POLITECNICO DI TORINO

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Master Degree Thesis

Development of a virtual environment for the study of upper limb movement illusions in neuroprosthetic applications

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Alla mia famiglia… che da sempre e per sempre crede in me.

"The world is an illusion, but it is an illusion that we must take seriously, because up to a certain point it is real, and it is true in those aspects of reality that we are able to understand. Our job is to wake up."

Aldous Huxley

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Abstract

In order to provide amputees with prosthetic devices that functionally resemble the lost natural limb, researchers have increasingly focused attention on restoring sensory feedback from the prosthetic device to the user. Lately, kinesthetic percepts have been considered along with the largely explored sense of touch and muscle vibration is considered a viable solution to provide homologous and somatotopic kinesthetic feedback non-invasively.

In a recent study, the group led by Prof. Micera demonstrated the possibility of eliciting several illusory movements of the hand by vibratory stimulation of the forearm of healthy subjects and the stump of transradial amputees. Elicitability of power grasping and hand opening percepts opened the possibility of providing kinesthetic feedback in closed-loop to one amputee controlling a robotic hand.

However, the variety of reported percepts outlined the need for a flexible environment for testing as well as training.

To this aim, the Translational Neural Engineering Lab (EPFL) bidirectional hand system has been integrated with a virtual environment for the bidirectional control of a virtual hand with 22 degrees of freedom, which potentially allows to study any elicited percept. A correct integration between the developed stimulation system and virtual reality has been obtained through modifications and further development of the software, so as to guarantee the specificity of the subject with respect to elicitable illusions.

Therefore, a software capable of interfacing with the central system previously developed and running on Raspberry has been developed in C++ exploiting the MuJoCo HAPTIX environment. The software allows simple control of the virtual hand, depending on the user intended movement as well as the possibility of performing a tracking experiment. The latter takes inspiration from a previously proposed paradigm and is aimed at allowing more structured assessment of kinesthetic feedback impact.

Pilot tests suggested proper integration of the developed virtual interface with the bidirectional hand system. This opens up the way for further investigations on non-invasive kinesthetic feedback, exploting muscle vibration.

Keywords: upper limb prosthetics, sensory feedback, proprioception, control, vibration, movement illusion, virtual reality.

Sommario

Al fine di fornire agli amputati dei dispositivi protesici che assomigliano funzionalmente all'arto naturale perduto, i ricercatori hanno concentrato sempre più l'attenzione sul ripristino del feedback sensoriale dal dispositivo protesico all'utente. Ultimamente, le percezioni cinestesiche sono state considerate insieme al senso del tatto, ampiamente esplorato, e la vibrazione muscolare è considerata una soluzione valida per fornire un feedback cinestesico omologo e somatotopico non invasivo.

In un recente studio, il gruppo guidato dal Prof. Micera ha dimostrato la possibilità di suscitare diversi movimenti illusori della mano, attraverso la stimolazione vibratoria dell'avambraccio in soggetti sani e del moncone in amputati transradiali. La percezione della presa di forza e dell'apertura della mano ha aperto la possibilità di fornire un feedback cinestesico, in una configurazione ad anello chiuso, ad un amputato che controlla una mano robotica.

Tuttavia, la varietà di percezioni riportate ha evidenziato la necessità di un ambiente flessibile sia per i test sia per l'addestramento.

A questo scopo, il sistema bidirezionale della mano del Translational Neural Engineering Lab (EPFL) è stato integrato con un ambiente virtuale per il controllo bidirezionale di una mano virtuale con 22 gradi di libertà, che potenzialmente permette di studiare qualsiasi percetto suscitato. Una corretta integrazione tra il sistema di stimolazione sviluppato e la realtà virtuale è stata ottenuta attraverso modifiche e ulteriori sviluppi del software, in modo da garantire la specificità del soggetto rispetto alle illusioni suscitate.

Pertanto, è stato sviluppato in C++ un software in grado di interfacciarsi con il sistema centrale precedentemente sviluppato e funzionante su Raspberry, sfruttando l'ambiente MuJoCo HAPTIX. Il software permette un semplice controllo della mano virtuale, a seconda del movimento voluto dall'utente e la possibilità di effettuare un esperimento di tracciamento. Quest'ultimo prende ispirazione da un paradigma precedentemente proposto ed è finalizzato a consentire una valutazione più strutturata dell'impatto di feedback cinestesico.

I pilot test hanno suggerito la corretta integrazione dell'interfaccia virtuale sviluppata con il sistema bidirezionale della mano. Questo apre la strada ad ulteriori indagini sul feedback cinestesico non invasivo, esplorando le vibrazioni muscolari.

1. Introduction

1.1 Upper limb prosthetics

Upper limb prosthetics aims at alleviating physical impairment and the psychological consequences of amputation. The latter has a negative impact on the ability to grasp and manipulate objects together with sensing and non-verbal communication [1]. Arms and hands are tools of expression, used in social interaction, and are crucial for personal comfort and private self-care.

Amputation of the upper limbs can be very complicated to accept [2]: in fact, even the loss of the simplest daily activities leads to a drastic decrease in the quality of life. It is assumed that amputation procedures date back to the Neolithic period and the first prosthetic replacement of a limb is reported in the Rig-Veda, an Indian poem written in Sanskrit between 3500 and 1800 BC ([2],[3]).

There are several conditions that can lead to amputation, including vascular disease, diabetes and trauma. Figure 1.1 shows the incidence of the various causes leading to amputation. Nowadays, amputation is more common in young people and the working population because they are more likely to be exposed to trauma [2]. However, it tends to affect men more than women and those who have a congenital absence of the limb: in this case, amputation is not always necessary and it is possible to apply a prosthesis to the rest of the limb [2].

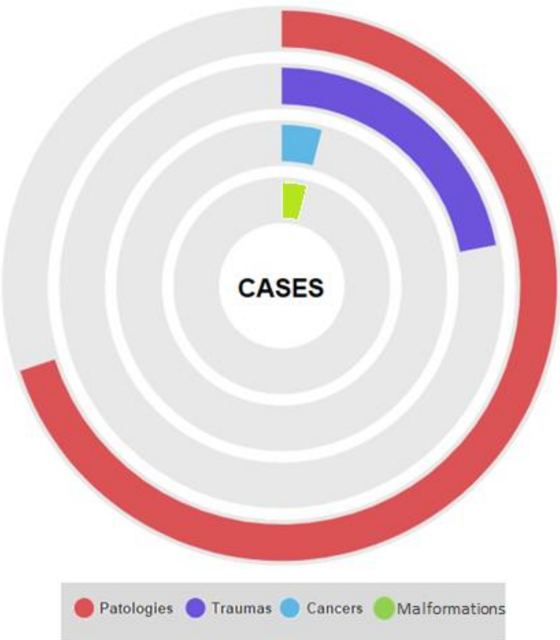


Figure 1.1 The main causes leading to lower or upper limb amputation. Adapted from https://crutechweb.altervista.org/corpo-tecnologia-e-cyborg/

To get a rough idea, consider that in 2005 there were 1.6 million amputees in the United States, with a prevalence that varies according to age, gender, race and aetiology of limb loss. Of these, only about 3% suffered a major upper limb amputation [4]. In the 1960s, Glattly also reported that the most frequent level of upper limb amputation is below the elbow and this finding was confirmed ten years later by Kay and Newmann ([5], [6]). Figure 1.2 shows the impact of amputation on individuals in the world.

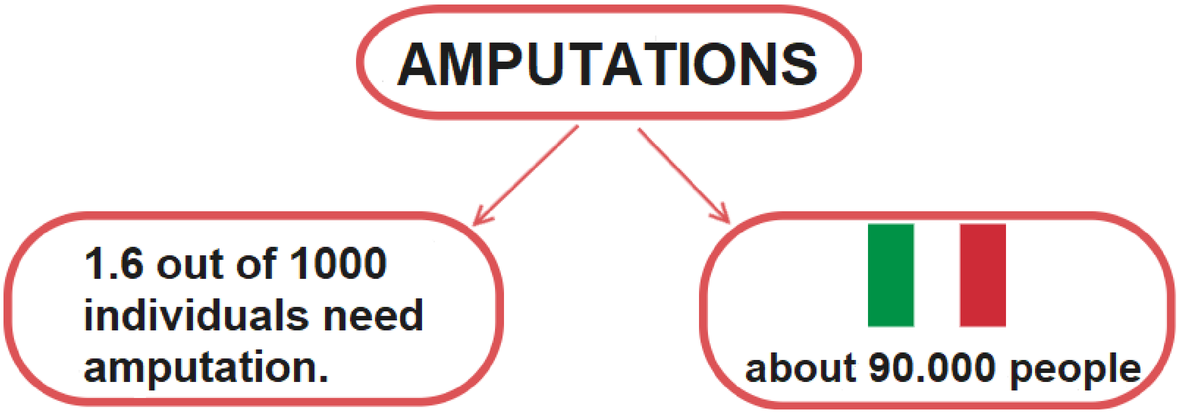


Figure 1.2 The impact of amputations on individuals. Adapted from https://crutechweb.altervista.org/corpo-tecnologia-e-cyborg/

The level of amputation is determined by the position of the lesion: once the damaged tissue has been removed, the surgeon seals the nerves and blood vessels and shapes the residual muscles to allow the future use of a prosthetic limb.

The possibility of providing amputees with prosthetic devices that resemble the natural lost limb as closely as possible, especially from a functional point of view, is therefore the most popular solution for permanent disability caused by amputation. However, despite recent technological advances and knowledge of human physiology, there is still a long way to go.

Recent progress in rehabilitation, prosthetic and surgical techniques give several possibilities to those who have amputated the upper limb. There are different types of amputation and, consequently, different prostheses to restore function. A first differentiation to be made concerns passive and active devices (Figure 1.3).

a)

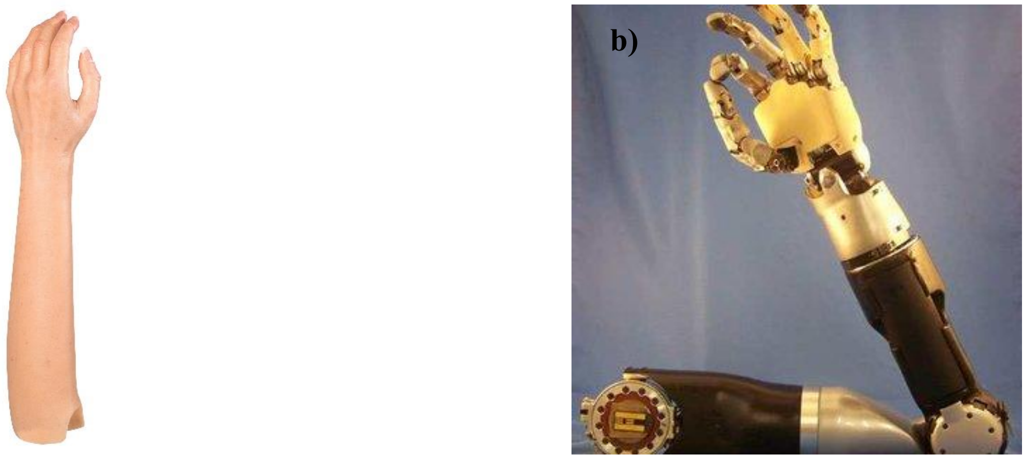


Figure 1.3 Types of upper limb prosthesis: a) passive device. Taken from https://www.ottobock.it/soluzioni-protesiche/arto-superiore/panoramica-delle-soluzioni/rivestimento-cosmetico-di-braccio-in-silicone/; b) active device. Taken from https://www.researchgate.net/publication/299483216_Stato_dell'arte_delle_protesi_di_arto_superiore

The former have primarily an aesthetic purpose, allowing only limited recovery of function limited to pushing and passive positioning. The latter include both myoelectric and body-powered devices (Figure 1.4). In this category, each type includes an end effector, a remaining limb socket, an anchoring system, and a power supply. The terminal device can be a hook, a hand, a passive hand, or a device customized for a specified scope. The power supply can be a portable battery, such as those used in myo-electric prostheses. It is activated by the patient's muscle contraction, which monitors the terminal device. [7]. In this case, the intention of the movement is decoded via electromyographic (EMG) signal, electroneurographic (ENG) signal [7] or through electrodes in contact with the epimysium[8].

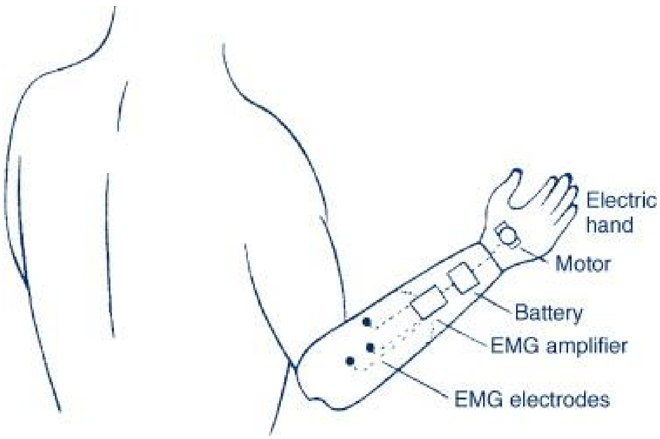


Figure 1.4 Electric-powered myoelectrically controlled, transradial prosthesis with an electromechanical hand terminal device activated by electromyographic potentials. Taken from https://www.sciencedirect.com/topics/medicine-and-dentistry/upper-limb-prosthetics

Depending on the surgical procedure the amputee underwent, the EMG may be recorded on the stump or chest muscle if Targeted Muscle Reinnervation (TMR) was performed during surgery.

In fact, there are upper extremity prostheses using implantable neurological detection devices or TMR. Targeted Muscle Reinnervation (Figure 1.5) is an invasive procedure that is based on the technology used in muscle sensing, in which residual peripheral nerves are used to reinnervate muscles in or near the residual limb [9]. It is used to increase the number of myosites available in the residual limb, so as to have an improvement in prosthetic control, and also allows signal amplification, as the chest muscles act as amplifiers.

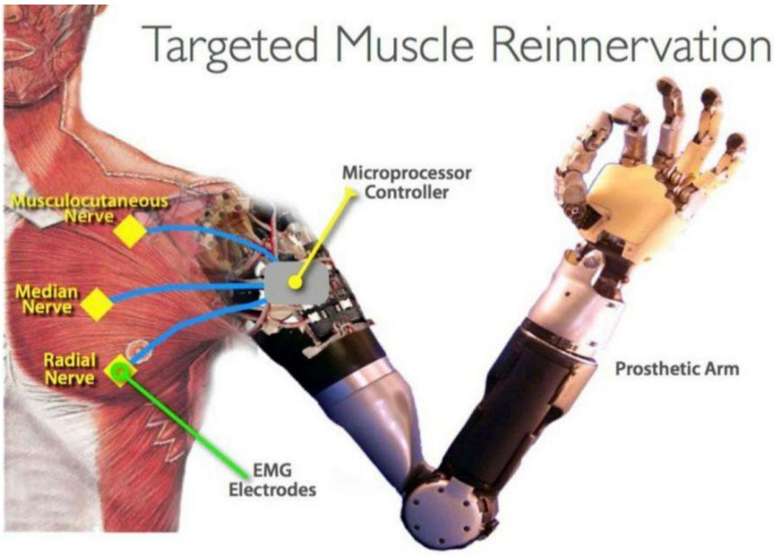


Figure 1.5 TMR. Taken from https://crutechweb.altervista.org/corpo-tecnologia-e-cyborg/

Another type of prosthetic control involves pattern recognition, which uses more surface electrodes than the typical two-site control scheme to recognize the pattern generated by muscle contractions in the residual limb. Pattern recognition does not require an isolated myosite for control, but allows to control the various movements of the prosthetic device thanks to the reproduction of natural movements of the amputated limb and thanks to the translation of that pattern into prosthetic control. To be effective, it requires an additional muscle input signal. In more proximal amputation levels, such as trans-humeral amputations and shoulder disarticulation, the use of TMR improves the myioelectric signals available for control. In fact, in order to get a more natural and intuitive prosthetic control for the myioelectric prosthesis, pattern recognition is combined with TMR surgery, so to optimize the myioelectric signals in the residual limb [10]

In contrast, osteointegration (OI) was developed as an alternative for individuals with upper and lower limb amputation who have difficulty using a conventional prosthetic system due to problems such as skin rupture, residual limb shape or length and who have significant limitations in function. This surgical procedure involves the direct attachment of the skeleton of a prosthetic device to the residual limb. An implant is surgically fixed in the bone of the residual limb, with an abutment penetrating the skin for skeletal attachment of the prosthesis.

This procedure eliminates the need for a suspension system or a prosthetic socket [10], providing improved sensory acuity and effectiveness in everyday activities [11].

However, it is important to assess consumer satisfaction with upper limb prostheses in order to identify design priorities for future developments. A specialist can use many approaches to measure the success of the implementation of upper limb prostheses, from counting the number of hours a person wears a prosthesis, to quantifying performance on standardized handling tasks, to asking the person about the improvement or otherwise of the quality of life [12]. If the user does not feel physically comfortable wearing or using the prosthesis or if, by chance, this causes pain, he or she is likely to use it unfrequently or even reject it. If control of the prosthesis requires excessive user attention, which leads to distraction from performing the necessary actions, it is likely that the user will not include the prosthesis in his/her activities. For some users, an important acceptation aspect is that the prosthesis resembles as closely as possible the appearance of the physiological limbs; other users prefer a more technical or non-physiological appearance. If people are satisfied with their appearance with the prosthesis and also find it comfortable to use, they are very likely to wear it regardless of whether or not they use it as a manipulative aid. On the other hand, if they feel that the appearance of the prosthesis is not acceptable and/or they are uncomfortable, they will not or rarely use it, regardless of how much they can improve their manipulative skills [12].

Actual prostheses, both passive and active, do not meet the requirements of amputees, with prosthesis abandonment rates of up to 30%. Rejection rates for myoelectric hands, passive hands and body-fed hooks were 39%, 53% and 50% respectively [13].

There are several aspects of design that are of greatest concern to consumers: the weight of the prosthesis, cost, appearance (in the case of cosmetic or passive prostheses), grip control, comfort of the harness, wrist movement and strength (in the case of body-powered devices). The lack of sensory feedback, durability of gloves and poor dexterity were also considered priorities of the design for electrical devices [10]. In particular, the lack of feedback makes control more difficult and promotes less predisposition of the subject to accept the prosthesis.

To provide amputees with sensory feedback about the current state of an artificial limb, both invasive and non-invasive techniques have been employed, often relying on sensory substitution approaches, especially in the latter case.

The success of long-term use of an upper limb prosthesis depends mainly on the perceived value of the amputee and comfort. Other factors that are essential for successful prosthetic rehabilitation include subsequent adjustments and revisions of prescriptions according to the changing needs of the amputee [13].

Therefore, life-long follow-up with a rehabilitation team, including a physiatrist, with attention to adaptations tailored to the patient's needs, improves prosthetic use outcomes in patients with upper limb amputation.

The focus of future research should be on the development of lighter, more comfortable and functional prostheses. Therefore, it is recommended to improve follow-up, information and repair services, combined with the active engagement of clients in the choice of prostheses that satisfy their specific needs and objectives [14]. At the same time, more and more attention should be focused on restoring sensory feedback for a better quality of patients' lives.

1.2 Bidirectional hand prostheses

Bidirectional hand prostheses are devices aimed at allowing skillful control while providing sensory information to the user.

The loss of the hand is a very invalidating factor that greatly influences the quality of life. To get an almost natural substitution of the lost hand, the user should be provided with the rich feelings that we normally perceive when we grasp or manipulate an object. Ideal bidirectional hand prostheses should incorporate both a reliable decoding of the user's intentions and the provision of almost natural sensory feedback through residual afferent pathways at the same time and in real time [15].

In this scenario, the user is part of a human-machine closed-loop system where the sensory feedback provided improves real-time control of the prosthetic device [14].

The evolution of a new hand prosthetics generation,ideally resembling human "physiological" dexterity and somatosensaton, still poses many challenges for research.

In fact, an important objective of neuroprosthetics is to determine the bidirectional communication between the user and the new prosthetic limbs endowed with an high number of degrees of freedom (DoF) [15]. In this respect, the most promising solutions aims at connecting the prosthetic limb with both the efferent and afferent fibres of the peripheral system through invasive or non-invasive neural interfaces [16].

To this aim, intelligent active prostheses with tactile and proprioceptive sensors needs to be integrated in closed-loop with the user, creating thus a bidirectional hand prosthesis.

1.2.1 Prosthesis control

In the past, different approaches to prosthetic control have been proposed, based on invasive or non-invasive recording techniques. The latter is by far the most commonly used approach, both in research and for commercially available prostheses [14]. Surface electromyographic (sEMG) signals have been applied in various different fields, in particular to identify the intention of the user to monitor the amputee, orthotic and exoskeleton assist devices in order to increase their capabilities.

Typically, the electromyographic signal (EMG) is used for prosthetic control (Figure 1.6), particularly the surface EMG signal (sEMG), because it is detected by the skin surface and is preferred for its ease of access and non-invasive procedure. However, the achievable dexterity of the prosthetic hand is minor due to the limitation of identifying different positions for signal acquisition. In fact, in this case, three to four possible positions can be identified from the residual limb to acquire signals for sequential control [17].

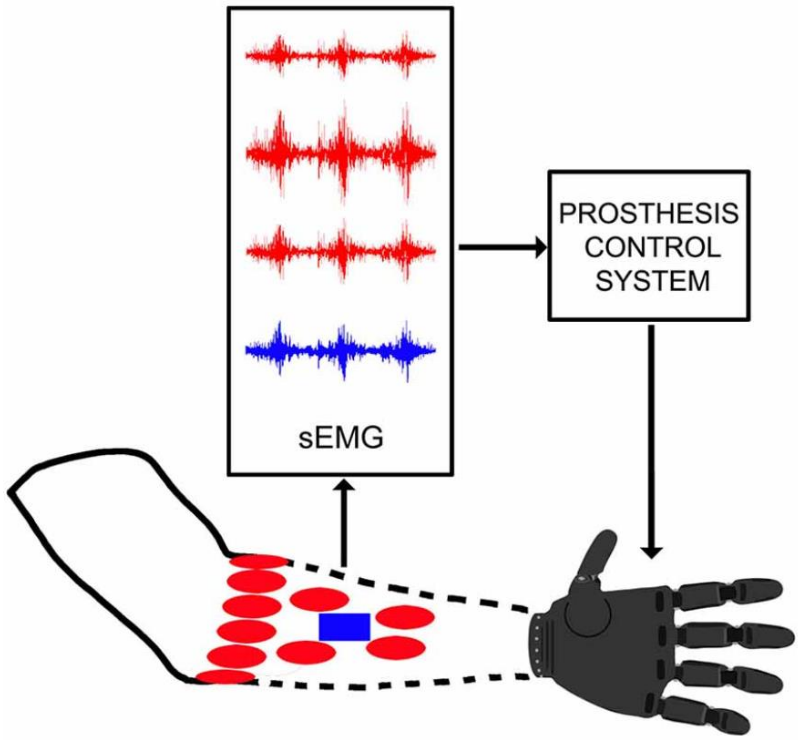


Figure 1.6 Scheme of a generic myoelectric control system. Taken from https://www.researchgate.net/figure/Scheme-of-a-generic-myoelectric-control-system-i-for-commercial-prosthesis-without_fig1_285216908.

From the sEMG, time domain or frequency domain features are commonly extracted to perform the classification: in fact, different EMG characteristics have been evaluated, for different time windows and for different noise levels, such as motion class discrimination, robustness and computational complexity, in order to control myoelectric upper limb prostheses [18].

As an alternative to this approach, many researchers have turned their attention to techniques that require a certain amount of invasiveness. Intramuscular EMG signals have the advantage of being able to access multiple positions to collect EMG signals so as to offer different degrees of control to the prosthetic hand.

The Figure 1.7 shows the differences between surface and invasive electromyography.

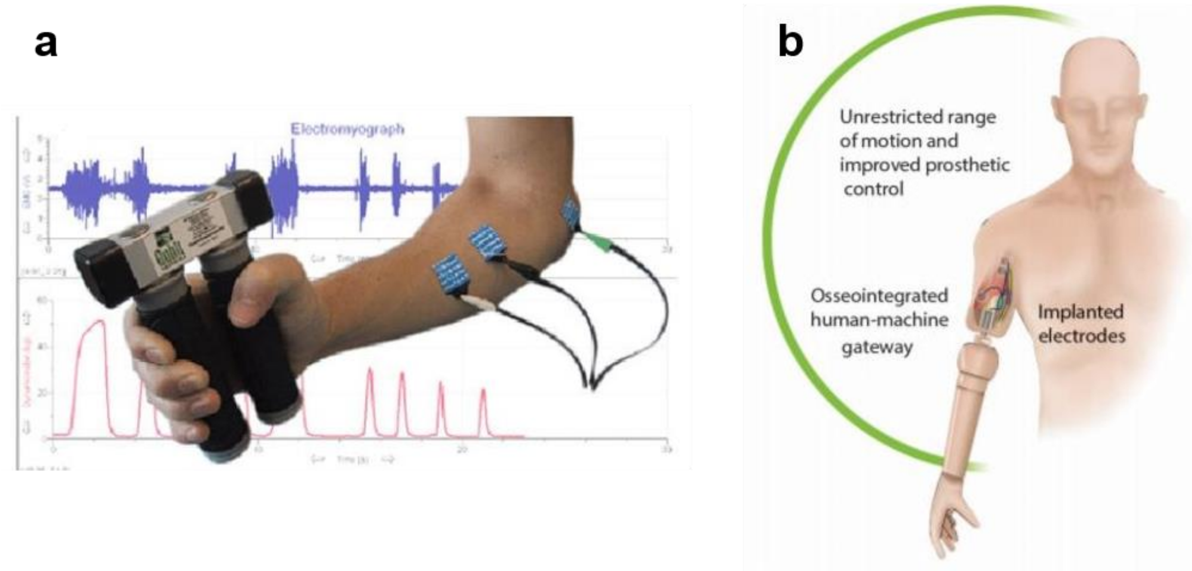


Figure 1.7 a) Surface recording of EMG signals; b) Invasive recording of EMG signals.

The ENG signal could also be a valid alternative to EMG: the high increase in invasiveness is clearly a disadvantage of this method and therefore an additional gain in performance or robustness must be widely demonstrated for this approach [19].

A direct connection of the prosthetic limb to the nervous system could greatly improve patients' quality of life [20]. Among the various possible approaches, intrafascicular electrodes are optimal candidates for the neural interface, representing a trade-off between high selectivity and relatively low invasiveness [20]. However, in order to provide stable, long-term bidirectional communication with the human body, some researchers have focused their attention on the possibility of using an osteointegrated percutaneous interface. The use of chronically implanted intramuscular electrodes has encouraged more robust and intuitive prosthetic control, simultaneously promoting a natural understanding of sensory feedback [21]. This is because, unlike surface electrodes, intramuscular electrodes have negligible crosstalk and a high signal-to-noise ratio (SNR) [8].

Despite the enhancements in sophisticated robotic hands, the intuitive control and of the prosthesis has usually been restricted to only 3 degrees of freedom (DOF) in closed-loop control. However, more and more progress has been made: in fact, the advanced capabilities of Utah Slanted Electrode Arrays (USEAs, Figure 1.8) implanted in the residual peripheral nerves of the human amputee's arm are able to restore control of 5 DOFs. The latter also provide a helpful source of feedback during virtual control of the closed-loop prosthetic hand [22].

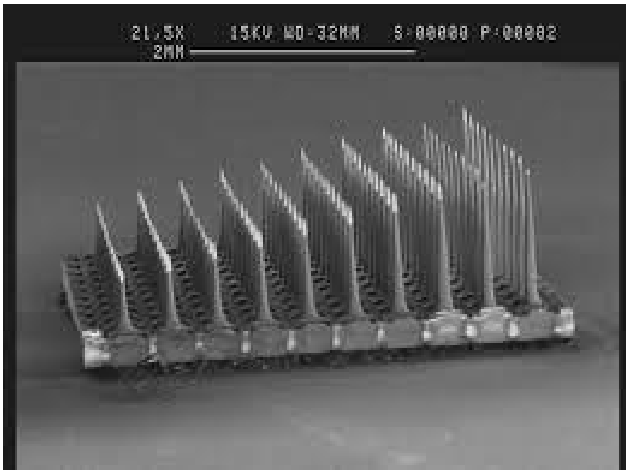


Figure 1.8 Utah Slanted Electrode Array (USEA). Taken from S. Wendelken et al (2017).

Therefore, if on the one hand surface EMG recordings are privileged for their non-invasiveness, on the other hand, they are often inconsistent and unreliable, due to the limitation of the electrodes because they have little skin contact, due to the grip rotation, the sweating, thus leading to high rates of prosthetic abandonment. At the same time, however, approaches that are more sophisticated require greater invasiveness, which can be compensated for by the simultaneous capture of EMG signals coming from different residual muscles, enabling natural control of multiple degrees of freedom, and improved prosthetic function of the upper limbs.

1.2.2 Sensory feedback

Haptic, proprioceptive and pain perceptions are essential parts of our daily lives, as they provide us with useful information about our environment, while at the same time protecting against harm to our body. Progress in prosthesis design and control systems can help amputees in recovering lost functions, but often, as already pointed out, there is still lack of tactile feedback, let alone of rich somatosensory feedback.

It is the task of the mechanoreceptors and free nerve endings in our skin to provide the necessary tools for somatosensory perception. The main mechanoreceptors in the skin that transmit tactile information are Meissner cells and Pacinian cells, which have rapid adaptation (RA) and respond to both onset and offset of tactile stimulation; Merkel's cells and Ruffini's terminations, which respond to sustained tactile loads due to their slow adaptation (SA) [23].

Since sensory feedback restoration, complete or partial, is not yet present in clinical practice, most amputees use myoelectric prosthetics based primarily on visual feedback. For this reason, the efforts of the scientific community have focused on developing approaches to provide appropriate and functional sensory feedback (scheme in Figure 1.9). Different solutions have been studied and improvements in dexterity have been demonstrated [24], with a more natural execution of movements and greater embodiment, also strengthening its control. In this regard, it is necessary to understand the importance of the somatosensory system: to provide extroceptive sensations to help us perceive and react to stimuli coming from outside our body [23].

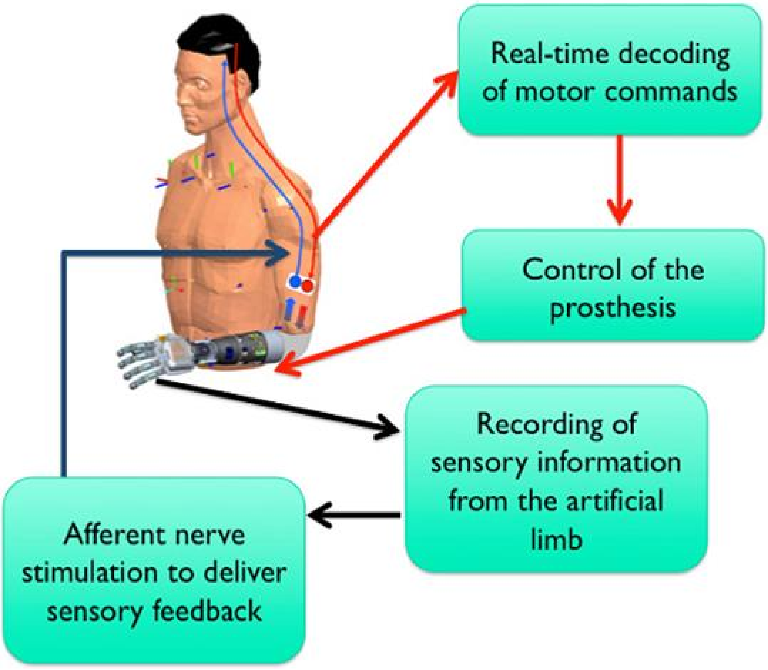


Figure 1.9 Prosthetic sensory feedback. Taken from http://www.nebias-project.eu/projects.

Among the possible feedback from their prosthesis, amputees consider of major importance the gripping force, followed by proprioceptive information [25]. Subsequently, the first contact during the gripping of an object and the end of contact during release also play an important role. In addition, the vibrations, electrical stimulation and pressure are also important aspects in the transmission of sensory information from the prosthesis to the user [25].

Sensory feedback strategies can be divided, firstly, into two categories: on the one hand, homologous approaches, in which the artificial feedback mode corresponds to the natural one; on the other hand, non-homologous approaches that use a different sensory path to provide feedback to users. In addition to this first distinction, we can proceed with a different subdivision: somatotopic and non-somatotopic approaches differ on whether or not there is a correspondence between the place where the sensation is perceived and the place where it would be naturally perceived. The ideal solution to have a completely natural sensory feedback should be to use both homologous and somatotopic approaches, for the simplicity and intrinsic intuitiveness [16].

To provide sensory feedback, two different approaches can be considered. Indeed. the feedback can be provided to the user either using invasive or non-invasive interfaces.

In this field, several studies have been conducted: these are those patients who use implanted neural interfaces. They are able to discriminate the stiffness and shape of objects [25] and carry out dexterous motor tasks [24].

In the latter case, sensory feedback can be restored through epineural or intraneural interfaces (Figure 1.10).

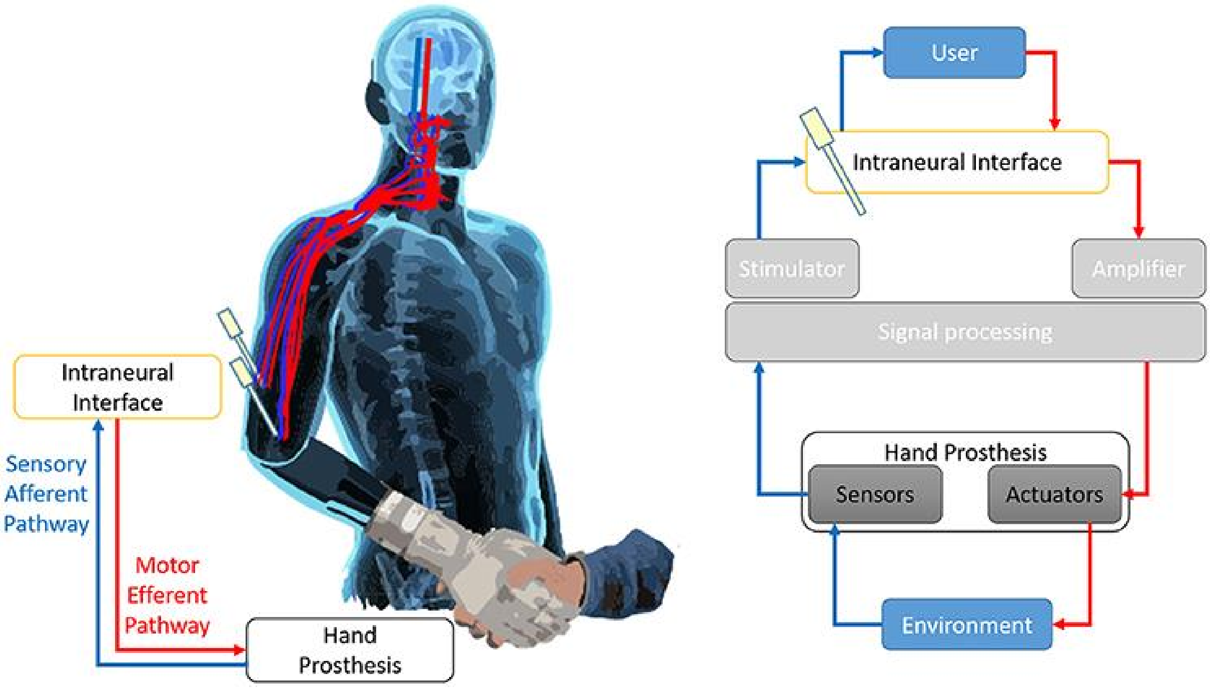


Figure 1.10 Prosthesis closed loop control, where Invasive intraneural interface mediates the information flow from the brain to the actuators of the prosthesis and from the sensors embedded on the prosthesis back to the brain. Taken from F. Lotti et al (2017).

Using a biomimetic approach based on frequency and amplitude modulation, both manual dexterity during a functional task and the level of manual precision have been improved. This has led to an important reduction of the so-called "telescopic effect", i.e. the abnormal feeling of the phantom limb position [24]. However, these strategies all require invasive intervention, which, in some situations, may not be possible to implement.

Non somatotopic and non-invasive approaches, which on the one hand might seem a solution, show, on the other hand, a difficulty in interpreting sensations, less accuracy in discriminating objects, and longer response and learning times [16]. For this reason, there are also non-invasive somatotopic restoration approaches, which use electrical or mechanical stimulation of the stump, based on a mapping of the hand on the stump itself, which is however not always available or complete.

To overcome this lack, the research moves towards an approach based on transcutaneous electrical nerve stimulation (TENS) to elicit sensations in the phantom hand of amputees stimulating nerves transcutaneously. Using these sensations as feedback during the control of the bidirectional prosthesis, they are capable of performing various functional tasks that otherwise would not have been possible. In addition, by means of this technique, it was possible to quantify the stimulation parameters useful to arouse painful tactile perceptions and not to the phantom hand. A multilayered electronic dermis (e-dermal) with features based on the mechanoreceptor and nociceptor behavior has been designed to give neuromorphic tactile information to an amputee, while the neuromorphic system implements neural components, such as tactile sensation, through spiking activity based on biologically guided models [22]. Figure 1.11 represents the system diagram.

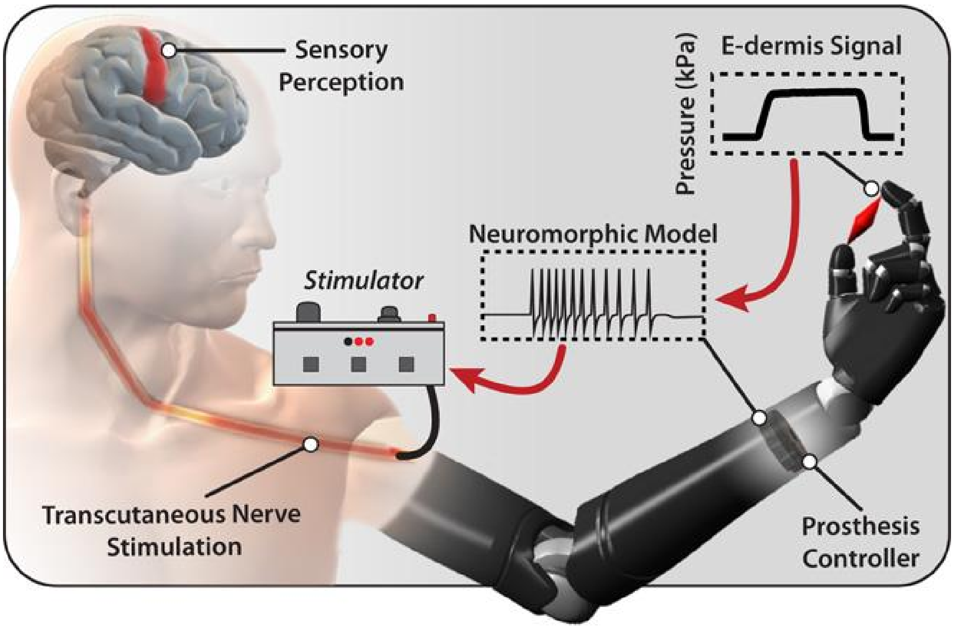


Figure 1.11 Prosthesis system diagram. Taken from L. E. Osborn et al (2018).

Targeted reinnervaton rerouting also sensory nerves, namely targeted sensory reinnervation (TSR) approaches have also been studied to provide useful sensory feedback from prostheses, as they provide an insight into the mechanisms of neural plasticity and peripheral regeneration in humans ([26], [27]).

Other authors have obtained good results for sensory restoration using transverse intrafascicular multi-channel electrode implants (TIME) in their median and ulnar nerves [28]; others are working on a technique known as "sensory regenerative peripheral nerve interface" (sRPNI), in which a "bioartificial interface" transfers sensory signals directly from a prosthetic sensor to the remaining nerve. However, the first steps have also been taken in the field of optogenetics which, using specific wavelengths, offers a valid alternative to direct electrical nerve stimulation [29].

Although more attention is paid to restoring tactile feedback, the position of the upper limbs and the perception of movement are also important. The sense of proprioception is not always easy to achieve through direct neural stimulation: successful studies have been reported and homologous proprioceptive feedback provided through direct neural stimulation has been exploited to recognize the properties of objects [30]. Instead, a nonhomologous approach based on intraneural stimulation has proven to be a good alternative [24]. On the other hand, Marasco and collaborators have exploited a non-invasive stimulation approach to provide amputees with a kinaesthetic perception of a robotic hand. Through vibration, illusory phenomena of complex movements have been produced in TMR patients and later on used to provide kinaesthetic feedback, leading to an improvement in motion control [31]. Exploiting the same phenomenon, researchers led by Prof. Micera have developed a muscle vibration stimulation system capable of providing homologous and somatotopic proprioceptive feedback, in a non-invasive way, to transradial amputees [14].

However, research on what is usually referred to as proprioceptive restoration can still be considered in its early stages. Much progress still needs to be made to identify both new strategies and the types of amputees who can benefit from the advantages of non-invasive, homologous and somatotopic proprioceptive feedback provided by muscle vibration.

1.2.3 Virtual prostheses

The capabilities of existing hand prostheses are generally restricted to the opening or closing of the hand for greater difficulty and strength found in decoding. In addition, many current prostheses do not have an active wrist and at most allow its manual positioning in different configurations. This is a major obstacle to the usefulness of the prosthesis compared to the many degrees of freedom of an undamaged hand [31]. Therefore, it is necessary to find more sophisticated mechanical solutions that allow more degrees of freedom and, at the same time, to find a way to control the additional dexterity of a prosthesis of this type. One of the greatest challenges for the development of prostheses is the production of devices that closely replicate their natural counterparts. As already mentioned, the control of the prosthesis is very unnatural and therefore involves a great mental effort, which is the reason why some patients abandon the use of such devices very early [32].

Virtual reality (VRE) software suites offer several advantages, such as high repeatability, elimination of some secondary sensory phenomena, reduction of human error. Researchers working in this field have demonstrated [32] the success and usefulness of VRE in neuroprosthetic research, as subjects tested with closed-loop control of prostheses in VRE have shown excellent results both in the identification of objects and in the execution of daily activities.

In this context, some researchers have tried to find a mechanism to help patients during the learning stages without the need to put the prosthesis on the whole time, i.e. a system with its own hardware and software for the detection and processing of the electromyographic signal (EMG) [33]. However, it was a mechanism that required several months of training with teams of doctors and therapists to achieve natural control [33].

In order to provide amputees with a training system for better control of the real prosthesis and optimization of the adaptation process, virtual reality systems have been developed, thus improving, on the one hand, the functional integration between amputee and active prosthesis [34] and, on the other hand, offering greater flexibility during the experimental phase.

To date, there are several types: for example, a virtual reality prosthesis simulator (Figure 1.12), which proves to be a promising tool for the development and evaluation of control methods, the prototyping of new prostheses and the training of amputees [35].

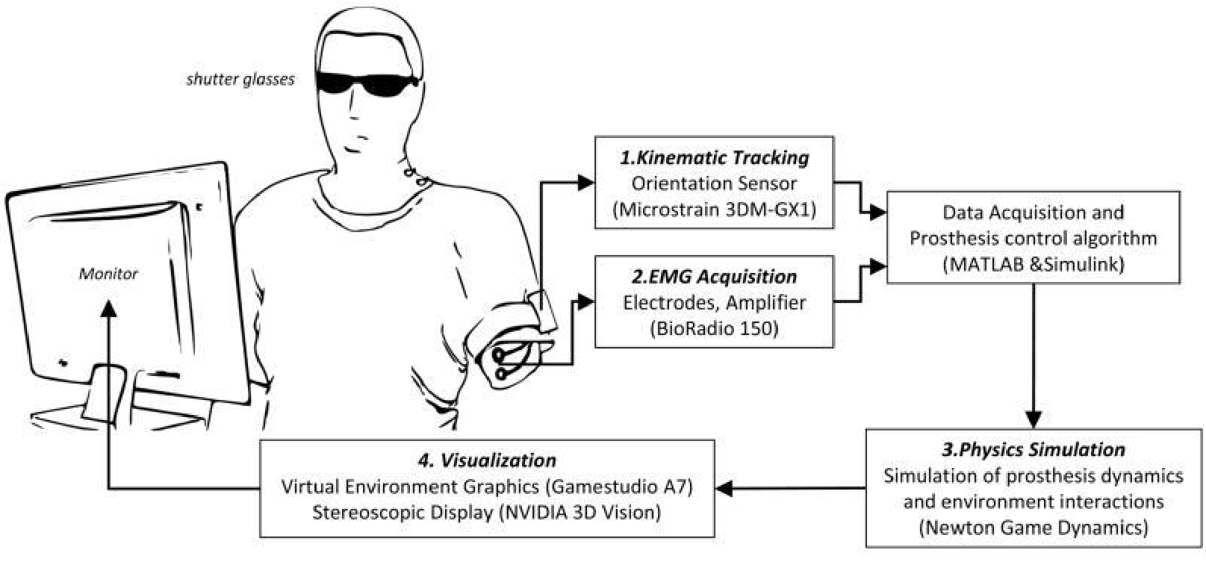


Figure 1.12 Scheme of the Transhumeral Prosthesis Simulator. Taken from J. M. Lambrecht et al. (2011).

Computerized systems have been proposed for amputees to operate a virtual prosthesis for gripping and/or releasing objects. However, these systems tend to be quantitative because they take into account the number of successfully completed tasks or the time needed to perform them [33].

Other researchers have developed a Virtual Reality environment in order to continuously encourage amputees to exercise their control skills without any risk [36]: it is an optical motion capture system (iotracker), used to trace the movement of the amputee's arm and head in order to provide 3D input and correct visualization of the virtual environment in a head-mounted display. In addition, electromyography is also used as input to capture control of the virtual prosthesis, providing a realistic simulation.

Technological progress in the design of upper limb prostheses offers significantly greater possibilities for motorized movement: in fact, the DEKA arm system (Figure 1.13) allows the user 10 degrees of motorized movement ([35], [36]).

Figure 1.13 DEKA arm system. Taken from J. M. Lambrecht et al. (2011).

However, in order to facilitate learning, a virtual reality program (VRE) has been introduced, which is particularly useful for amputees who need a structured learning environment due to cognitive deficits.

Therefore, a VR-based training system for the control of myoelectric prostheses [37] is useful, as it is designed to improve the skills regarding the efficient control and movement of the prostheses themselves with a natural posture [38].

1.3 Proprioception of limb position and movement

Several experts have tried to define what proprioception is; some of them have defined it in the following way: “Proprioception is the ability to perceive and recognize the position and movement of one's body in space, the state of contraction of one's muscles, the sense of strength, effort and balance without the support of sight” [39].

It was introduced by Charles Scott Sherrington "as a sixth sense because it is regulated by a specific part of the brain" [39]. In modern use, it is often used interchangeably with the term kinesthesia, coined by Bastian in 1887, which instead concerns only the sense of position and movement of the limbs and trunk [40].

At the basis of proprioception, over the years, different theories have alternated and debated. Traditionally, speaking of proprioception, reference is made to the receptors related to conscious sensations, i.e. sense of position, movement, and strength. However, the receptors of the vestibular system also contribute to provide conscious sensations, unlike the eyes or ears which are not able to provide identifiable sensations [41].

In addition, it is also possible to generate an artificial proprioceptive signal by means of muscle vibration, while at the same time, involuntary sensations are generated.

The study of proprioception has its roots between neurophysiology and neuropsychology [41]: on the one hand, some contemplated a central origin of the muscular sense; on the other, the peripheral component was supported. However, over the years, proprioception has received great interest, both for the better understanding of daily sensory experiences and for its importance. In fact, it affects both the control mechanism for a correct execution of the movement and the correction mechanism in case unpredictable external phenomena disturb strategically programmed motor projects. It can therefore be said negative feedback circuits control that proprioception: the action performed is compared with the programmed one and any difference (error) is signalled to the system in order to trigger the appropriate corrections [41].

Proprioception therefore describes the sensory inputs that originate, during centrally guided movements, from particular structures: the proprioceptors. Their main function is to provide feedback information on the movements of the body itself, in other words to signal, instant by instant, which movements the body itself is performing; precisely on the basis of this information the higher centers are able to correct or modify the movement in progress [42].

The receptors responsible for proprioception are found in the skin, muscles and joints. Limb position and movement information is not produced by individual receptors, but by afferent populations. The different signals produced during a movement are elaborated to codify the position of the endpoint of a limb, while the afferent input is related to a central body map to identify the position of the limbs in space [42].

The movements of the limbs are accompanied by stress and tension in all the tissues surrounding the affected joint, such as the skin, ligaments, muscles and tendons. It would therefore be intuitive to look for proprioceptors in the joints: for a long time, the joint receptors were considered the main kinesthetic receptors. Today, instead, the muscle spindles, together with Golgi's tendon organs, are considered the main actors, since they are receptors sensitive to the state of muscle stretching and therefore play an important role both in proprioception and in motor control mechanisms.

In reality, however, the proprioceptive sense organs are much more than the previous ones mentioned and they can be divided into three groups: the muscle receptors (neuromuscular spindles, Golgi tendon organs, Pacini receptors at muscular collocation and the free muscle endings of the muscle, perimysium and epimysium); the articular receptors; the cutaneous mechanoreceptors (Merkel, Meissner, Ruffini and Pacini corpuscles) [42].

Mammalian muscle spindles include different types of fibers: the primary Ia afferent fibers, which are wrapped around the nucleated portion of three types of intrafusal fibers, i.e. bag 1, bag 2 and the nuclear chain that does not exceed the spindle capsule; the afferent fibers of the smaller Group II have secondary endings on bag 2 and the chain fibers. These fibres have a response proportional to the amount of stretching. Beyond these afferent fibres that act as muscle length sensors, there are two types of afferents, the γ dynamic fusimotor fibres that innervate bag 1 and the γ static fusimotor fibres that innervate bag 2 and the chain fibres [14]. A schematic representation of the muscle spindles is shown in Figure 1.14.

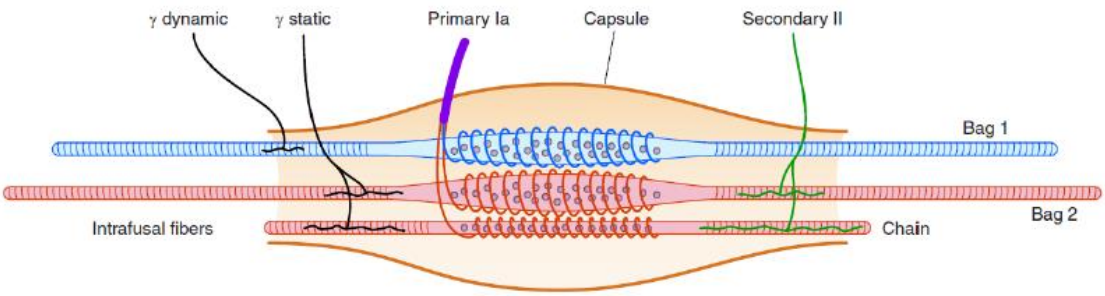


Figure 1.14 Structure of mammalian muscle spindle. Taken from U. Proske and S. C. Gandevia (2012).

The tendon organs of Golgi, instead, are considered high threshold sensors, as they are sensitive to voltage variations. For their schematic representation, see Figure 1.15. Each tendon filament is innervated by a branch of a Group Ib axon, penetrating the capsule, and is attached to a muscular fibre referred to a given drive unit, different for all tendon filaments. The contraction of the muscle stretches the tendon filament producing activity in the Ib fibers [41].

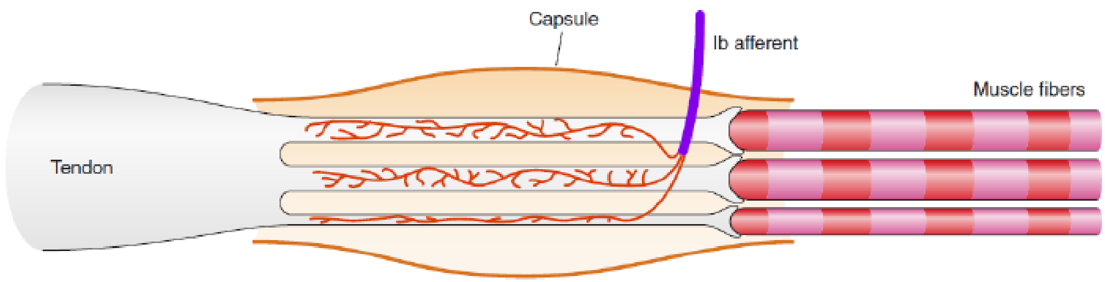


Figure 1.15. Structure of mammalian muscle spindle. Taken from U. Proske and S. C. Gandevia (2012).

The articular and cutaneous receptors play a more important role in the sense of position (conscious proprioception). The stimulation of the fibers coming from Merkel's corpuscles gives the sensation of skin pressure, while the one coming from Meisssner's corpuscles gives the sensation of localized vibration.

On the other hand, stimulation of the fibers coming from Ruffini's corpuscles gives the occasional sensation of articular movement and that coming from Pacini's corpuscles gives the sensation of a diffuse vibration. Instead, the sensation coming from the articular receptors is of deep focused pressure, movement or joint stress [42].

The signals of the muscle spindles alone seem to be ambiguous when concerning the hand proprioception given the distance of the muscle moving the fingers, whether they are positioned in the forearm or the hand, and the large number of joints their tendons have to pass through [41]. Although all four types of glabrous skin mechanoreceptors are involved in kinesthesia, the slow-adapting Ruffini type II terminations are considered the most relevant in the position of the signaling limbs [43].

Exercise may disturb proprioception, involving musculoskeletal injury. In addition, proprioceptive senses, in particular limb position and movement, become deteriorated with age and are associated with an higher risk of falls in the older age group [41].

1.4 Kinesthetic illusions

The spatial awareness of the body is due to a series of sensory inputs from muscles, tendons, joints and skin [31]. The execution and control of motor tasks are mostly influenced by proprioceptive feedback, i.e. information about the body's position and movement. In 1972, it was discovered that non-invasive vibratory stimulation on a muscle or tendon induced an illusion of movement [44] (Figure 1.16) consistent with stretching of the vibrated muscle/tendon ([45], [46]), as neuromuscular spindles are sensitive to stretch rate. Stretching is associated with an exciting tonic response in antagonistic to vibrated muscles (antagonistic vibratory response, AVR), i.e. in muscle groups normally contracted if the illusionary movement had been performed. This response is important, since a relationship between the parameters of AVR (sEMG, activation delays, motor unit types, shutter speeds) and those of the kinaesthetic illusion has been found ([[47], [48]).

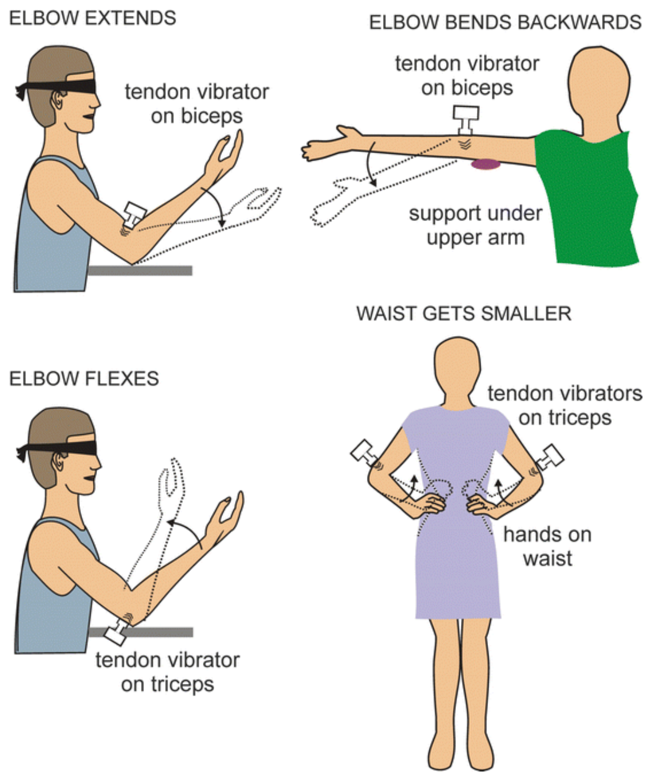


Figure 1.16 Kinesthetic illusions induced by muscle or tendon vibration. Taken from J. L. Taylor (2013).

Illusions are the demonstration that the representation of the body's sense of position and awareness of limb movement derive from the cross-calibration of visual and proprioceptive signals. Studies on vibrational illusion and the phantom limb phenomenon indicate that the perception of movement and limb position are independently coded and can be dissociated [49].

However, this phenomenon still has many unresolved points, due to different stimulation parameters that alter the sensation such as frequency, duration, position.

A vibration at 100 Hz on the biceps or brachial triceps tendon caused an illusory perception of the movement and displacement of the forearm in the direction of the elongation of the vibrato muscle. No illusion, however, was perceived during the vibration of the elbow joint. Subsequent studies have shown that vibratory antagonist muscles do not lead to illusory perceptions of movement [50], while the simultaneous vibration of several non-antagonist muscles is approximately resolved as a complex illusion resulting from the vector sum of the directions that compose it [51].

The local factors that cause the illusory effect of vibration involve the vibration stimulus's properties, such as its frequency, amplitude and duration, and the vibrato muscle's properties, such as contraction and fatigue. Contextual factors (gestalt), on the other hand, concern the relationship of the vibrated body part with the rest of the body and the environment [53].

When you vibrate a muscle, it can also cause activity in nearby or antagonistic muscles [52], which can distort or disturb the illusionary movement.

In this regard, the size of the vibrator plays a fundamental role. The positioning, holding and stability of the stimulator is an important aspect of correctly targeting the muscle of interest, as even light movements of the subject could move the vibrator or influence its preload force, which is usually difficult to control. The vibration amplitude from hundreds to thousands of micrometers can be very different depending on the pressure applied to the vibrator. As far as vibration frequencies are concerned, on the other hand, it has been shown in many studies that the range between 70 and 110 Hz induces illusions of movement. While some groups found greater effects for frequencies of 70-80 Hz [53], others found no difference in the perceived illusion of movement compared to the vibration frequency. The muscle state (relaxed or contracted) also contributes to the perceived illusion.

Moreover, illusions are influenced by the movement of the limbs, both passive and voluntary, and by the history of voluntary contractions. They can be classified into "first order" illusions due to a link between the muscle spindle activity and the concept, and into more complex illusions involving other sensory modalities and external objects [53].

At the moment of vibration, it can happen that the muscle contracts by the so-called tonic vibration reflex (TVR) [54]: in normal muscles, it can be effectively controlled and counteracted by voluntary effort, so that the vibration has no effect on the maximum voluntary power. After the vibration ceases, there is often a transitory sensation in which the vibrating limb returns to its original position (kinesthetic effect), even in the absence of the afferent inputs recruited by the vibration.

This collateral kinesthetic effect seems to derive from a sensory process and to depend on previous illusory movements. The duration of this effect generally depends on the duration of the previous stimulation and the displacement is about 70% compared to that during the vibration [55].

It is assumed that the illusion originates from somatosensory areas that are normally engaged in kinesthesia. It has been noted that when vibrating the left biceps tendon at 10 Hz (low condition), 70 or 80 Hz (illusion condition), or 220 or 240 Hz (high condition), only vibrations at 70 and 80 Hz cause severe illusory arm strains. Assessing regional cerebral blood flow (rCBF) in the delusional condition, two groups of activations were found, one in the additional motor zone (SMA) also affecting the caudal cingulate motor zone (CMAc) and the other in the 4a zone of the primary motor reaching the dorsal premotor cortex (PMd) and the 4p zone of the primary motor. When, on the other hand, the main effect of vibration prevailed, zones 4p of the primary motor, 3b and 1 of the primary somatosensory cortex, the frontal and parietal operculum and the insular cortex came into play.

This indicates that SMA, CMAc, PMd, and area 4a of the primary motor (Figure 1.17) are related to the kinesthetic illusion: this, against our expectations, implies that the motor areas rather than the somatosensory areas seem to transmit the illusion of limb movement [55].

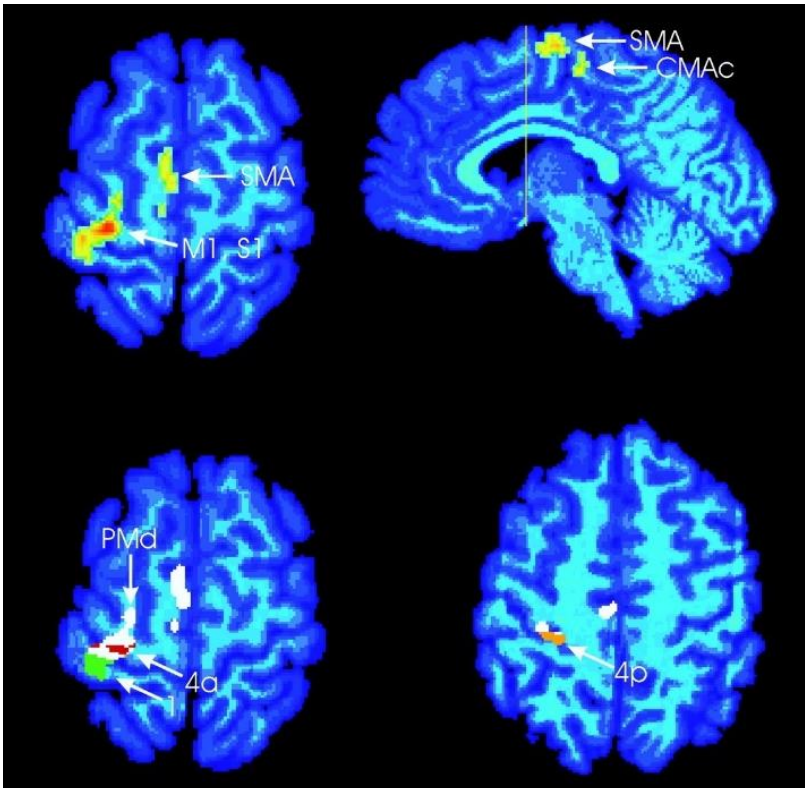


Figure 1.17 Active areas obtained in the illusion condition compared to low and high condition. Taken from E. Naito et al. (1999).

1.4.1 Movement illusions in neuroprosthetics

As most prostheses do not offer kinesthetic feedback during movement, amputees often do not have control over their body movements (sense of freedom of movement [31]) when they master a prosthesis. The brain needs feedback from the body so that an intentional movement can be completed effortlessly. Therefore, the presence of a kinaesthetic sense makes prosthetic systems more controllable.

Recently, muscle vibration has been successfully employed by Marasco and colleagues to provide kinaesthetic feedback to TMR patients controlling a robotic hand [31]. A neural-machine interface capable of instilling kinesthetic sense in amputees has been developed to allow greater control of movements in the absence of visual feedback. This approach seems to be an excellent solution for improving motor performance and quality of life.

A preliminary investigation isolated 22 different complex and functionally relevant movement concepts among the six amputees involved in the study. Contrary to expectations, vibrational stimulation of the muscle reinnervated by the median nerve produced the illusion of flexion instead of extension, while the muscles innervated by the radial nerve produced the perception of extension instead of flexion. In addition, the illusion felt on the vibration of biceps, triceps, brachial or pectoral muscles were synergistic hand gestures. From this, it was deduced that the reinnervation of the elbow and shoulder muscles with the hand nerves may have reassigned their sensory neural structure and that a key role in kinaesthesia could be played by the fibres that signal active contraction [14].

It is the only example of non-invasive homologous and somatotopic kinesthetic feedback implemented in a closed-loop configuration with a prosthetic hand: this approach opens the way to a perfect integration of minds and machines, although there is only restricted evidence of its functioning on amputees who have not received TMR [14].

1.5 Aim of the master project

The central role of hand position information for movement control has been widely established, as has the sense of ownership and agency derived from kinesthetic perceptions. The congruence between sensory feedback and intentional movements gives a sense of agency, which allows to discern own actions from those of others [44]. Therefore, establishing a sense of agency helps amputees to have control of the artificial limbs, allowing the acceptance of the device by the user.

Illusions of movement have proven to be a suitable means of providing natural, non-invasive kinesthetic feedback to TMR patients. Moreover, promising evidences outline also the possibility of exploiting illusions of movement also in transradial amputees [14]. Indeed, muscle vibration has been employed to elicit hand related movement illusions in two transradial amputees. Furthermore, one of the two patients received kinesthetic feedback while controlling bidirectional prosthesis.

In light of this, the aim of this project was to investigate further the possibility of eliciting hand related illusory sensations by vibration of the forearm in healthy subjects and of the stump in transradial amputees. Moreover, given previous findings on the variety of elicitable sensations as well as the massive presence of wrist related illusory movements, a flexible environment for testing and training was needed.

To this aim, the bidirectional hand system developed at the Translational Neural Engineering Lab (EPFL) ([56], [14]) has been endowed with communication to a virtual environment (MuJoco Haptix) for the bidirectional control of a virtual hand. The flexibility provided by the virtual environment will allow to take into account the specificity of the subject with respect to the elicitable illusions, while evaluating the benefits provided by sensory feedback and gathering information and indications useful for further development.

2. Materials

2.1 Bidirectional hand system

The heart of the bidirectional hand system developed by Prof. Micera's research group is a software implemented on a single board computer that can be easily interfaced with several external devices that may be needed for closed circuit control.

The entire code is mainly developed in C++, although some important C libraries are used. The hybridization of these two programming languages C/C++ allows, on the one hand, portability between different embedded platforms and, on the other hand, a high ability to interface with external devices. The entire code follows a modular architecture, possible thanks to the abstraction tool given by object-oriented programming, in order to separate the control of each device. In particular, several "controllers" (i.e. classes) are implemented, each of which represents the abstraction of a device together with its functionality. For all classes there are few high-level public functions, which hide the low-level implementation. The Table 2.1 shows the description of the main controllers.

Controller class	Description
Main Controller	It is the executive director of the code: it executes an infinite cycle from which the functions of the other classes, previously instantiated, are called. He takes care of the creation and timing of the threads.
Hand Controller	It manages the control of the different possible types of hands.
Stimulation Controller	It manages the activation of the stimulator: ensures communication and defines the stimulation parameters.
EMG Controller	It manages communication with the EMG recorder, reading data from it.
Session Recording Controller	It allows to save different data to files, in different ways.
Classification Controller	It abstracts the concept of classifier. It is used to train the classifier and to obtain a classification output for the expected movement from the EMG input data.

Parameter Load Controller	It is used to read the settings file, saving the parameters in the corresponding program variables.

Table 2.1 Classification of the main controllers implemented in the code.

The main controller plays a major role, as it is dedicated to creating the instances of all the other controllers and calling their functions. In fact, since classes cannot communicate directly, the main controller facilitates the transfer of information. The independence of controllers means that they can be added, removed or modified without influencing others. In addition, the main controller creates and manages the threads, ensuring that they are correctly timed.

Multithreading is a key feature of the program. Multi-core hardware, such as the Raspberry Pi 3 Model B (4 cores), allows you to run different parts of the code in parallel. In this way, the different independent subtasks that the manual bidirectional system has to perform can be executed simultaneously and at different times.

The modularity and readability of the program makes it easy to add functionality, creating new levels of abstraction or extending existing ones. In particular, within the hand controller, the stimulation controller and the EMG controller, the code necessary to communicate and control different devices is implemented. The parameters that are provided externally are managed by the parameter load controller. This information is then used to recall the appropriate functions for the connected devices. In this way, for example, such a system can be used to control both a virtual hand (MuJoco Haptix) and a robotic hand (already implemented for IH2 Azzurra and i-Limb (Ossur)), in a closed loop configuration with transcutaneous or intraneural sensory feedback [16], [56]).

The designed system was previously used with Prensilia's commercially available IH2 Azzurra robotic hand (Figure 2.1). Unlike most prosthetic hands, it incorporated both force and position sensors, which are essential to implement a bidirectional closed-loop control scheme.

IH2 Azzurra has 5 degrees of freedom: it is, in fact, a man-sized, programmable anthropomorphic hand, autonomous and reasonably light for a robotic device. However, one disadvantage has been noted: the presence of louder noise than other prosthetic hands, as it can act as an external disturbance in experimental

Figure 2.1 IH2 Azzurra Robotic Hand. Taken from https://www.prensilia.com/

2.2 Stimulation System

The previously developed [14] system is able to provide kinesthetic feedback based on muscle vibration in a closed-loop manual prosthesis.

In order to elicit illusions and provide feedback on hand position and movement, a stimulation system is required. However, taking into account the different degrees of freedom that a hand can have, several actuators, at least two, are required, while also taking into account the limited space available on the stump.

The stimulation system comprises, on the one hand, an actuator component, considered as the source of vibration, and, on the other hand, a central control system, including the hardware and software necessary to correctly monitor and control the actuator.

The actuator consists of an ERM motor (Precision Microdrives 320-100 ERM). It is a standard DC motor with a staggered (i.e. asymmetrical) mass attached to the shaft.

The motor is contained within two shells. In particular, one shell is interfaced directly with the user's skin, while the other has a special space to position the IMU and a slot to pass a Velcro strap, allowing a more stable positioning of the device.

In addition, an inertial measurement unit is allocated in the stimulator housing to allow frequency monitoring (Figure 2.2)

The overall system (Figure 2.3) was developed as a breadboard prototype.

Figure 2.2 Stimulation system. Taken from S. M. et al (2019).

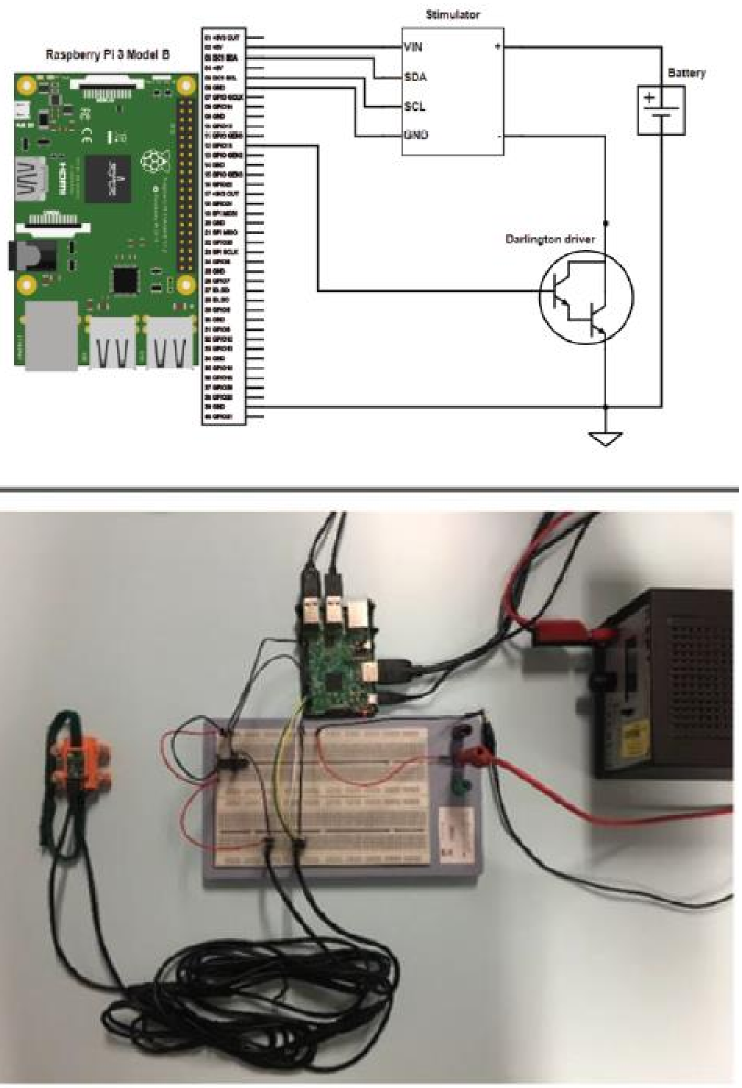


Figure 2.3 Above, the prototype stimulation system; in the middle, the schematic diagram of the overall system; below, the breadboard prototype. Taken from S. M. et al (2019).

As for the software, this was developed [14] in C/C++. For the code implementation, several libraries were used, such as the external WiringPi library, or the FFTW library.

The Figure 2.4 shows the pseudocode of the whole cycle.

```
Settings instructions
Loop
  Acquire data from the accelerometer
  Estimate the vibration frequency
  Write to the PWM pin
  Save data
End loop
Quit
```

Figure 2.4 Scheme of the main loop of the stimulation system.

Each code cycle lasts 4 ms, during which a new sample is acquired from the accelerometer, the vibration frequency is estimated and it is written to the PWM pin, the data is saved. However, if the time required to execute these instructions is less than 4 ms, the system waits so as to have a constant frequency of 250 Hz.

As far as the estimation of the vibration frequency is concerned, the method adopted [14] provides first, the calculation of the discrete Fourier Transform (DFT) of the signal, then a non-parametric estimate of the spectral power density (PSD).The frequency of the main peak was considered as an estimate of the vibration frequency of the stimulator.

Finally, in order to exit the loop condition, different conditions were set, depending on the need, such as, to be, the time, or the number of iterations, or even a shutdown request by the user.

As far as the characterization of the frequency estimation is concerned, it falls within a range of 20-120 Hz, instead, the estimated vibration amplitude in terms of displacement is in the range 160-230 µm. In this regard, it has been assumed [14] that the points on the edge of the stimulator at the skin interface are subject to uniform circular motion.

In addition, in order to have an intuitive and reliable control of the central unit of the device, a PI controller was adopted.

2.3 EMG recorder

The neural interface processor of the vine (Ripple Neuro), also known as the NIP of the vine (Figure 2.5), is used to acquire muscle activity through the sEMG. This is a complete system equipped with several components that can be used to acquire both electrophysiological and neurophysiological data. Stimulation front ends are also available.

Figure 2.5 Grapevine Neural Interface Processor. Taken from https://rippleneuro.com/

The Grapevine EMG front end can record up to 16 differential electrodes and is designed for both surface and implanted differential signal. Each channel is sampled at 2 kS/s and a bandpass filter with cut-off frequencies of 15 and 375 Hz respectively is applied. In addition, notch filtering of the first three power line harmonics (50-100-150 Hz) is performed. The Grapevine Touchproof adapter (Figure 2.6) is used to interface the EMG front end with the electrode cables, which terminate in 1.5 mm safety DIN connectors.

For each pair of disposable snap-on electrode pads, the two units are positioned approximately 1 cm apart. The reference and ground electrodes can be positioned either on the elbow or on other prominent reference points.

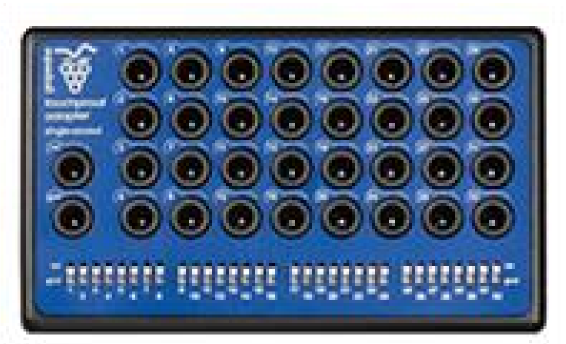


Figure 2.6 Grapevine Touchproof adapter. Taken from https://rippleneuro.com/

This system is designed for clinical use with humans. The Grapevine NIP can be connected to a computer via a Gigabit Ethernet connection and the Trellis software suite, containing a set of C headers, allows you to control instrument settings, as well as data logging and display. These can be useful for writing custom programs for the control of the Grapevine NIP and for reading the signal acquired from the product datastream. These C headers are then used by the bidirectional code of the manual system to access the acquired sEMG via the Raspberry Pi Ethernet port.

2.4 Virtual hand

A new modification made to the system previously illustrated concerns the addition of a new output, in addition to those already present, such as the IH2 Azzurra robotic hand. This new interface is a virtual hand built using the MuJoco software, This allows us to take advantage of the flexibility offered by this virtual environment, taking into account the specificity of the subject with respect to elicitable illusions.

2.4.1 MuJoco

MuJoCo (Multi-Joint dynamics with Contact) was developed by Emo Todorov for Roboti LLC [57]. Initially it was used at the Movement Control Laboratory of the University of Washington, then it was adopted by a large community of researchers and developers. The development started in 2009, motivated by the awareness of the inadequacy of existing tools for optimal control research, status assessment and identification of the system.

It is a physical engine that aims to facilitate research and development in robotics, biomechanics, graphics and animation and also in other areas where fast and accurate simulation is needed. It offers a combination of speed, precision and modelling power: it is the first complete simulator designed from scratch for model-based optimisation and, in particular, for contact optimisation. MuJoCo allows you to scale intensive computational techniques and to apply them to complex dynamic systems. It also has more traditional applications such as testing and validation of control schemes, scientific interactive visualization, virtual environments, animation and game. (Figure 2.7).

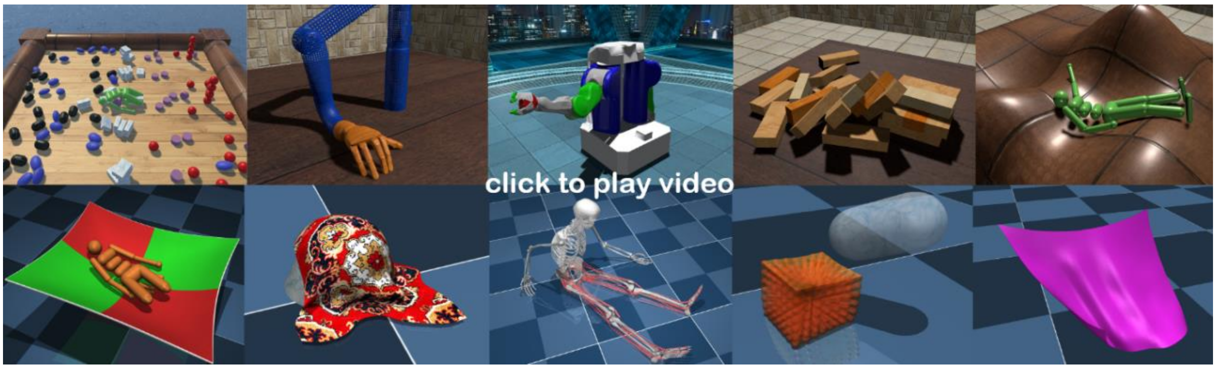


Figure 2.7 Representation of possible MuJoco functions. Taken from E. Todorov (http://www.mujoco.org/).

MuJoCo manages to match user convenience and computational efficiency. The development environment is C and runs on low level data structures. The MuJoCo suite includes the main product, which is simply called MuJoCo, and several add-ons that create functionalities superior to the main product. The product description is provided in Table 2.2.

MuJoCo products	Description
MuJoCo	It is a dynamic library with API C, compatible with Linux, Windows and maxOS. This library allows the synthesis of control, system identification, status evaluation, data analysis through reverse dynamics, mechanism design, parallel sampling for machine learning applications. It can also be used as a more traditional simulator, including game applications and virtual interactive environments.
MuJoCo HAPTIX	It is a product for the end user with a complete graphical user interface, only 64-bit Windows compatible. It has a socket-based API that contains a subset of functions and data structures, which are available in the main library. It can be used either as a generic simulator or as a custom simulator according to the demands of the DARPA Hand Proprioception & Touch Interfaces (HAPTIX) program. It also incorporates real-time motion capture.
MuJoCo Unity Plugin	Gives the user the ability to take advantage of Unitys' editing and rendering capabilities.

MuJoCo VR	It is useful to implement an interactive virtual environment.

Table 2.2 MuJoCo product line

2.4.1.1 MuJoCo HAPTIX

MuJoCo HAPTIX is based on the commercial MuJoCo Pro library for visualization and simulation. This is expanded with a graphical interface and real-time motion capture option. The user code can interface with it via a socket API. MuJoCo HAPTIX can be used in two different ways:

-generic simulator, based on the MuJoCo Pro library;
-specialized simulator, adapted to the DARPA Hand Proprioception & Touch Interfaces (HAPTIX) program requirements.

MuJoCo HAPTIX runs only on Windows, even though the MuJoCo Pro library is cross-platform.

Socket API

The API, used to interface with the user code, can be simple or native and is accessible from both C/C++ and MATLAB. The Table 2.3 shows the characteristics of each API.

API	Features
Simple	- it is intended to be used in the DARPA HAPTIX program; - it is useful for the simulation of prosthetic hands, optimizing their ease of use. - it makes some hypothesis on the model structure; - for functions and definitions, it uses the hx- prefix.
Native	- it allows more extensive simulator access; - it makes no hypothesis on the model's structure; - it provides a feature superset available via the simple API; - for functions and definitions, it uses the mj- prefix.

Table 2.3 Features of the two different API types.

However, there is a difference in the way arrays of variable size are determined. On the one hand, in the simple API, the size is determined a priori; on the other hand, in the native API, the size of arrays is variable. Both API types are implemented in the same communication libraries and can be merged in the same user program.

The software distribution contains the necessary libraries of communication for C/C++ and MATLAB.

In the project, the C/C++ API was used. Therefore, the *"haptix.h"* library has been inserted in the code, connecting to the stub library *"mjhaptix_user.lib",* which, in turn, will load the actual *"mjhaptix_user.dll"* library at runtime. In addition, the simple API has been used rather than the native API.

The simple API is focused on the hx_update function, which sends the engine data structure, hxCommand, to the simulator and receives the sensor data structure, hxSensor, from the simulator.

Below is the general outline:

```
#include "haptix.h"

hxRobotInfo info;
hxSensor sensor;

int main(void)
{
hx_connect(0,0);
hx_robot_info(&info);
hx_read_sensors(&sensor);
hx_close();
return 0;
}
```

The Table 2.4 describes the functions contained in the simple API.

Functions	Description
hx_connect	It creates the connection of the socket to the simulator.
hx_close	It closes the connection previously established with the simulator.
hx_robot_info	Provides information about the structure of hxRobotInfo, saving the result internally in order to determine the variable array size in hxSensor and hxCommand.
hx_update	It is the main function of updating.
hx_read_sensors	It behaves similar to the hx_update function, with the difference that it is not updated.

Table 2.4 Functions in the simple API.

User Interface

The graphical user interface (GUI), which appears once the program is started, is shown in Figure 2.8.

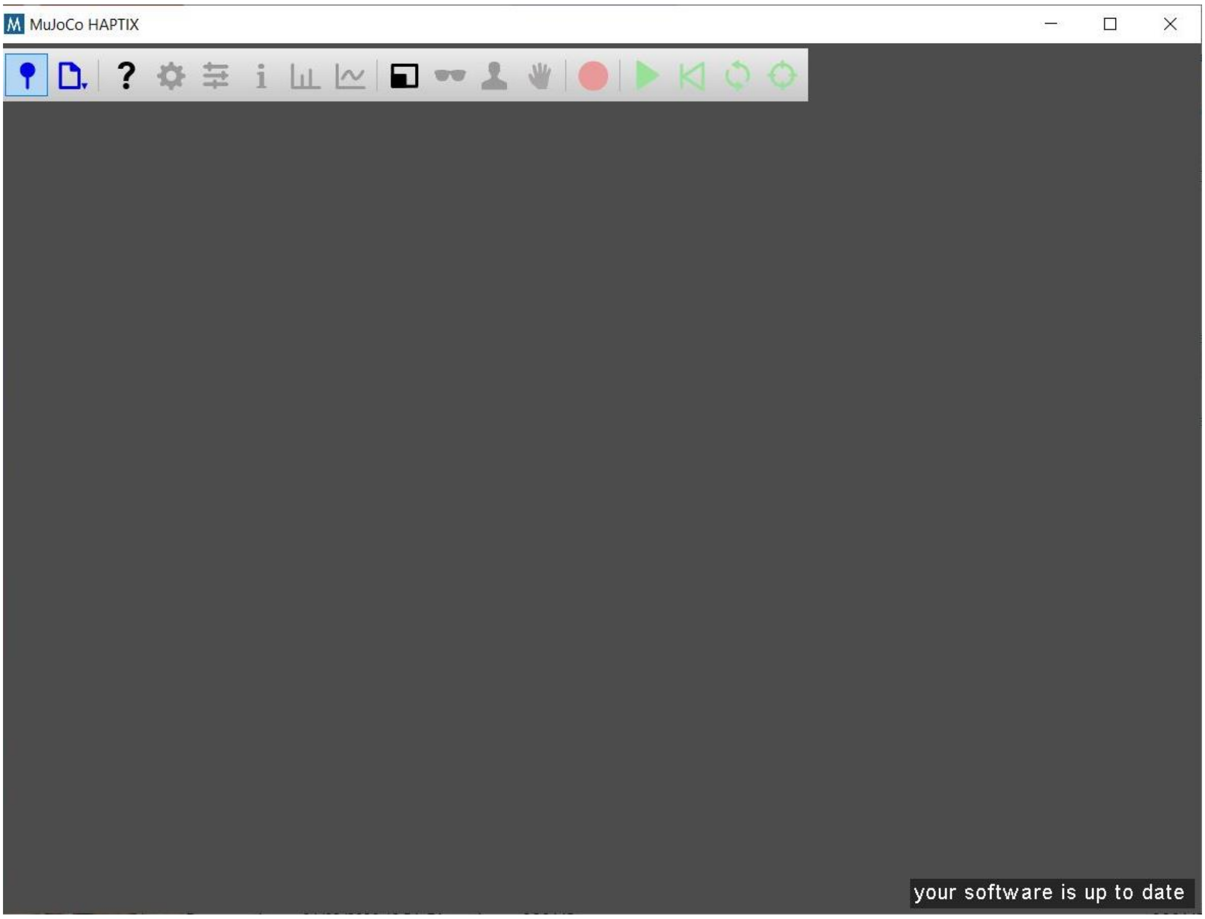


Figure 2.8 GUI in MuJoCo HAPTIX.

It is centered around a toolbar (Figure 2.9) that offers several functions. The fundamental one is represented by the second icon (Menu File), useful to load the model needed for the project.

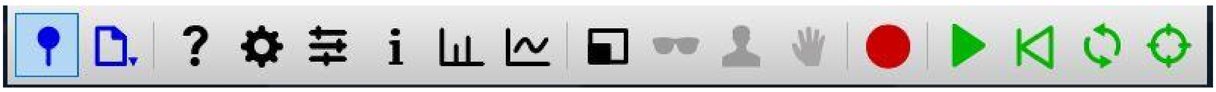


Figure 2.9 Toolbar.

HAPTIX models

The available software provides a series of ready-made models with the presence of a hand with the possible addition of objects, even geometric ones. The first operation to perform, once the program is started, is to load the model of interest.

MuJoCo HAPTIX (as well as MuJoCo Pro) can load models in different formats: if it is XML, it will be analyzed and then built. In this way, the template shows up in the 3D window and is done for simulation. In case of errors during the analysis or compilation, these are printed in a message box.

MuJoCo HAPTIX is distributed with two state-of-the-art prosthetic hand models: the Modular Prosthetic Limb Hand (MPL) and the Luke Hand. These are simulation models used by researchers who develop new neural interfaces to enable amputees to monitor and sense the next generation of prosthetic hands. They are models in XML format: the one we are interested in is the MPL hand model.

The latter is the most sophisticated prosthetic hand currently available. It has 22 hinged joints in the wrist and hand, which are actuated by 13 independently controlled motors. There are fewer motors than there are joints, this is because some of them act on more joints. It also has joint position and speed sensors, motor position sensors, speed and force sensors and IMUs in each fingertip. The polarity of each coupling and motor, which have their own name defined in the model file, is determined by the right hand rule.

The Figure 2.10 shows, on the left, the model of the hand with its 22 joints, suitably labeled; on the right, the 13 motors present in the model, also suitably labeled.

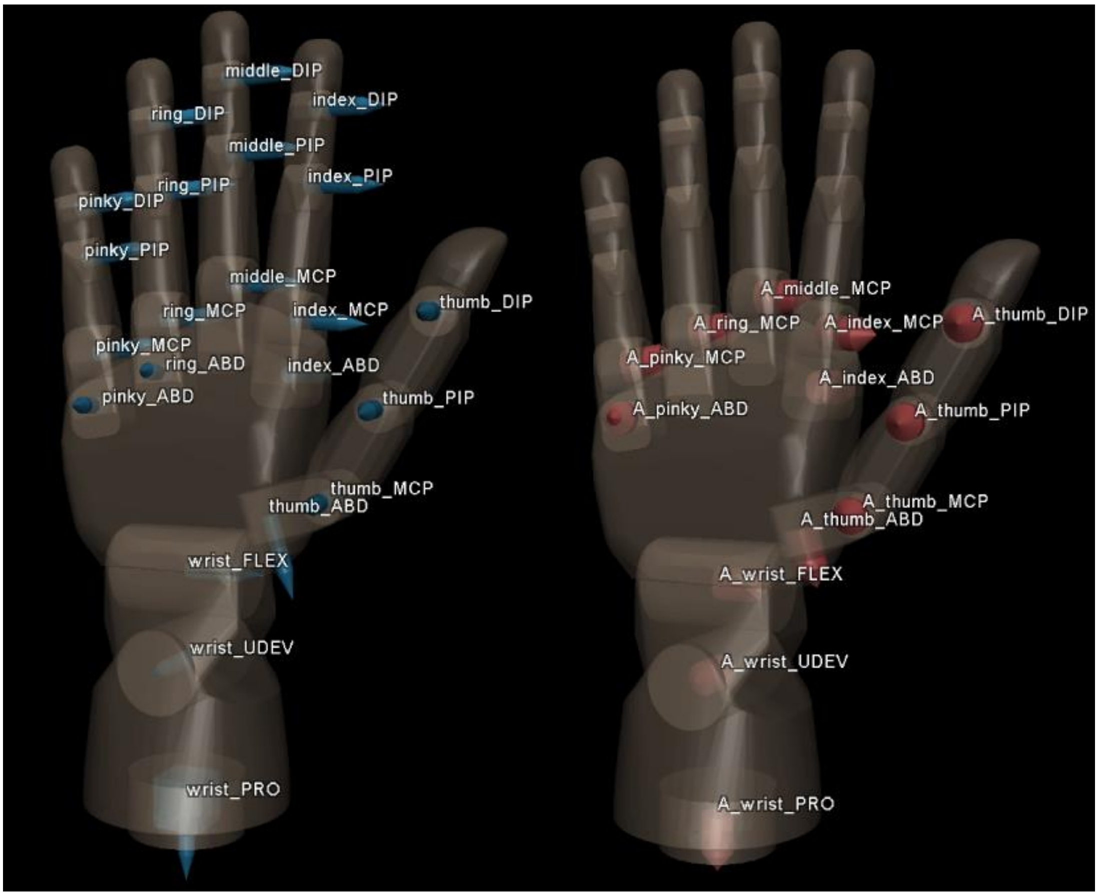


Figure 2.10 On the left, the model of the hand with its 22 joints; on the right, the 13 motors present in the model. Taken from http://www.mujoco.org/book/haptix.html

As far as the sensors are concerned, there are seven different types:

- joint positions: measures the position of the joint, in standard units;
- joint speed: measures the speed of the joint, in standard units;
- motor positions: measures the position of the motor, in standard units;
- motor speed: measures the speed of the motor, in standard units;
- motor torques: reflects the internal simulation of a servomotor;
- contact sensors: measures the forces, in Newton (N). They are always positive, because contact forces cannot pull;
- inertial unit of measure (IMU) sensors: measure linear acceleration (in m/s^2) and angular velocity (in rad/s).

In the Figure 2.11, the last two types of sensors are shown.

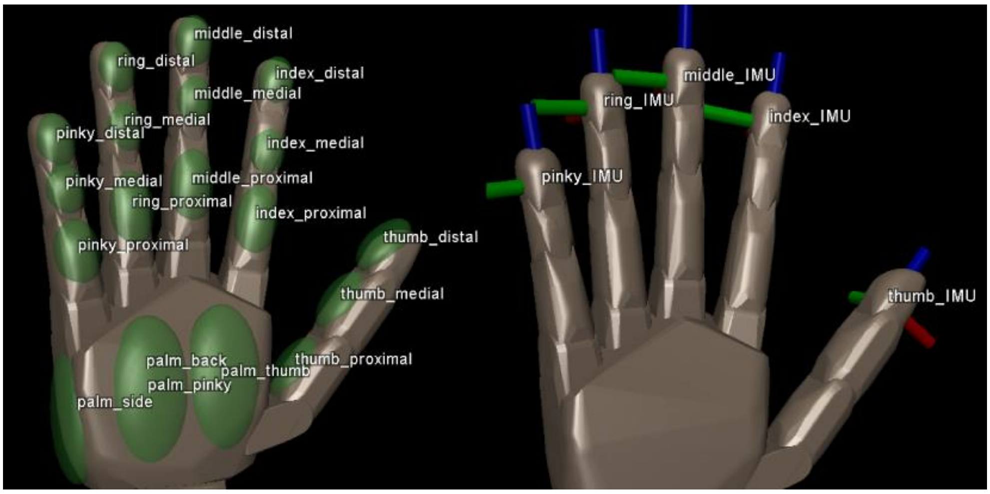


Figure 2.11 On the left, the contact sensors; on the right, the IMUs. Taken from http://www.mujoco.org/book/haptix.html

2.4.2 Serial Communication

In order to create a connection between the Raspberry Pi 3 Model B and the virtual hand in MuJoCo, a serial communication must be adopted.

Serial communication (Figure 2.11) is the most widely used approach to transfer information between data processing equipment and peripherals. Each device, such as a Personal Computer (PC) or mobile phone, operates on serial protocol. In serial communication, data is in the form of binary pulses (0-1) [58], where you can assume that the binary number 1 represents a high logic port (or 5 Volt), while the number 0 represents a low logic port (or 0 Volt). In this communication, the information (or data) is transferred one bit at a time: you therefore have a source (or sender) and a destination (or receiver).

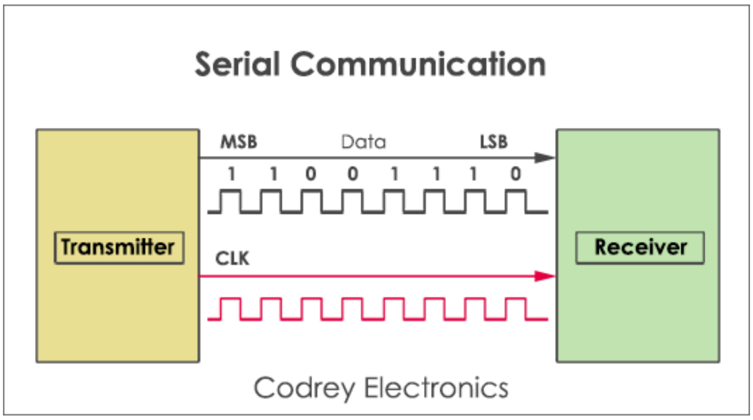


Figure 2.12 Representation of serial communication. Taken from https://www.codrey.com/embedded-systems/serial-communication-basics/

In this way, fewer I/O (input-output) lines are required, taking up less space and being more resistant to crosstalk. It also requires a low installation cost and is capable of transmitting data over long distances. The transmission modes can be different: Simplex, Half Duplex and Full Duplex. The Figure 2.12 shows the differences between the different modes.

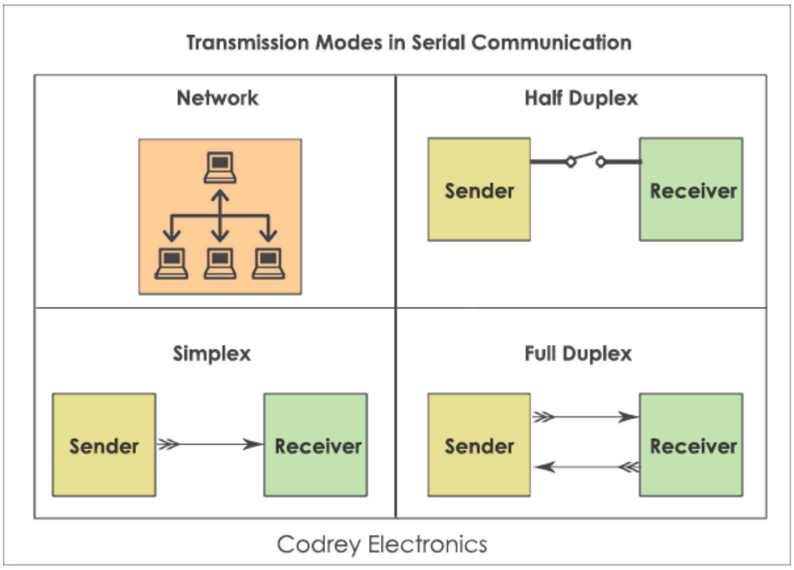


Figure 2.13 Representation of different trasmission modes. Taken from https://www.codrey.com/embedded-systems/serial-communication-basics/

For serial devices to work efficiently, the clock is the main source. It is different for each serial device and is classified as synchronous and asynchronous protocol.

In the synchronous serial interface, devices use the single CPU bus to share both data and the clock, allowing faster transfer and use fewer I/O lines. In the asynchronous serial interface, on the other hand, there is no external clock signal, allowing stable, long-distance communication.

The latter has been used in our project, taking into account the 4 parameters on which it is based: control of the baud rate, the errors, the data flow, the transmission and recepetion.

To enable communication, a cable (Figure 2.14) had to be used to connect the Raspberry Pi 3 to your PC.

Figure 2.14 The cable adopted to create the connection between Raspberry and PC. Taken from https://www.reichelt.com/

UART (Universal Asynchronous Receiver/Transmitter) is a serial communication protocol, which uses a frame structure (Figure 2.15) that, in asynchronous communication, consists of:

- START bit: indicates the beginning of the serial communication. It is at a low logic level.
- Data bit packet: from 5 to 9 bits. Normally, an 8-bit package is used.
- STOP bit: usually it is one or two bits long. It indicates the end of the frame and is always at a high logical level.

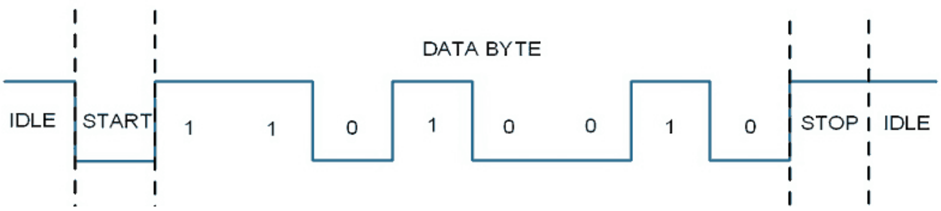


Figure 2.15 Basic frame structure. Taken from https://www.electronicwings.com/raspberry-pi/raspberry-pi-uart-communication-using-python-and-c

Once the cable is properly connected to the exact pins of the Raspberry Pi 3 (Figure 2.16) and the serial communication is configured on it, the connection is established.

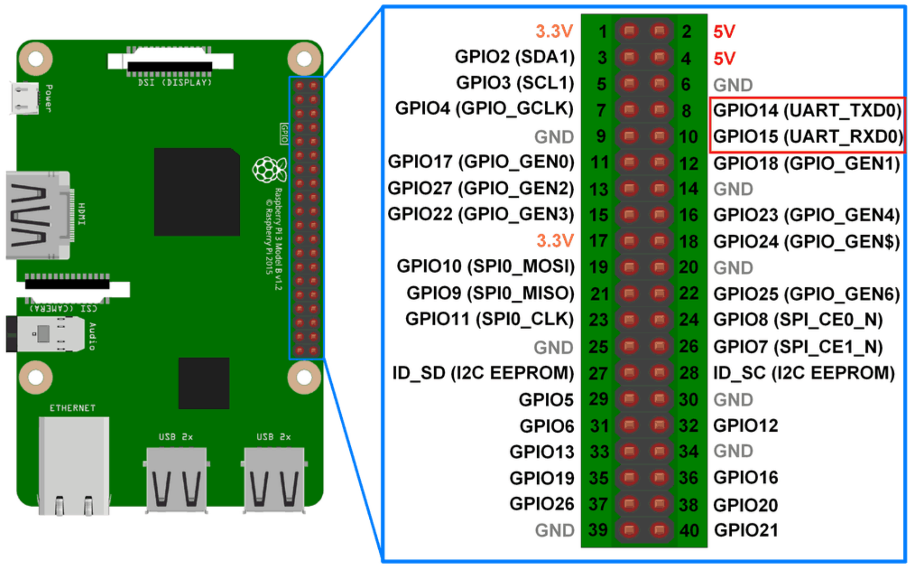


Figure 2.16. Raspberry Pi 3 UART pins. Taken from https://www.electronicwings.com/raspberry-pi/raspberry-pi-uart-communication-using-python-and-c.

3. Methods

3.1 Virtual hand control

In order to be able to study kinesthetic feedback restoration in a broader and more flexible fashion compared to what had already been done with the robotic hand, it was necessary to develop a virtual system capable of controlling a virtual hand with 22 degrees of freedom.

To this aim, it was first necessary to create a model of the virtual hand that would suit our purposed, then develop the algorithm for the control and finally perform the characterization to evaluate the correct integration of the developed virtual interface with the bidirectional hand system.

3.1.1 Virtual hand model

For our project, we modified one of the provided XLM models in order to remove the presence of any geometric object, not useful and that could disturb the attention of the subject, from the environment and in order to set the model of the MPL hand according to the initial position desired (palm up or palm down, palm facing right or left) and the initial width of both hand and fingers desired (hand totally open, ajar, completely closed, fingers more or less spaced apart). In the Figure 3.1, an example is shown.

Figure 3.1 a) example of a newly created model; b) zoom in on the hand.

3.1.2 Software development

The entire software is developed in C/C++. It allows the connection with MuJoCo HAPTIX, serial communication to interface the Unix-based bidirectional hand system [14] and the virtual environment running under the Windows operating system, and the actual control of the virtual hand.

Below, in Figure 3.2, it is a pseudocode of the entire code.

```
Settings instructions

MuJoCo connection
Opening serial port
Setting port parameters and timeouts
Mode choice

   Conditional loop
      Saving timing
      Reading class
      Control algorithm
      Saving data
   End conditional loop

MuJoCo disconnection
Closing serial port
```

Figure 3.2 Entire pseudocode of the software.

The main fulcrum of the code is the conditional loop, within which timing is saved, defined as the duration of the cycle and measured in milliseconds; the reading of the class, in which the entire program waits to receive a character encoding the class on the serial port before continuing; the proper control of the virtual hand, described in the next paragraph; the saving of data, i.e. the positions of the motor sensors active in the movements.

As first instructions before entering the main loop, to the software was developed in order to proceed with the connection to MuJoCo HAPTIX, then with the opening of the serial port and the setting of the parameters and timeouts (Table 3.1 shows the functions used in this context), finally the choice of the control mode.

Functions	**Description**
CreateFile()	It is used to open the port: you specify the name of the port, the type of access, because the serial port is bidirectional, the way to create the file.
GetCommState(), SetCommState()	They are used for setting the parameters. In particular: - BaudRate: data transmission frequency; - ByteSize: number of bits before the rising edge of the stop bit; - StopBits: number of stop bits; - Parity: parity (even, odd, none).

Table 3.1 Functions used in serial communication.

Before exiting, at the end of the conditional loop, the software disconnects from MuJoCo HAPTIX and the serial communication is closed.

3.1.2.1 Control algorithm

The algorithm for the control of the virtual hand is dependent on the movement intention (i.e., the class) that is streamed from the bidirectional hand system to the external laptop on which our software runs and interfaces with the MuJoCo HAPTIX environment.

In the virtual hand control, the main objective is to take into account wrist movements, in particular pronation and supination, therefore the 5 movement intentions the bidirectional hand system kNN classifier is able to classify have been associated as reported in the Table 3.2.

Class	Description
0	Rest condition
1	Closing hand
2	Pronation wrist
3	Supination wrist
4	Opening hand

Table 3.2 Classes implemented in the virtual hand system.

It is important to note that while we are currently focusing on pronation and supination wrist movements, the virtual environment is actually a flexible test bench for the analysis of any complex movement.

The Figure 3.2 shows the movements of the hand in MuJoCo Haptix.

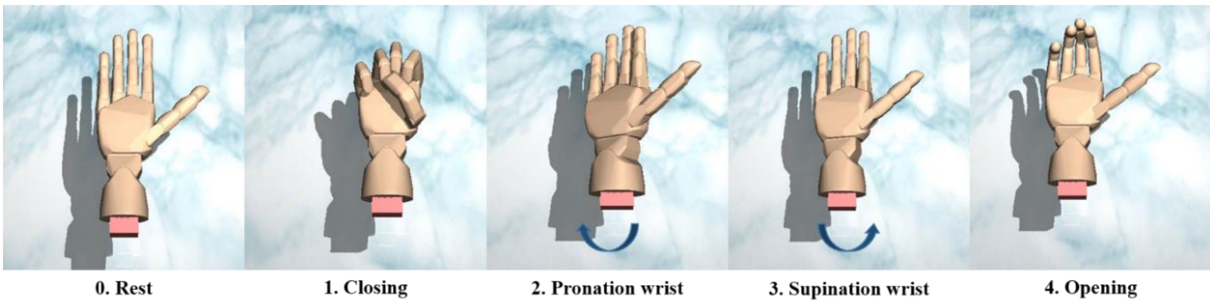


Figure 3.2 Movements hand in MuJoCo.

Once the class is read, the position of the motors is initially saved. Depending on the class, i.e. the desired movement, the position of the motors will change. In particular, in the case of class 1 and 4, corresponding, respectively, to the closing and opening of the hand, the motors concerned are 10 of the 13 available and are shown in the Table 3.3.

Actuator name	Joint name	Range
A_thumb_ABD	thumb_ABD	0 - 1.5
A_thumb_MCP	thumb_MCP	0 - 1.0
A_thumb_PIP	thumb_PIP	0 - 1.0
A_thumb_DIP	thumb_DIP	0 - 1.0
A_index_ABD	index_ABD	0 - 0.34
A_index_MCP	index_MCP	0 - 1.6
A_middle_MCP	middle_MCP	0 - 1.6
A_ring_MCP	ring_MCP	0 - 1.6
A_pinky_ABD	pinky_ABD	0 - 0.34
A_pinky_MCP	pinky_MCP	0 - 1.6

Table 3.3 The actuators used with their joints and range of motion in the closing/opening movement.

In the case of class 2 and 3, i.e. wrist supination pronation, only one motor is considered (Table 3.4). No motor is considered in the case of class 0, i.e. in resting condition.

Actuator name	Joint name	Range
A_wrist_PRO	wrist_PRO	0 - 3.14

Table 3.4 The wrist actuator used with their joint and range of motion in the pronation/supination

Below, the general pseudocode for hand control function is shown (Figure 3.3).

```
Loading the initial motor positions

Switch case

    Variation of motor position depending on speed
    Sending commands to virtual hand

End switch case
```

Figure 3.3 Pseudocode about virtual hand control.

The hand control function is centered on the switch case: depending on the class received, the movement is executed, activating the motors of interest.

For the control, 3 different incremental/decremental steps are chosen in advance to define the speed of movement of the hand. In the case of the wrist motor, a step of 0.025 has been chosen; in the case of the finger motors, on the contrary, a step of 0.008 has been used for almost all of them, with the exception of the motors related to the index and little finger abduction movement, where an increase/decrease of 0.004 has been chosen.

The difference in step values depends on the range of movement of the motor of interest. for example, in the case of the wrist, having a wide range of movement, from 0 to 3.14, it was necessary to choose a larger step to allow neither too fast nor too slow a movement. In contrast, hand motors have a much smaller range of motion.

However, it is possible to make minor changes to the movement speeds, depending on what is to be assessed or achieved.

In order to be able to move the hand step by step, it is necessary to verify, at each increment/decrement, that the position of the motor sensors is within the maximum range.

Once verified, the position will be increased or decreased, then transmitted to the motors and saved. It is clear that in the next cycle, the previously saved position will be the initial position.

3.1.2.2 Integration with the bidirectional hand system

The bidirectional hand system has been modified so that it can be interfaced with the virtual environment.

First of all, a further output of the system concerning the virtual hand has been added, in addition to those already present for IH2 Azzurra and i-Limb (Ossur). Then, a serial communication between the two systems has been created.

In particular, the control, line, input and output options of the port have been modified. The control options control the baud rate, set to 115200 baud, number of data bits, equal to 8, parity, stop bits, equal to 1, and hardware flow control. The input options control any input processing that is done to characters received on the port and have been set to ignore parity errors. The line options, which control how input characters input are managed by the serial driver, and the output options are set to 0.

In addition, the function relating to the setting of the parameters have also been modified and the function relating to the transmission of input/output data has been set so that data received but not read is removed.

Next, it has been added, in the Hand Controller, the possibility to control the virtual hand. In this case, the class provided by the Classification Controller has been taken into account and has been written on the serial port.

Since the bidirectional system of the hand had been previously implemented for the IH2 Azzurra and for i-Limb (Ossur), the consideration of a third hand type, the virtual hand, involved the addition of some conditions so that the system always works, regardless of the hand to be controlled.

On the other hand, in the code in MuJoCo HAPTIX, it was also necessary to implement the part related to reading from the serial port, through the *ReadFile* function (Table 3.5).

Functions	Description
ReadFile()	It allows you to read the data. It is a blocking function, i.e. the program will wait if there are no characters to receive and will not respond to user input until it has sent all the defined bytes along the physical channel.

Table 3.5 ReadFile function for serial communication.

Another change that has been made concerns the mapping modification relative to the classes, therefore to the hand movements.

In the previous development, also 5 classes were considered. The Table 3.6 describes which class is associated with a particular movement.

Class	Description
0	Rest condition
1	Power grasp
2	Pinch grasp
3	Ulnar grasp
4	Hand opening

Table 3.6 Classes implemented in the bidirectional hand system.

Unlike the classes described in the algorithm, wrist movements were not taken into account.

3.1.3 Tracking experiment mode

The previously proposed control algorithm can be used in a tracking experiment. The latter is inspired by a previously proposed paradigm [31].

In this experiment, the virtual hand controlled by the subject is not visible to him. However, the subject is shown a virtual hand controlled externally, exactly as if he was watching a video and had to replicate its movement. In this last case, the class must be known a priori: it is the operator who decides which movement of the hand to show to the subject and then make him replicate it. The class, then, in this case, is provided through an array structured in the following way: for a certain number of positions of the array, the class, for example, will be relative to the closing movement, for other as many positions, the class will be associated to the opposite movement, of hand opening. this can be repeated as many times as you want depending on the size of the array, also chosen a priori.

Instead, for the control of the invisible virtual hand, the class must always be provided through serial communication, since it is the subject who controls it, replicating the movement shown to him.

Once the class is known, in both cases, the previously illustrated virtual hand control algorithm can be applied, with the same modes and parameters described above.

However, it is always necessary at the end to save the data relative to the positions of the sensors, both in the case in which the hand is controlled externally, and in the case in which the subject controls an invisible virtual hand.

In this way it is possible to obtain a more structured evaluation of the impact of kinesthetic feedback.

Below, we report the pseudocode related to the tracking experiment (Figure 3.4).

Reading class from array
Reading class from serial port

Switch case

    Variation of motor position depending on speed
    Sending commands to virtual hand

End switch case

Saving data

Figure 3.4 Pseudocode about virtual hand control.

3.1.4 Characterization

Once the development of the virtual interface was finished, it was necessary to verify its correct functioning.

A first analysis has been done considering the 5 possible movements, taking into account the motor sensors positions of both wrist and hand. Then, a second analysis has been carried out on the cycle timing.

3.1.4.1 Virtual hand DOFs analysis

The 5 possible movements during the virtual hand control are shown in Figure 3.5.

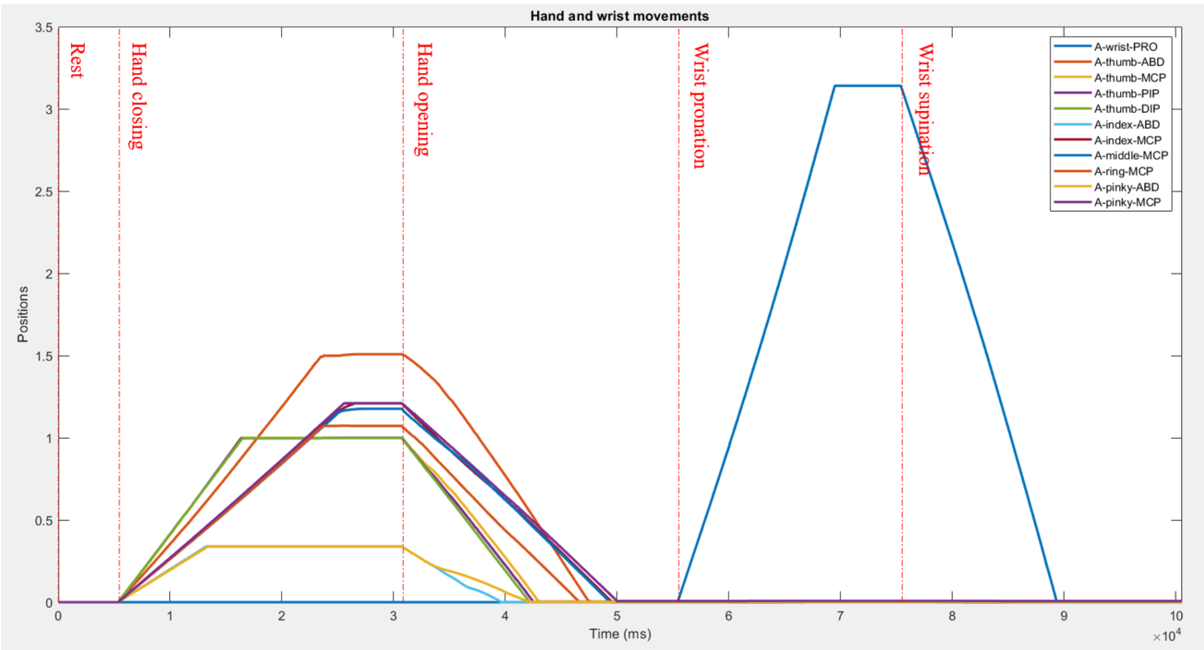


Figure 3.5 Motor sensors positions during the hand and wrist movements.

The test performed lasted about 100 seconds. During this time, the five possible movements, resting condition, hand closing, opening, wrist pronation and supination were verified.

The above graph (Figure 3.4) relates the positions taken by the motor sensors, measured in motor-specific units, as a function of time, measured in milliseconds.

It can be seen that, in the first 5 seconds, the hand, which initially, from model, is open, was at a state of rest. Therefore, no motor has varied its position; therefore, correctly class 0 has been read and transmitted.

Subsequently, the subject performed a closing movement of the hand followed by an opening movement.

It can be noted, as correctly, that the active motors are only those related to the hand, while the wrist motor is stopped at 0. However, the motors increase, step by step, their position, in the case of the closing movement, until they reach the maximum of their range, and then decrease and return to the initial position, in the case of the opening movement. In addition, the presence of a plateau marks the achievement of the maximum or minimum value of the range. In fact, for example, if the class continues to be "closing hand", but the hand is already completely closed, the motors will not move, so the hand remains stationary in that position until a different class is provided.

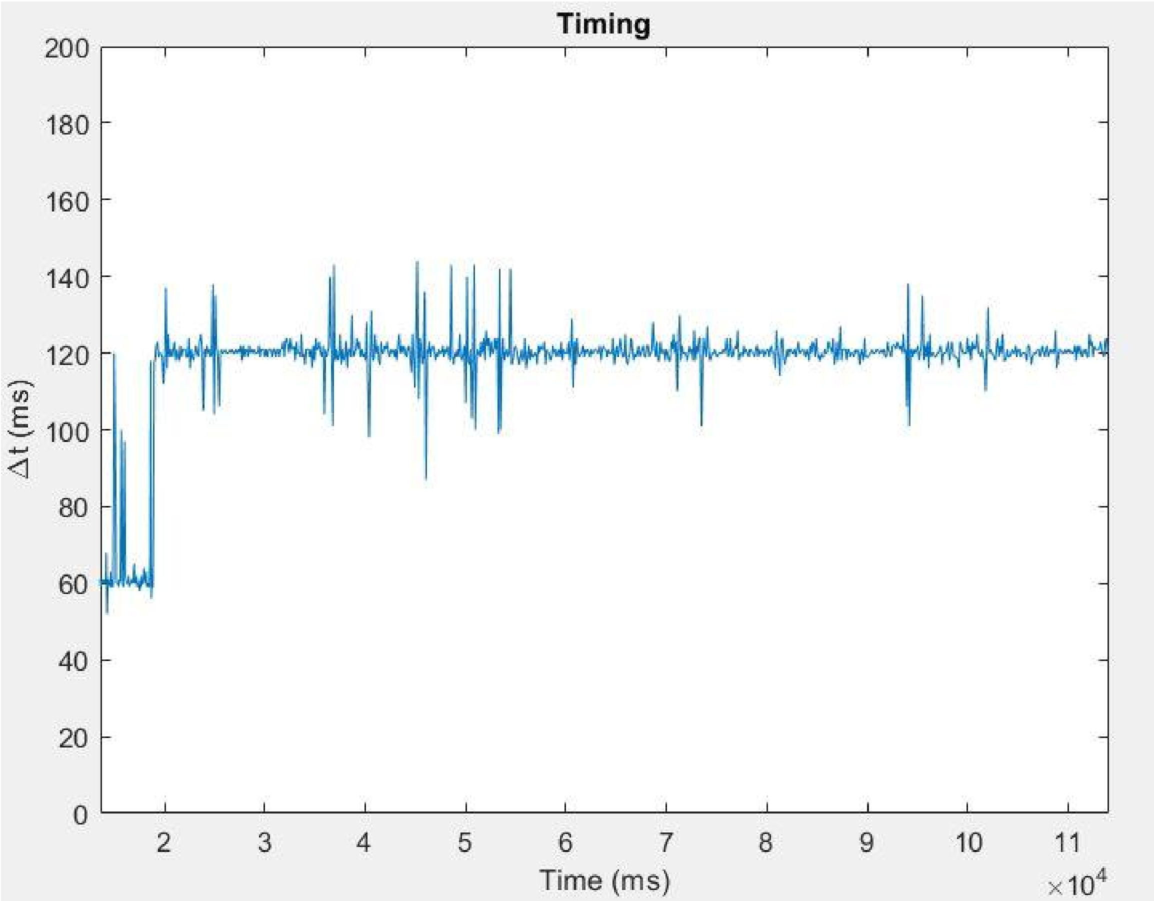
Eventually the wrist was set in motion. Also in this case, only the motor of the wrist is correctly active, while all the others are stopped. First, the wrist is pronated, the maximum possible range value is reached, and then there is the supination movement, which returns the wrist to its initial position.

This test, so, confirms both the correct reading of the intended movement from the bidirectional hand system via serial communication, and the correct implementation of the virtual hand control.

3.1.4.2 Delays analysis

A qualitative analysis of time delays has been conducted. In general, the control loop in the bidirectional hand system has a timing of 60 milliseconds.

Taking into account the time of the previous analysis, we obtain what is shown in Figure 3.6.



Initially, it is in rest condition, which is why the time intervals are centered at 60 ms, except for a few outliers. Once a class is read, then the virtual hand is controlled, the time intervals are centered at 120 ms, except for a few outliers. This difference is due to the interfacing of the software with MuJoCo HAPTIX. Moreover, it is also confirmed by the number of bytes read from the serial at every cycle of the software's main loop. Indeed, in rest condition the number is on average 1.06, while for all the other classes is 1.99.

Making a further consideration on the average of the time intervals, class by class, we have obtained the results reported in the Table 3.7.

Class	Mean (ms)
0	79
1	120.38
2	120.39
3	120.43
4	120.41

Table 3.7 Mean values class by class in normal virtual hand control.

These are average times that can be considered acceptable, especially since the frequency of the EMG Controller of the bidirectional hand system is 10 Hz, so it has a timing of 100 milliseconds.

By comparing the normal control of the virtual hand with the tracking experiment, we obtain the following graph showing the time intervals, measured in milliseconds, shown in Figure 3.7.

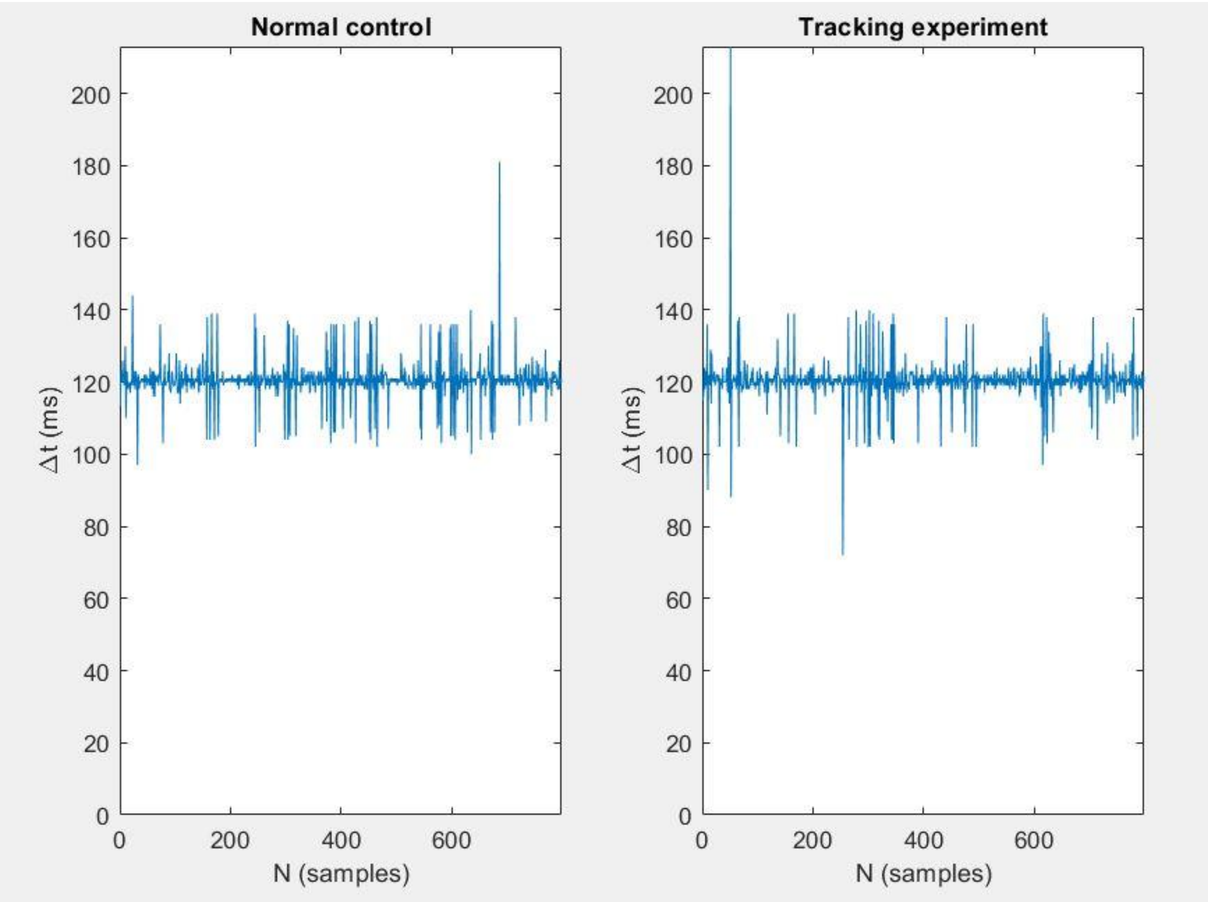
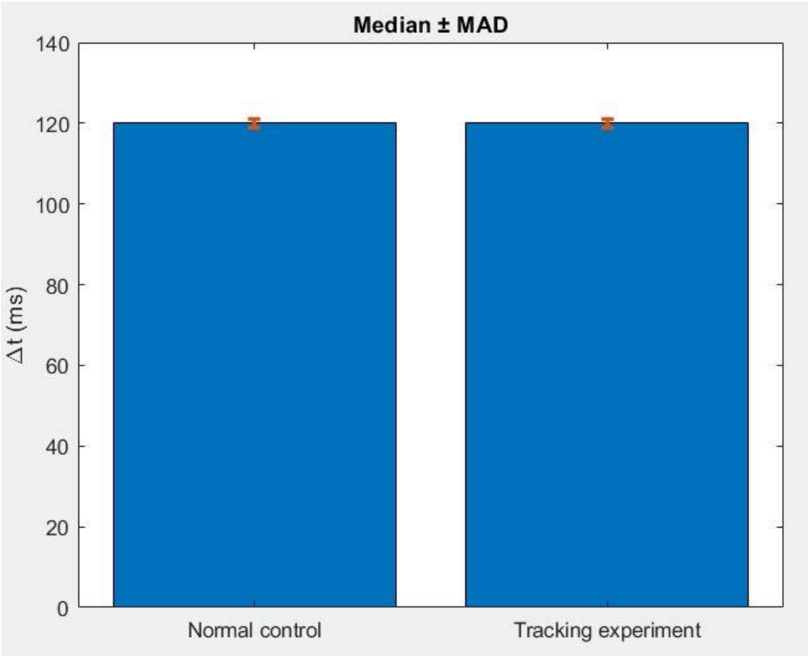


Figure 3.7 Timing intervals in normal control compared to tracking experiment.

In both cases, the time intervals are centered around 120 milliseconds: with the exception of a few outliers, the timing is the same, even in the case of the tracking experiment where two virtual hands are controlled. In this regard, we report the intervals defined as the median plus or minus the median absolute deviation, shown in Figure 3.8.



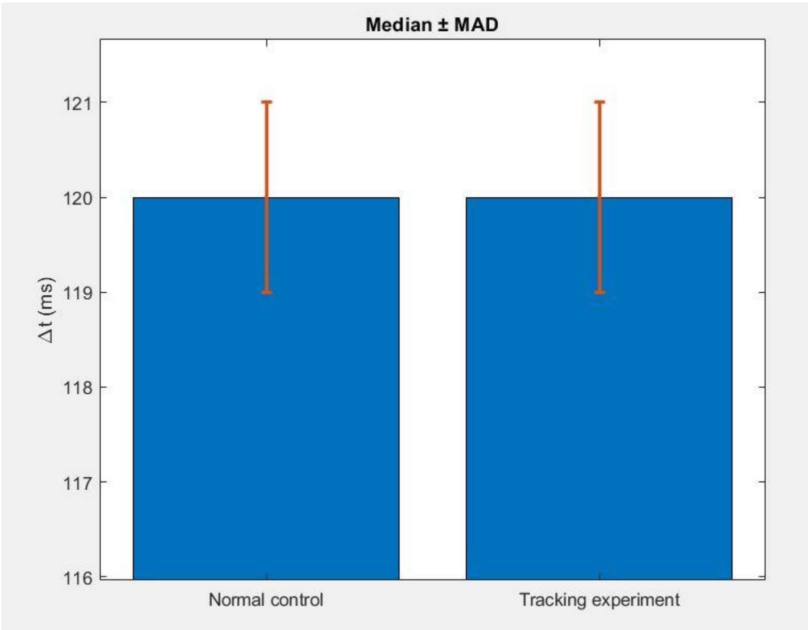


Figure 3.8 Above, median ± MAD intervals in normal control and in tracking experiment; below, zoom on intervals.

In order to test the significance of the above statement, we first checked whether the time distributions were Gaussian exploiting the Lilliefors test was performed, which is a composite normality test based on Kolmogorov-Smirnov's test. Given the rejection of the null hypothesis, a non-parametric test, the Wilcoxon signed-rank test, was exploited to assess whether the average ranks of the two distributions differ. If, on the other hand, the test result had confirmed the normality of the distributions, a t-test would have been performed.

The results of the test are shown in the Table 3.8.

Wilcoxon signed-rank test	
α	0,05
p-value	0,986

Table 3.8 Results obtained by Wilcoxon signed-rank test.

From the results obtained, we deduce that the null hypothesis cannot be rejected, because the p-value is greater than 0.05. Therefore, there is a no statistical difference between the two distributions, which confirms our qualitative assessment reported above.

The results on timing analysis do not show, therefore, particular delays neither in the normal control of the virtual hand, nor in the tracking experiment mode. They, therefore, confirm, again, the correct functioning of the developed system.

4. Discussion

The project presented in this master thesis aims to develop a virtual environment for the study of illusions of movement of the upper limbs in neuroprosthetic applications. In this regard, a previously developed system [14] was considered, which aimed at restoring proprioceptive feedback to transradial amputees, focusing on muscle and tendon vibration as a means to provide homologous and somatotopic non-invasive sensory feedback.

In order to achieve the objective initially established, an in-depth study of the field was necessary. The increasing interest of researchers in upper limb prostheses comes from a large number of subjects, mostly young, who have undergone amputation. The different causes, in this regard, have been highlighted, finding a significantly higher prevalence of the pathologies compared to the other causes considered. In order to offer amputees a good quality of life, different types of prosthesis are available today. However, being able to control them is still the most studied and discussed aspect today. Among the methods presented, the most common and also used in this project was the control by electromyographic surface signal, for its ease of access and non-invasiveness. Although non-invasiveness is a fundamental requirement, very often EMG recordings can be unreliable and inconsistent due to poor electrode contact with the skin, sweating, reduced electrode placement space. Therefore, more sophisticated approaches that allow natural control of more degrees of freedom and improved prosthetic function would be preferable. Establishing a sense of agency could help amputees inaccepting the device.

Lack of sensory feedback is one of the most studied and essential aspects of prosthetic control to help amputees recover lost function. Several feedback strategies have been discussed, however, the homologous and somatotopic approach is the ideal solution for completely natural sensory feedback due to its simplicity and intrinsic intuitiveness.

Illusions of movement have been investigated since the 70s and recently have proved to be an adequate means of providing natural, non-invasive kinesthetic feedback to TMR patients and, moreover, promising evidence was also found in the previous project [14], in which the illusions of movement were exploited in transradial amputees.

With the previous study [14], several illusory perceptions have been raised, showing a certain specificity of the subject, in terms of type of illusory movement, stimulation site and stimulation frequency. However, the most perceived perceptions were related to the wrist and the most receptive ones were studied.

The need for a flexible environment stems from previous discoveries about the variety of illusions aroused and the massive presence of illusory movements tied to the wrist.

Therefore, in order to develop a system capable of achieving the intended goal, an in-depth study of the bidirectional system of the hand was necessary, as the latter can be easily interfaced with various external devices that may be necessary for closed circuit control.

A further study was conducted, in particular, on the stimulation system developed to allow the bidirectional hand system to provide kinesthetic feedback based on muscle vibration in a closed loop manual prosthesis. Finally, the modular architecture and readability of the bidirectional hand system source code made it easy to add functionality, creating new levels of abstraction or extending existing ones. As a result of these considerations and evidence, it was also chosen to use this system to achieve our goal.

However, changes had to be made to this system to facilitate the integration of the virtual interface with the bidirectional hand system. In particular, it was necessary to add a new output for the system to interface with the virtual environment.

The virtual interface was created in MuJoCo HAPTIX. The latter was an excellent software to achieve our goal, thanks to the availability, within the suite, of a virtual hand with 22 degrees of freedom.

Not having found among the models of the virtual hand already available in MuJoCo the one that would suit our case, it was necessary to create a new one, proving to be valid for the goal to be achieved. They have been eliminated all the geometric objects, so as not to disturb the attention of the subject, and it has been assumed an initial position of the hand such to have clear and evident the movements that it will go to carry out.

To interface the two different systems, the serial communication protocol was chosen, since in this case, the data transfer takes place bit by bit and the data reading is possible every time an event is heard.

Subsequently, the implementation of the EMG signal classification system has been modified, since the main objective is to take into account the movements of the wrist, in particular pronation and supination. The choice of this movement alone is dictated by the results of the previous study, in which the most perceived illusion was related to the movement of wrist pronation. However, it is important to note that the use of a flexible environment allows with few modifications the study of any type of movement, therefore to consider any degree of freedom of the virtual hand.

The implementation of the virtual hand control algorithm is the real core of the system. The choices on the speed parameters, the virtual hand motors to be used, the communication for the streaming of the movement intention from the bidirectional hand system, the logging of data related to the time and positions of the motor sensors have proved to be satisfactory for the achievement of our goal.

Moreover, it has been implemented also the possibility to use this virtual hand control algorithm on a tracking experiment, taking inspiration from a paradigm previously proposed by Marasco [31]. The author, through the use of a neural-machine interface, has shown an improvement in motion control, thanks to the integration of kinaesthetic feedback produced by vibration. Also in our case, the possibility of a tracking experiment aims to allow a more structured evaluation of the impact of kinesthetic feedback.

To verify the correct functioning of the entire system, pilot tests were performed, which suggested the correct integration of the virtual interface developed with the bidirectional hand system.

Pilot tests were carried out both on timing and hand control. In particular, the correct reading of the class and the correct execution of the movements were verified. As far as timing is concerned, depending on the class, the time intervals were evaluated, noting that in resting condition, these are centered at 60 ms, while for the other classes at 120 milliseconds, due to the interfacing of the bidirectional system of the hand with MuJoCo HAPTIX and the different number of bytes read, on average 1.06 byte in resting condition, on average 1.99 bytes for all other classes.

In the comparison between a normal control and the tracking experiment, the intervals (median ± median absolute deviation (MAD) were initially calculated, obtainingan overlap between the two. The normality of the time interval distributions was also tested, with negative results. Therefore, the Wilcoxon signed-rank test was performed to assess the presence of a difference between the average ranks of the distributions. The results obtained did not show a statistical difference between the two distributions, as a p-value of 0.986 was obtained, therefore greater than 0.05.

Due to the spread of the epidemiological health emergency Covid-19, it was not possible, however, to perform the experiments on healthy subjects and amputees. In particular, the plan was to carry out the tracking experiment in order to evaluate the impact of kinesthetic sensory feedback provided by muscle vibration in a tracking task. In order to do so, first a mapping of the elicitable sensations would be performed, by vibration of the forearm in healthy subjects and of the stump in amputees. Then, depending on the perceived sensations the subjects or patients would have been asked to perform the tracking experiment. It is worth to note that in the case of healthy subjects, the control would be performed with the controlateral arm with respect to that receiveng the vibratory-induced kinesthetic feedback. This clearly to avoid proprioceptive information coming from their intact receptors.

While the tracking experiment will be carried out in the future, the results obtained while characterizing the interface are to be considered auspicious. Indeed, the developed interface paves the way for further investigation of non-invasive kinesthetic feedback by exploring muscle vibration.

5. Conclusions

The high rate of myoelectric prosthesis failure could be greatly reduced by restoring sensory feedback from the prosthetic device to the user. Sensory restoration is the missing link needed to make current state of the art prostheses widely accepted by amputees. Researchers have increasingly focused attention on this need to provide amputees with prosthetic devices that functionally resemble the lost natural limb. Several studies have been conducted on the sense of touch and more receintly kinesthetic perceptions have became subject of investigation.

In particular, providing homologous and somatotopic non-invasive kinesthetic feedback exploting muscle and tendon vibration is a new promising approach.

A previous study tackling vibratory transradial stump stimulation as well as forearm stimulation in healthy subjects showed elicitability of a great variety of illusory percepts, with a significant prevalence of wrist related movements. The same work proved the possibility of achieving bidirectional control of a robotic hand based on opening and closing movement intention decoded from sEMG electrodes with vibratory stimulation providing the corrisponding kinesthetic percepts in closed loop.

In light of this it was deemed necessary to integrate the bidirectional hand system developed by researchers led by Prof. Micera with a flexible virtual environment for both testing and training.In particular, a correct integration of the bidirectional hand system with a virtual environment for the bidirectional control of a virtual hand with 22 degrees of freedom has been achieved, allowing, on the one hand, the possibility to study any perception, guaranteeing, on the other hand, the specificity of the subject compared to such perception.

The characterization on hand and wrist movements and timing has been performed to verify the correct functioning of the developed system, obtaining satisfactory results.

However, the outbreak of the Covid-19 pandemic prevented from performing on healthy and amputated subjects.

In the future, the entire system will be tested on both healthy and amputee subjects in order to analyse the results for possible improvements with the aim of obtaining an increasingly intuitive and skilful control of the device. In addition, further investigations of non-invasive kinesthetic feedback could be carried out, trying to combine it with the widely explored tactile feedback, so as to provide complete sensory feedback as close as possible to the natural one.

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