to be taken into account in order to 2151**52**100 prosthetic 2152 avoid misclassification and unwanted 52101 movements, because as soon as the signals change, the 2153 2154 52102 classifier is no longer able to behave properly. 2155 58

To cope with these problems, a possible solution consists in the adaptation of the control algorithm while using the prosthesis. This is of paramount importance, since the biggest issue of ULP control lies in the variability of the sEMG input signal due to electrodes shift, muscle fatigue, sweat, etc. ML algorithms are highly performing after training, but deterioration of the input signal or subsequent doffing/donning of the prosthesis can lead to misclassifications. For these reasons, amputees must regularly perform the training from scratch of the algorithm, which typically takes long time (Phinyomark and Scheme, 2018). To address this issue, the incremental learning focuses on the adjustment of internal weights of the model without the need of re-training- (Gijsberts et al., 2014). In this way the training data is continuously updated, and the control system is capable to cope with possible sources of errors (i.e., unwanted changes in input signals).

A promising approach to innovate the ULP field is the adoption of co-adaptive features through bidirectional human-machine interfaces (De Santis, 2021). In this case, the human and the machine reciprocally adjust their activity in order to improve their task-specific joint performance as a human-machine system. Co-adaptive features constitute a convergence of user activity and machine activity (including feedback towards the user and the machine), i.e., an "agreement" between human and machine on the biosignals produced by the first and on their interpretation performed by the second. Co-adaptation can modulate both (human and machine) training processes within the same framework (DiGiovanna et al., 2008, Zbyszynski et al., 2019, Yeung et al., 2019, Igual Bañó, 2021). This is performed through the feedback of human and machine on each other, further supporting the opportunity of designing feedback-to-user and feedbackto-prosthesis. Such a research effort requires innovative approaches to training processes as interactions between human and machine. In the next we present two building blocks for a user-prosthesis co-adaptation: closed-loop sensorimotor systems and interactive training.

#### 6.3.1. Toward closed-loop sensorimotor prosthesis

While great progress has been made in recognizing human motor intention and translating it into prosthesis joint movements, sensory feedback restoration is one of the many challenges that many research groups are still addressing (see section 3.2) (Farina et al., 2021). Obtaining a reliable and efficient way to artificially convey sensory information to prosthetic users would allow to develop smart devices able to truly mimic the behavior of human limbs, establishing the premise for a true co-adaptation between user and machine.

However, such a *sensorimotor* prosthesis would still need to face technological barriers for its development and

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32156 use in ADLs. For example, all the circuitry and components 2209 42157 needed to operate the device (i.e., acquire signals for motor 221052158 intention decoding and translate sensory information into 2211 62159 stimulation patterns) should fit into the socket space. One 2212 <sup>7</sup>2160 <sup>8</sup>2161 possible solution to obtain an embedded device is to rely 2213 on a hybrid approach. For example, a non-invasive 2214 <sup>9</sup>2162 sensorimotor prosthesis could use EMG signals to extract 2215 <sup>1</sup>2163 motor intentions and vibrotactile feedback to deliver 2216 1216412165sensory information. This configuration requires the 2217 embedding of an ADC amplifier to acquire EMG data, and 2218 <sup>1</sup>2166 motor drivers to control vibromotors. All these components 2219 12160 12167 15168 could be placed on the same board, overcoming the 2220 2221 problem of electrical coupling.

12168 12169 12170 12170 12171 12171 12172However, although this design is very articulated, we 2222 believe that this is not the real end point for a fully-2223 integrated prosthetic system capable of maximizing patient 2224 2<del>0</del>172 acceptance. It simply turns out to be a developmental test 2225 \_2́4173 bench for what will be the next generation of prostheses on 2226 23174 a longer temporal horizon, namely neuroprostheses. By 2227 23175 creating a modular architecture, in fact, it will be possible 2228 2176 to maintain the physical prosthetic system and to 2229 2**≩**177 progressively replace the non-invasive input and feedback 2230 22178 sources with implanted ones, namely: (i) the standard 2231 22179 sensors for surface electromyography replaced by an intra 2232 228180 neural implant; (ii) the hardware for feedback delivery 2233 22181 replaced by a chronic implant; and (iii) the hardware on 2234 30/182 which run the control strategies replaced by a smaller and 223532183 more performing dedicated hardware able to process 2236 3**2**184 2237 neuromorphic algorithms (e.g., ASIC).

32185 The realization of bidirectional ULP systems able to 2238 32186 restore both sensory and motor functions will open new 2239 32187 research scenario for embodiment process and neuroplastic 2240 **32**188 phenomena. Indeed, about neuroplasticity in amputees 2241 37189 using bionic hands as prostheses, Di Pino et al. (2009) 2242 32190 highlighted how the reorganization of the central nervous 2243 <sup>32</sup>191 system after the usage of the device can be the source of 2244 49192 indices of prosthetic effectiveness in functional recovery. 2245 42193 Furthermore, the effects of the device on the central 2246 4<u>2</u>194 nervous system can make the prosthesis work as a 2247 4<u>3</u>195 neurorehabilitative solution mitigating aberrant plasticity 2248 44 2195 42 196 45 197 phenomena and facilitating positive neural changes. 2249 Finally, novel human-machine interfaces should consider 2250 2197 452198 42198 42209 42200 52201 2202neuroplasticity principles for restoring the efferences and 2251 afferences of the central nervous system with the lost limb 2252 in order to exploit them for connecting a prosthesis. 2253

The processes described above are an excellent 2254 5<u>7</u>202 expression of the technologies that can lead to a user-2255 -52203 prosthesis co-adaptation. They care for providing the 2256 53204 human with sensations matching the motor activity and the 2257 5**4**205 events occurring on or for the artificial limb, which needs 2258 5**2**206 to learn how to offer appropriate feedback to the user. Next 2259 52207 paragraphs will describe how this can happen. 2260 2261

Establishing interactions between user and prosthesis requires a human-centered design of the technology "behavior". Since the term co-adaptation implies that two or more entities are adjusting to each other, possibly learning through the interaction itself for reaching a goal that can be the improvement of the human-machine performance. The attention to the interactive aspects of learning and training was recommended in Castellini et al. (2016). In this context, intriguing opportunities come from theoretical frameworks in psychology like the constructivism to define and improve the paradigm of interactive ML in prosthetic training and control (Nowak et al., 2018, Bettoni and Castellini, 2021). Accordingly, a myocontrol system should learn and forget on demand, under request of each one of the components of the humanmachine system. For instance, the users can label the violation of their expectations on the prosthesis interpretation of their commands, starting a novel data collection cycle. Additionally, the machine itself can highlight the need of collecting further data (especially from correct execution of a training exercise) through acoustic feedback to the user. Through this, the myocontrol models are updated.

Moreover, certain biosignal features could guide an automated labeling of the violation of the observer's expectations without any explicit command, as in neuroprosthetic interfaces using Error-related Potentials (Chavarriaga et al., 2014). Such an advance (still explored in laboratories) could enable self-calibrating intention detection processes, leading to a true (and fruitful) humanmachine symbiosis. Such symbiosis is based on the online processing of users' neurocognitive states. The machine interprets such states for implicitly adjusting (without direct and declarative commands of the user) its activity to the individual current capabilities and preferences. Exploiting this process as a further example of the closedloop previously envisioned, the human-machine system will become a fully functional unit able to enact manual and bimanual biomimetic behaviors (Chavarriaga et al., 2014).

However, when the practical applications of this kind of implicit learning will move outside the laboratories, its advantages should be evaluated in real-world cases of prosthetic learning. Currently, a human-machine explicit communication component in initial co-training sessions can highlight an active role of the users with positive impact on their self-efficacy and engagement. In this context, biofeedback strategies (self-regulation of perceptually represented physiological changes) in coadaptive systems could be especially useful for easing the integration of both implicit and explicit aspects within the user-prosthesis co-training (even during daily recalibrations) (Kalampratsidou and Torres, 2017).

5**2**208 6.3.2. Innovation in Interactive Training

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32262	6.4. Amputation matters: the key role of the	2311
<sup>4</sup> 2263	surgeon	2312
5		2313
62264	A further reflection that emerges in order to maximize	2314
72265	patient acceptance is related to the clinical situation	2315
82266	immediately preceding amputation. In fact, although it is	
92267	clear that in case of injury/accident the doctor/surgeon has	2316
12268	to manage a situation of immediate danger in which the	0017
12269	priority is to secure the patient trying to save "as much as	2317
12270	possible of the injured limb", on the other hand, on the	2318
12271	engineer side, the ideal would be to be able to standardize	2319
1 <del>\$</del> 272	the level of amputation. In this case, in fact, it would be	2320
15273	possible to avoid "extreme" situations in terms of	2321
<sup>1</sup> <b>6</b> 274	amputation levels: a very distal amputation does not allow	2322
$1\overline{2}275$	the orthopedic technician, and therefore also the engineer.	2323
18276	to have enough space to integrate the circuitry and the	
19277	power system inside the cavity between the internal and	2324
20278	external lamination of the reservoir itself on the other	2325
27279	hand a very proximal amputation does not allow the	2325
$2\tilde{7}280$	orthonedic technician to create a socket canable of	2327
$2\frac{3}{7}\frac{200}{281}$	allowing the patient's stump to support the weight (thus not	2328
24201	anowing the patient's stump to support the weight (thus not	2329
25202	the electromy graphic signal) of the dedicated prosthetic	2222
26203	the electromyographic signal) of the dedicated prostience	2330
27/204	system. Therefore, having the possibility, even in case of	2331
28203	extreme danger, to be able to define a "standard" level of	2332
29280	amputation in which the surgeon is able to have a slightly	2333
30287	longer-term vision, would allow a greater number of	2334
34288	patients to take advantage of these fantastic biomedical	2335
32289	technologies. In fact, at present, many patients find	2336
33290	themselves having to request an additional surgical	2337
34291	operation, thus further compromising the patient's	2338
323292	willingness to use these solutions.	2339
36		2340
3 <b>2</b> 293	7. Conclusions	2341

204 In this manuscript, we have detailed and discussed 2342 several strategies to substitute and restore the functionality 2343 295 of human upper limb when missing. We specifically 2344 296 297 focused on input and feedback signals for bidirectional 2345 298device control and on aspects regarding the user needs that 2346 299 should be addressed with a user-centered prosthetic design 2347 approach. We also stressed that in order to have a fully 2348 **⊿2**300 embodied prosthetic system it is essential to implement a 2349 42301 components: 2350 of three 47302 synergistic collaboration 2351 42303 mechatronics, control algorithm and the user perception. 2352 **423**04 These have to be combined by a real rehabilitation process 50305 2353 that is necessarily user-centered. 2354

#### 52306 8. Conflict of Interest

The authors declare that the research was conducted in 2356307 the absence of any commercial or financial relationships 2357308 55-56<sup>3</sup>09 2358 that could be construed as a potential conflict of interest. 2359

#### <sup>57</sup> 58310 9. Author Contributions

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A.M., N.B., F.T., D.D.D., G.B., and M.S. conceived the study. N.B., A.M. and M.S. designed the figures. N.B. and A.M. prepared the figures. All the authors contributed to the writing, read and approved the final version of the manuscript.

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