Current Achievements and Future Directions of Hand Prostheses Controlled via Peripheral Nervous System

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Abstract The human hand is a powerful tool to feel and act on the environment and a very sophisticated means for physical and social interaction. This is why hand loss can be perceived as a devastating damage that changes people lifestyle. It causes a severe impairment for the amputees and can significantly alter their quality of life, since it affects personal and working fields by reducing the level of autonomy, the capability of performing activities of daily living (ADLs), and the capability to gesture and interact with other people. The upper-limb amputation involves almost 4000 people per year in Italy and about the 20% of amputations in USA. The relevance of the upper-limb loss in the international scenario motivates the flourishing research in the field of upper-limb prosthetics. This chapter intends to provide an overview on hand prostheses driven by non-invasive and invasive interfaces with the peripheral nervous system (PNS), taking into account technical aspects related to hand control, peripheral interfaces, and clinical features about the restoration of sensory feedback. The international scenario of off-the-shelf and on-the-shelf prosthetic hands is explored, and pros and cons of technologies are analyzed. This chapter is especially focused on the recent studies on the restoration

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of tactile perception in amputees through neural interfaces and first evidence on bidirectional hand control. Current achievements on this thorny topic are in-depth explained in this chapter and future directions are finally roughed out.

Keywords PNS-based prosthetic hand · Upper-limb prosthesis · Sensory feedback · Grasping · Manipulation

1 Introduction

The human hand is a powerful tool characterized by a complex mechanical structure and a sophisticated sensory system that enables dexterous grasping and manipulation tasks through a bidirectional communication with the brain. The hand loss causes the interruption of this communication and, consequently, severe impairments for the subjects may arise, regarding both motor control and sensory feedback. The subject's quality of life is altered for the personal as well as the working spheres; the capability to perform activities of daily living (ADLs) and interact with other people is significantly affected.

Worldwide, an estimated three million of people suffer from an arm or hand amputation (LeBlanc 2008). Approximately 3500 and 5200 upper-limb amputations are reported each year in Italy and in UK, respectively. The different levels of upper-limb loss have the following incidence on the total amputations: 16% transhumeral, 12% transradial, 2% forequarter, 3% shoulder disarticulation, 1% elbow disarticulation, 2% wrist disarticulation, 61% transcarpal, and 3% bilateral limb loss.

In the last 70 years, the advances in technological and surgical field have produced significant improvements in the upper-limb prosthetics. Hand design, control, and sensory feedback have been fostered to realize prostheses able to reproduce aesthetical as well as functional features of the lost limb, in order to meet prosthetic user needs (Cordella et al. 2016). However, despite the advances, today's upper-limb prostheses are still affected by relevant limitations: lack of an intuitive and reliable interface, lack of sensory feedback, noise produced by the actuators.

This chapter intends to critically review the state of the art on hand prostheses, by reporting main requirements coming from the analysis of users' needs and describing main recent technical and clinical achievements. This chapter is especially focused on the technologies enabling the restoration of tactile perception and bidirectional control in amputees and reports the latest human studies on hand control via neural interfaces.

This chapter is structured as follows: In Sect. 2, an overview of the users' needs is provided and main requirements for upper-limb prostheses are reported. Section 3 discusses off-the-shelf and on-the-shelf prosthetic hands and myoelectric control. In Sect. 4, peripheral neural interfaces for prosthesis control and afferent stimulation are introduced and compared. Section 5 provides an overview of recent human experiments on the restoration tactile sensing and bidirectional hand control. Finally, Sect. 6 draws the conclusions.

2 User Needs

Over the years, many attempts have been made to provide the amputees with a valid prosthetic substitute for the lost limb. Therefore, several studies have been devoted to identify (i) the type of activities that the prostheses can help perform (Van Lunteren et al. 1983); (ii) the reason why several amputees prefer not to use the prosthesis (Biddiss and Chau 2007; Peerdeman et al. 2011); and (iii) job-related problems before and after amputation (Wright et al. 1995). Table 1 summarizes main studies on user needs, accounting for user experience with myoelectric,

Table 1 Main studies focused on the analysis of user needs, considered population (in terms of type of prosthesis and level of limb loss), main questions shared among the studies and corresponding answers

Study	Type of prosthesis	Level of limb loss	Questions	Answers
Kyberd and Hill (2007)	60% C, 27% Myo, 13% other	58% Tr, 31% Th, 7% Sd	1	More natural appearance Improvements in movement and grip functions
Biddiss and Chau (2007)	BP, C, E	54% Tr, 21% Th, 7% Sd, 16% Wd, 15% Bi	1	Comfort, Function, Comfort
			2	Household maintenance Cooking, eating, dressing, personal hygiene, typing
Jang et al. (2011)	80.2% C, 1% Myo, 79.2% other	6.6%Sd, 20.5%Th, 48.4%Tr, 6.6%Wd, 17.9%Tc, 11% Bi	1	Cosmesis and comfort
			2	Cooking, eating, dressing, personal hygiene, typing
Pylatiuk et al. (2007)	Myo	76.9%Tr, 14.8%Th, 5.5% not specified	1	Sensory feedback
			2	Using cutlery
Østlie et al. (2012)	19.9% C, 34.2% Myo, 29.8% BP, 16,1% other	85% Tr, 15% Th	2	Cooking, eating, dressing, personal hygiene
Østlie et al. (x2012)	7% BP, 8% Myo, 25% both	71.2% Tr, 28.8% Sd and Th, 4% Bi	2	Eating, personal hygiene, employment and recreation
Lucchetti et al. (2015)	Myo	Tr	1	Functionality
			2	Eating and dressing

Legend:
Tr Transradial, *Th* Transhumeral, *Sd* Shoulder disarticulation, *Tc* Transcarpal, *Bi* Bilateral, *Wd* Wrist disarticulation, *BP* Body-powered, *E* Electric, *C* Cosmetic, *Myo* Myoelectric
Question 1 = Consumer design priorities
Question 2 = ADLs the subjects would like to perform

electric, body-powered, and passive upper-limb prostheses. Notwithstanding the high variability of the users' answers, a common set of needs and requirements can be identified (Cordella et al. 2016). They are listed below:

- To perform activities of daily living mainly related to eating, dressing, type writing, handling a cell phone, and opening the door (Kyberd and Hill 2007; Biddiss et al. 2007; Cloutier and Yang 2013). This entails that the prosthetic system needs to perform basic grasping actions (i.e., power, pinch, lateral, neutral, and pointing of the index finger) and simple manipulation tasks enabling the execution of activities of daily living (ADLs).
- To feel what is grasped or manipulated through sensory feedback.
- To perform actions in a more coordinated manner and with less visual attention. In particular, the use of a control system able to manage position and force exerted by the fingers on the objects can lighten the role of the visual feedback giving more importance to sensory feedback.
- To perform actions requiring fine force control.
- To change position and orientation of the grasped object, thus entailing capabilities of object manipulation; to move each finger independently, as in free manipulation; to improve the performance of thumb, index, and middle finger, in order to increase precision and efficient handling of small objects; and to provide the prosthetic hand with a wrist module, given the fundamental role played in ADLs.
- To wear prostheses with high level of anthropomorphism (in terms of size, weight, shape, color, and achievable grasping configurations) and with low motor noise.

Most of the required grasping and manipulation capabilities depend on the technical features of the multifingered prostheses and on the implemented control strategies that notably affect functionality.

Although several attempts have been done to provide the user with an intuitive and effective prosthesis control, the so far proposed solutions are not able to manage and properly combine basic hand movements to generate the desired complex motion. The literature is especially focused on intuitive control approaches, where the user's intention is extracted from peripheral signals through pattern recognition techniques (see Sect. 3).

On the other hand, upper-limb prosthesis users also express their necessity to feel and interact with the world through the prosthesis. This requires to provide the prosthetic hand with a tactile sensory system for the twofold purpose of performing a force control during grasping and returning force/tactile sensation to the user by means of peripheral interfaces on the afferent pathway. Over the years, different approaches have been proposed for eliciting tactile sensations (Antfolk et al. 2013; Schofield et al. 2014) as it will be detailed in Sect. 5.

3 Hand Prostheses and Myoelectric Control

Upper-limb prostheses can be classified into two main categories based on their functioning: passive and active prostheses (Fumero and Costantino 2001). Passive prostheses are in turn divided into cosmetic and functional ones; active prostheses include body-powered and externally powered prostheses, which are further classified into myoelectric and electric.

The most advanced commercially available myoelectric multifingered prosthetic hands are Touch Bionics i-Limb,[1] Ottobock Michelangelo[2] and RSL Steeper BeBionic[3] (Fig. 1). Table 2 summarizes the main characteristics of multifingered commercial and research hands. Further details about mechanical characteristics of anthropomorphic poliarticulated prostheses are available in Belter et al. (2013).

The commercial hands are able to provide different grip patterns but they are still characterized by a limited number of active Degrees of Freedom (DoFs) (5 at most) and do not provide the user with sensory feedback (Table 2). The research hands can guarantee a major number of active DoFs, applying lower force level respect to commercial prostheses. In both cases, the noise produced by the actuators during movements makes the prosthetic hands still far from fully addressing the users' needs (Clement et al. 2011). Moreover, all the myoelectric prostheses only use a position loop to control hand grasping, forcing the user to continuously look at the object for trying to regulate the grasping force, also for preventing object slippage. Therefore, the user requirement to control the grasping providing less visual attention is not fulfilled.

Providing a prosthetic device with reliable tactile information still represents a challenge in the robotic and prosthetic fields.

The subject intention of movement is extracted from muscular signals through EMG interfaces.

The on/off control is a simple and intuitive control modality allowing the activation of a defined prosthesis function when the EMG signals exceed a threshold. This modality requires many sites to extract the EMG signal, one for each function to control.

The agonist/antagonist myoelectric control (Popov 1965) is the most adopted solution for commercially available myoelectric prostheses, thanks to its simplicity and robustness (Jiang and Farina 2014). A couple of electrodes on agonist/antagonist muscles allows to associate to the contraction of one muscle the motion of opening and to the contraction of the other muscle the motion of closure, both with a constant speed (Popov 1965). The simultaneous contraction of both muscles permits to switch between different functions.

Proportional control (Fougner et al. 2012) allows to vary force and speed proportionally to the amplitude of the EMG signals recorded from a pair of

[1]http://www.touchbionics.com/.

[2]http://www.living-with-michelangelo.com/home/<.

[3]http://www.bebionic.com.

Fig. 1 Most advanced commercially available prosthetic hands

agonist/antagonist muscles. Hence, the voltage command for the motors is taken as proportional to the contraction intensity. Muscles co-contraction allows to select the degree of freedom to control.

In this control, only a limited number of DoFs can be independently controlled (far from the multifunctional control of the human hand) (Popov 1965). In particular, it is possible to perform a limited number of hand configurations, but it is not possible to move each finger independently (as it is desired by the users).

The commercially available myoelectric prostheses use classical myoelectric control with on/off or agonist/antagonist EMG control for selecting the DoF to be controlled.

In order to overcome these limitations, several alternative approaches can be found in the literature, such as ultrasound imaging (Gonzales and Castellini 2013), force myography (FMG) (Wininger et al. 2008), and, most importantly, pattern recognition techniques (Cloutier and Yang 2013) applied to EMG signals acquired through implantable (IMES Pasquina et al. 2015) or surface electrodes (Dohnalek et al. 2013). Most of them are still used only in the research field. Pattern recognition consists of the following steps (Fig. 2): (a) feature extraction in time or frequency domain (Cloutier and Yang 2013); (b) dimensionality reduction; and (c) classification. Pattern recognition classifiers can be grouped into linear classifiers, such as linear discriminant analysis (LDA) or perceptron or support vector machine (SVM), nonlinear classifiers, such as nonlinear logistic regression or SVM with nonlinear kernels, and multilayer perceptron or multilayer SVM (Ortiz-Catalan et al. 2014; Ciancio et al. 2016). Performance is affected by arm posture modifications, the complex nature of forearm muscles synergies, inherent cross talk in the surface signal, and displacement of the muscles during contraction. Furthermore, performance in the real context seems different from the laboratory settings (Li et al. 2012), thus limiting the clinical applicability of pattern recognition approach. The first commercial device based on pattern recognition and surface electrodes is the COAPT,[4] which appeared on the market is in January 2015.

[4]COAPT Complete control, 2014. Available: http://www.coaptengineering.com/.

Table 2 Characteristics of poliarticulated commercially available prosthetic hands (i-Limb, Bebionic and Michelangelo) and of research hands with application in prosthetics (Southampton, UB hand III, IH2 Azzurra) (Belter et al. 2013)

Hand and company name	i-Limb by Touch Bionics	Bebionic by RSL Steeper	Michelangelo by Ottobock	Southampton hand	UB hand III	IH2 Azzurra by Prensilia
Weight (g)	443–515	550–598	420	400	–	640
No of actuators	5 DC motors	5 DC motors	2 DC motors	6 DC Motors	20 DC motors	5 DC motors
Active DoFs	F/E of MCP joint of each finger and thumb opposition	F/E of MCP joint of each finger	F/E of all the fingers contemporarily and thumb opposition	F/E of MCP joint of each finger and thumb opposition	F/E of MCP, PIP and DIP of thumb, index abduction, and middle, index abthumb opposition, F/E of MCP and PIP of ring and little.	F/E of MCP joint of thumb, index, middle, ring (coupled with little) and thumb opposition
Joint coupling mechanism	Tendon linking MCP to PIP	Linkage spanning MCP to PIP	Cam design with links to all fingers	Worm wheels gears	Tendon driven mechanism	Tendon driven mechanism
Grasping configuration	Power, Precision, Lateral, Hook, Finger-point	Power, Precision, Lateral, hook, finger-point	Opposition, Lateral, Neutral Mode	Power, Precision, Lateral, Hook	Power, Precision, Lateral, Hook, Finger-point	Power, Precision, Lateral, Hook, Finger-point
Maximum applied force	100–136 N	140 N	70 N	Fingertip forces: 9 N	Tendon force: 70 N	35 N

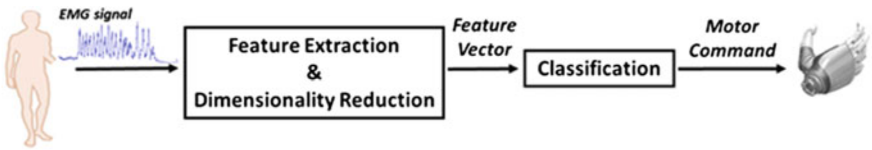

Fig. 2 Block scheme of a myoelectric hand control

In order to provide intuitive and stable myoelectric control, the adoption of IMES has been tested on transradial amputees (Pasquina et al. 2015) with very promising preliminary results (especially for robustness to limb position and environmental conditions). However, IMES cannot be employed when the sensing sites are very close each other, or when the target muscle is small or thin.

Notwithstanding the huge amount of research on myoelectric control, great effort is still required for improving hand control and interfaces, and move toward clinical translation of research results. Currently, active research challenges are related to (i) real-time, direct, robust, and simultaneous control of multiple DoFs in a natural and intuitive manner, (ii) bidirectional communication with the peripheral nervous system (PNS), and (iii) fast learning of hand control.

4 Neural Interfaces for Prosthesis Control and Afferent Stimulation

Electrodes can be used as interface between a technical system and biological tissue to record bioelectrical potentials or to stimulate electrically neuronal structures. They are transducers to transform current: ionic into electric or electric into ionic. Electrode design and material selection are based on factors such as access to and location of the application site and the application duration. The selectivity depends on the invasiveness and the size of electrode contacts (Navarro et al. 2005). Stiff and flexible electrode structures are used.

Structural or backbone materials of the electrodes are often polyimide, silicone, or silicon. Advantages of polyimide structures are the high flexibility and thinness (10–15 μm), the low density (1.42 g/cm^3), the water uptake (<0.5%), and the good biostability (>12 months). Electrode contact materials, the electrically active part of the electrode, are metals (e.g., gold, platinum), metal compounds (e.g., titanium nitride, iridium oxide), or intrinsically conductive polymers (e.g., PEDOT). All materials have to be biocompatible and longtime biostable. Stimulation electrodes should have a high charge injection capacity to transfer charge without causing chemical reactions. The stimulation has to be charge-balanced. Thereby the influence of redox reactions and corrosions is reduced, and the tissue can be protected (Neural Stimulation and 2008).

To evaluate the microfabricated electrodes, electrochemical, mechanical, optical, and biological characterizations are necessary. Preferred tests in addition to validation of biocompatibility are impedance spectroscopy as well as determination of charge injection capacity using pulse tests.

The final step is sterilization before the electrodes can be used in in vivo studies. ethylene oxide (ETO) sterilization allows the treatment of electrodes that are already packaged for shipment.

Bionic hand prostheses have to restore both motor and sensory functionalities. Therefore, the neural interface should achieve a bidirectional communication with afferent and efferent nerve fibers. The required selectivity could be realized with implantable microelectrodes. They are very invasive and are placed around (circumneural, e.g., cuff electrode, FINE), within (interfascicular e.g., shaft electrode or intrafascicular LIFE, TIMES, ds-FILE), and between (intraneural, e.g., sieve electrode) the nerves. Invasiveness and selectivity increase in referred order. They acquire bioelectrical activity from motor nerve fibers to control the hand prostheses as well as to stimulate the sensor fibers to realize a sensory feedback.

The feasibility with tf-LIFE (thin film—Longitudinal Intrafascicular Electrode) was shown by Rossini et al. (2010). The electrodes were placed in median nerves and ulnar nerves of an amputee. Individual fingers of the hand prostheses could be selectively moved. The electrical nerve stimulation evoked sensations. The sensory feedback with TIME (transverse intrafascicular multichannel electrode) allowed the discrimination between the shape and texture of different objects (Raspopovic et al. 2015). A comparative analysis of CUFF, tf-LIFE, and TIME shows that the threshold for muscle activation with TIME and tf-LIFE is significantly lower than with CUFF. The selectivity to activate muscles is higher for TIME compared with tf-LIFE (Badia et al. 2011). To increase the selectivity of CUFF electrodes and to decrease the stimulation thresholds, the shape of this electrode structure is flatten. The FINE (flat interface nerve electrode) is described by Tyler and Durand (2002).

A future-oriented development is the ds-FILE (double-sided filament electrode) (Poppendieck et al. 2015). In Figure 3), the design and details of the ds-FILE are shown. Table 3 gives an overview about three different intrafascicular electrode structures.

The papers (Navarro et al. 2007) and (Ciancio et al. 2016) give a good overview and critical review on interfaces with the PNS to control prosthetic hands.

Electrical nerve stimulation is a proven method to activate peripheral nerves. Sometimes, the electrode contacts are not in the optimal position for stimulation or recording. Microactuators embedded in the flexible electrode structures on the basis of shape memory alloys could change the electrode contact position and could improve the electrical connection to the nerve tissue (Bossi et al. 2007).

The use of electrodes includes also disadvantages. The invasive access and the positioning directly on or in the nerve depend on mechanical nerve manipulation. tf-LIFE, TIME, and ds-FILE penetrate the nerve. The electrode and electrical stimulation could change the ambient tissue. This could decrease the longtime stability. So, new stimulation techniques such as ultrasound, optogenetic, or biochemical

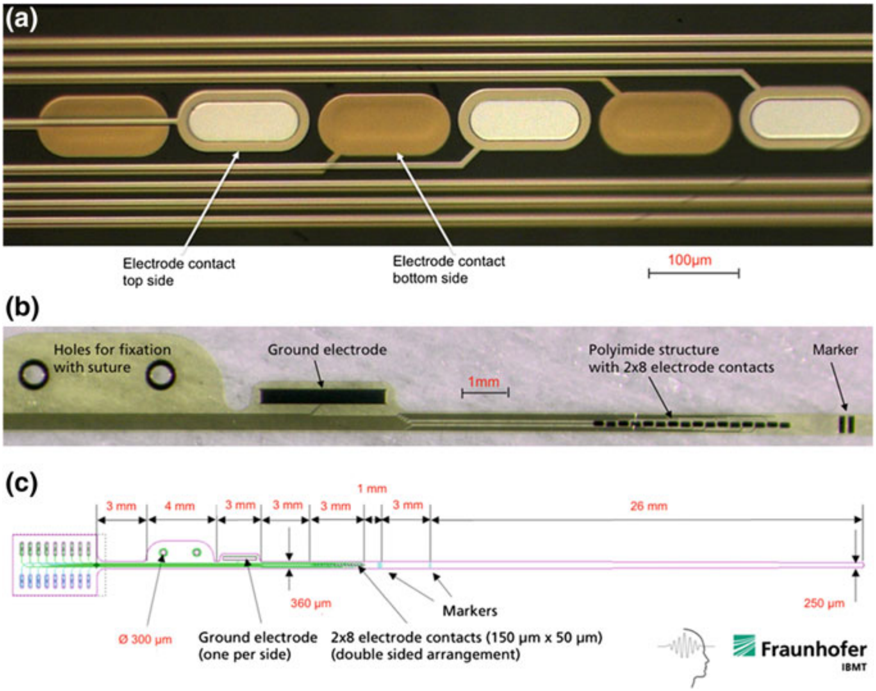

Fig. 3 Double-sided filament electrode (ds-FILE) for stimulation and re-cording **a** detail **b** polyimide structure **c** design

stimulation have to be developed to achieve a longtime stable stimulation. This will be an important step in restoring the sensor functionality of hand prosthesis.

5 Tactile Feedback and Neural Control of Upper-Limb Prostheses

A closed-loop control around the user (Antfolk et al. 2013) is characterized by a bidirectional communication between the user (mainly the PNS) and the prosthetic system (Fig. 4) via the following modules:

(1) The interface combines recording and stimulation capabilities and is responsible for the communication with the PNS through the efferent and afferent pathways (Sect. 4).
(2) The control system drives the prosthesis actuators on the basis of proprioceptive and tactile/force sensory information. User intention is decoded by the signals recorded on the efferent pathway by means of EMG or ENG interfaces and used to generate the control commands (Sect. 3).

Table 3 Comparison of different intrafascicular electrodes

	tf-LIFE	TIME	ds-FILE
Type	Thin film—Longitudinal Intrafascicular Electrode	Transverse Intrafascicular Multichannel Electrode	Double-sided filament electrode
Form	Loop, electrode contacts single sided	Loop, electrode contacts single sided	Single filament, electrode contacts double sided
Materials	Platinum on a sub layer of polyimide	Platinum and iridium oxide on a sub layer of polyimide	Microrough platinum on a sub layer of polyimide
Electrode contacts	8 electrode contacts	10 electrode contacts	16 electrode contacts
	2 ground contacts	2 ground contacts	2 ground contacts
Size of electrode contacts	40 μm × 100 μm	Ø 60 μm	50 μm × 150 μm
	4.000 μm^2	2.827 μm^2	7.500 μm^2
Implantation tool	Polyimide loop with needle	Polyimide loop with needle	Surgical needle directly connected to the polyimide filament
Application	Recording and stimulation	Recording and stimulation	Recording and stimulation
References	Micera et al. (2008), Benvenuto et al. (2010), Hoffmann and Micera (2011)	Boretius et al. (2010), Jensen et al. (2010), Badia et al. (2011)	Poppendieck et al. (2015)

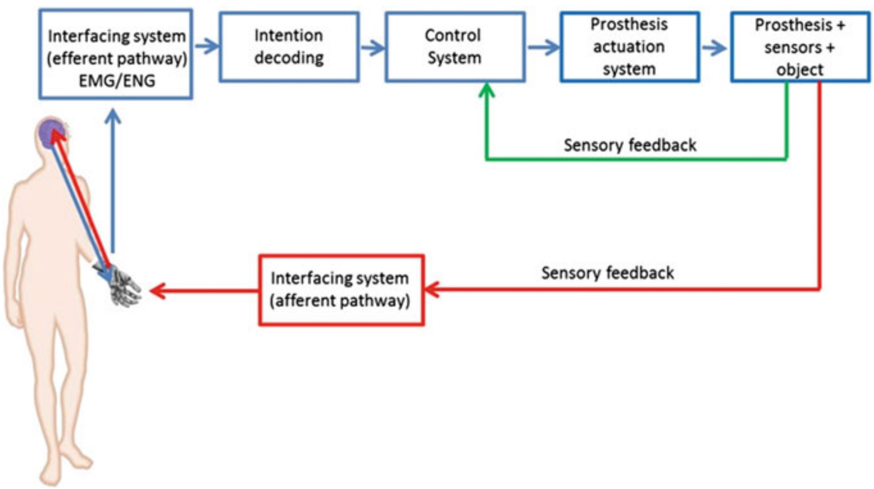

Fig. 4 Block scheme of the PNS-based control of a prosthetic system

(3) The sensory system returns the tactile feedback about the manipulated object to the control system and, also, to the amputee via the peripheral interface.

The restoration of sensory information regarding the interaction between prosthesis and environment (tactile perception, proprioception, pain, and temperature) (Farina and Aszmann 2014) is carried out through the afferent pathway. In (Childress 1980), three different afferent pathways were proposed, based on (i) visual or auditory feedback signals; (ii) somatic sensory signals, i.e., tactile, proprioception, and vibration; and (iii) feedback signals intrinsic to the prosthesis control system, which use information of the sensors embedded in the prosthesis for automatically adjusting the grasping force.

Somatic sensory signals can be generated through non-invasive or invasive interfacing techniques (Antfolk et al. 2013) (Schofield et al. 2014) such as vibrotactile, electrotactile, mechanotactile, targeted sensory reinnervation (TSR), and neural stimulation. Despite the recent interest in the literature, neural stimulation represents the most promising technique because it allows to exploit the physiological pathways of communication between the hand and the PNS.

Over the years, several studies have been performed in order to investigate the possibility of restoring sensory feedback in individuals with limb loss by means of peripheral nerve stimulation. Clippinger et al. (1974) performed one of the first experiments implanting an induction-powered radio receiver-pulse generator for motor stimulation of the median nerve of 15 patients. This study provided evidence on the possibility of restoring the pressure sensation applied to the grasped object.

In Dhillon and Horch (2005), it has been demonstrated the feasibility of performing a natural control of the prosthesis and returning a natural sensory feedback to the amputee in a closed-loop control by means of implantable peripheral interfaces. Implanted peripheral nerve electrodes were used to (i) elicit touch and movement sensations and (ii) record motor neuron activity usable as hand control signals, without exploring closed-loop, non-visual control of the prosthesis. More recent experimental studies (Rossini et al. 2010; Raspopovic et al. 2015; Ortiz-Catalan et al. 2014; Tan et al. 2014) have also shown that it is possible to restore the natural tactile sensory feedback through peripheral neural interfaces. Table 4 and Fig. 5 provide a brief overview of the aforementioned experimental studies and their results.

The work in Rossini et al. (2010) investigates the feasibility of (i) controlling a hand prosthesis by means of the neural signal directly extracted from median and ulnar nerves of an amputee; (ii) using afferent neural stimulation to elicit tactile sensory feedback. Four tf-LIFE4s (Hoffmann and Kock 2005) electrodes have been implanted, by means of a surgical intervention, two in median and two in ulnar nerves in a parallel way respect to the main nerve axis. Initially, motor output from efferent fibers has been recorded in order to control the prosthetic hand. The classification improved from 75 to 85% in two days. Subsequently, the experimenters stimulated afferent fibers to elicit sensation. The stimulation was artificially triggered by the experimenters without the use of sensors embedded in the prosthesis and the delivering of electrical current in the tf-LIFE4s electrodes allowed to

Table 4 Summary of results on neural implant studies for sensory feedback restoration

	Rossini et al. (2010)	Raspopovic et al. (2015)	Ortiz-Catalan et al. (2014)	Tan et al. (2014)
Number of subjects	1	1	1	2
Experimental period	4 weeks	4 weeks	Up to 16 months	Up to 24 months
Electrodes	tf-LIFEs (thin-film Longitudinally-implanted Intra Fascicular Electrodes)	TIMEs (transversal intrafascicular multichannel electrodes)	Cuff electrode (Ardiem Medical)	FINE (flat interface nerve electrodes)
				Cuff electrode (Ardiem Medical)
Number of electrodes	4	4	1	Subject 1: 2 FINEs, 1 cuff
				Subject 2: 2 FINEs
Nerves	Median and ulnar nerves	Median and ulnar nerves	Ulnar nerve	Subject 1: median and ulnar nerves
				Subject 2: median and radial nerves
Trains of pulses	Rectangular cathodal pulses	Rectangular cathodal pulses	Single active charge-balanced biphasic pulse	Square electrical pulses
Frequency	10–100 Hz	50 Hz	8–20 Hz	10–125 Hz
Current	10-100 μA	Maximum stimulation current: 240 μA (at 100 μs) for the index finger and 160 μA(at 50 μs) for the little finger	30–50 μA	1.1–2 mA
Pulse width	10–300 μs	–	–	24–60 μs
Charge	0.1–4 nC	Median nerve: 14–24 nC	100-180 μA	Subject 1: 40.7–95.5 nC
		Ulnar nerve: 4–8 nC		Subject 2: 95–141 nC
Elicited hand areas	Figure 6a	Figure 6b	Figure 6c	Figure 6d–e

(continued)

Table 4 (continued)

	Rossini et al. (2010)	Raspopovic et al. (2015)	Ortiz-Catalan et al. (2014)	Tan et al. (2014)
Grasping task	Power grip, pinch grip, little finger flexion	Palmar grasp, pinch grasp, ulnar grasp	Tripod grasp during arm oscillation, power grasp in different limb position	–

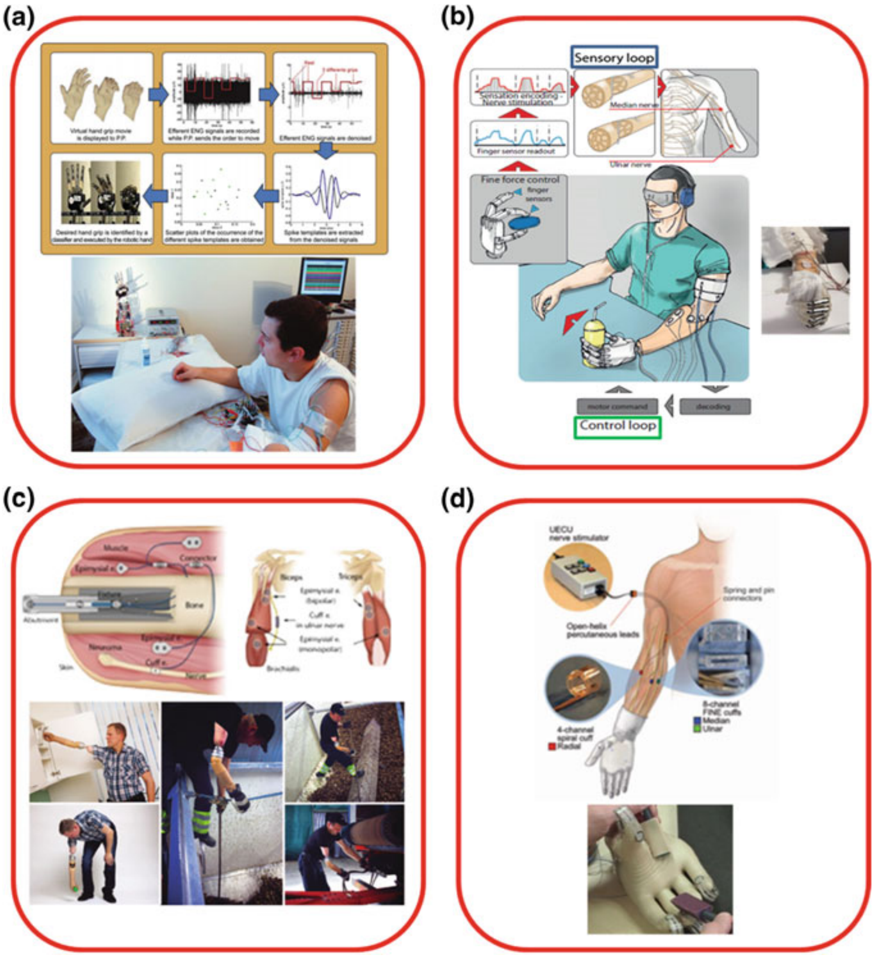

Fig. 5 Experimental studies on the restoration of the natural tactile sensory feedback stimulating the nerve in upper-limb amputees: **a** Rossini et al. (2010), **b**) Raspopovic et al. (2015), **c** Ortiz-Catalan et al. (2014), **d** Tan et al. (2014)

elicit sensations (parameters in Table 4). A mapping phase of the 32 electrodes allows identifying the elicited sensations on the afferent fibers (Rossini et al. 2010) (Fig. 6). Different contacts permitted to elicit different sensations. Moreover, the improvement of the phantom limb pain symptoms has been observed by means of McGill Pain Questionnaire (sfMcGill), Present Pain Intensity (PPI) and Visual Analogue Scale (VAS).

The work in (Raspopovic et al. 2015) reported the results of a surgical implant of four transversal intrafascicular multichannel electrodes (TIMEs, Boretius et al. 2010), two in median nerve and two in ulnar nerve, for the bidirectional control of the hand prosthesis. The control has been achieved by means of a myoelectric control of the prosthesis on the efferent pathway and a sensory loop that, reading the hand sensor readouts, was able to elicit tactile sensations on the afferent pathway.

In the first phase, a mapping of all contact sites allowed identifying all the possible elicitable sensations and the related territories. In the second phase, the closed-loop control around the user has been experimented by decoding the user intention. The Prensilia IH2 Azzurra hand provided with tension sensors on the tendons has been used during the experiments.

Figure 2b reports the hand areas elicited from the electrical stimulation of median and ulnar nerves. The amputee has been able to voluntarily control three levels of pressure exerted on the object with index and little fingers with a success

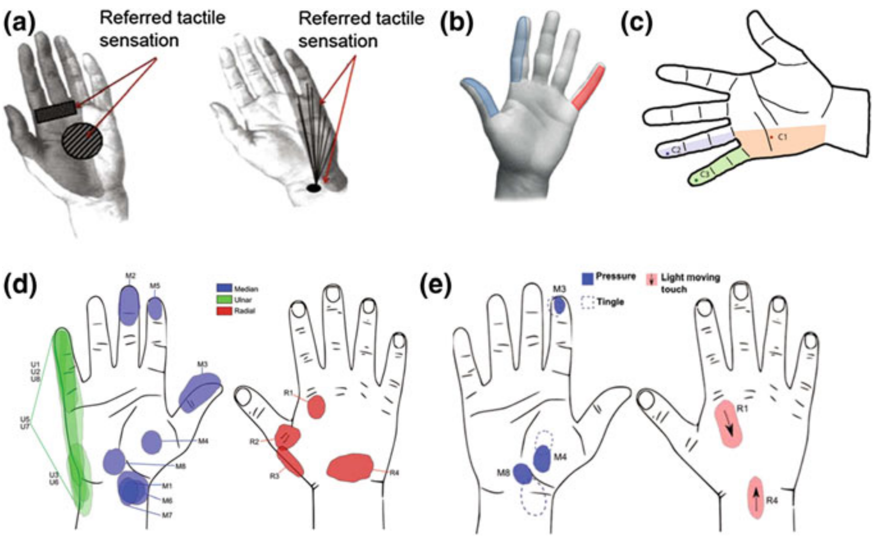

Fig. 6 **a** Perceived localization of sensation after median nerve tf-LIFE4 stimulation on left and after ulnar nerve tf-LIFE4 stimulation on right (Rossini et al. 2010); **b** Elicited hand areas in Raspopovic et al. (2015); **c** Tactile perception in Ortiz-Catalan et al. (2014). The *dark points* represent the electrode-specific projected field; **d** Sensation locations (Tan et al. 2014). The *letter* represents the nerve and the *number* represents the stimulus channel; **e** Pressure tactile perception on varying of impulse duration (Tan et al. 2014)

rate >90%. Moreover, the subject has been able to identify three object shapes with mean accuracy of 88% and three different consistency levels with performance of 78.7% (Raspopovic et al. 2015).

The study in Ortiz-Catalan et al. (2014) demonstrates the improvement of hand controllability using implanted EMG sensors and the feasibility of eliciting tactile sensations in chronic implants. One cuff electrode has been permanently implanted in the ulnar nerve of one patient with transhumeral amputation treated with an osteointegration procedure.

The controllability of the prosthesis has been improved and the time of usage of the robotic hand increased of 6 h per day respect to the use of superficial EMG sensors. The results achieved with the prosthetic hand are comparable with those obtained with the healthy hand. Eight different movements (hand opening/closing, wrist pronation/supination, wrist and elbow flexion/extension) have been performed with an accuracy of 94.3% ($\sigma = 1.6\%$).

The evolution of the phantom limb pain and the use of the prosthesis have been evaluated through the use of sfMcGill measuring a decrease of 40% in the phantom limb pain between two months before and 10–16 months after the implant.

Finally, the study in Tan et al. (2014) shows the feasibility of eliciting tactile sensations in a stable manner up to 24 months and demonstrates that the perceived sensations and the perceived areas can be modulated changing pulses parameters (Table 4).

Two subjects have been implanted with FINE (flat interface nerve electrodes) (Tyler and Durand 2003) cuffs or with CWRU (Case Western Reserve University) spiral electrode (1988). The first patient has been implanted with two FINE cuffs with eight contacts in median and ulnar nerves and one CWRU spiral electrode with four contacts in radial nerve, with totally 20 active sites. The second subject has been provided with totally 16 active sites: two FINE cuffs with eight contacts implanted in median and radial nerves.

The control of a prosthetic hand taking advantages from the sensory feedback has been investigated in (Schiefer et al. 2015). The EMG signals have been used to control the SensorHand Speed provided with FlexiForce sensors on thumb and index tips.

The impact of the sensory feedback on the prosthesis use has been assessed by means of three different functional tests. The first test aimed at evaluating the subject's ability to distinguish the position of a wooden block during index/thumb and middle/thumb pinch grip. The second test, a modified version of the box and blocks test, has been performed to verify if the amputee was able to locate and move a block. Finally, the amputee ability to perform ADLs (Schiefer et al. 2015) has been evaluated by means of the southampton hand assessment procedure (SHAP) applied with and without sensory feedback. Despite the SHAP score has been improved with sensory feedback, mainly during Power, Tip, and Lateral grasps, the assessment highlighted for both subjects a major focus on visual feedback than tactile feedback.

The analyzed studies provide an evidence of the possibility of using afferent neural stimulation to elicit sensory feedback and establish a bidirectional control with the user. Notwithstanding the reviewed studies have to be acknowledged for the contribution they have brought in the prosthetic field, a number of challenges still need to be faced by the future research studies. For instance, current prostheses do not fully exploit hardware potentiality they embed to perform complex grasping and fine manipulation tasks. More advanced solutions for sensorization and control of upper-limb prostheses should be developed. Moreover, performance of the prosthetic device is still too dependent on the interfacing system and its limitations. Finally, biostability and reliability of neural interfaces need to be further investigated for clinical translation of currently achieved preliminary scientific results and, possibly, less invasive solutions for the restoration of close-to-natural sensations need to be explored. Most of these challenges are faced in the currently active project PPR2—control of upper-limb prosthesis by invasive neural interfaces—involving the authors of this chapter and supported by Italian Institute for Insurance against Accidents at Work (INAIL).

6 Conclusions

This chapter has provided an overview of the main achievements and current trends in the field of upper-limb prostheses.

Requirements coming from the analysis of users' needs have been presented. They mainly regard the hand dexterity and sensory feedback and can be satisfied by working on the prosthesis control and the recovery of the bidirectional communication with the PNS through a closed-loop interface.

Hence, special attention has been devoted to the neural interfaces for prosthesis control and afferent stimulation and to the neural implants for the restoration of sensory feedback. This chapter also analyzes the most eminent human experiments on bidirectional hand prostheses that close the user in the control loop by means of neural interfaces.

Notwithstanding the encouraging results, current solutions are still far from being translated into clinical practice for a number of open issues regarding invasiveness, reliability, robustness, long-term stability. The deployment of the discussed solutions in the clinical practice mainly depends on the stability and reliability of the developed hardware and software solutions over long periods of time. This chapter reveals the necessity to improve hand control and the interfaces between the prosthesis and the human body in order to restore in a reliable and robust way the amputee sensation during interaction with environment and the way of exchanging sensory information between the environment and the user. Future challenges will be focused on (a) the increase of dexterity of currently available prosthetic hands, working on control and sensory system, (b) the improvement of tactile selectivity and discrimination capabilities by combining multimodal sensory system intraneural with peripheral interfaces, and (c) the development of biostable and biocompatible neural interfaces able to permanently restore the bidirectional communication with the PNS.

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