Thesis for the Degree of Licentiate of Engineering

Embedded Controller for Artificial Limbs

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Front Cover: The figure on the front cover is composed by an illustration of the Artificial Limb Controller (ALC) connected to a prosthetic arm and to the Osseointegrated Human-Machine Gateway (OHMG). It also includes a picture of the first OHMG patient grasping a delicate item while blinded.
ALC illustration and front cover graphics by Jason Millenaar and Sara Manca.

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Dedicated to the memories of my mother Rosanna (1960-2016) and my friend Luca (1986-2016).

Abstract

Promising developments are currently ongoing worldwide in the field of neuroprosthetics and artificial limb control. It is now possible to chronically connect a robotic limb to bone, nerves and muscles of a human being, and use the signals sourced from these connections to enable movements in the artificial limb. It is also possible to surgically redirect a nerve, deprived from its original target muscle due to amputation, to a new target in order to restore the original motor functionality. Intelligent signal processing algorithms can now utilize the bioelectric signals gathered from remaining muscles on the stump to decode the motor intention of the amputee, providing an intuitive control interface. Unfortunately for patients, clinical implementations still lag behind the advancements of research, and the conventional solutions for amputees remained basically unchanged since decades. More efforts are therefore needed from researchers to close the gap between scientific publications and hospital practices.

The ultimate focus of this thesis is set on the intuitive control of a prosthetic upper limb. It was developed an embedded system capable of prosthetic control via the processing of bioelectric signals and pattern recognition algorithms. It includes a neurostimulator to provide direct neural feedback modulated by sensory information from artificial sensors. The system was designed towards clinical implementation and its functionality was proven by amputee subjects in daily life. It also constitutes a research platform to monitor prosthesis usage and training, machine learning based control algorithms, and neural stimulation paradigms.

Preface

This thesis is a fulfillment for the degree of Licentiate of Engineering at Chalmers University of Technology within the context of the Author's industrial doctorate project.

The work resulting in this thesis was carried out between October 2014 and June 2017 between the Biomechatronics and Rehabilitation Laboratory within the Biomedical Signals and Systems Research Unit at the Department of Electrical Engineering of Chalmers, and Integrum AB, Mölndal.

Professor Bo Håkansson is the examiner. In addition, Assistant Professor Max Ortiz-Catalan and Associate Professor Sabine Reinfeldt are main supervisor and co-supervisor, respectively.

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Lastly, to Veronica. For being her and there, as always, still following and supporting my dreams, as always, and for coming in a country far away to rescue my mental health from a certain breakdown. Grazie Veno'.

List of Publications

This thesis is based on the work contained in the following appended papers:

Paper I
Mastinu, E., Ortiz-Catalan, M., and Håkansson, B., "Analog Front-Ends comparison in the way of a portable, low-power and low-cost EMG controller based on Pattern Recognition", *Proceedings of the 37th Annual International Conference of the IEEE Engineering in Medicine and Biology Society, August 25-29, 2015, Milano, Italy*, vol. 64, no. 4, pp. 2263–2269, 2016.

Paper II
Mastinu, E., Håkansson, B., and Ortiz-Catalan, M., "Low-cost, open source bioelectric signal acquisition system", *Proceedings of the 14th Annual International Conference on Wearable and Implantable Body Sensor Networks of the IEEE Engineering in Medicine and Biology Society, May 9-12, 2017, Eindhoven, Netherlands*, vol. 26, no. 4, pp. 261-263, 2017.

Paper III
Mastinu, E., Doguet, P., Botquin, Y., Håkansson, B., and Ortiz-Catalan, M., "Embedded System for Prosthetic Control Using Implanted Neuromuscular Interfaces Accessed Via an Osseointegrated Implant", *IEEE Transactions in Biomedical Circuits and Systems*, vol. 11, no. 4, pp. 867-877, 2017.

Paper IV
Mastinu, E., Ahlberg, J., Lendaro, E., Håkansson, B., and Ortiz-Catalan, M., "A novel approach to myoelectric pattern recognition for the control of hand prostheses: A case study of use in daily life by a dysmelia subject", Submitted to *IEEE Journal of Translational Engineering in Health and Medicine*, 2017.

Other related publications of the Author not included in this thesis:

- Mastinu, E., Ortiz-Catalan, M., and Håkansson, B., "Digital Controller for Artificial Limbs fed by Implanted Neuromuscular Interfaces via Osseointegration", *Proceedings of the 38th Annual International Conference of the IEEE Engineering in Medicine and Biology Society, August 16-20, 2016, Orlando, Florida, U.S.A.*, 2016.

- Mastinu, E., Håkansson, B., and Ortiz-Catalan, M., "Digital Controller for Artificial Limbs fed by Implanted Neuromuscular Interfaces via Osseointegration", *Proceedings of the Trent International Prosthetic Symposium, September 28-30, 2016, Glasgow, Scotland, U.K.*, 2016.

- Mastinu, E., Håkansson, B., and Ortiz-Catalan, M., "Embedded Controller for Pattern Recognition and Neural Stimulation via Osseointegration", *Proceedings of the 16th World Congress from the International Society for Prosthetics and Orthotics, May 8-11, 2017, Cape Town, South Africa*, 2017.

- Lendaro, E., Mastinu, E., Håkansson, B., and Ortiz-Catalan, M., "Real-time classification of non-weight bearing lower limb movements using EMG to facilitate phantom motor execution: engineering and case study application on phantom limb pain", Accepted for publication on *Journal of Frontiers in Neurology, section Neuroprosthetics*, 2017.

- Gusman, J., Mastinu, E., and Ortiz-Catalan, M., "Evaluation of Computer-Based Target Achievement Tests for Myoelectric Control" Submitted to *IEEE Journal of Translational Engineering in Health and Medicine*, 2017.

- Naber, A., Mastinu, E., and Ortiz-Catalan, M., "Stationary Wavelet Processing and Data Imputing in Myoelectric Pattern Recognition on a Low-Cost Embedded System", Manuscript ready for submission to *Journal of NeuroEngineering and Rehabilitation*, 2017.

Abbreviations and Acronyms

ALC	Artificial Limb Controller
DC	Direct Control
DoF	Degrees-of-Freedom
DSP	Digital Signal Processor
EMG	Electromyography
ENG	Electroneurography
IMES	Implantable Myoelectric Sensor
MCU	Microcontroller Unit
MPR	Myoelectric Pattern Recognition
OHMG	Osseointegrated Human-Machine Gateway
OPRA	Osseointegration Prostheses for the Rehabilitation of Amputees
FPGA	Field Programmable Gate Arrays
RPNI	Regenerative Peripheral Nerve Interface
TMR	Targeted Muscle Reinnervation
TSR	Targeted Sensory Reinnervation

Contents

Part I

Introductory Chapters

Chapter 1

Introduction

The human hand consists of 27 bones, 28 muscles, 3 major nerves, multiple tendons, as well as arteries, veins and soft tissue. It is an incredibly complex system with a huge spectrum of functionality. Hands are essential not only to interact with different objects daily, but also necessary for social interactions, such communication and arts. The loss of a hand is a terrific traumatic experience, usually followed by significant psychological and rehabilitation challenges. The interaction between engineering and science has, since a long time, been pointed towards the restauration of the functionality of a lost limb, and this thesis aims to contribute to such goal.

1.1 Scope and Structure of the Thesis

This Licentiate thesis is focused on the natural and intuitive control of an artificial limb to replace the lost functionality in cases of upper limb amputation. Electromyographic (EMG) (also defined as myoelectric) signals and their application for prosthetic control is an imperative background concept for this thesis.

Most of the efforts gathered in this thesis is a logic consequent step to a previous study where an Osseointegrated-Human-Machine-Interface (OHMG) was developed and implanted on a pilot subject [1]. The OHMG achieved a long-term interface to bone, muscles and nerves of a patient thanks to an osseointegrated titanium implant, epimysial and cuff electrodes, and bidirectional feedthrough mechanisms. Osseointegration creates a stable mechanical attachment of the prosthesis, while the implanted electrodes provide long-term stable access to bioelectric signal sources and sites for peripheral nerves stimulation. The work carried within this thesis should be seen, in part, as an answer to a particular demand: the need of an advanced electronic control system compatible with the OHMG, and capable of state-of-the-art processing algorithms, and of direct neural stimulation. Thereby, the focus was on the development and the validation of an embedded system needed to exploit the advantages of the

OHMG for closed-loop prosthetic control, meaning to concurrently enable intuitive motor control and sensory feedback. Moreover, it was shown that it can be used in combination with implanted electrodes (within the context of the OHMG) as well as with less invasive sensors (surface EMG electrodes). Lastly, in order to promote the research in the field, an open-source complete package (hardware and software) for advanced investigations into myoelectric prosthetic control was made available in the scientific community.

The first part of the thesis is structured as an introduction to the field providing the reader of some of the background knowledge needed for the attached articles. Chap. 2 presents the current conventional clinical solutions for prosthetic applications while Chap. 3 introduces the reader to some of the most advanced surgical techniques available today for amputees. Chap. 4 briefly points out the contraposition between the conventional control strategy for operating artificial upper limbs and the state-of-the-art strategy proposed lately by researchers (myoelectric pattern recognition), defined as capable of providing natural prosthetic control, and of which, some applications and examples are furtherly reported on Chap. 5. Chap. 6 collects some of the main challenges and achievements in matter of neural interfaces, while Chap. 7 describes the concept of closed-loop prosthetic control.

In the second part of this report, four scientific articles developed within the time of this thesis are included. A brief description of their contributions can be found in Chap. 8.

Chapter 2

Conventional Clinical Solutions

Despite the amount of research spent over the last decades in the field of prosthetics, the main solutions clinically available for patients remained basically unchanged in the last 40 years. In order to restore the functionality of a lost limb, two challenges need to be addressed: how to attach the prosthesis to the body, and how to functionally control the artificial limb. Suspended sockets are usually provided to patients to secure, by compression of the skin, the prosthetic extremity. The terminal devices can then be driven via either a system of cables (body-powered) or via bioelectric signal measured on the skin surface at the stump level (myoelectric), as shown from Fig. 2.2.

2.1 Suspended Sockets

The conventional method to attach prosthesis to the patient's stump is via a suspended socket. Sockets rely on mechanically compressing the tissue in the stump to secure the artificial limb. Therefore, skin contact and friction are essential elements for the attachment. The socket must be custom made according to the stump of each patient. There are several drawbacks related to the use of suspended sockets, major ones are listed in the following:

- skin irritation or inflammation
- poor fit and mechanical reliability
- limited range of motion
- limitations in use due to environment temperature conditions
- sweating causing unpleasant smelling.

Depending on the patient and his/her level of physical activity, these problems can escalate from an uncomfortable situation to a point where they can actually prevent the patient to wear the prosthesis. Today, suspended sockets are widely identified as one of the major source of issues for amputees all over the world.

2.2 Body-Powered Prostheses

The concept of an upper limb prosthesis driven by remaining parts of the body was pioneered in Germany at the beginning of the 19th century. This device represents the first documented example of a so called ”body-powered” prosthesis. It relied on trunk movements transferred from a shoulder girdle to a terminal device through leather straps (Fig. 2.2, left). Since then, the biggest technologic improvement for body-powered prostheses came in 1948, when the first device using a Bowden cable was introduced. The body-powered prostheses available today are essentially optimizations of that design [2].

Regardless the simplicity of their design and the not-anthropomorphic appearance (most commonly a two-pronged hook), body-powered prostheses are still widely diffused in the amputees' community [3]. This longevous success is due to their high value for money. They are lightweight, robust and require relatively simple maintenance; a skilled user can achieve an impressive range of functional motions, moreover, to some extent force discrimination and proprioperception is inherently possible by sensing the cable tension.

In 2016, the first edition of the Cybathlon was held in Switzerland (Fig. 2.1), meant as an Olympic-inspired competition for people with disabilities exploiting assistive technologies. Interestingly, the upper limb prosthesis category was won by a body-powered user. Even though this event was mostly meant as a competition for robotic devices, the commitment to this event of the winning team was actually to proof the still superior efficacy of body-powered prostheses compared to state-of-the-art advanced robotic devices.

2.3 Myoelectric Prostheses

The mechanical effort to maneuver a body-powered prosthesis can often be fatiguing. Electrically-powered artificial limbs try to solve this by actuating motors through an electronic control system (Fig. 2.2, right). These devices, commonly defined as myoelectric prostheses, are based on the utilization of electrical activity measured at the stump from the remaining muscles (myoelectric signals), which is triggered by the user to drive the prosthesis. Myoelectric prostheses were firstly proposed in the first half of the 20th century. Some early studies were carried out by De Luca *et al.* (starting from the 1970's) about the scientific definition of neuromuscular signals

Figure 2.1: Medal ceremony of Cybathlon 2016 - ARM category (image from Cybathlon webpage). A body-powered prosthesis user won, followed by a myoelectric user operating one of the most advanced terminal devices, followed by the OHMG user operating a standard myoelectric device.

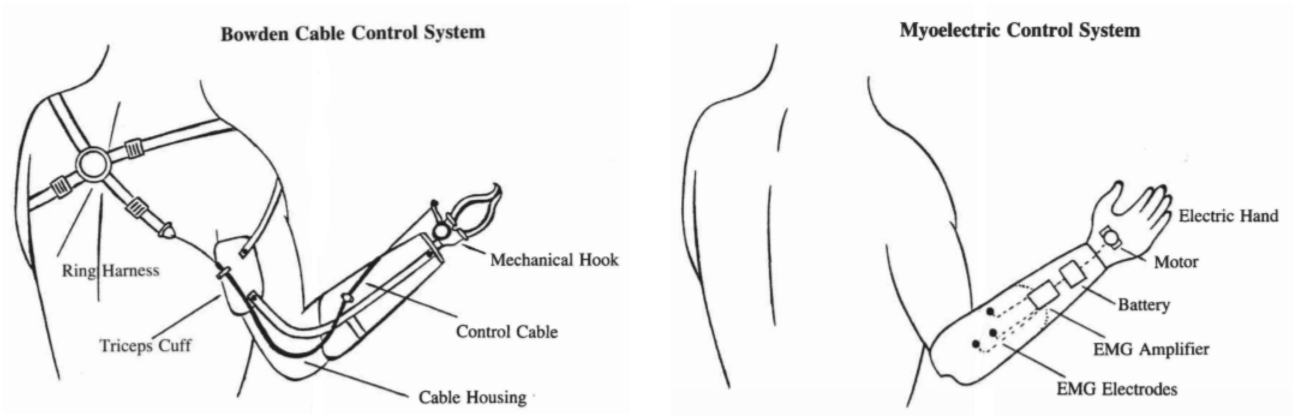

Figure 2.2: Representation of two typical solutions for below-elbow prosthesis [5]. Left) Body-powered Bowden cable prosthesis controlled by "gross" movements of the body. Right) Myoelectric prosthesis controlled by electomyographic (EMG) signal captured from residual muscles at the stump.

and the challenges behind their use for prosthetic control [4]. Indeed, due to critical technology limitations, myoelectric prostheses became a clinically valid solution only around the 1980's [2]. Since then, the technology has remained essentially the same.

Source electrodes are commonly non-invasive and placed over the skin surface of two groups of antagonist muscles. Proportional control is allowed by varying the intensity of the muscles' activity. Besides some "incidental clues" like noise or vibrations from electric motors, sensory feedback is still not part of a standard myoelectric device prescription and therefore, visual feedback is constantly required to properly operate these devices. Most commonly, their aesthetics is superior of any body-powered prosthesis; the mechanics can be hidden under life-like hand silicone gloves available in different skin tonalities. The primary disadvantages of this type of prostheses are currently their cost and weight, but fragility and maintenance are also major concerns.

The biggest breakthrough of myoelectric terminal devices is represented by the advent of multi-functional robotic hands. Manufacturers started recently to equip their robotic terminal devices with microprocessors which allow for more complex functioning. Hand with multiple grips or postures are now an option on the market. Each pre-defined position can be reached by triggering some pre-defined pattern of EMG activity, e.g., a series of triple impulses on the "open hand" control signal. These gestures are meant to facilitate the user manipulation of items through functioning fingers.

Chapter 3

Advanced Surgical Techniques

Considering the relative low efficacy of standard clinical solutions and their major limitations, alternative approaches have been suggested over the years from researchers, typically, involving a surgical procedure. The outcomes of a modern hand transplants surely identify it as one of the most promising and intriguing techniques. Alternatively, amputated nerves can be now redirected to new target muscles for both control and sensorial purposes. Osseointegration allows for direct skeletal anchorage of the prosthesis, its popularity is growing fast and it is often recognized as the future in the prosthetic field.

3.1 Targeted Muscle Reinnervation and Targeted Sensory Reinnervation

There are precise technology challenges regarding the recording of activity from the peripheral nervous system. Neural action potentials have characteristic amplitude of few micro volts and their direct use for prosthetic control imposes hard technological requirements. Due to amputation, some nerves are deprived of their original target muscle. In 1980, Hoffer and Loeb suggested a novel surgical technique to naturally amplify neural signals via reinnervating a cut nerve on a new target muscle, namely Targeted Muscle Reinnevation (TMR). After the reinnervation process settles, it is possible to use these new sites for prosthetic control via EMG acquisition from the surface of the skin. This idea, represented in Fig. 3.1, had its first clinical implementation in 2004 thanks to Kuiken *et al.*, where TMR allowed a bilateral shoulder articulation patient the control of a 3 Degrees-of-Freedom (DoF) prosthesis [6]. The TMR technique was more formally assessed by Kuiken *et al.* in 2009, where residual arm nerves where successfully transferred to alternative muscle sites in five patients and their ability in controlling a virtual prosthetic limb was measured, together with experimentations over multiple-DoF prostheses [7].

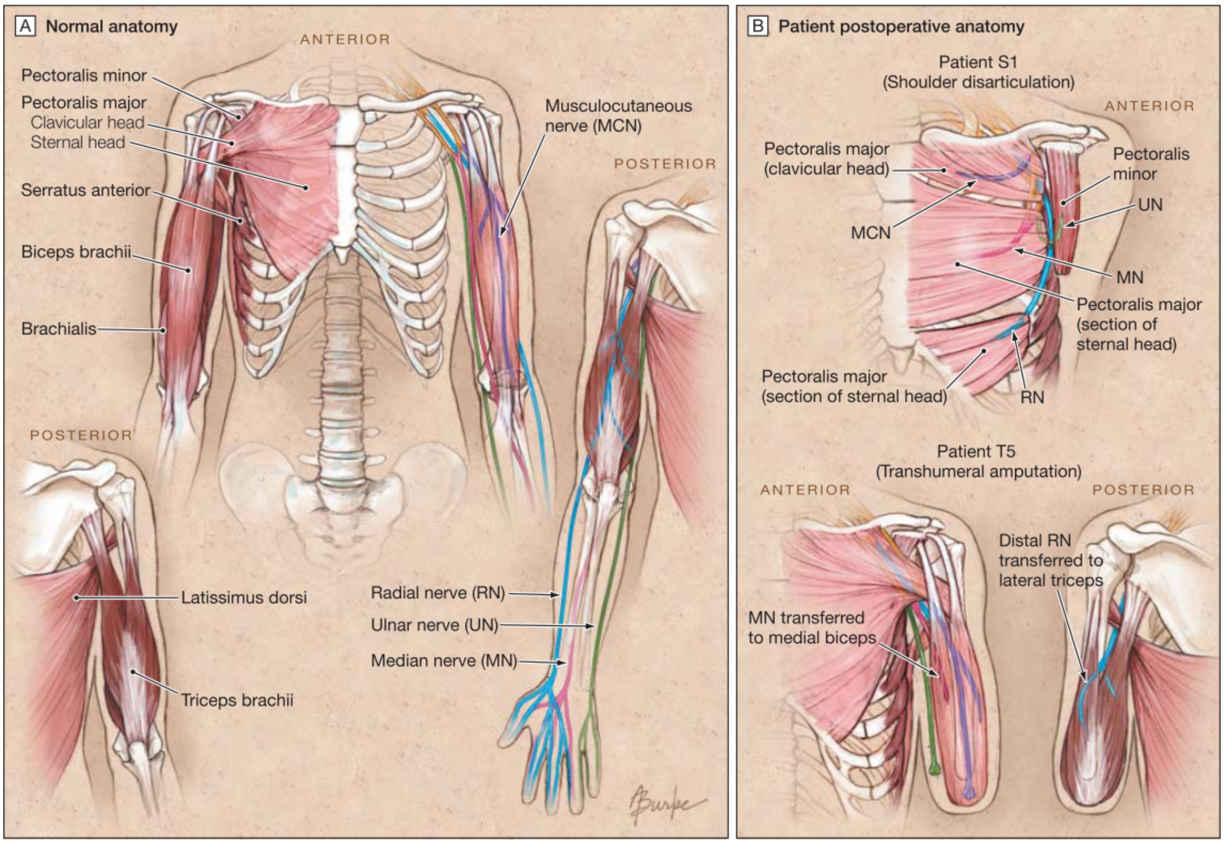

Figure 3.1: Representation of Targeted Muscle Reinnervation from Kuiken *et al.* [7].

It has been estimated that over 60 patients have been treated with this procedure since 2002.

An unexpected outcome of the first TMR patients was a sensory recovery on the preceptors of the skin overlaying the reinnervation sites. This was further investigated by extending the TMR to reinnervate sensory nerves to the main peripheral nerve trunk, developing a new surgical procedure defined as Fascicular Targeted Sensory Reinnervation (TSR). The idea is to create a discrete spatial sensory hand map on a skin area relatively distant from the prosthesis. Early results on a single patient showed the effectiveness of the TSR to recover pressure sensation discrimination on amputees [8].

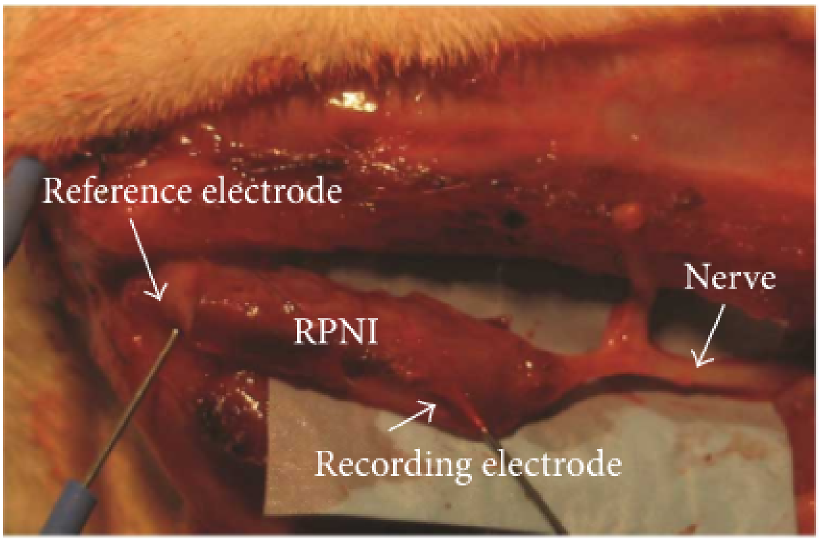

Figure 3.2: Representation of Regenerative Peripheral Nerve Interface (image from [10]). Small portions of muscles can be transplanted to serve as a target for nerves deprived of a functional target muscle after amputation.

3.2 Regenerative Peripheral Nerve Interface

The TMR technique has been further improved in the so called Regenerative Peripheral Nerve Interface (RPNI) [9, 10]. Here, small portions of muscles can be transplanted to serve as a target for nerves deprived of a functional target muscle after amputation (Fig. 3.2). Multiple transplants can be executed on the same patient to create a matrix that can be further used for EMG acquisition and prosthetic control. Due to the small portion of muscle transplanted, this technique imposes the use of implanted electrodes for EMG acquisition for a reliable control of the prosthesis [11]. The RPNI has been tested successfully on both animal models and humans as a treatment for post-amputation neuroma pain.

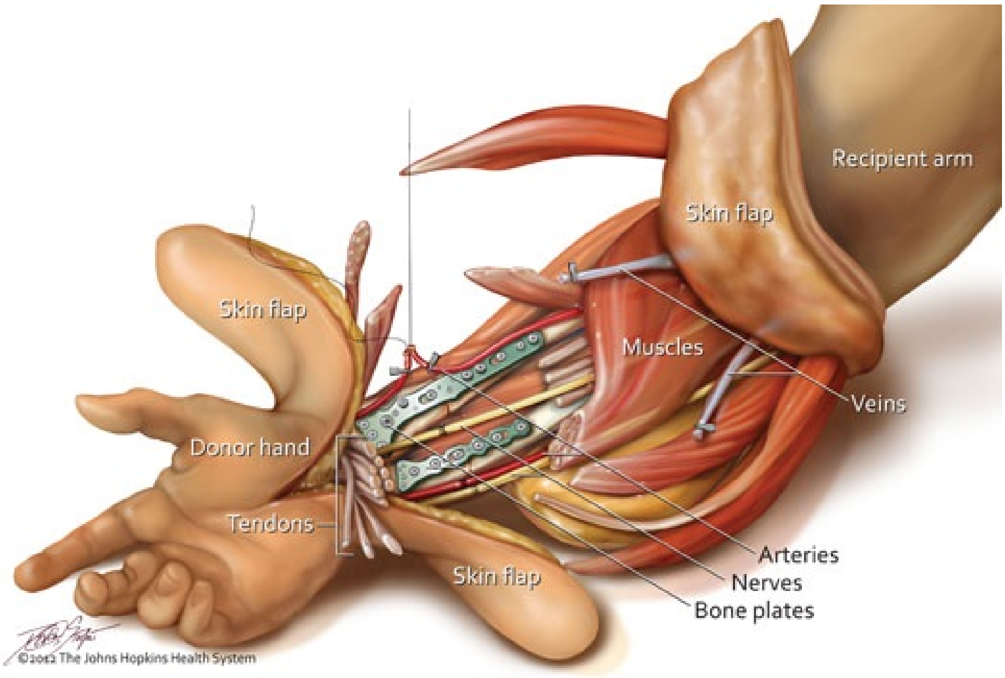

Figure 3.3: Representation of a hand transplantation (image from John Hopkins Medicine University, Comprehensive Transplant Center webpage).

3.3 Transplantation

Hand and upper limb transplantation represents certainly one of the most fascinating ways to restore the cosmesis and functionality of the lost peripheral limb. It is a complex surgical procedure which aims to transfer a hand (or a full forearm) from a donor to a recipient. The surgery can last from 8 to 12 hours and it involves bone fixation, reattachment of arteries, veins, tendons, nerves and skin (Fig. 3.3). It is followed by a heavy immunosuppression medication and a tedious rehabilitation procedure, which results can strongly vary from a patient to another. That is why patient selection is widely considered the most important aspect of the transplant technique, where a special emphasis on medical, behavioral, psychological, social factors, as adherence to immunologic and rehabilitative therapy is mandatory to achieve optimal outcomes [12].

Several failures are associated with the first reported attempts of this surgery, mostly due to primitive and insufficient immunosuppression medications and rehabilitation post-transplantation. This technique is not considered experimental anymore: its improvement in the quality of life is heavily recognized thanks to the modern outcomes in the matter of functionality and survival time (longest-lasting period of 16 years, [12]).

3.4 Osseointegration

Bone-anchored prostheses are a solution to the drawbacks related to coupling artificial limbs via suspended sockets (described in Section 2.1) which is the conventional way of attaching limb prostheses. Bone-anchored prostheses allow for direct transfer of external loads from the artificial limb to the skeleton, eliminating the need of a suspended socket. Direct skeletal attachment of the prosthesis is currently pursued thanks to the concept of osseointegration. Osseointegration was defined as ”close adherence of living bone tissue to an implant surface without intervening soft tissue, thus allowing for a structural functional connection between a load bearing implant and the bone tissue” [13]. A strong structural connection between living bone tissue and a foreign material is thus possible, provided the biocompatibility of that material. It was discovered in the early 1960's by Dr. P. I. Brånemark in Gothenburg, Sweden, and now it is a world-wide consolidated clinical practice for dental implants. Its application for artificial limb attachment started in the 1990's with titanium custom made implants that consequently led to the establishment of the Osseointegration Prostheses for the Rehabilitation of Amputees (OPRA) Implant System (Integrum AB, Mölndal, Sweden). The OPRA (Fig. 3.4) is based on the implantation of a titanium externally-threaded cylindrical platform (fixture) into bone tissue in the stump. Another titanium unit (abutment) is then fixated (press-fit) into the fixture extending percutaneously from the residual limb and allowing for attachment of an external prosthesis. A third element (abutment screw) is then used to clamp and secure the abutment to the fixture. The OPRA Implant System was initially meant for lower limbs amputation, but it was shortly after applied to upper limb as well.

Other typologies of implants and anchoring technologies have been proposed around the world and are currently available, or under development, or under clinical validation. Some examples are:

- Integral Leg Prosthesis (ILP), Orthodynamics GMbH, Lübeck, Germany
- Osseointegrated Prosthetic Limb (OPL), Permedica s.p.a., Milan, Italy
- Intraosseous Transcutaneous Amputation Prosthesis, Stanmore Implants Worldwide (ITAP), Watford, United Kingdom
- Keep Walking Advanced, Tequir S.L., Valencia, Spain
- Percutaneous Osseointegrated Prosthesis (POP), DJO Global, Austin, USA
- COMPRESS, Zimmer Biomet, Warzaw, USA

A wide collection of scientific publications (mostly regarding the first Swedish system) is validating the improvement of the quality of life for bone-anchored amputees [14, 15]. Additional benefits of direct skeletal attachment of prosthetic limbs include:

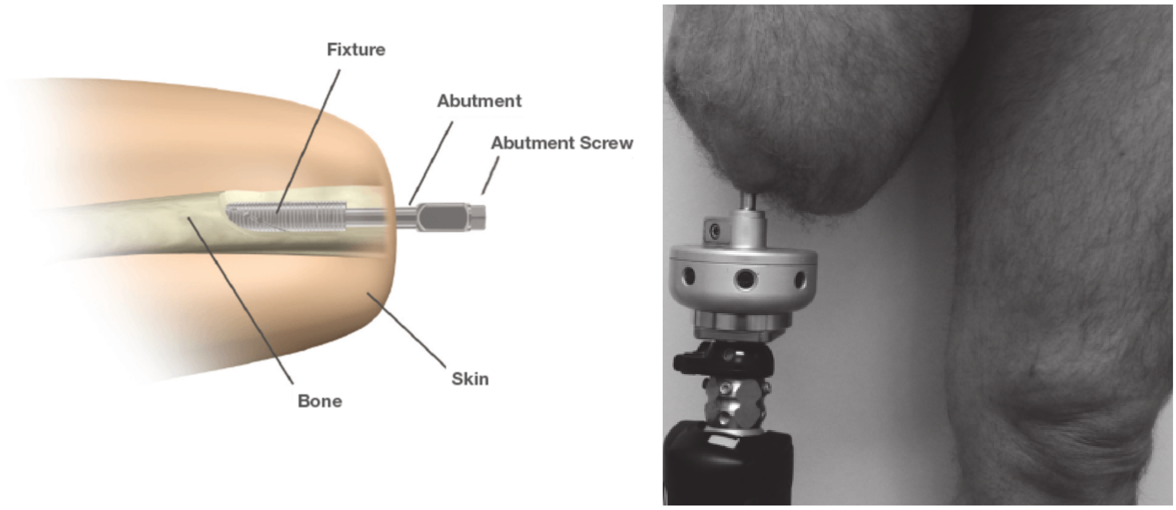

Figure 3.4: The OPRA Implant System. Left) Schematic of the implant (image from Integrum AB webpage). The OPRA implies the implantation of a titanium platform (fixture) into bone tissue in the stump. Another titanium unit (abutment) is then fixated into the fixture and extends percutaneously, while a third element (abutment screw) is then used to clamp the abutment to the fixture. Right) Clinical photograph showing a patient with the osseointegrated implant attached to an external prosthesis [16].

- improved range of motion (for both upper and lower limbs)
- improved walking ability and reduced energy expenditure
- improved comfort during sitting position
- improved awareness via osseoperception.

Osseointegration, like any other surgical procedure, implies risks. Superficial infections can arise at the percutaneous interface, requiring an antibiotics treatment. Deeper infections are rare but, if not promptly treated, can led to the implant removal [16, 17].

The commercial interest in this technology is growing fast as well as the list of countries where the treatment is available. Moreover, the FDA of U.S.A. recently approved the first bone-anchored implant (OPRA Implant System) and surgical procedure, and the U.S. Army has started a clinical trial, where lower limb amputees are treated with this system.

Chapter 4

Control Strategies for Myoelectric Prostheses

Despite the advances in prosthetic hardware that allow an increasing number of artificial joints to approach those of the lost limb (Modular Prosthetic Limb, [18], DEKA arm, [19]), a major issue remains unsolved, namely, how to achieve a reliable and natural control of the prosthetic limb. After decades of research and development on upper limb myoelectric prosthetics, current clinical applications for amputees still rely on a 30-years-old strategy for control, namely direct control (DC) [20].

4.1 Direct Control

Direct Control, also known as one-for-one or one-muscle-to-one-function, implies the utilization of rectified myoelectric signal from two groups of antagonist muscles (e.g., biceps and triceps for above elbow amputation, flexors and extensors for below elbow) to trigger the terminal prosthetic device (Fig. 4.1). For instance, hand open and close can then be driven via a set of two complementary movements (e.g., elbow flex and extend for above elbow amputation, wrist flex and extend for below elbow). Proportional control, defined as speed-controllable movements, is then achieved by modulating the intensity of the electrical activity measured at the stump: a strong contraction will be interpreted and converted as a fast prosthetic activation of that particular movement. For cases in which limited control sites are available, a configuration of one-muscle-to-two-functions is also possible, by matching different activation thresholds to different prosthetic movements (e.g., a weak and a strong elbow flexion for hand open and close). Adaptation is usually required to get the user familiar with the new set of muscles-contraction and expected-limb-movement. The DC approach is pervasive mostly owing to its simplicity, relative good reliability, and ease to learn. Unfortunately, the functional outcome is commonly related to the specific patient predisposition, thus often resulting in rejection of the myoelectric prosthesis,

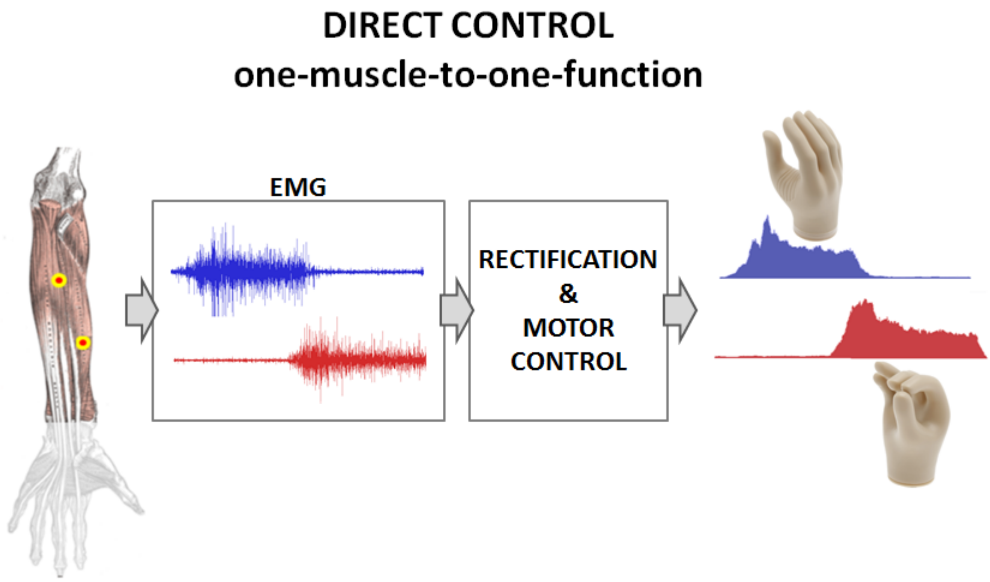

Figure 4.1: Representation of Direct Control strategy for myoelectric prostheses. It implies the utilization of rectified myoelectric signal from two groups of antagonist muscles (e.g., flexors and extensors for below elbow amputation) to trigger the terminal prosthetic device.

or in reduction of the robotic potential (independent fingers control, wrist rotation, elbow joint angulation) to a simple prosthetic claw [21]. Different variations of the standard DC approach are available nowadays to provide more controllable DoF, but unfortunately, always with a cost of improved complexity and reduced intuitiveness of the control interface.

4.2 Myoelectric Pattern Recognition

Around the mid-1960's the field of neural prosthetics started to involve computer intelligence for improving the control experience for the user (and to reduce the training burden) [22]. The need of a more natural control interface met the growing potential of pattern recognition algorithms. Pattern recognition (namely also machine learning) is an umbrella term which covers a variety of algorithms, ranging from statistical to biologically inspired, which have in common the same task: identify patterns or regularities in data and consequently recognize them when a new sample of data is presented. These algorithms are usually defined as supervised, when the decision regarding new data is made in reference to analogous pre-labeled data used as a training set, or unsupervised, when no pre-labeled data is available. Moreover, we differentiate between classification and regression problems, when the decision of the algorithm has the form of a class (or a label), or continuous values, respectively.

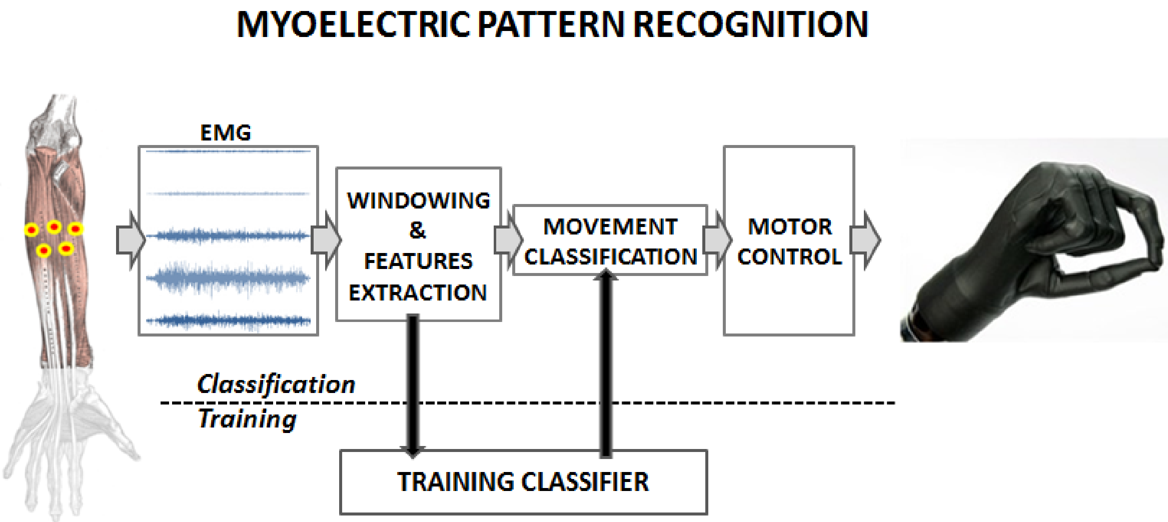

Figure 4.2: Representation of myoelectric pattern recognition strategy for a classification problem. The acquired EMG signals are windowed and a proper set of features is then extracted to reduce the dimensionality of the problem. These features are feed the classifier, which was previously trained with analogous data (supervised learning), to classify the motor intention of the user.

Natural control is defined in this context as the ability of providing control of the prosthesis in the same way as an intact physiological system would do, thus intuitive and spontaneous movements of the phantom arm are properly translated to the artificial limb. This approach is often defined as myoelectric pattern recognition (MPR), meaning machine learning applied for motor volition prediction using the EMG as input signal. Single-muscle targeting is not necessary for MPR, but instead multiple channels are spread over the stump to gather as much useful information needed to characterize (and thus differentiate) each movement.

The first investigations of MPR started in the mid-1960's at the Rehabilitation Engineering Center of Philadelphia, and a complete report was published later by Wirta *et al.* [22] (Fig. 5.1). A multivariate statistical program was used to classify four movements fed with myoelectric signal previously recorded from six surface EMG sites from an able-bodied subject. Shortly after in 1973, Herberts *et al.*, reported MPR applied for the simultaneous control of a three DoF prosthesis [23]. The Discriminant Analysis in linear configuration (LDA) was deemed as the classification algorithm and currently, it is still one of the most renowned tools for MPR researchers. It was also in those same years (mid-1970's), that MPR researchers started to realize that targeting the muscles was not necessarily the optimal electrodes configuration anymore, but instead it was more convenient to find other configurations able to exploit the most of the information available on the stump (e.g., electrodes in between muscles [24]).

MPR became slowly more and more popular among the prosthetic research field because of its appealing potential [25,26]. Generally, all major promising algorithms developed over the years in the machine learning field were exploited by researchers for prosthetic MPR applications. Some examples are:

- Neural Network,
- Support Vector Machine,
- K-Nearest Neighbor,
- Gaussian Mixture Model.

More recently, modern deep learning algorithms started to be used and evaluated for prosthetic control purposes [27,28].

Even though MPR represents today the state-of-the-art for prosthetic control interface, its clinical implementation is still far from being a concrete reality for amputees. Up to date, there is only one commercially available MPR system, namely Complete Control from COAPT (Chicago, Illinois, U.S.A.), and although clinical investigations are ongoing, no results have been made publicly available in the scientific community. A still high rejection rate appears to be towards this technology, from both patients and clinicians. Potential reasons for the slow take off of MPR are due to well-known difficulties related to multiple channels surface EMG acquisition. Issues such as motion artifacts, electromagnetic interferences, frequent changes at the interface skin-electrode, socket manufacturing cost, contribute to make MPR still unpractical for wide dissemination.

Chapter 5

Upper Limb Myoelectric Pattern Recognition Systems

The first MPR embedded system for the control of a prosthetic arm was developed in the mid-1960's and it was a simple weighted network of resistors (Fig. 5.1) [22]. For the first time, a MPR system was able to recognize different movements taking as input EMG activity recorded simultaneously from different channels. More precisely, it was fed by six EMG sites and capable of predicting four movements with reported accuracy around 90%. Shortly after, Herberts *et al.*, reported a similar pure-analogic MPR system applied for the simultaneous control of a three DoF prosthesis [23]. The battery-powered portable system was able to drive the robotic arm for hand prehension, wrist rotation and elbow flexion/extension and tested on an above-elbow amputee.

Opposed to portable systems, computer-based MPR systems started to appear in the literature around the 1980 [29]. Computer-based platforms were, and still remains, a very prolific source for literature studies, used as a test-bench for MPR algorithms and control performance [7, 30, 31], but also for "serious gaming", training and rehabilitation purposes [32], and for phantom limb pain reduction [33].

The advent of microprocessors and of microcontroller units (MCU) was a crucial breakthrough towards any modern portable and wearable device, and this includes prosthetic controller as well. The first attempt of a MCU-based MPR system is dated 1977, included in a work published from Graupe *et al.* [24]. It relied on one of the first MCU, the 8080 from Intel (Santa Clara, California, U.S.A.), for real time autoregressive analysis of EMG signal to classify motions and to properly actuate a robotic device. The reported classification accuracy was between 85% and 95%. The interest on MPR prosthetic control systems grew constantly and developing in parallel with the computation capabilities of new emerging processing units. An interesting discussion was carried out by Xiao *et al.* about the advantages of having a GPU core for MPR prosthetic applications [34]. Approaches using Field-Programmable Gate

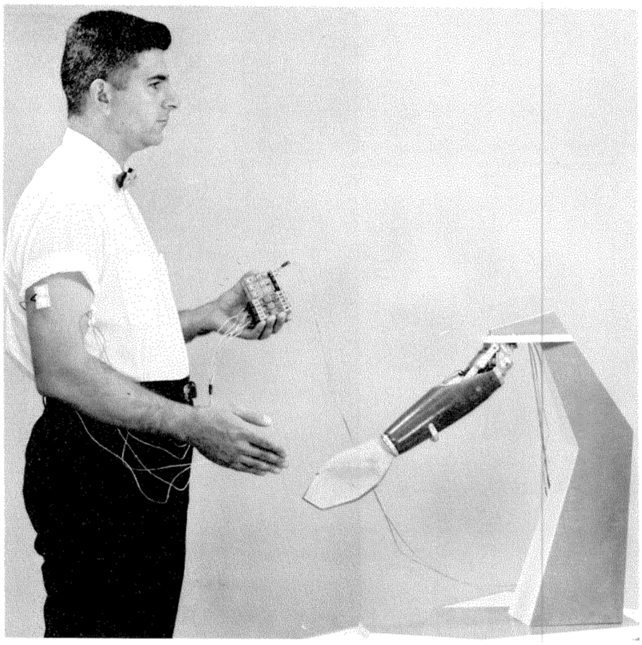

Figure 5.1: The first embedded system employing pattern recognition for the control of a prosthetic arm [22]. Developed in the mid-1960's, it was composed by a simple weighted network of resistors.

Arrays (FPGA) have shown to be highly beneficial for accelerating the computation of pattern recognition algorithms [35]. FPGAs represent a valuable solution for prosthetic control which is predestined to appear in future embedded MPR systems, but currently no clinical implementation of such system has been reported. Digital signal processor (DSP), like the popular series TMS320 from Texas Instruments (Dallas, Texas, U.S.A.), have been selected for the development of portable MPR systems [36,37]. A portable speech recognition DSP-based system was also suggested by Lin *et al.*, as a solution for prosthetic control [38]. Other system designs involved more powerful but also more power demanding processors like the PXA270 from Intel or the CortexA8 from ARM (Cambridge, England, U.K.) [39,40]. This approach obviously poses energy consumption challenges but still provides a remarkable processing capability for a wearable device. Processor cores from the Cortex-M family recently started to be a popular choice for MPR systems' design given their efficient compromise between power consumption and computation capabilities [41]. This core was also chosen for the system presented in Paper III attached in this thesis. To date there is a single commercially available embedded MPR system from which limited information is available due to its commercial nature (Complete Control, COAPT).

Chapter 6

Neural Interfaces for Myoelectric Prostheses

The functional challenges of any myoelectric prosthesis, MPR or not, are related to the sensors used to acquire the EMG signals. Clinical solutions typically include non-invasive electrodes, where conductive parts are located on the surface of the skin above the target muscles. The selectivity of this approach is limited due to the signal traveling through different tissues before reaching the sensing parts or cross-talk between neighboring muscles. Any electrode misplacement or electromagnetic field in proximity can potentially create artifacts able to involuntary drive the prosthesis. Moreover, environmental conditions (humidity and temperature) cause impedance changes in the interface skin-electrode which can contribute to reduce the reliability of these systems and force to exhaustive recalibration.

Since all these aspects can greatly threat the overall functionality of non-invasive myoelectric devices, several invasive approaches have been investigated to potentially solve these problems. Invasive solutions basically rely on implanted electrodes for sensing the myoelectric signal. Several configurations for implanted neuromuscular electrodes are available today. Besides all the risks involved in the surgery and in foreign-body reactions, the major system-design challenge for invasive solutions has been historically how to functionally access the control signals sourced by implanted subcutaneous parts. Several solutions have been thus proposed.

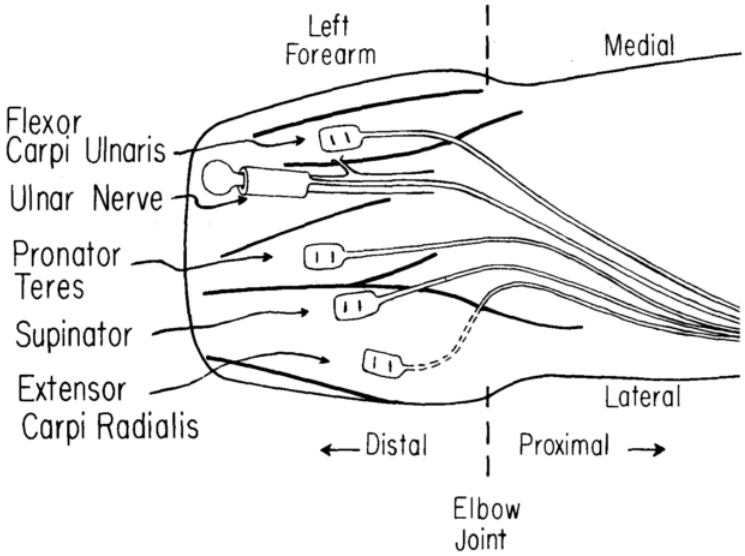

Figure 6.1: First attempt of a percutaneous neuromuscular interface for prosthetic control, 1980 [42]. A transradial amputee was implanted with four epimysial electrodes and a cuff electrode which leads converged on a percutaneous connector emerging from the skin of the upper arm.

6.1 Percutaneous Leads

Percutaneous leads have been explored and utilized in literature, and despite not being regarded as a long-term stable solution due to obvious problems at the interface between leads and skin, they played a crucial role in research for neural prosthetics. The first pioneering attempt of a percutaneous neuromuscular interface for prosthetic control is dated back to 1980, reported by Hoffer and Loeb [42] (Fig. 6.1). A transradial amputee was implanted with four epimysial electrodes on the muscles and a cuff electrode planted around one large fascicle of the ulnar nerve (proximal to the neuroma). Leadout cables converged onto a 12-pin socket percutaneous connector emerging from the skin of the upper arm. The difficulty in securing the cables at the interface and prevent skin inflammation eventually led to an infection followed by the percutaneous connector removal.

To our knowledge, the longest reported time of implantation for percutaneous implants is over four years [43], but it is widely recognized that these solutions will eventually reach a functional failure. Currently, they do not represent a clinical viable solution for amputees but still they are an important source for basic (and not only) science research in the field of neural prostheses.

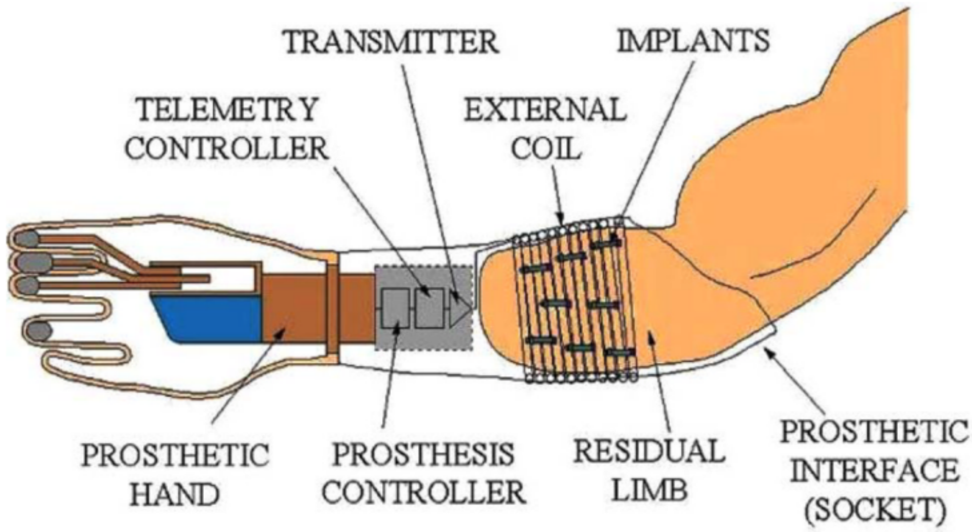

Figure 6.2: Representation of the IMES system [47]. The EMG sensors are implanted in the forearm and communicate wirelessly to the external coil laminated in the prosthetic socket.

6.2 Wireless Interfaces

Provided the limitations of percutaneous solutions, wireless neural interfaces have been suggested and developed over the years. Implanted telemetric systems can be used to bidirectionally transfer information between the body and the robotic control system. The first experimentation of a wireless system for prosthetic control was done by Herberts *et al.* in the 1968 [44]. Here, the six implanted electrode-capsules were wirelessly energized from a single external processing unit placed on the skin. EMG signals were successfully transferred via frequency modulation of the carrier wave. Two able-bodied subjects and two below-elbow amputees were recruited for experimentation; the implantation lasted from 3 up to 15 months, and some primitive foreign-body reactions were reported. Few years later, in 1974, Clippinger *et al.*, presented a wireless neural stimulation system aimed to integrate sensory feedback on a body-powered prosthetic system [45]. Here, oppositely to Herberts' system, all implanted electrodes converged to a centralized transmission unit connected wirelessly to the main external unit. The implant was removed several weeks after. The next clinical implementation of a wireless prosthetic system was not reported until 2014, where Pasquina *et al.* provided two transradial amputee subjects with the Implantable Myoelectric Sensor (IMES) technology [46]. The IMESs are small, cylindrical electrodes (16 mm long and 2.5 mm of diameter) capable of detecting and wirelessly transmitting EMG data [47] (Fig. 6.2). Thanks to these telemetric sensors the test subjects could functionally control a 3 DoF prosthetic arm.

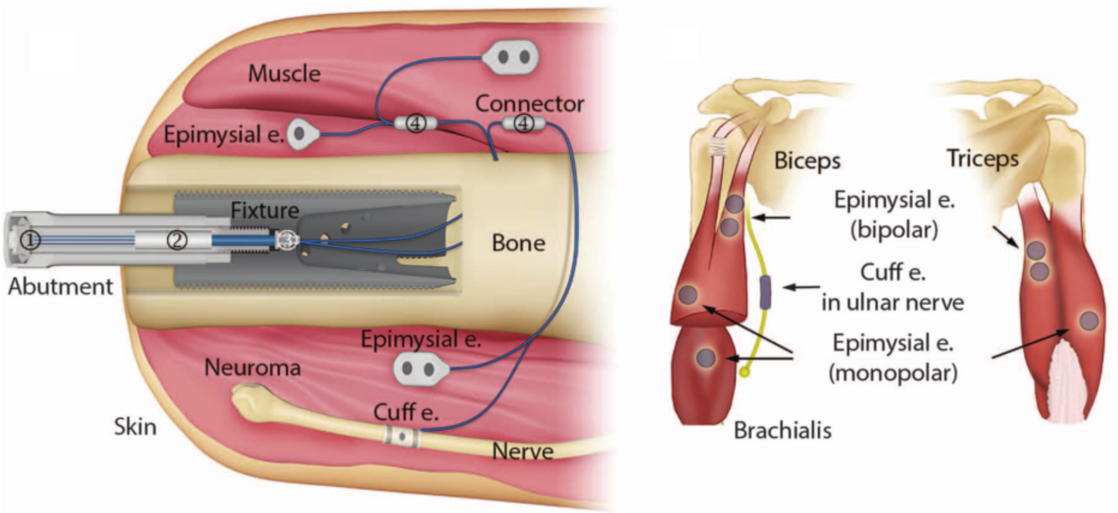

Figure 6.3: Osseointegrated Human-Machine Gateway (OHMG). Left) Representation of the modular system. Right) Placement of epimysial and cuff electrodes in the right upper arm [1].

6.3 Osseointegrated Human-Machine Gateway

The technology for the direct skeletal attachment of a limb prosthesis (started in 1990 [17]) provided the framework for an alternative method to gain access to the peripheral nervous system. In fact, osseointegration inherently predisposes of a percutaneous interface between the skin and the titanium abutment. In 2014, Ortiz-Catalan *et al.* demonstrated the possibility of a long-term bidirectional communication between the artificial limb and implanted neuromuscular interfaces by incorporating signal feedthrough mechanism into the osseointegrated implant [1]. Here, some of the parts constituting the OPRA Implant System were modified to integrate feedthrough connectors, which interface to the implanted electrodes' leads outside the bone in the soft tissue. The system included epimysial electrodes, in both monopolar and bipolar configuration, targeting biceps and triceps muscles, as well as a cuff electrode located around the ulnar nerve. This technology, named as the Osseointegrated Human-Machine Gateway (OHMG) and shown in Fig. 6.3, was implanted on a transhumeral amputee subject and it is still currently functional at the 4th year follow up. The advantages of implanted EMG sensors for prosthetic limb control were proven as well as the functionality of the cuff electrode for direct neural stimulation.

Three more transhumeral amputees have recently been implanted as part of an ongoing clinical trial.

Chapter 7

Sensory Feedback and Closed-Loop Control

Even though active prosthesis can provide an acceptable restoration of functionality, sensory feedback is still missing and not purposely pursued in clinical practice. Several surveys reported this to be a cause for preventing a wider acceptance of prosthetic devices over the amputees' community [48,49]. Exteroception (sense of the surrounding environment) and proprioception (sense of the proper state, joint angles, etc) are mandatory requirements for any prosthetic device which wishes to be referred to as "able to provide a functional natural sensation". Tactile feedback is essential in the interaction with items, and researchers agree on the necessity of investigating viable methods to provide a closed-loop control of the prosthesis. In the last decades, several approaches have been proposed but none has been yet unanimously approved from clinicians to be usable and suitable for daily operation. Sensory substitution is an approach that has been widely explored in research. It is based on the idea of providing sensory information to the body through a sensory channel that differs from the natural one, e.g., substitute touch with hearing, or via the same channel but in a different modality, e.g., substitute pressure with vibration. Vibrotactile and electrotactile are two examples of sensory substitution techniques investigated since decades [50].

Vibrotactile sensory substitution transfers information to the user by vibrating the skin at frequencies not higher than 500 Hz [52]. The information can be modulated acting on two main parameters, amplitude and frequency of the vibration. The discrimination capabilities of the user are strictly related to the location where the vibrating parts are applied. Electrotactile stimulation uses a local current to evoke sensations and convey information to the user [52]. Major parameters are current amplitude, shape, frequency and duration of the pulse waveform. Oppositely to vibrotactile, no mechanical parts are involved, therefore, electrotactile-capable devices are characterized by low power consumption and fast response. Mechanotactile

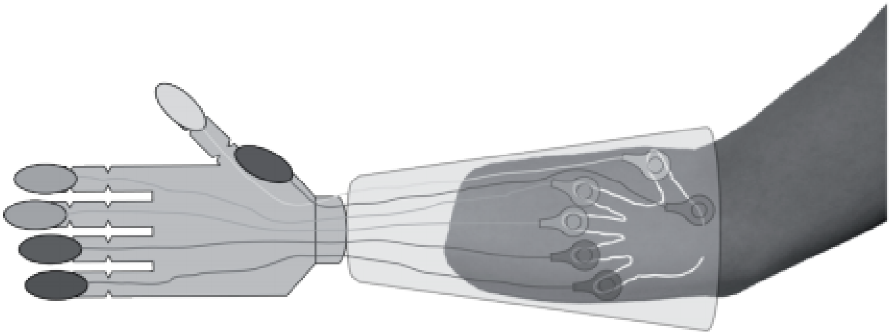

Figure 7.1: Non-electric device to provide mechanotactile feedback, developed by Antfolk *et al.* [51].

stimulation operates force application on the skin. It is most often combined with a phantom hand map used as target for sensory feedback. It is a technique appealing because of its simplicity and effectiveness. Antfolk *et al.*, investigated further this idea developing a non-electric device (Fig. 7.1) and proving its efficacy with 12 amputee test subjects [51].

Direct neural stimulation is the most exciting approach for sensory feedback, since it can potentially restore somatic sensory deficiencies. For this reason it has gathered many attentions from researchers around the world. The first attempts on using implanted electrodes to restore sensory feedback were conducted over 40 years ago [53], and several others were reported more recently [54–56]. Unfortunately, a more systematic knowledge of the interactions between the peripheral and central nervous systems is imperative and still missing. Moreover, current technology limitations in matter of neural interfaces prevent amputee patients to exploit their daily robotic prostheses via "natural feeling" closed-loop control. The poor selectivity of neural interfaces is one of the major limitations. Furthermore, the selectivity is inversely proportional to the functional duration of the implanted electrodes; the most promising studies in recent literature are carried in controlled laboratory environments for several months, after which the implants are removed.

Chapter 8

Summary of the Thesis Contributions

In the last part of this report are appended four scientific articles written within the time of this thesis, three of them are already published and the fourth is currently under reviewing process. A brief description of their contributions is presented in what follows.

- Paper I presents tests and considerations needed during the design phase of the embedded system aim of this thesis. It focuses on the identification of the most suitable analog front-end for EMG signal acquisition in the context of a low-power and low-cost prosthetic controller. Two popular analog front-end chips available on the market were analyzed and compared. Preliminary tests are also included regarding its feasibility for myoelectric pattern recognition applied to prosthetic control. These considerations might be beneficial to other researchers and developers in the field of prosthetic.

- Paper II describes a low-cost and open-source bioelectric signals acquisition architecture. It was designed as a modular system where each single unit can provide up to 8 differential or single-ended channels with a resolution of 24-bits and reprogrammable gain up to 24 V/V. It was meant as a hardware complementary to an open-source software platform already available online from our group, namely BioPatRec. This integration provide a complete system for researchers interested on intuitive prosthetic control based on pattern recognition algorithms.

- Paper III reports the development and the functional validation of the embedded system designed to exploit the advantages of the OHMG technology. The *Artificial Limb Controller* allows for bioelectric signals acquisition, processing and decoding of motor intent towards prosthetic control. It includes a neurostimulator to provide direct neural feedback thus enabling closed-loop robotic limb control. The system was validated and its functionality was proven in a first pilot OHMG-patient. This embedded controller allows for out-of-the-lab applications of closed-loop prosthetic control.

- Paper IV presents the report of a short-term clinical application of the developed prosthetic controller (presented in Paper III) utilized in combination with non-invasive EMG electrodes and pattern recognition methods. The intuitive-control approach allowed for the discrimination of three fine grips and open/close hand in a multifunctional prosthetic hand. The system was used by a dysmelia subject for five consecutive days in a out-of-the-lab context while information about prosthesis usage and real-time classification accuracy were collected. The functionality of the proposed approach was compared with the conventional myoelectric control approach. This work presents an alternative to the conventional use of myoelectric signals in combination with multifunctional prosthetic hands, moreover it is also a further validation of the Artificial Limb Controller.

Chapter 9

General Conclusions and Future Work

Some of the most exciting advancements in the field of upper limb prosthetic from all around the world have been introduced within this thesis, with its main focus set on intuitive myoelectric prostheses, which, fed by ”natural” muscles’ activity on the stump, can trigger movements on the prosthesis. Promising developments are still ongoing worldwide, moreover the popularity of the prosthetic field is growing rapidly, perhaps dragged by the science-fiction-biased appeal of robotics. Unfortunately for patients, clinical implementations still lag behind the advancements of research in matter of robotic limbs, prosthetic control and sensory feedback. More efforts are therefore needed to fill the gap.

Within this work, it was developed an embedded system capable of prosthetic control via the processing of bioelectric signals with pattern recognition algorithms. The Artificial Limb Controller includes a neurostimulator to provide direct neural feedback based on sensory information. The system was ultimately designed to be reliably used in activities of daily living for real clinical implementations, as well as a research platform to monitor prosthesis usage and training, machine learning based control algorithms, and neural stimulation paradigms. It was shown that it can be used in combination with the implanted electrodes on nerves and muscles provided by the OHMG technology.

However, considering the early clinical test stage of the OHMG implant, restricted inclusion criteria and implant costs preclude a massive distribution of this solution. For this reason, many efforts of our Biomechatronics and Rehabilitation Laboratory are still addressed to alternative and more accessible solutions, such as less invasive sensors (surface EMG electrodes). Therefore, a clinical proof-of-concept in activities of the daily life was conducted, by designing a complete prosthetic system based on the Artificial Limb Controller. The system was used by a dysmelia subject for five days for the natural control of three fine grips and open/close in a multi-functional prosthetic hand.

A low-cost hardware for bioelectric signal acquisition was designed and shared with the scientific community. It is a complete open-source package, comprising hardware and software, made freely accessible via GitHub platform. This integration provide a complete system for intuitive myoelectric control where signal processing, machine learning, and control algorithms are used for the prediction of motor volition and the control of robotic and virtual prostheses.

This thesis work provided the hardware (Artificial Limb Controller) needed for further investigations in many directions. The ultimate focus is set on the intuitive control of a prosthetic limb. We aim for a control interface that is "as natural as it can be", where the user is relieved from the burden of training and adaptation. We believe that the combination of the OHMG technology and the TMR procedure, strengthened by the advancements of signal processing techniques, can very well improve the *status quo* for amputees in matter of functional control of their prosthetic limbs. We truly believe in the advantages of osseointegration and in the breakthrough represented by the OHMG technology, it is now mandatory to deliver further assessments of their benefits to the community. We think that sensory feedback should be an essential requirement of any modern upper limb prosthesis, and it is now a concrete clinical possibility thanks to the long-term stable access to nerves via the OHMG. The same access channel on the nerves is going to be also used to investigate the chances of using nerves' signals for control purposes. More intelligent signal processing algorithms can be studied to optimize the control, as well as their feasibility for clinical applications. These are some of the ideas and directions that are likely to be taken in the following time of this industrial doctorate project.

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