Tesi di dottorato in Ingegneria Biomedica, di Luca Rossini,
discussa presso l'Università Campus Bio-Medico di Roma in data 16/04/2010.

UNIVERSITÀ CAMPUS BIO-MEDICO DI ROMA

SCHOOL OF ENGINEERING

PHD COURSE IN BIOMEDICAL ENGINEERING

(XXII - 2007/2009)

NEUROINSPIRED INTERFACES FOR HUMAN-MACHINE INTERACTION

A THESIS PRESENTED BY LUCA ROSSINI

IN PARTIAL FULLFILLMENT OF THE REQUIREMENTS FOR
THE DEGREE OF DOCTOR OF PHILOSOPHY
IN BIOMEDICAL ENGINEERING

UNIVERSITÀ CAMPUS BIO-MEDICO DI ROMA
SCHOOL OF ENGINEERING

COORDINATOR :	PROF SAVERIO CRISTINA
SUPERVISOR :	PROF EUGENIO GUGLIELMELLI
CO-SUPERVISORS :	PROF CECILIA LASCHI, DR LOREDANA ZOLLO, DR DARIO IZZO

JANUARY 2010

UNIVERSITÀ CAMPUS BIO-MEDICO DI ROMA
SCHOOL OF ENGINEERING
PHD COURSE IN BIOMEDICAL ENGINEERING
(XXII - 2007/2009)

NEUROINSPIRED INTERFACES FOR HUMAN-MACHINE INTERACTION

LUCA ROSSINI

CONTENTS

CHAPTER ONE

-

INTRODUCTION TO NEUROINSPIRED INTERFACES

I. NEW HUMAN-TECHNOLOGY INTERFACES CAN LEAD TO TECHNOLOGICAL DEMOCRACY

The proliferation of progressively more sophisticated electronic devices is a characteristic of our time. The direct access to informational contents and to applications' interfacing and controlling is steadily increasing, while the new phenomenon of digital divide (here intended in its general sense) is also growing at the same rate: the use, with the related benefits, of new technologies is not accessed by all potential users. Geographical discrimination is only one of the gaps, which the digital revolution is struggling to bridge. Another discrimination regards knowledge. Any new device often requires the know-how related with the interface of its predecessor, plus a learning process associated to the new features offered. Hence, who does not manage to keep the pace, for reasons related with motivation, age, education level, work experience among the others, is eventually overwhelmed by devices each time more complex and advanced. Henry Ford once said that "true progress is made only when the advantages of a new technology are within reach of everyone": a great challenge that lies ahead our digital era.

A solution is the improvement of actual interfaces or the development of new ones, since they are responsible for our communication with machines, and thus for the definition of a universal language able to provide everybody with the possibility of controlling present and future devices. It is possible to argue that the best accessibility will derive from interfaces able to exploit at best the natural communication pathways characteristic of the human being. Bailey (1989) defines an interface as "the boundary shared by interacting components in a system" in which "the essence of this interaction is communication, the exchange of information back and forth across the boundary". Information between human and technology is, therefore, exchanged across human/technology interface. This exchange of information is bidirectional, since it includes both the interface that allows the person to control the device and the interface that provides feedback to the person regarding the device's operation.

The effectiveness of human/technology interfaces depends on three interrelated elements that contribute to the operation of a device: the control interface, the selection set, and the method. The control interface, or input device, is the hardware with which the human operates the device (i.e. keyboard, mouse, joystick, etc,.). The control interface generates from one to an infinite number of independent inputs, or signals, defined as the input domain (Morasso et al., 1979). The selection set is the group of items available from which choices are made (Lee and Thomas, 1990). The strategies with which the user makes selections using the control interface are the selection methods.

A "natural" interface learns and adapts itself to user's interfacing modalities, and not the opposite, extending the use of new technologies towards population sectors which are typically struggling to interface with technologies. The characteristic feature of natural interfaces is the fact that they almost lack a physical control interface. Since the user is asked to behave "as he/she normally would" while trying to get the device to perform the desired action, he does not have to operate any physical interface-device interfacing him to the technology. The control interface in a natural interface monitors user's natural behaviours and detects those related with the technology interaction (Rauterberg and Steiger, 1996). The set of discernable behaviours is the selection set of a natural interface. The selection method is direct, meaning that the user is able to use the control interface to randomly choose any of the items in the selection set (he/she can perform any recognizable behaviour at any time).

Non-natural interfaces are operated by predefined user's motor actions, and typically different action kinematics are associated with different interfaces (i.e. computer keyboards and mouse). As a consequence, their use inevitably requires a re-modulation of connections between user's brain sensorimotor areas involved with the device utilisation (i.e. the neuronal networks involved with the actual formulation of a task), and those dedicated to the motor task for the interface operation (i.e. the hand and fingers control to obtain a correct typing of the related task's commands). Obviously, operating a classical interface carries a high cognitive load which - when several different interfaces have to be operated within a short period, or when the operator is less re-active in its internal re-modulation - can easily decrease the operator's mental performance due to mental fatigue and increase the error rate (Olsen and Goodrich, 2003).

Here a new class of natural interfaces is defined, named Neuroinspired Interfaces: they are systems that, relying on the intrinsically physiological ways of human information transfer and action execution, permit a fully natural interaction between users and machines. Neuroinspired Interfaces are regarded as technological devices aimed at improving everyday life of a large number of common people by providing a universal language.

II. NEUROINSPIRED INTERFACES

Neuroinspired Interfaces are here defined as systems that rely for their operation on the physiological ways of human (neural) information transfer and (muscular) action execution.

As any natural interface, a Neuroinspired Interface has its characteristic feature in the ability of monitoring and detecting human behaviours, which it translates into technology operation. The difference from other natural interfaces is in the fact that these behaviours are extracted from physiological and involuntary events related with the natural transferring of information on user's intentions that inevitably happens between the arising of a need or a task decision (intention) and the manifestation of an action (Fig.1).

Any human intention is originally conceived within the brain, thanks to the synchronized electrical activity of networks of dedicated neurons. Always within the brain, any action requested by the intention is planned and its accomplishment status continuously controlled. Only low level information containing the individual commands to human effectors, namely limb and postural muscles, exit the brain and are conveyed trough fascicles of peripheral nerves. This commands can travel the whole body until reaching the motor plaque, where they are translated into muscular activity and, thanks to the structure offered by bones, joints and ligaments, produce movements.

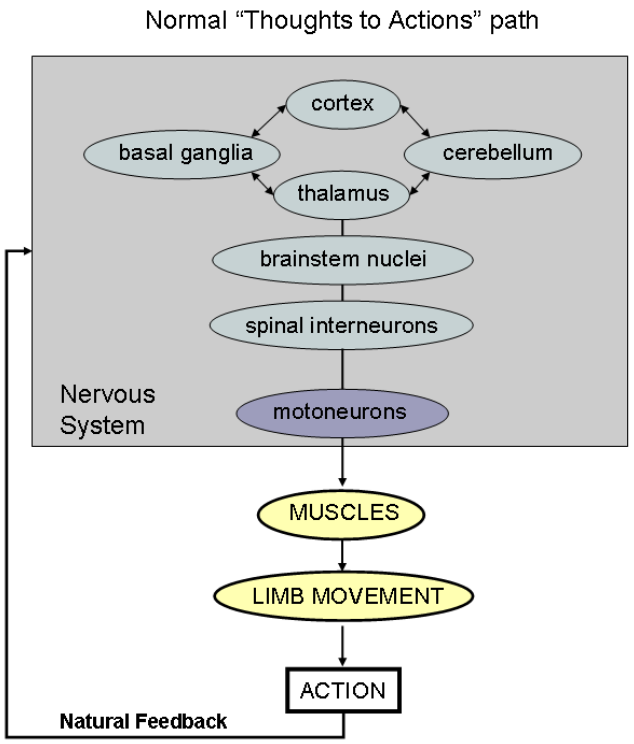

Figure 1. Normal information path which separates human's thoughts from actions. An intention is generated and integrated in the central nervous system (light blue ovals). It leaves the central nervous system at the level of spinal interneurons and is conveyed in the motoneurons fibres (dark blue oval) towards its actuation (light yellow ovals). The action (white box) is the result of the intention actuation, and produces a natural feedback which goes back to the nervous system.

Only low-level information (like the commands for opening and then closing the hand) leaves the brain and travels along nerve fibres towards limb muscles. Information at this level does not contain any "high-level" target intention anymore (that is, the concept of blue bottle is lost even if the command contains all the relevant instructions to shape the hand/fingers and regulate force in order to grasp and lift a bottle like the blue one). On the other hand, information at this level ended its formulation and integration path before leaving the brain: it is, hence, in its final form for intention execution (Micera and Navarro, 2009). The lack of any non-invasive technology for accessing peripheral neural activity makes this information accessible only by invasive procedures, like intra-neural electrodes implantation (Rossini et al., 2009).

Finally the electrical commands end travelling along nerves, they reach and activate a motor plaque at the muscle fibres level. Here commands are immediately translated into actions, that is, muscle contractions. The latter can produce or not movement, but surely produce a specific electrical activity which can be invasively or non-invasively monitored (Carpi and De Rossi, 2009). When movement occurs, it can be monitored too thanks to several non-invasive techniques.

Summarizing, Neuroinspired Interfaces can extract information on user's intentions from the following sources: (1) the place where information naturally originates and for the most stays, by monitoring user's brain activity (Fig. 2); (2) the place where information's low-level fully integrated version is naturally conveyed, by monitoring peripheral neural activity (Fig. 3); (3) the place where information naturally manifests itself in form of actions, by monitoring and detecting muscular activity and limb movement (Fig. 4). Obviously, the decision on where to extract the information makes a big difference on which kind of information can be extracted, how invasively it can be accessed, and how easily it can be separated from the multitude of information human beings are constantly producing, elaborating, and conveying into actions.

The main goal of the present Thesis is to prove the theoretical potentials of Neuroinspired Interfaces at all the three main levels of prospected human-interface connections. The work follows the same "thoughts to actions" path, from the central nervous system (CNS), passing from the peripheral nervous system (PNS), and arriving at the muscular action execution producing limb movements.

III. NEUROINSPIRED INTERFACES WITH THE CENTRAL NERVOUS SYSTEM

In theory, by extracting and decoding user's brain activity it would be possible to access any kind of information on user's intentions at any level of integration. There is a class of interfaces designed to monitor brain activity and translate the voluntary modulation of some of its feature into commands to a device: the Brain Machine Interfaces (BMI) (Wolpaw, 2002). When the required modulation is related with the natural one happening during intention formulation (i.e. during motor planning of the upper limb) for controlling a similar device action (i.e. a robotic upper limb movement), the BMI is also a natural interface. In an ideal natural BMI, hence, the motor commands, instead of being sent to the physiological musculo-skeletal effectors, reach an artificial actuator (a robot) (Fig. 2).

The worldwide excitement generated by the work of Nicolelis in the year 2001 was caused by the clarity with which this ideal model was demonstrated. In a long video sequence, the world witnessed a monkey in the act of controlling a robotic arm and feeding itself by doing so. The monkey was sitting and behaving normally while, at the same time, controlling with its brain neurons the actions of the robotic arm (Nicolelis, 2001). It was suddenly clear that BMIs are not only potentially able to restore lost abilities, but they also are a realistic option to augment human capabilities. An insight that equally generated hopes and doubts in the general public and among scientists and opened a healthy discussion on ethical implications related to the use of this technology.

In Chapter 2, the study focuses on open issues like the invasive/non-invasive BMIs dilemma and the potential long-term neuro-plasticity effects on user's ability to control the interface. After matching the performance of the current system to the requirements of different assistive and augmenting devices, the study targeted two main class of potential users for current BMIs: seriously paralyzed subjects (i.e., with solely limited control of eye muscles), and astronauts.

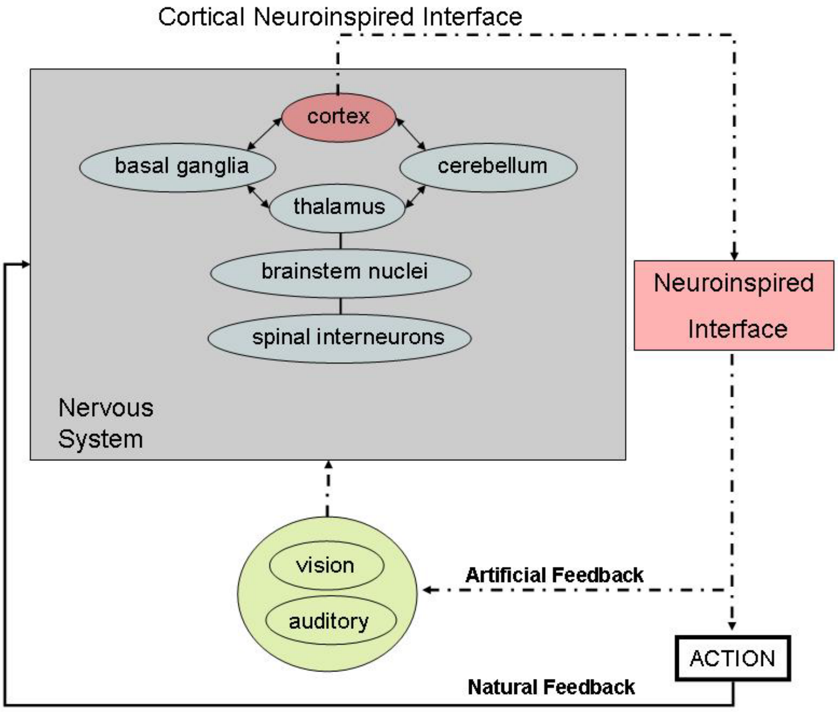

Figure 2. Information path which separates human's thoughts to actions in a cortical Neuroinspired Interface. User's intention is generated and integrated in the central nervous system (light blue ovals), but the interface access the information solely at the cortex level, loosing part of the information. The action (white box) is controlled vie the interface, which produces also artificial feedback to the subject.

III.I Neuroinspired Interfaces for Space Applications

A dedicated study focused on astronauts, exploring the difficulties faced by this very particular class of workers during orbital flight or space travel expeditions, and studying the known effects of microgravity exposition to the cortical activities related with BMIs (Rossini, Izzo, and Summerer, 2009). Astronauts (a particular highly motivated, trained and skilled category) are also suffering, when in orbit, from what can be seen as a case of digital divide (Summerer, Izzo and Rossini, 2009a). On Earth, the high versatility of humans motor abilities allows for a huge range of elaborated motor behaviours, such as dancing, playing soccer, doing acrobatics or playing music instruments. However, human motor performance is strictly bounded to the physical conditions that govern our planet. Human perception and planning of movement, for example, are related to the identification of the gravity axis (Clement, 2003). Inevitably, human sensory-motor system encounters a loss of performance in situations of changed or annihilated gravity. Under microgravity conditions, this loss is so important that, from certain perspectives, astronauts are in a similar situation to people affected by motor disabilities on Earth: both have, for different reasons, a deficit in the performance required to accomplish their motor tasks (Gordon et al., 1995). The reduction of physical and mental ability suffered by astronauts can be addressed by assistive devices (Cook and Hussey, 2002) once they are redesigned for functioning in space (Solov'yev, 1991), though weightlessness condition affects astronaut's uses of any kind of human/technology interface that requires physical interaction. Potentially independent from the user's physical abilities, BMIs can in principle access the user's intentions at a higher level, were they naturally originate: in the brain. Hence they can predict directly the user's motor intentions, not related with users' abilities. BMIs have the potential to provide the most direct control over complex systems and, since they are expected to operate in principle very similar in space and on Earth, they could assist astronauts by helping them to perform in space as efficiently as on the Earth.

In Chapter 3, the study focuses on addressing the potential of brain-machine interfaces for space applications and on reviewing expected issues related with microgravity effects on brain activities. Information on the latter had to be indirectly extrapolated from studies related on specific changes in the cortical activity between ground (i.e. planet Earth) and orbital recordings. This information is very scarce, due to the difficulty in performing experiments with astronauts during orbital flights, and none of the published studies have ever approached the problem of using BMIs in Space. Because of these limits, a new experiment was performed to test the ability of a BMI classifier to work on the cortical activity recorded during short-term expositions to microgravity during parabolic flight. The results of the experiment are shortly presented in Chapter 3.

Since the next step would necessarily be to test a whole BMI system performance during orbital flight operations, the main goal of the study was to provide a detailed analysis of the potentials of BMIs for Space applications as far as the current knowledge would permit, and to suggest the research and development steps necessary to include brain-machine interface technology in future architectures for human space flight.

IV. NEUROINSPIRED INTERFACES WITH THE PERIPHERAL NERVOUS SYSTEM

Neuroinspired Interfaces relying on the information extracted from user's brain activity are fundamentally flawed by serious physical and technological limitations related with current brain-imaging techniques, which make BMIs a valuable solution solely for severely paralyzed subjects or for human subjects performing complex operations in very unnatural environment, as Astronauts during microgravity exposition (Tonet et al., 2008; Citi et al., 2009; Rossini, Izzo and Summerer, 2009b). The limitations of current BMIs are not only related with the level of invasiveness of the brain-imaging techniques. Independently on the resolution of the recording technique, in fact, the extracted information would always be in its non-final stage, that is, some of the processing and integration which in the brain transforms intentions into action commands would be inevitably missing (Rothwell, 2009).

The only way to access neural information at its final and fully integrated stage is by a Neuroinspired Interface which monitors and detects user's intentions at the peripheral nervous system (PNS) level (Micera and Navarro, 2009). At this level, on the other side, any high-level information (i.e. the final target of the action) is lost. Despite the high degree of invasiveness of current PNS activity imaging techniques (neural electrodes), these interfaces could provide bidirectional, multi degrees of freedom, and natural control of sensorized robotic prosthesis, i.e. a robotic hand prosthesis for hand amputee subject (Rossini et al., 2009). Since the information extracted from the PNS contains the low-level commands once directed from the CNS to the muscle actuators, which in the amputee were usually lost together with the amputated hand and are therefore no longer part of his/her body, the specific role of the interface is to artificially close the communication line once directed to muscles with the prosthetic robotic actuators (Fig. 3).

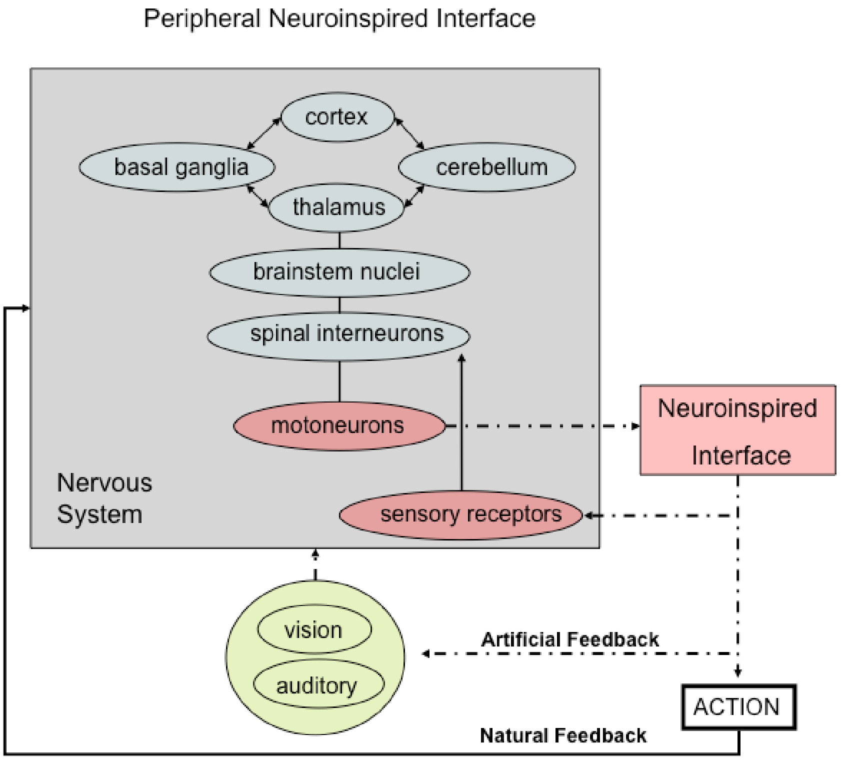

Figure 3. Information path which separates human's thoughts from actions in a peripheral Neuroinspired Interface. User's intention is generated and integrated in the central nervous system (light blue ovals), before being conveyed to the motor neurons, where the interface access the information and gives back natural feedback as the natural sensory receptors would do. The action (white box) is controlled vie the interface, which produces also artificial feedback to the subject.

In Chapter 4, the study aims at testing the potentials of Neuroinspired Interfaces with the PNS for the bidirectional control of a robotic prosthetic hand. The study was performed within the FP6 Neurobotics Project experiments. Three open questions were particularly addressed: 1) is the recorded peripheral neural activity really modulated by motor cortical activity?; 2) is the user of an invasive interface with the PNS really able to voluntary control his/her efferent neural activity in order to control more than one degree of freedom of the robotic prosthesis operation?, and; 3) is the artificial production of afferent neural activity able to produce natural sensorial feedback that the user can use in closed-loop for voluntary modulation of his/her efferent activity?

V. NEUROINSPIRED INTERFACES WITH ANTICIPATORY MOVEMENTS

The same neural information at its final and fully integrated stage, which can be accessed by Neuroinspired Interface with the PNS, produces within few tens of milliseconds a muscular contraction, which may or may not induce limb or postural movement (Fig.1). This is the regular scenario, of course, if the target muscles and limb are still present and healthy. Neuroinspired Interfaces designed to extract information on user's intentions from his/her muscle contraction (Carpi and De Rossi, 2009) or limb movements can, in theory, have access to final-stage intentions information with non-invasive techniques which could be applied to the largest human population (Fig. 4). On the other hand, since these interfaces require the final step of the path from thought to action to be performed, they cannot be used neither by paralyzed nor amputee subjects.

By monitoring involuntary behaviours related with user's intentions, it is in principle possible to predict the same intentions in a natural and transparent fashion (Laschi et al., 2007). A subclass of Neuroinspired Interfaces, which rely on anticipatory unconscious behaviours, is here addressed as Anticipatory Interface. Before exploiting any physiological anticipatory movement into an

Anticipatory Interface, it is necessary to prove the existence of such movements also during the tasks that need to be performed by the user. If Anticipatory Movements persist, their features have to be characterized in order to extract important information regarding 1) how the anticipation time relates to tasks conditions; and 2) the physical magnitude of the anticipation movement that has to be automatically detected by the Anticipatory Interface. Two involuntary and anticipatory movements were taken into consideration in two studies, which are separately reported in Chapter 6 an 7.

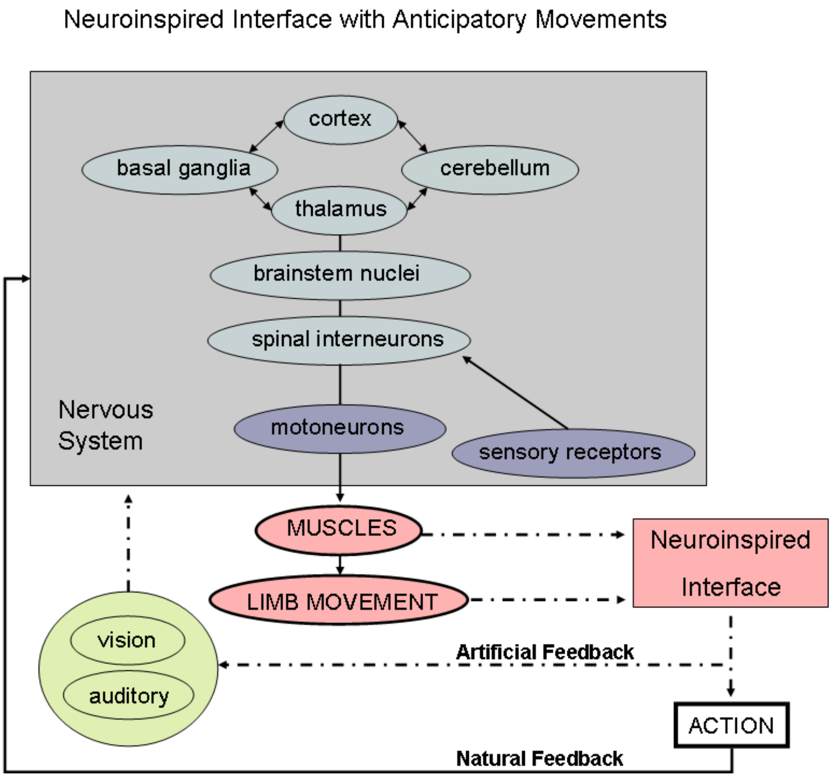

Figure 4. Information path that separates human's thoughts from actions in a Neuroinspired Interface with Anticipatory Movements. The interface accesses the information at this very last level. The action (white box) is controlled vie the interface, which produces also artificial feedback to the subject.

The goal of the first study was to determine the persistence of anticipatory head rotation during teleoperation of a navigating robot. The characteristics of anticipatory movements during this peculiar task are presented, and the exploitation of head-rotation anticipatory movements is discussed in the design of Anticipatory Interfaces as novel means to enable teleoperation with reduced command-signal delays.

The goal of the second study was to determine the existence of anticipatory movements related with upper limb motion during reaching tasks. Differently to the head anticipatory rotation during locomotion considered in the first study, a formally accepted model of human upper limb movement and control is still lacking (Ferraina et al., 2009). It is here hypothesized, as possible involuntary anticipatory behaviour, the production of common shaped velocity commands produced by a rhythmic neuro-controller. Together with the rhythmic neuro-controller, the concept of a "quantum of movement" is here proposed and tested: a standard velocity pulse that is produced in series, with a fixed frequency, to control any voluntary upper limb movement. Finally, a completely new human upper limb movement decomposition algorithm suitable to be included in a Neuroinspired Anticipatory Interface is proposed, the Predictive Decomposition algorithm.

CHAPTER TWO

-

NEUROINSPIRED INTERFACES WITH THE CENTRAL NERVOUS SYSTEM

I. INTRODUCTION TO CENTRAL NEURAL INTERFACES

Neuroinspired Interfaces may extract information on user's intentions by monitoring and detecting user's brain activity and translating the extracted information into commands towards technological devices. Neuroinspired Interfaces with the central nervous system (CNS) belong to the class of Central Neural Interfaces, also known as brain-machine interfaces (BMIs) or brain-computer interfaces (BCIs). This class of Human-Technology interfaces is aimed at restoring or augmenting human communication and control skills (Wolpaw et al., 2002) by directly interfacing the brain activity with the controlled devices.

A BMI records the neural activity related to the message/command intention at the cortical level by an invasive or non-invasive brain activity measurement system. This activity is decoded into the intended message/command, and finally actuates the user's intention by means of an external actuator (like a cursor on a PC monitor, a robotic hand, or a wheelchair). Invasive systems directly record the electrical activity of a group of few neurons (usually about one hundred) via electrodes inserted in the user's brain cortex (Wesseberg et al., 2000). As demonstrated by Nicolelis (Nicolelis, 2001; Nicolelis, 2003), by invasively recording the activity of even such a small number of neurons randomly selected in the primary motor cortex, it is possible to decrypt the user's intended limb movement in a 3D space, and then to make a robot arm replicating it in the real world. The monkeys used for these experiments succeeded in operating the robot without moving their own limbs, as if the robot arm had been integrated in their own bodies, as an extra limb. The invasive techniques require severe and potentially dangerous neurosurgery operations, which are unsuitable on subjects not affected by severe paralysis. But paralyzed subjects do not have any natural feedback anymore, which makes the first training phase of implementation of these interfaces impossible, and their subsequent use largely ineffective (Kennedy, 2000).

As a consequence, non invasive systems, which operate by recording brain activity from "the outside" of the skull, appear today as the most suitable platform for studies on healthy subjects. The non-invasive recording of brain activities takes place via well known clinical non-invasive diagnostic devices (Babiloni et al., 2009a) such as electro-encephalogram (EEG), magneto-encephalogram (MEG), functional magnetic resonance (fMRI), positron emission tomography (PET), and near red spectroscopy (NIRS). Most of these devices have a poor temporal resolution of the signals (e.g. fMRI, PET, the current NIRS) and hence do not suffice for real-time operations.

Both EEG and MEG however, do measure brain activity with the desired temporal resolution. The EEG records the projection of the electric field generated by the activity of a large group of neurons on the scalp of the subject by surface electrodes. The MEG monitors, instead, the magnetic field associated with the same activity. The differences between them are apparent. The electric field produced by neural activity is shielded by the layers of protecting tissues and fluids that separate the brain from the outside world before being recorded by EEG instruments. Hence, the spatial resolution is drastically limited, which makes impossible any precise identification of the group of neurons generating the signal. For this reasons, BMIs based on EEG are still far from achieving the capabilities of the best invasive BMIs (Tonet et al., 2008). Since the same layers of living tissues and fluids that shield the neuro-electrical activity are instead "transparent" to the magnetic field, MEG instruments can identify with high spatial definition the topological origin of the detected activity. However, the magnetic field is so weak that, in order to detect it, the device has first to be wholly shielded from any other magnetic source (even Earth) by enclosing it in a room delimited by thick lead walls; secondly the signal can be successfully amplified only by mean of extremely sensitive device such as cooled superconducting quantum interference devices (SQUIDs).

All in all, MEG-BMIs are currently not feasible due to the bad portability, but might become an interesting application with future, not yet envisaged, technological advances.

I.I Cortical non-invasive interfaces

Cortical non-invasive (C-NI) BMIs can measure and correctly classify specific signals of brain activity intentionally and automatically produced by the subject and translate them into device control signals. Such signals are recorded from the scalp and suffer from the limitations of their transit through the extracerebral layers (severe amplitude reduction, filtering of frequencies particularly in the high-frequency range, spreading of the generator source identification, increased contamination of the signal from the generator(s) by far-field volumetric potentials).

Features commonly used in experimental studies derive from brain signals that include alterations of the electrical activity recorded through electroencephalography (EEG) such as mu or beta rhythms (Wolpaw et al., 1991), event-related potentials (ERPs), including the P300 and N400 evoked potential and visual evoked potentials (VEPs), either transient (to individual, low-rate stimuli) or steady-state (to prolonged trains of high-rate, repetitive stimuli) (Farwell and Donchin, 1988; Sutter, 1992; Middendorf et al., 2000; Kelly et al., 2005a/b), transient variations of the background rhythms, i.e. event-related (de)synchronization (ERS/ERD) (Pfurtscheller et al., 1993), slow cortical potentials (SCP) (Birbaumer et al., 1999), and activation patterns induced by mental task strategies (Curran and Stokes, 2003; Kostov and Polak, 2000). To avoid the need of skin preparation and electrolytic gels, dry recording electrodes are being studied (Mason, 2005). Today's wet electrodes are not suitable for daily use in normal living environment; dry electrodes would guarantee a good electrode/skin contact and allow acceptable signal-to-noise ratio for longer session times.

Other features recorded with different modalities include neuromagnetic signals recorded through magneto-encephalography (MEG) (Tecchio et al., 1997; Georgopoulos et al., 2005), blood oxygen level-dependent (BOLD) responses recorded through functional magnetic resonance imaging (fMRI) (Weiskopf et al., 2004) and localised activity-related brain oxygenation measures recorded through near infrared spectroscopy (NIRS) (Coyle et al., 2004a).

Current cortical non-invasive HMIs are mono-directional interfaces, in which brain signals are used to drive a machine, and not the opposite. Stimulating the CNS by means of non-invasive technologies, such as transcranial magnetic stimulation (TMS) is not selective (Rossini et al., 1994; Rossini and Rossi, 2007; Rossini, Rossini and Ferreri, 2010). Therefore natural afferent pathways are commonly used for communication feedback.

Examples of applications of non-invasive cortical interfaces are, among the others:

- ERP, ERD/ERS: classification of mental states, related only to motor imagery (Kauhanen et al., 2006), or including also mental tasks (such as cube rotation or calculation) (Obermaier et al., 2001; Nykopp, 2001; Lehtonen, 2002; Millán and Mouriño, 2003; Millán et al., 2004), or imagination of sensory stimulation (Dornhege et al., 2004).
- P300 evoked potentials: selection of items in a sequence, such as four-choice paradigm (Sellers et al., 2006a), or arranged into square matrices, typically of size 6x6 or differently (Wang et al., 2005).
- Slow Cortical Potentials: 1-D cursor movement tasks (Birbaumer et al., 2000; Blankertz et al., 2004).
- Sensorimotor cortex rhythms: 1-D cursor movement tasks (McFarland et al., 2003; Fabiani et al., 2004; Buttfield et al., 2006) and 2-D cursor movement tasks (Wolpaw and McFarland, 2004; Fabiani et al., 2004; Geng et al., 2006; Vuckovic and Sepulveda, 2006).
- Steady-State Visual Evoked Potentials: 1-D cursor movement tasks (Middendorf et al., 2000) and nominal selection of a variable number of targets, from 2 (Kelly et al., 2005a), to 12 (Cheng et al., 2002; Wang et al., 2006).

I.II Cortical invasive interfaces

Cortical invasive (C-I) interfaces are based on the voluntary control of the firing rate of individual neurons in the primary motor cortex. Neural signals recorded in cortical invasive interfaces range from small neuronal samples to large ensembles, including local field potentials (LFPs), spread over a single or multiple recording sites (Lebedev and Nicolelis, 2006). Commonly used intracortical electrodes are microwires (Marg and Adams, 1967), multiple electrode arrays (MEAs) (Maynard et al., 1997), and neutotrophic electrodes (Kennedy, 1989). An alternative, less invasive, recording modality is electro-corticography (ECoG) based on epidural or subdural implanted mesoelectrodes (Jerbi et al., 2009). In humans, many experiments exploit ECoG signals measured on epilepsy patients requiring invasive monitoring of cortical activity for localization and eventual resection of an epileptogenic focus Kennedy and Bakay (1998). Also studies using MEAs are being carried out (Hochberg et al., 2006).

Cortical invasive interfaces have the potential to be bidirectional. However, most studies currently use them only for recording neuronal activity, relying on visual stimuli for feedback, as in the case of cortical non-invasive interfaces. Signals used in cortical invasive interfaces are usually generated by the subject through motor imagery tasks (Leuthardt et al., 2004; Graimann et al., 2004; Hochberg et al., 2006). Also, interfaces exploiting LFPs generated by non-motor imagery (e.g. in the auditory cortex) have been investigated (Wilson et al., 2006).

Examples of applications of invasive cortical interfaces are, among the others:

- 1-D cursor movement: (Kennedy and Bakay, 1998; Kennedy et al., 2000; Leuthardt et al., 2004; Wilson et al., 2006);
- 2-D cursor movement: (Hochberg et al., 2006);
- nominal selection of up to 4 mental states (Graimann et al., 2003, 2004).

Research on the use of cortical invasive interfaces as BMI started on animals over three decades ago (Fetz, 1969; Humphrey et al., 1970). Indeed, being more invasive than human studies, animal experiments showed higher performance. Animal studies, on rats, cats and monkeys, are demonstrating the potential of invasive technology for applications such as:

- switches (Chapin et al., 1999; Laubach et al., 2000)
- 2-D cursor movement: (Serruya et al., 2002; Santhanam et al., 2005)

- 3-D movement of cursor and robot arm: (Wessberg et al., 2000; Taylor et al., 2002, 2003; Carmena et al., 2003; Nicolelis, 2000, 2003)

Besides MEA, also LFP have been exploited (Bokil et al., 2006).

II. CURRENT CORTICAL INTERFACES PERFORMANCE

In Tab. I a summary of latency and throughput values for all classes of HMIs is shown (Tonet et al., 2008). MEG-based BCIs have recently shown performance comparable to EEG (Kauhanen et al., 2006). However MEG devices are expensive, immobile and extremely vulnerable to body-generated and urban magnetic noise, when operative outside magnetically shielded rooms. fMRI scanners are also expensive and immobile. fMRI-based BCIs, such as (Yoo et al., 2004), suffer from poor temporal discrimination due to the haemoglobin relaxation time which produce BOLD effects. On the other hand, NIRS-based BCIs, such as (Coyle et al., 2004b) are inexpensive and portable. However they suffer from very low throughput (in the order of 0.01 bit/s). For all these reasons, BMIs based on MEG, fMRI and NIRS are not suitable to control a Neuroinspired Interface.

Concerning BMIs, apart from SCP-based interfaces, in humans many BMIs have comparable values of throughput and latency, which means that there is currently no best choice for a given application. Factors that influence the choice, besides the application itself, could be the user, their training, and the feature extraction method. Throughputs higher than 1 bit/s are very difficult to achieve, cannot be attained by all users and sustained for a long time. Concerning scalp EEG, limitations could mainly arise from its low sensitivity, rather than from the signal classification techniques. In fact, at the current stage of technology, the generation/selection of signals detectable by EEG cannot be performed at much higher rates. This is surprisingly true also for invasive interfaces that, in human experiments, have not (yet) shown their superiority. However, this is probably due to the more pioneering status of electrodes and to the higher disability of the patients: consent to electrode implant is sought and given only in cases of very severe disabilities. However, as patients degenerate toward the locked-in state, their ability to learn and communicate with a BCI decreases (Birbaumer, 2006). In monkeys, thanks to more invasive BMIs, such systems have lower latency and higher throughputs, the latter also thanks to longer training periods. In summary, while the invasive approach can be promising for the future, open issues (Micera et al., 2006) and ethical aspects have to be investigated before they can be considered suitable for rehabilitation and for applications in able-bodied people; such concerns cannot be overcome at the present.

TABLE I

Maximum and minimum values of throughput and latency for all classes of HMIs

Interfaces	Throughput (bit/s)			Latency (s)		
	Min	Median	Max	Min	Median	Max
Cortical non-invasive	**0.01**	**0.42**	**1.63**	**0.50**	**2.10**	**126.00**
ERD/ERS	0.12	0.38	0.69	1.00	1.50	5.00
P300	0.09	0.47	1.63	0.84	1.58	3.90
SCP	0.02	0.06	0.09	5.50	65.75	126.00
Sensorimotor	0.01	0.28	1.25	1.00	2.20	7.00
SSVEP	0.16	0.44	1.13	0.50	2.10	7.20
Cortical invasive on human	**0.02**	**0.15**	**0.70**	**2.35**	**4.50**	**8.60**
Cortical invasive on monkey	**0.39**	**1.80**	**3.30**	**0.20**	**0.36**	**1.50**
Non-cortical non-invasive	**0.44**	**2.61**	**27.02**	**0.14**	**0.70**	**9.50**
Keyboard	1.00	3.00	27.02	0.18	0.47	0.70
Mouse	2.00	3.20	8.50	0.14	0.50	1.70
Speech	2.63	5.04	6.13	1.00	1.40	1.49
EMG	0.44	1.66	2.66	0.69	0.96	5.00
Non-cortical invasive	**0.33**	**0.78**	**0.92**	**0.33**	**1.25**	**2.00**

Adapted from Tonet et al., 2008

The main problem of cortical invasive interfaces is the limited robustness and the time-decay of their efficacy, due to the encapsulation with scar tissue around the recording area, the presence of proteins adsorbed onto electrode surface, and the micro-movements between the brain and the interface damaging the nervous system and degrading the precision of the recorded signal. Recent studies exploiting MEAs recording LFPs from a sample of hundred or thousands neurons located in the relevant cortical area, open encouraging scenarios because, even with the progressive loss of a number of neurons in contact with recording tips, the remaining amount of information is sufficient to allow the essential features of the cortical output (Rickert et al., 2005; Bokil et al., 2006).

ECoG combines advantages over intracortical electrodes (no cortical invasiveness, reduced clinical risk, greater long-term stability) and EEG technology (larger amplitude of recordings, higher spatial resolution, reduced artefacts, less attenuation in the higher spectrum), while not incorporating many of their limitations (Moran, 2003). Nonetheless, ECoG is still an invasive technique requiring craniotomy and dural meningeal opening, which limits its use on specific clinical conditions (Jerbi et al., 2009).

III. CORTICAL INTERFACES AND THEIR POTENTIAL USERS

BMIs have so far been extensively studied as a communication means for people that are affected by most severe disabilities – such as severely advanced (terminal) stages of amyotrophic lateral sclerosis (ALS) or muscular dystrophies, brainstem lesions etc. – who, because of the underlying pathology, have no voluntary control of muscles (Wolpaw et al., 2002; Donoghue, 2002; Mussa-Ivaldi and Miller, 2003) (Fig. 1).

In this case, despite having a normally working brain in terms of cognition and self-perception, they possess no communication means with the outside world and a BMI may represent their only way to interact with other people and objects. For these cases, BMIs of even relative efficiency still represent a significant improvement in daily living abilities, so even interfaces with low bit rates can be considered as prosthetic applications (Fig. 2).

On the other end of the spectrum there are able-bodied users (Fig. 3). For these users, a BMI as an alternative communication device is not useful, due especially to their low bandwidth and the fact that current BMIs impose a high cognitive load, with long training periods, and do not allow the user to perform activities besides interacting with the BMI itself, to avoid the generation of artefact signals that are not directly related to the driving of the BMI. In such conditions, a BMI would only be practical if conceived as an augmenting interface, i.e. an interface that allows users to perform actions in addition to what they already can do with their normal abilities. Some of the potential augmenting capabilities of brain machine interfaces have already been demonstrated in ground experimental labs.

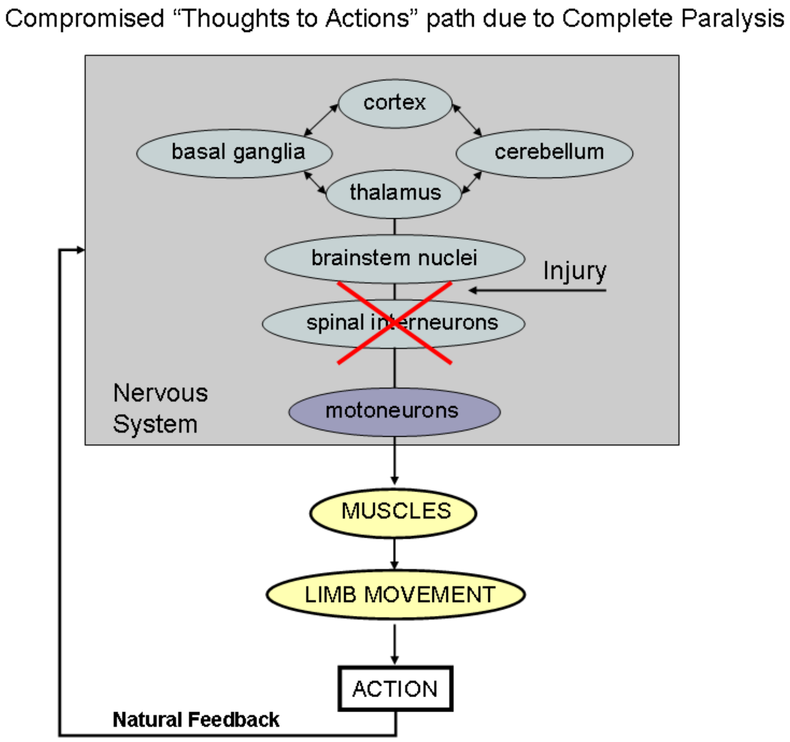

Figure 1. Complete paralysis compromise the normal Information path which separates human's thoughts from actions. The intention is still generated and integrated in the central nervous system (light blue ovals), though it cannot leave the central nervous system due to the lesion at the level of spinal interneurons.

The most advanced systems currently conceived are able, in ground experimentation, to serve as general purpose computer interfaces, replacing the use of mouse and keyboards in dedicated environments (Krusienski and Wolpaw, 2009). Systems have been proposed for use with off-the-shelve software, and in particular in connection to virtual navigation systems or 3D virtual object manipulation software (Scherer et al., 2009). Other BMI systems have also been optimized to interface with specific tools in order to reach the best possible performance for controlling domotic environments (Babiloni et al., 2009b).

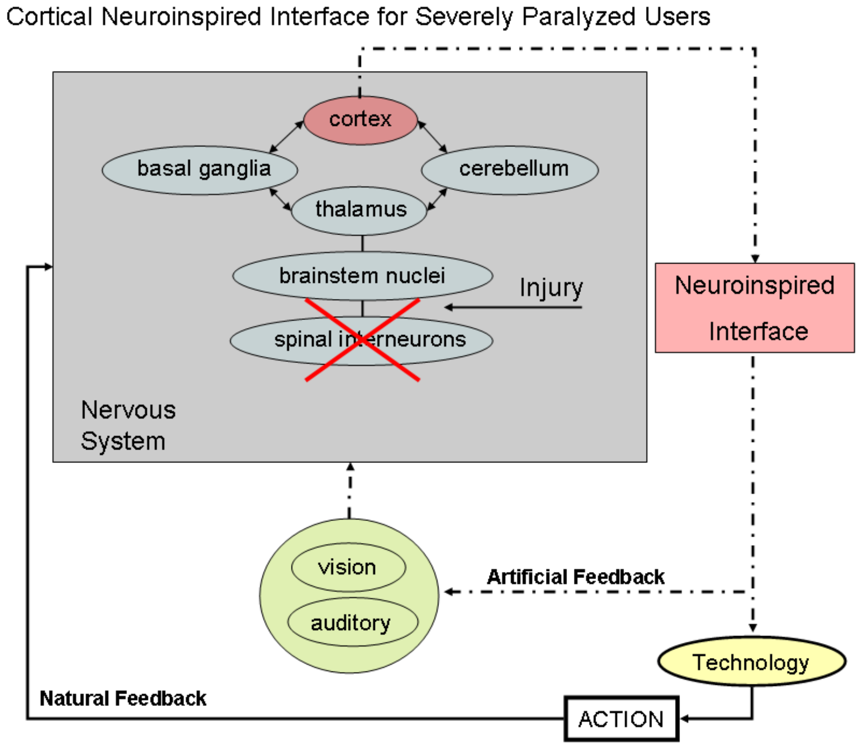

Figure 2. The information on user's intentions can be extracted at the cortical level and translated by a Neuroinspired Interface into actions of an assistive device.

BMI devices considered in these works have been originally conceived and implemented to restore part of the lost abilities of people seriously affected by different kinds of motor paralysis (for clinical perspectives on BMIs see

Birbaumer et al., 2009) and not in the framework of a general effort to augment human interactions with its environment (Tonet et al., 2007).

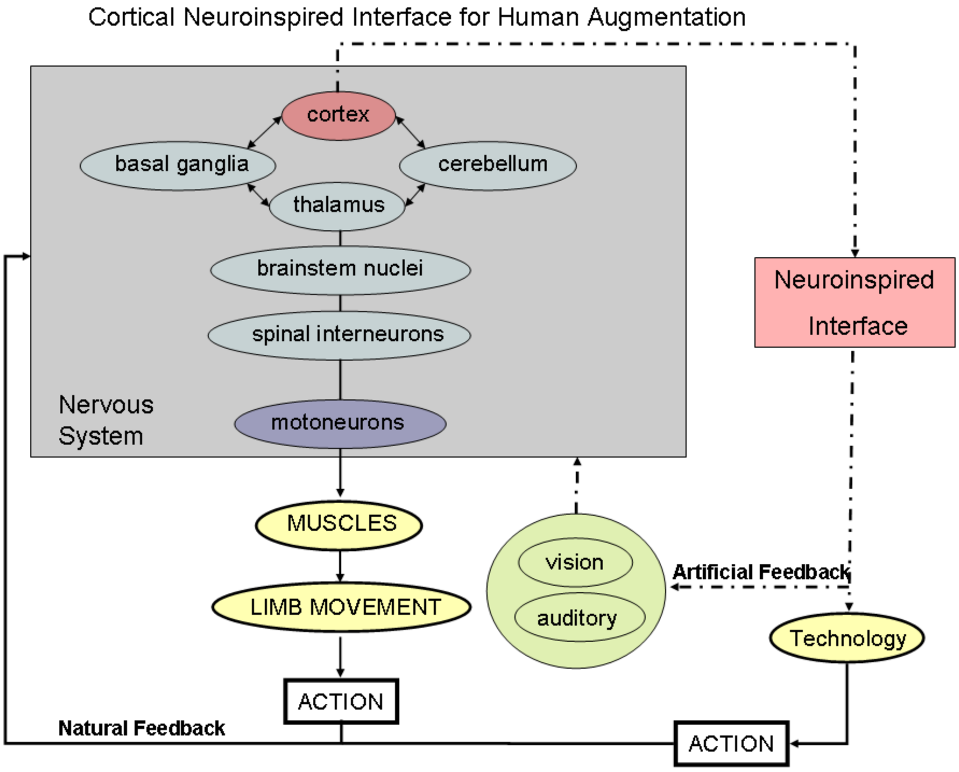

Figure 3. Cortical interfaces can be useful for human augmentation only if they allow users to operate multitasking. User's intentions are contemporary generated and integrated in the central nervous system (light blue ovals), but the interface access the information on its operation solely at the cortex level, loosing part of the information, while the unrelated information is left free to follow his normal path towards motoneurons and ultimately muscles. The actions (white boxes) are contemporary produced by user's muscles and by the neurally-controlled technology.

In order to understand the applicability of the current concepts, it is necessary to understand up to what extent one can make use of devices designed to be the main (if not only) source of communication or the only mean to control the external environment. When the brain motor frequencies, the logic and the associative areas and the attention markers are all included into multi-degrees of freedom interface and constantly monitored, user's brain activity has to be completely focused on the operation of the interface. Any other thought, in fact, would produce noise and would risk to be translated into undesired commands. The inevitable outcome is that using a BMI usually brings almost to zero any possible level of multitasking, intended as any other action different from operating the BMI itself (Neumann et al., 2003). As a consequence, in those cases where some of the potential applications for BMIs for augmenting human capabilities have been demonstrated in labs, it is not obvious that the same BMI devices can be used as an hands-free interfaces for real daily life activities: the user would in fact need to avoid any other activity apart from those mental tasks required to control the interface, otherwise producing brain activity which would interfere with the signals used by the BMI. This introduces a need to rethink BMIs in order to optimize the multitasking capabilities of the user and adapt therefore its functioning to the requirements that are typical of healthy subjects.

In an exploratory phase, the first generation of BMIs in use for human augmentation is likely to be based entirely on non-invasive brain-imaging techniques. This is primarily because of the high risks associated with neurosurgery, which make implementation of invasive cortical systems on healthy subjects unacceptable, but also to the strong cultural feelings against what is sometimes referred to as "cyborgization", literally the enhancement of a biological being with mechanical devices or capabilities.

IV. MATCHING CORTICAL INTERFACES AND APPLICATIONS

Feeder robots and domotic devices are suitable applications to be controlled by means of a BMI. This is not surprising: indeed, the control panel of domotic applications is usually a simple interface composed of switches and sliders, controls that are easily implemented by means of a BMI (Gao et al., 2003; Cincotti et al., 2006). Feeder robots have even simpler interfaces: a trigger signal is needed to activate the robot, that then executes the feeding task autonomously without further feedback from the user. Even SCP-based low-throughput BMIs can be used to control feeder robots. However, feeder robots are more easily controlled by means of puff/sip switches, which only require breath control abilities.

Concerning more complex rehabilitation applications, there is an overlap for higher-performance BMIs with robotic devices that have few DOFs, i.e. BMIs can be used to control grasping with a prosthetic hand (Guger et al., 1999; Aggarwal et al., 2006) or a hand orthosis (Pfurtscheller et al., 2000; Kennedy et al., 2000; Müller-Putz et al., 2005b) and a smart wheelchair (Millán et al., 2004; Tanaka et al., 2005). All other rehabilitation applications require higher throughputs.

Performances measured in monkeys suggest that cortical invasive interfaces could be used successfully for controlling wheelchairs and prosthetic hands with greater interactivity. With future developments, performance could increase to allow driving more complex robots, such as 3/6-DOF arms. However, with cortical invasive interfaces, humans have not reached the same performance as monkeys. In (Hochberg et al., 2006), the quadriplegic human subject that received the 96-MEA, was able to control a computer cursor to interact with home appliances, operate the opening and closing of a prosthetic hand and perform rudimentary actions with a multi-jointed robot arm. An interesting note is that he could perform these actions even while conversing, which suggests that invasive interfaces have greater capabilities of discriminating shared output, i.e. simultaneous orders of different content, and are probably more suitable than non-invasive BMIs for multitask operations.

Besides throughput and latency, there are other variables that affect performance of BMIs and that have to be taken into account for the development of a complete system. BMI performance is not constant over time: on one hand, the duration of any single experimental session is limited by cognitive and physical fatigue of the user and by degradation of the BMI over time due to external factors; on the other hand mutual adaptation of user and algorithms can boost interface performance over repeated experimental sessions, by increasing the automatic component of the task and decreasing the cognitive and attentive load (Bailey et al., 2006). In fact, task repetition favour skilful performances due to progressive loss of cortical and voluntary control in favour of partly or entirely automatic behaviour. Moreover, the more automated a task is, the less is the involvement of high-level control centres, the smaller the amount of involved synapses and relays, the faster the task execution. However, BMI control efficiency reduction due to fatigue has been reported also in automatic control systems (Kennedy et al., 2000); this is, sometimes, caused by user attempt to speed up the control (Kübler et al., 1999).

It is possible to overcome limitations of the interface by improving the effectiveness of the commands sent to the device, i.e. by developing smart high-level controllers, which are able to perform parts of the tasks autonomously. Systems with low-level controllers and no autonomous behaviour will leave all decisions to the users and will require many simple commands to be driven interactively. The commands will be simple (few bits/command) but frequent (many commands/s).

On the other hand, an embedded high-level controller with a high degree of autonomy will accept complex commands from the user and then act autonomously, typically in a closed feedback loop based on data read from internal sensors. Such a controller will require complex commands from the user (many bits/command) but less often (few commands/s). Controllers with a modular degree of autonomy allow the user to switch between lower and higher levels of control, ensuring that the user is always in control of the device, but freeing them from the burden of controlling it continuously. Modulating degrees of autonomy could also be a means to overcome gaps between interface performance and application needs, by developing more deeply integrated human-machine systems.

V. BRAIN PLASTICITY AND BMI SYSTEMS

Any voluntary task is performed by physiological actuators (i.e. subcortical, spinal relays and muscles), which translate into an action the intentions planned by the subject. When the task is accomplished with good performance, the cortical networks which took part in controlling the actuators are strengthened (in terms of their connections and/or their reciprocal sensitivity to their mutual activation/inhibition) (Will et al., 2008). The actuators, though, are relatively blind to those plastic modifications in the cortical neuronal networks following learning or training. From the actuators' point of view, the only effect of any plastic changes is that they perform the same task 'faster and better'.

If this is true for any task performed with human's physiological actuators, it can be radically different, and somehow paradoxical, when the task is executed with a Brain Machine Interface. In a BMI operated task, planners and actuators happen to coincide, since the actuators are the same cortical neural networks which plan the task and, hence, could undergo plastic changes during learning (Rossini, 2009). In order to operate a BMI system, subjects must first of all encode their acquired skill (i.e. how to drive a cursor in a computer display) in a cortical network as accessible as possible to be retrieved by a "reader" (the imaging techniques implemented in the interface architecture) that probes the brain through the scalp. If the BMI is not "natural", such a cortical network might be quite different from the one routinely activated in physiological condition to perform a similar task, and hence usually needs to be learned from scratch. The specific activity of the cortical network required to operate the BMI needs to achieve a certain level of automation, so that the mental effort required to the user to operate the BMI is reduced while a sufficient communication bit-rate is maintained. The level of automation, though, should not be too high, otherwise a reduction of cortical activity in favour of subcortical networks could happen (as normally happens for lot of tasks, like the finger tapping control of a piano player) (Elbert et al., 1995), and subcortical networks' activity is trickier to access.

V.I Monitoring Plasticity during BMI Control

Learning how to control a BMI, in other words, can change the actuators in a totally new and unpredictable way. The factual effects of plasticity on the neuronal networks devoted to BMIs control, and the relative differences with the 'normal' plasticity, can be explored. Plastic brain changes in healthy humans can be measured and followed-up via non-invasive methods, namely those based on local changes of blood flow and metabolism in the brain (i.e. Positron Emission Tomography, PET and functional Magnetic Resonance Imaging fMRI) and those reflecting electromagnetic signals (EEG, MEG, TMS) (Rossini, 2009). Both these sources of information stem from the amount and duration of neuronal firing as well as on the developing and dynamic connectivity of neuronal assemblies which bind and unbind time by time to sustain a given function (Babiloni et al., 2009a). Needless to say, combination and integration of the two methodologies represent the best solution since they combine the best of structural and temporal discrimination. It is hence conceivable to build-up an instrumental approach through which individual training schedules could be tailored on the basis of the surviving neural networks which could be utilized in individual patients according to their residual abilities. Training protocols should be rendered appropriate to be carried out within the fMRI environment and under the helmet of MEG sensors. Meanwhile, High Density EEG recordings should be acquired and TMS/EEG sessions should also be carried out. From the analysis of the resulting integrated data, we can extract information on: 1) the main neuronal networks utilized to optimally perform the task for BMI control; 2) the localization and chronological hierarchy of the relays constituting individual and distributed networks; 3) time-varying coherence modifications of the examined brain rhythms as well as directions of such modifications; 4) time-varying synchronization likelihood modifications; 5) cortico-cortical connectivity examined via EEG/MEG as in the previous two points and TMS/EEG recordings. Once the main picture of the brain activities pivotal for sustaining the BMI/BCI tool is depicted, possible 'reinforcements' of the relevant aspects to maintain (or even improve) them along time should be envisaged.

VI. FUTURE TRENDS OF CENTRAL NEURAL INTERFACE

The results in the field of invasive BMIs have made possible substantial scientific advances, and invasive systems are expected to keep playing a crucial role in the future. With current technology, only invasive interfaces, especially those using cortical electrodes, can interact with neurons as intimately as to be able to listen to the single spikes produced by the surrounding neurons, and potentially to answer with a similar electrical activity (Lebedev and Nicolelis, 2006). This currently unique spatial and temporal resolution therefore makes them the most suitable research tool to understand the full potentials of BMIs in general.

The importance of cortical electrodes in BMI research leads scientists to address the many technical difficulties related with performing research on animal models (Taylor et al., 2002; Serruya et al., 2002; Nicolelis, 2003; Fagg et al., 2008; Fetz, 2007; Schwartz, 2007; Velliste et al., 2008). Typically such experimental work requires a prolonged training period during which the animal, often a monkey, learns to perform a control task with a normal interface (be it to use a joystick in order to correctly position a mouse pointer on a screen or to move a robotic hand in a three dimensional environment). Only after the monkey reaches good performance in these "simple" tasks, the cortical electrodes are implanted to record and decode the electrical activity produced by the brain during the control of the system. Eventually, the BMI will replace entirely the normal interface during the execution of the whole task.

Non-invasive systems have so far never been reported to allow for the execution of a complex task that requires comparable brain activity. This, together with the observation that task learning would be much faster in humans, are arguments that make many scientists optimistic on the possible performances achievable by invasive systems on humans.

Along these lines, the American Food and Drug Administration (FDA) exceptionally authorized few human experiments with invasive cortical electrodes specifically designed for invasive BMIs on humans (Kennedy and Bakay, 1998; Hochberg et al., 2006; Truccolo et al., 2008). The selected subjects were affected by complete paralysis and hence were able to communicate with the external environment only via BMIs. The results, contrary to the expectations of the involved scientific community, showed that this set-up was not able to achieve better performances than non-invasive systems (Tonet et al., 2008).

The fact that human experiments with non-invasive and invasive BMIs provide similarly defective control suggests that the problem is independent from the recording system (Wolpaw, 2007). One explanation suggests that these results could be due, in part, to the training protocols adopted, and specifically to the feedback protocol. In general, while complete and coherent feedback helps speeding up and maintaining long lasting skill achievements, a feedback only based on visual signals makes it harder for the user to understand how to systematically gain good results and hence keeps the execution of any motor activity far from reaching its best performance (Gordon et al., 1995). Invasive BMIs' monkey subjects are trained to control the system via classical "limb controlled" interfaces, i.e. joysticks. During joystick control, the monkey receives tactile and proprioceptive information on the position of all its upper limb's joints, as well as information regarding the force applied to any muscle, the mechanical resistance of the joystick and any other mechanical parameter that plays a role in the task's outcome. This multimodal information is then proficiently integrated by and within the monkeys' brain, and coupled with the associated task's outcome. Thus, the neural networks devoted to the most efficient approach are quickly selected and reinforced with respect to all the others, almost hard-wiring the neural pathway associated with the whole task execution. At the end of this training phase, when the cortical interface is finally invasively implanted, it finds a stable and repeatable neural signal associated with task execution, easily recognizable and decipherable. From then on, the monkey has to rely only on its visual feedback, which is sufficient for an already acquired and reinforced skill.

Human subjects, which tested invasive BMI systems, instead, were already severely paralyzed and deprived of any tactile or proprioceptive sensory information about most of their body (Kennedy and Bakay, 1998; Hochberg et al., 2006). The training phase was based on the imagination of limb movements (i.e. the right hand closure/disclosure) and could not be associated with any other feedback than visual ones (i.e. a virtual hand performing the same movement). The interface was intended to bypass the damage which prevented the patients to normally control their muscles, by connecting few tens of neurons of cortical areas not directly affected by the pathology or the condition causing the paralysis with the external "effectors" (i.e. a mouse pointer, a prosthetic hand, or a speller). Without any tactile or proprioceptive feedback provided during neither the training nor the execution phases, the neural networks related with the task of movement imaging received very little reinforcements. This probably made the neural signal much less stable and repeatable, which in turn made the mathematical classifiers perform worse than expected.

Since it is currently inconceivable to implant BMI cortical electrodes in healthy subjects, and is still very difficult to obtain permissions for implanting them in severely paralyzed subjects (in Europe this has never been done as far as known to the author), the only other possible approach to pursue invasive interfaces research on humans in the near future is to exploit other kind of electrodes which are, for clinical reasons, already implanted in patients' brain. Even though those electrodes, like the electro-cortical (ECoG) electrodes used in the therapy of the most severe cases of epilepsy (Kahane et al., 2004), lack the specificity and selectivity of BMI cortical electrodes, they can be tested with subjects still provided with the natural feedback pathways (Jerbi et al., 2009), and the first results on BMI systems are indeed holding promising results. Possibly, the joint research on non-invasive techniques and ECoG invasive experiments, tailored towards understanding the deep and specific events which underlay the neural activity related to BMI operations, will lead to new design solutions able to overcome many of the limits of current BMIs. On the other hand, in the long term, should neurosurgery become less risky and complex, and some level of cyborgization accepted by society (e.g. robotic prosthesis neurally controlled) the expected superior performances of invasive BMIs could eventually justify their implementation on humans, firstly on severely disabled persons, and subsequently even on healthy persons. In such a scenario the performances of the resulting BMIs would be substantially enhanced.

CHAPTER THREE

-

NEUROINSPIRED INTERFACES FOR SPACE APPLICATIONS

I. INTRODUCTION TO INTERFACES FOR ASTRONAUTS

While the high versatility of human sensorimotor system allows for a large range of elaborated motor behaviours, its performances are strictly bounded to the physical conditions it has been adapting to over its evolution. In particular, our perception and planning of movement depend on the identification of the gravity axis. Situations of perceived annihilated gravity (i.e. orbital microgravity) inevitably affect human's sensory-motor system (Clement, 2003). The subsequent losses of performances are so important that, from certain perspectives, humans operating in microgravity are in a similar situation to people affected by motor disabilities on Earth (Souvestre and Landrock, 2007): both have, for different reasons, a deficit in the performances required to accomplish their motor tasks (Gordon et al., 1995) (Fig. 1).

On Earth, disabled people can take advantage of assistive systems, which are technologies designed to fill the gap between user's residual abilities and required ones (Cook and Hussey, 2002). The answer to the reduction of physical and mental ability suffered by astronauts can hence be addressed (and it already partially is) with assistive technologies, once they are redesigned for functioning in space. The required assistive technologies for astronauts are, essentially, computer interfaces, robotic hands, and robotic arms. Most of them are already technologically well developed, but are still lacking in operability. In fact, the reduction in sensorimotor performances affects the use of any kind of physical interface as well (Solov'yev, 1991). The adoption of natural interfaces (Perzanowski et al., 2001) could enhance the communication and control abilities of humans in space, allowing to fully focus on the task instead of on the interface use.

Natural interfaces, with respect to traditional ones, exploit natural human communicative channels and hence allow intuitive and universal use without elongated training sessions. Natural interfaces commonly are based on, and integrate, speech recognition, gesture recognition, facial expression recognition, and gaze tracking. However, their usefulness for severely disabled people and – in an analogue way - for astronauts has constraints. Gesture and facial expression recognition efficiency is affected by the inability for the impaired user to perform within strict tolerances, while speech recognition reliability presents extreme challenges when implemented in spacecraft environments (Clement, 2003), where the background noise can be as high as 64 dBA for the air conditioning to 100 dBA for vent relief (Payette, 1994). Gaze tracking alone tends to lack precision and the ability to permit the control of complex systems.

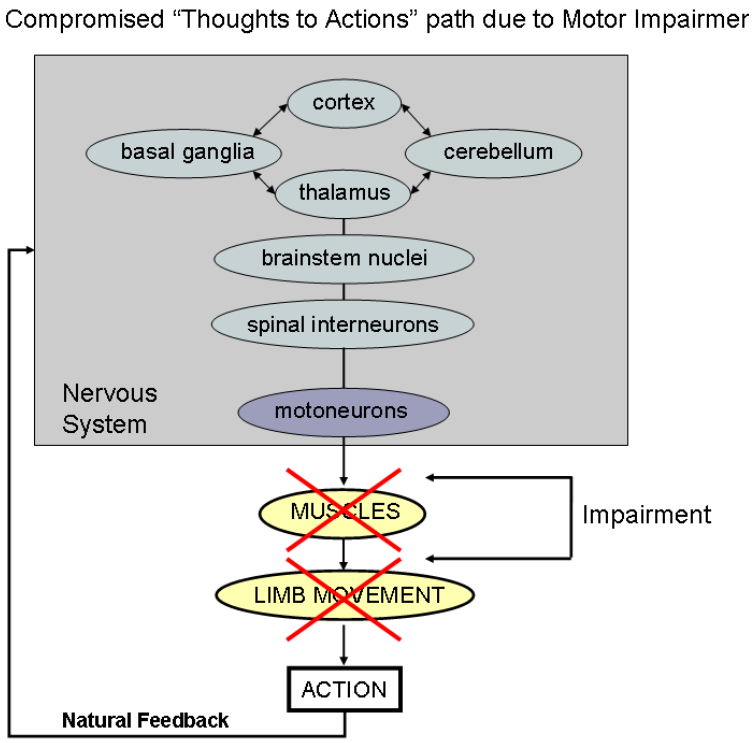

Figure 1. Microgravity exposition compromises the normal information path, which separates astronaut's thoughts from actions. Due to the effects of microgravity, the muscle contractions fail to properly control limb movements, affecting the overall astronaut's motor performances.

While not yet as mature as some of the mentioned options, brain machine interfaces (BMIs) are instead virtually independent from the user's physical abilities, by accessing the user's intentions at a higher level, where they naturally origin: in the brain. They predict directly the user's motor intentions, not related with users' abilities, by monitoring the activity of neurons (individually or in networks) and translating these signals into actions. Since they are expected to operate in principle very similar in space and on Earth, BMIs could assist astronauts by helping them to perform in space as efficiently as on Earth (Fig. 2).

II. MICROGRAVITY EXPOSITION EFFECTS ON HUMAN BRAIN

Exposition to micro-gravity causes specific modifications in the way the human brain behaves (Pletser and Quadens, 2003). As the brain is the main element of BMIs, any changes due to short time or long-time exposition to "space environments" have to be taken in consideration in the design and set up of BMIs for space applications.

For example, the main brain rhythm, the alpha, and the main motor cortical rhythm, the mu, show important modifications in their power spectrum, which result significantly increased with respect to ground measurement, when recorded during prolonged microgravity exposition (i.e., during EEG session with astronauts in the International Space Station - ISS) (Leroy et al., 2007). These adaptive changes could result from a coherent cortical drive from the thalamus coincident with a lack of other input due to the general reduction in tactile and proprioceptive feedback under microgravity (Cheron et al., 2009). The distribution of basic EEG rhythms appears to reflect some adaptive changes in brain activity during long exposures to microgravity. NeuroCog ESA virtual navigation experiment, performed both on ground and on board the ISS, showed that the initial presentation of a virtual 3D tunnel was differently accompanied by a power increase in the theta and in the alpha bands, while a power increase in the alpha, beta and gamma bands occurred during the whole task in weightlessness (Vidal et al., 2003).

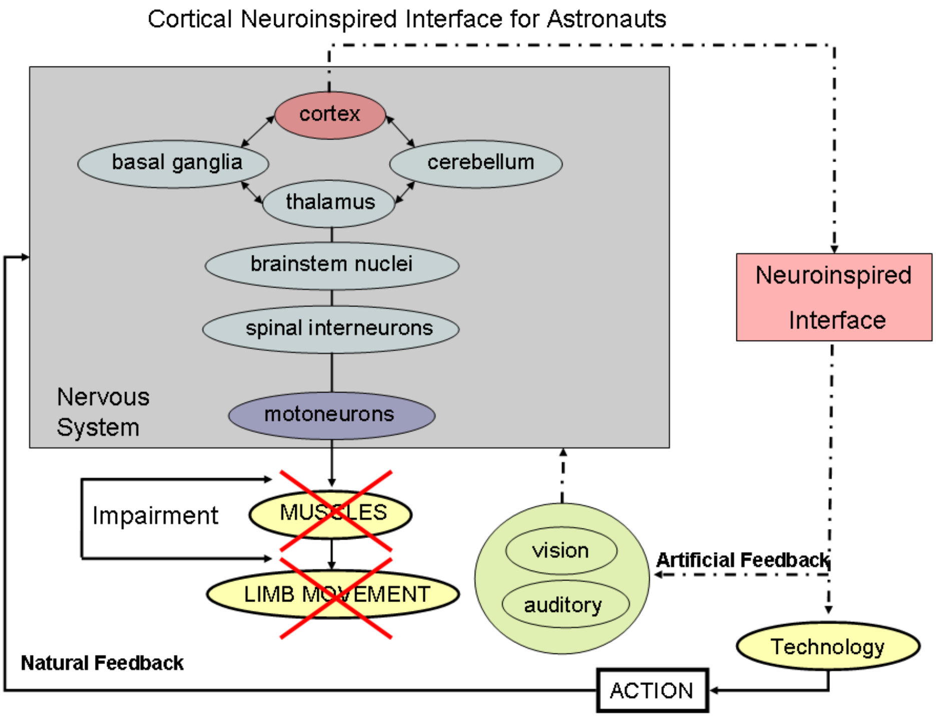

Figure 2. While microgravity reduces performance of astronauts' actions, it does not affect the related intention. This can hence be extracted cortically and translated by a Neuroinspired Interface into the same actions performed by a technology.

A first step towards appreciating the effects of microgravity on BMI operations was done during a 2007 parabolic flight campaign of the European Space Agency (ESA). During parabolic flights the human body experiences repetitive short exposures to micro and macro-gravity (Fig.2). Two subjects, both male, in their 20s, with prior BMI and no microgravity experience, were EEG recorded on ground (calibration sessions) and on the parabolic flights during three gravity conditions (1G, as on Earth; 2G, double weight; and 0G, microgravity). Subjects were asked to mentally move a virtual blue balloon on a computer display to its left or right. The mental tasks corresponding with the left and right movement directions were, respectively, left hand movement imagination, and words association; the balloon was artificially moved by the system with a 30% error rate (the same as usually associated with BMI operation), regardless of the subjects' EEG.

Even though this approach did not allow subjects to operate the BMI system, it permitted to record the EEG activity associated with the two different mental states, which were compared with the one recorded during on ground sessions. An online classifier for parabolic flight session prepared on on-ground data could not have predicted the potential effects of the extreme gravity changes and noisy environment of parabolic flights. The off-line analysis computed for the two subjects achieved a mental-task classification accuracy between 72% and 79% (Millàn, Ferrez, and Seidl, 2009), and demonstrated that the relevant brain activity features related with the tasks remained almost unaltered by the three gravity conditions (Fig.2), despite the stress, noise and novelty of parabolic flight.

The results are certainly circumscribed to the particular experimental protocol, and need to be confirmed with further experiments with online controlled BMI systems in parabolic flights.

III. BMIS FOR SPACE APPLICATIONS

Some potential uses of brain-machine interfaces (BMIs) for space applications (Menon et al., 2008; Citi, Tonet, and Marinelli, 2009) have already been demonstrated in ground experimental labs, like general purpose computer interfaces, replacing the use of mouse and keyboards in dedicated environments (Krusinenski and Wolpaw, 2009), systems for use with off-the-shelve software (Scherer et al., 2009), systems optimised to interface with domotic environments (Babiloni et al., 2009b).

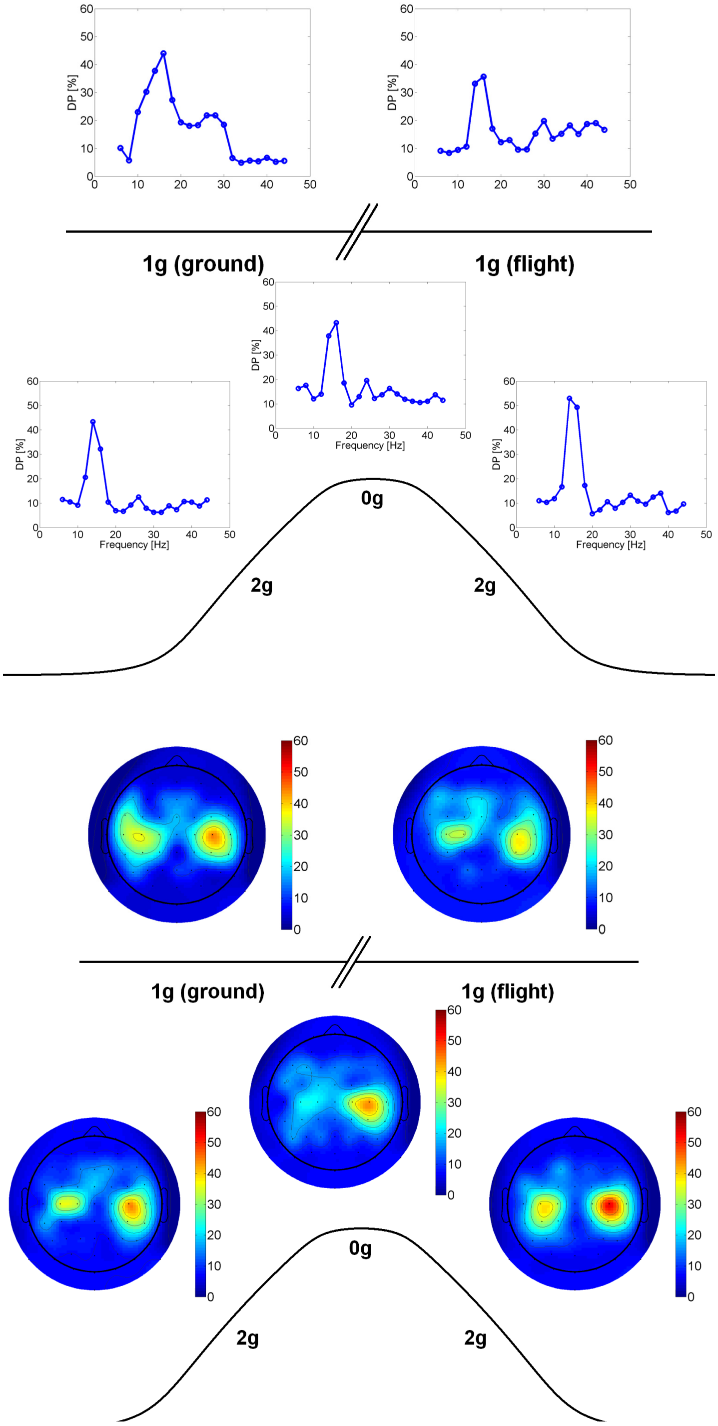

Figure 2. BMI features, as degree of relevance of EEG frequencies (first two on the top) and EEG electrodes (last two in the bottom). Those better associated with the tasks remained stable during the three gravity conditions. Adapted from (Millàn, Ferrez, and Seidl, 2009).

However, these systems have been originally conceived and implemented to restore part of the lost abilities of people seriously affected by different kinds of motor paralysis) and are not tailored to facilitate astronaut operations (Rossini et al., 2007). It is not evident that these same BMI devices can be used as hands-free interfaces for human space flight: for example, in order to avoid the production of brain activities which would interfere with the signals used by the BMI, astronauts would need to avoid postural movement, even those necessary to keep a stable position in microgravity conditions. BMIs for space applications would hence need to be first of all adapted in order to optimise the multitasking capabilities of the subject. The first generation of BMIs specifically designed for space applications is likely to be based entirely on non-invasive brain-imaging techniques, primarily because of the high risks associated with neurosurgery. On the other hand, the research in the field of invasive BMIs made substantial progress, and invasive systems are expected to play a crucial role in the future of BMIs (Summerer, Izzo, and Rossini, 2009b).

IV. FUTURE MANNED SPACE PROGRAMS – PLANNED OR ENVISIONED

Almost 40 years after the last humans have ventured beyond low Earth orbit and landed on the lunar surface in 1972, renewed interest in such mission has led to the announcement of human space exploration plans for returning to the Moon and eventually reaching Mars before the mid of this century (NASA, 2009; Bodeen, 2009). The traditional space faring nations with human space exploration programmes, the United States (US) and Russia, have been joined by China that has recently become the third country with an independent capability to launch humans into space. A similar programme has been announced by India so that by 2020, there could be four independent, possibly competing human space exploration programmes. Private enterprises are also taking the first steps into human space flight. Private sub-orbital space flight has been successfully demonstrated and several commercial companies based on business plans centred on what is generally called "space tourism" are advancing the field. At time of writing, at least one private company has already arranged for the "visit" of space tourists in the ISS and has announced an ambitious lunar mission (Space Adventures, 2009). There are observable, stable research trends that favour the introduction of more human-centred research in human space flight. Most of the current life sciences research related to human space flight is performed within the European Programme for Life and Physical Sciences and Applications (ELIPS) Programme of ESA (ELIPS, 2009), dedicated to life and physical research on the ISS and especially to take full advantage of the unique opportunities provided by the European Columbus laboratory onboard the ISS.

V. NEXT STEPS TOWARDS BMIS FOR SPACE APPLICATIONS

Future BMI systems for space applications will have to be able to operate continuously in reduced gravity conditions, allowing for multiple tasks to be performed concurrently with the BMI protocol execution. While current non-invasive BMI systems have reached a maturity that makes their consideration to support astronaut activities a concrete possibility, the current state of the art devices are however not directly applicable to human space exploration and exploitation activities. Hence, additional research driven by space requirements is necessary. A step by step approach with clear, uncritical, and simple tasks would not only put BMIs to real space world tests but also facilitate their acceptance among astronauts. Because of the singular and difficult to simulate conditions in which astronauts operate, it is crucial to involve astronauts from the earliest discussion and development stages as to identify in detail those situations where astronauts may benefit from using BMIs (Rossini, Izzo and Summerer, 2009b). From this application bouquet, a set of possible BMI systems might be selected to be tested and their protocols refined first in short-time microgravity exposition experiments, such as parabolic flight campaigns. Benchmark tests (Citi, Tonet, and Marinelli, 2009; Tonet et al., 2008) need to be implemented in order to assess the fitness level between systems and their target applications. Once the best BMI systems are identified, these would undergo long-term microgravity exposition tests, i.e. onboard the ISS. Apart from evaluating the effective usefulness of such systems in the accomplishment of specific astronauts' tasks, it remains very important to assess the effects of microgravity conditions on the use of BMIs once long-term neural adaptations have happened in astronauts' brains (Rossini, 2009). It is predictable that the effects of brain adaptation will differently affect the performance of different signal-processing techniques, as well as of different interface technologies, and it is crucial for the future of BMIs in space that those differences will emerge.

Developments of technologies and knowledge required to design brain-machine interfaces are happening at a great pace. These are driven by terrestrial applications and in particular targeted by biomedical research. While of interest, such achievements are not directly applicable to microgravity operations where the specific tasks and the unique environment are not considered by the mainstream research efforts on BMI. As a consequence, important research steps are still needed to prove the potential of BMI for human space flight with the early involvement of the final users (astronauts) and space experts. These steps are necessary to construct a critical set of data which will eventually allow for a matching between BMI systems performances and their related applications' requirements, paving the road towards the very first complete design of BMI for space applications. At the same time, the results of the December 2007 ESA parabolic flight campaign suggest that it is at least possible for a subject with prior BMI experience to achieve stable performances of EEG modulation during short-time exposures to micro-gravity. The logic next steps are parabolic flight experiments with online controlled BMI systems and the further comparison with long duration microgravity exposure data.

CHAPTER FOUR

-

NEUROINSPIRED INTERFACES WITH THE PERIPHERAL NERVOUS SYSTEM

I. INTRODUCTION TO PERIPHERAL NEURAL INTERFACES

Neuroinspired Interfaces can currently extract information from the peripheral nervous system (PNS) solely by means of invasive implantation of electrodes (Micera and Navarro, 2009). The bidirectional electrical interaction between the PNS and the Neuroinspired Interface makes possible a hybrid integration between user and technology which is currently impossible with any other interface: the user "feels" the interfaced device as it was part of his/her own body and controls it as it was one of his/her limbs (Rossini et al., 2009). This is possible since both the information on user's intentions and on sensory feedback is conveyed in the natural information pathway of the PNS (Fig. 1).

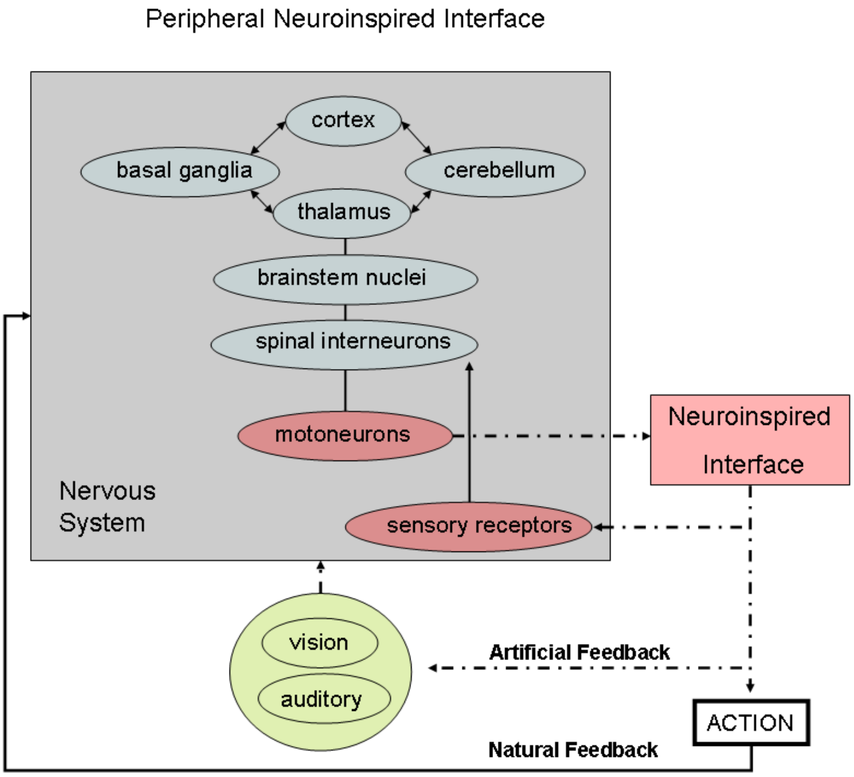

Figure 1. Information path that separates human's thoughts from actions in a peripheral Neuroinspired Interface.

The PNS is constituted by neurons whose cell bodies are located in the spinal cord or within spinal ganglia and their axons, which extend through peripheral nerves to reach target organs. Peripheral nerves contain two main types of nerve fibres, afferent sensory fibres and efferent motor fibres. Most of the peripheral nerves are mixed, providing both motor and sensory innervations to the corresponding projection territory (Fig. 2). Nerve fibres, both afferent and efferent, are grouped in fascicles that eventually give origin to branches that innervate distinct targets. Intrafascicular electrodes (e.g., LIFEs) measure the activity of and act upon the population of axons in their immediate vicinity.

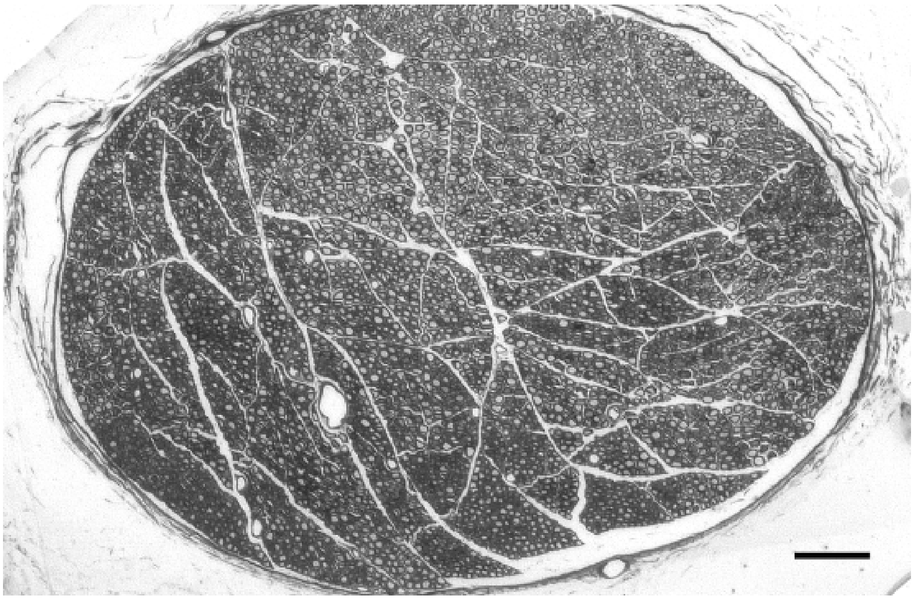

Figure 2. Structure of the peripheral nerve: transverse section of the rat sciatic nerve showing subfascicles of nerve fibres. From Micera and Navarro, 2009.

Afferent sensory fibres convey tactile, thermal, pain and proprioceptive information, depending upon the specialized terminal receptor of each somatic sensory neuron. They terminate at the periphery either as free endings or in specialized sensory receptors in the skin, the muscle and deep tissues. Signals are transmitted by the corresponding axons in series of action potentials, with intensity of the signal mainly coded by impulse frequency. Intra-neural electrodes can trigger the activity of these afferent fibres by injecting electrical biphasic stimulation pulses in the intra-fascicular space. Since the brain cannot discriminate between normal peripheral activity and induced peripheral activity, intra-neural electrical stimulation can reproduce tactile, thermal, pain and proprioceptive sensations, which are conveyed along the natural afferent information path and are integrated as natural sensorial feedback.

Efferent motor fibres originate from motoneurons in the spinal cord and end in neuromuscular junctions in skeletal muscles. These fibres convey all the information required to activate and modulate muscular contraction, which produces any human movement and action. Each spinal motoneuron makes synaptic contacts with a number of muscle fibres, constituting a motor unit. Graded contraction of each muscle is produced by increasing the number of motor units activated, and by increasing the frequency of impulses to each motor unit (Henneman et al., 1974). Intra-neural electrodes can access the overall electrical fluctuation in the intra-fascicular space, which contains the overlapping activity of both afferent sensory and efferent motor fibres. Signals related to different nerve fibres must hence be identified and extrapolated (Micera et al., 2009a,b).

II. NEUROINSPIRED INTERFACES FOR AMPUTEE USERS

By means of Neuroinspired Interfaces with the PNS it is theoretically possible to restore sensorimotor functions to users who lost limbs due to disease, trauma or amputation. These users have the "Thought to Actions" path compromised at its Actuation stage, though they retain a potentially functional pathway from CNS to PNS (Fig. 3). Once fully integrated into motor commands, the information leaves the central nervous system at the level of spinal interneurons and is conveyed in the motoneurons. Due to the amputation, though, this information never reaches the target muscles (lost with the amputation) or rather the remaining muscles does not produce the intended movement due to limb amputation.

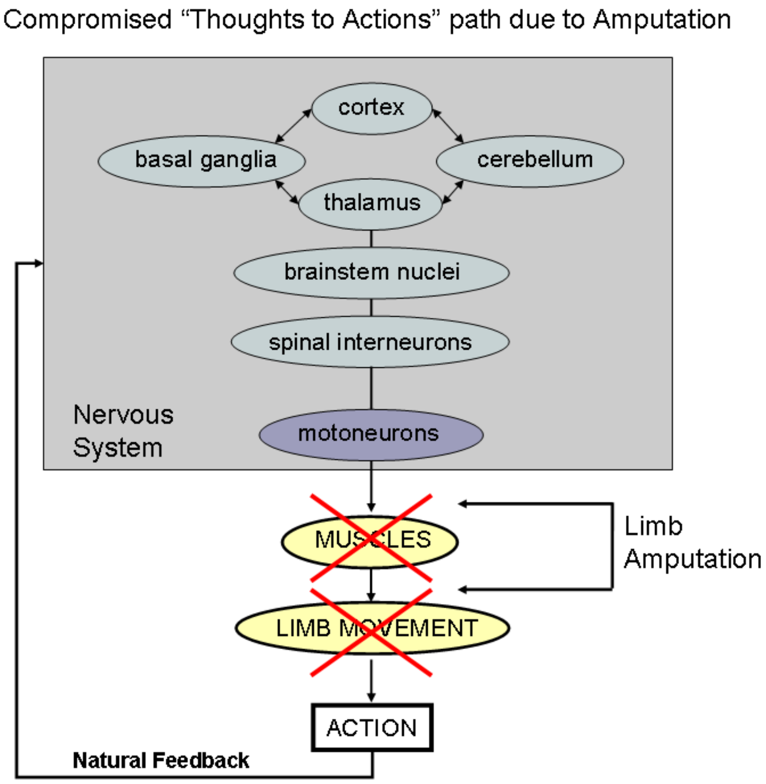

Figure 3. Limb amputation compromises the normal Information path that separates human's thoughts from actions. The intention is still generated and integrated in the central nervous system (light blue ovals).

A Neuroinspired Interface can be connected to the amputated nerves by multipolar intra-neural electrodes that may re-create the bidirectional link between the user's nervous system and the prosthesis. Current commercial prosthetic limb devices are unable to provide enough functionality and to deliver appropriate sensory feedback to the user so as to functionally replace the lost limb. A robotic prosthesis bridged with the PNS thanks to a Neuroinspired Interfaces could, on the other hand, provide both functionality (thanks to the many degrees of freedom offered by the robotic device and controlled by the motor efferent information naturally produced by the user) and sensory feedback (thanks to the tactile, temperature and proprioceptive information gathered by the artificial sensors embedded in the robotic device and translated via intra-neural stimulation into natural sensorial feedback) as shown in Fig. 4.

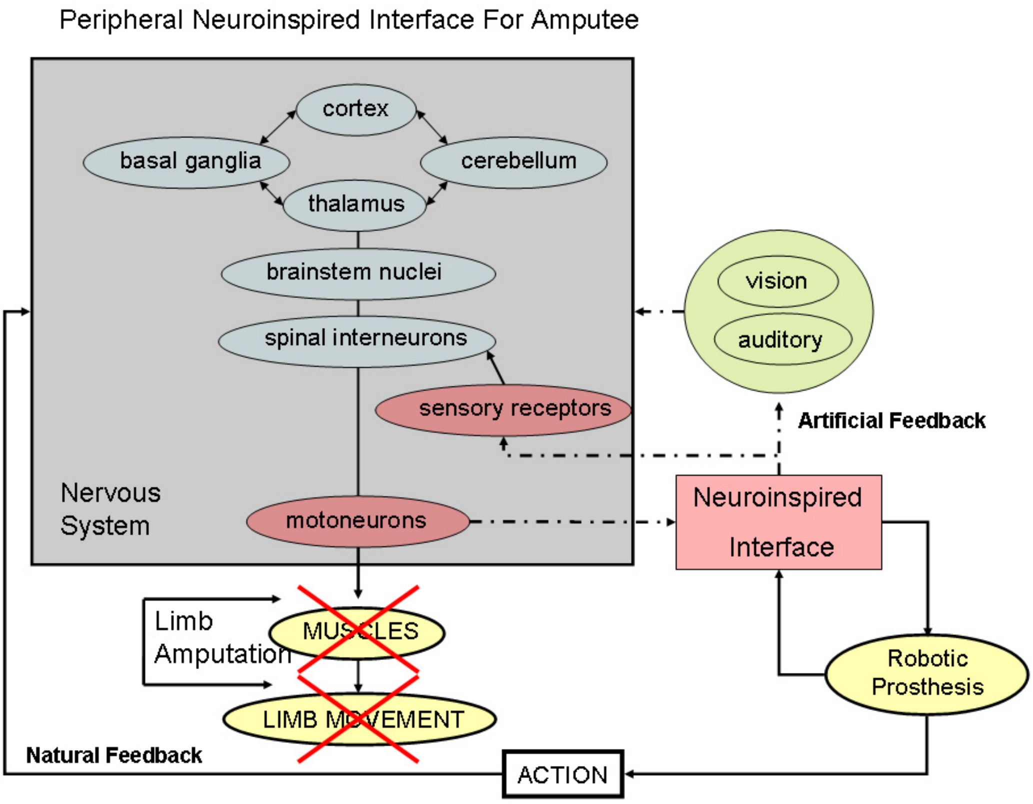

Figure 4. The information on user's intentions can be extracted at the peripheral level and be translated by a Neuroinspired Interface into actions of robotic prosthesis device. Information can be sent back to the user in the form of bio-feedback and/or artificial feedback.

First experiences with Intrafascicular electrodes and amputees were performed with LIFEs (Longitudinal Intrafascicular Electrodes) (Dhillon et al., 2004, 2005). LIFEs were implanted into median or ulnar nerves proximal to the stump. The results indicated that the motor signals recorded using LIFEs could be used to control prosthetic systems. During these trials the possibility of stimulating afferent nerves to provide sensory feedback to the subjects was also investigated. Subjects were able to feel tactile or proprioceptive sensations localized to individual phantom digits elicited through different electrodes (Dhillon et al., 2005). In some cases plastic stimulus-induced reorganization on somatosensory cortex by the afferent stimulation made the localization of elicited sensations better defined with time.

However, there are some important questions yet to be investigated in order to fully understand the risk/benefits of invasive Neuroinspired Interfaces with the PNS: i) whether the peripheral neural activity recorded by the Neuroinspired Interface is actually modulated by the user's motor cortex; ii) whether it is possible to extract motor commands to control more than one degree of freedom from efferent signals recorded from the user, and; iii) whether the biofeedback provided by intra-neural electrical stimulation can be successfully used by the user to regulate the electrical efferent neural motor activity accessed by the interface. To address these questions, a new version of LIFEs was implanted in a right-handed male (referred to in the present study as P.P.) who had suffered left arm transradial amputation due to a car accident two years earlier.

III. SUBJECT AND METHODS

A 26 years old, right-handed male was selected amongst several amputees volunteering in participating to the study. He had suffered traumatic trans-radial amputation of the left arm due to a car accident. Previous medical history was negative for significant systemic diseases or surgeries. During selection phase the subject underwent a complete neurological examination, as well as neurographic and electromyographic exams to exclude systemic Peripheral Nervous System disorders. He was submitted to neuropsychological and neuropsychiatric tests (MMPI-2, WAIS) to evaluate his comprehension, intellectual capacity and to exclude personality disorders. The patient did not report subjective/objective sensory deficits at the stump level. The local Ethics Committee approved the study and a written consent was obtained by P.P. after full explanation of the experimental protocol aims in front of a witness from his family who also signed the document.

The neural electrodes used in the implant belong to the family of tf-LIFE4 (thin-film Longitudinal Intra Fascicular Electrodes, 4th generation). Thanks to thin-film fabrication technology, each wire electrode was equipped with 8 active sites, plus 4 additional sites for references and grounds. Two tf-LIFEs (Hoffmann and Kock, 2005) (Fig. 5a,b) were inserted under surgical microscope (Opmi Vario/NC33, Zeiss) in each nerve following epineural microdissection separated by 3 cm (Fig. 5c). tf-LIFEs were introduced 45° obliquely to assure stability and high probability of intercepting nerve fibres. Four weeks later, tf-LIFEs were explanted via the same surgical access.

Four integrated Grass amplifiers (QP511 Quad AC Amplifier System), each one amplifying four channels, for a total of 16 channels simultaneously amplified were employed. ENG (from median and ulnar nerve as specified in the following) and EMG signal (from deltoid, biceps and triceps via surface electrodes in a belly-tendon montage, skin-electrode impedance < 10 KOhms) were recorded. ENG signals were amplified with a factor of 10,000, and band-pass filtered between 0.1 and 10 kHz. EMG signals were amplified with a factor of 5,000 and band-pass filtered between 0.03 and 3 kHz. Each channel was connected to the amplifier via a dedicated 3-pole cable (signal, reference, and ground). Those 48 poles (16 channels, 16 references, and 16 grounds) were connected to the 34 poles of the connector box via ground and reference grouping, ground being unique for all the channels (as well as for the whole instrumentation), while the reference was unique for each amplifier, requiring actually only 4 different reference poles, since also the tf-LIFE electrodes are fabricated for working with a single reference for each four channels. The connector box allowed to group all the single-pole wires into a multi-pole cable that could be simply and quickly plugged/unplugged. This box can be connected to the tf-LIFE electrodes through M/F SAFELEAD connectors.

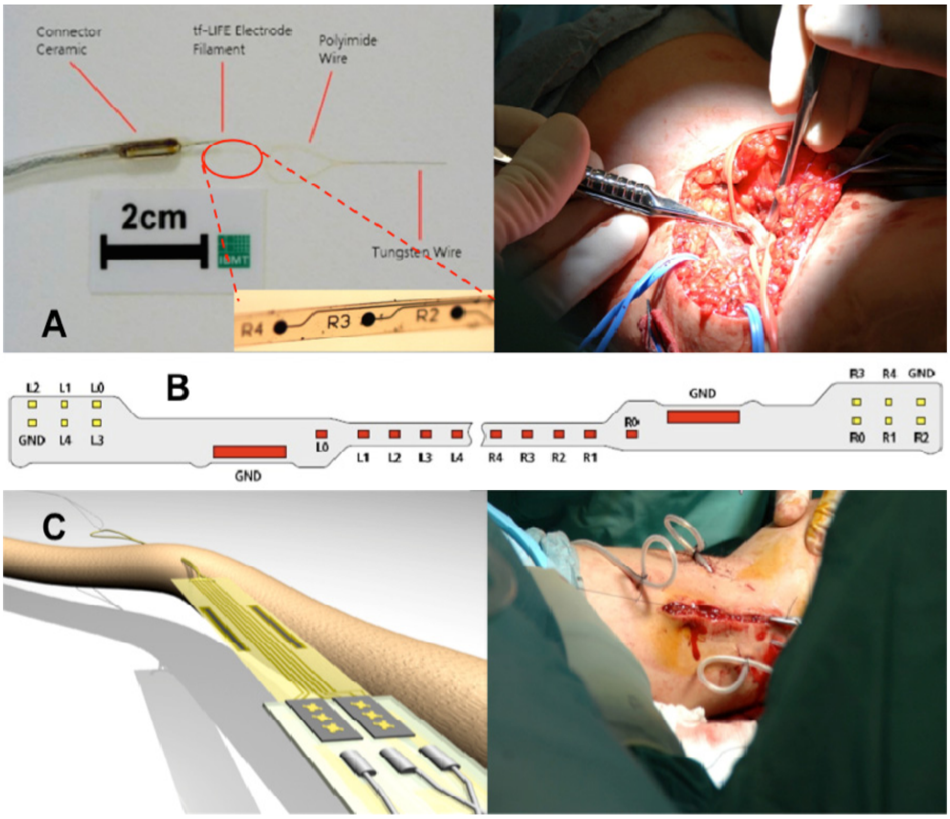

Figure 5. Overview of the implant. From Rossini et al., 2009.

Post-processing of tf-LIFE and EMG signals were obtained via selective filtering between 800 and 2500 Hz for the former and 10-1000 Hz for the latter. tf-LIFE electrodes are axial-symmetric, with four active pads for signal detection, one reference pad, and one ground pad on each side. Since the connector box has only one input plug for the ground (GND), an adaptation stage was included to pair the instrumentation with the electrodes. Eight ground pads were hence connected to the GND plug on the connector box via specific purpose-made adapting cables. A 16 channels, 16 bit, 1 Ms/s analogue-to-digital converter (ADC), rack mounted and connected to a rack mounted PC, was used.

III.I Cortical output in the efferent activity

Transcranial magnetic stimulation (TMS) is a non-invasive and painless technique that allows researchers to stimulate discrete brain areas. The technique involves delivering a brief magnetic pulse to the scalp through a coil; the stimulating effect depends on the geometry of the stimulating coil with respect to the head and of the waveform of the current pulse flowing through the coil (Fig.4). With the commonly used stimulation intensities and coils producing relatively focal types of stimuli, the cortex is activated within an area of a few square centimetres.

The physical basis of TMS is described by Maxwell's equations. Because the electromagnetic fields associated with TMS are of low frequency, the quasi-static approximation of the equations (Plonsey, 1969) can be applied to the computation of the tissue-induced fields and currents. A time-varying current pulse in the stimulation coil produces a magnetic field according to the Biot–Savart law. The time-varying magnetic field, in turn, induces an electric field according to Faraday's law. The induced electric field moves charges in the direction of its field lines. If the coil is parallel to the surface of the conductor (head), no surface charges appear due to induction, and the computation of the electric field inside the conductor is simple (Grandori and Ravazzani, 1991). Otherwise, charges accumulate at the conductor surface as well as at the interfaces between tissues with different conductivity, generating a secondary electric field. The intensity of the magnetic field can be represented by flux lines around the coil and is measured in Tesla (T). The magnetic field is oriented perpendicular to the coil and, for currently commercial devices, has average values of maximal stimulating intensities around 2T (Barker et al., 1985).

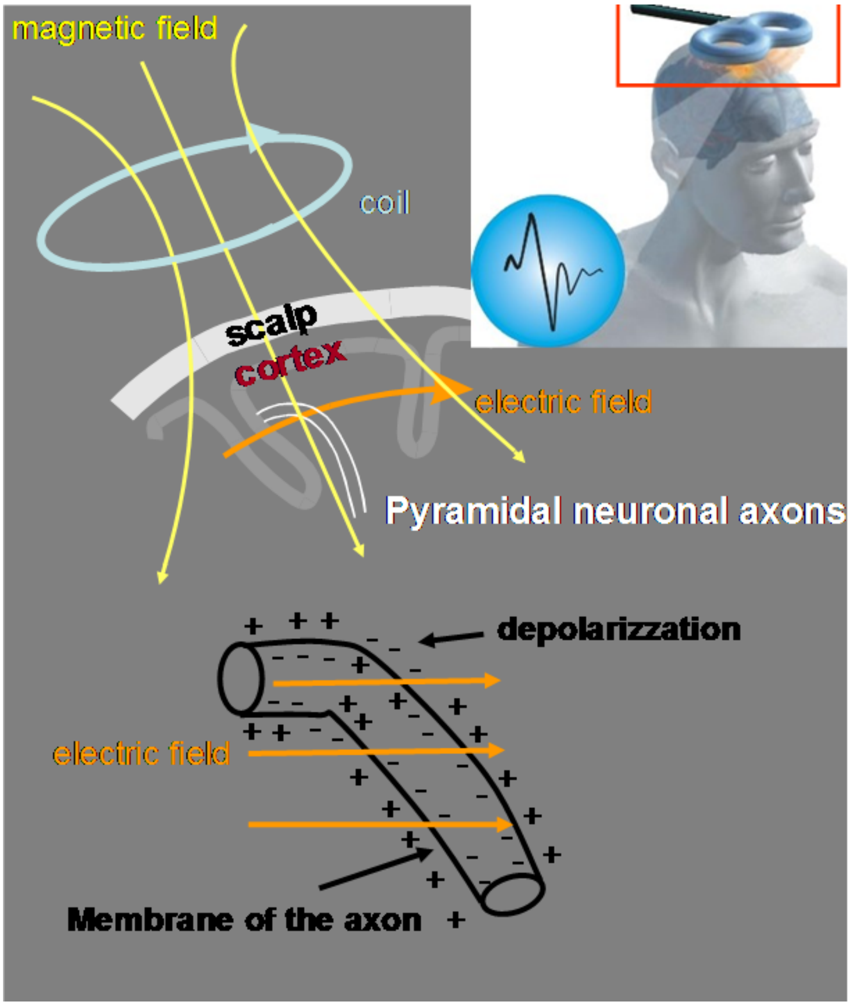

Figure 4. The electric current flowing in the TMS coil(s) induces a magnetic field, which penetrates the layers of tissues separating the brain from the outside (scalp). The magnetic field induces an orthogonal electric field in the underneath brain cortex, which drives ions movement. Neuron axons orthogonal to the electric field are maximally perturbed in their membrane potential, and undergo to depolarization or hyper polarization depending on orientation with respect to the current flow direction. In the case of depolarization, if the electric potential between the outside and the inside of the axon goes below the activation threshold, the neuron responds by an action potential. From Rossini, Rossini and Ferreri, 2010

Because the total induced electric field is strongest at the boundaries of any homogenous conductor compartment (Heller and van Hulsteyn, 1992), the stimulating effect of TMS in the brain is concentrated at the cortical surface. The electric field induced in tissue causes cell membranes to either depolarize or hyperpolarize. If the depolarization of the membrane overcomes its threshold, an action potential is generated (Fig. 4). Macroscopically, the locus of activation in the brain seems to be where the induced field is maximal (Kriggs et al., 1997). Focal activation is achieved by using a figure-of-eight coil or a double-cone coil, with two loops in which the current flows in opposite directions. The induced electric field peaks at the intersection of the coil windings (virtual stimulating cathode) (Fig. 5). The stimulating field experienced by a neuron has its duration equal to the first phase of the dB/dt waveform. A greater amount of stored energy is required for longer-duration stimuli to achieve the same change in transmembrane voltage (Barker et al., 1991). Therefore, short pulses with rise times of less than 100 μs are usually applied.

Latency is the interval between the delivery TMS impulse and the resulting response and reflects the total motor conduction time from cortex to the target muscle. The latency may be measured at the onset of the motor response and it is expressed in milliseconds (ms). Conduction times along the 'central' tracts (i.e. pyramidal fibres) are around 6 msec for those governing upper (proximal and distal muscles) and 12 msec for those governing the lower limb.

While recordings from spinal cord and corticospinal tracts have been repeatedly obtained -therefore providing information on the characteristics of the "central" signals elicited by TMS- very little has been investigated until now from the peripheral nerve except during the early stages of transcranial electrical stimulation (Rossini et al 1985) and with a number of technical bias which limits the value of those pioneering contributions. The reason for this lack of information is easily ascribable to the fact that invasive and relatively painful microneurographic recordings should be carried out either in normal volunteers or in Patients, able to selectively record from the nerve without excessive cross-talk interference from neighbouring muscles in which large amplitude MEPs are elicited at more or less the same time of the small nerve signal triggered by TMS. The use of tf-LIFEs in amputees offers an excellent opportunity for recording efferent signals directly from nerve fascicles while stimulating the motor tracts via TMS. Despite stump nerve contingents are partially degenerated, the number and physiological characteristics of the remaining fibres is still sufficient to infer relevant information on the fibre recruitment in the motor nerves during motor cortex TMS.

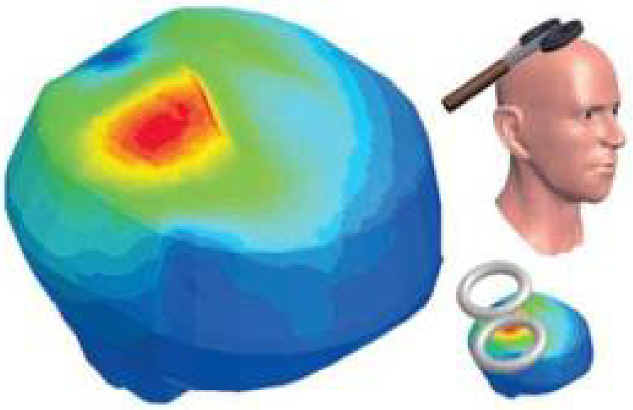

Figure 5. Magnetic field distribution over the scalp induced by a figure-of-eight coil (also known as double-cone coil). When the coil is placed parallel to the scalp as shown in the figure, the achieved activation is focal, with a field peak occurring at the intersection of the coil wings. From Rossini, Rossini and Ferreri, 2010

TMS was employed to monitor eventual 'plastic' changes of motor maps during training with the cyber hand control via tf-LIFE. During these TMS sessions, signals from LIFE hereby reported have been acquired. Transcranial Magnetic Stimulation (TMS Magstim200; eight-shaped coil with an inner wing diameter of 70mm) of the right hemisphere was carried out while simultaneously recording from tf-LIFEs electrode and Motor Evoked Potentials (MEPs) from proximal – biceps and triceps- muscles (stimulus rate 0.1-0.2c/sec; at various intensities below and above excitability threshold defined with standardized methods; Rossini et al., 1994). Briefly, MEPs were originally elicited with a suprathreshold stimulus and then by decreasing progressively until reaching a level around threshold; at that point, by 1% output adjustment, the excitability threshold level was defined at an intensity able to elicit clear responses of about 50 microV in amplitude in 50% of a series of 10 stimuli. The 'hot spot' corresponded the scalp point where the minimal intensity triggered MEPs of largest amplitude and shortest latency. The figure-of-eight coil was positioned with an approximate 45° angle of the handle with respect to the line of the Central sulcus as appreciated by structural MRI.

III.II Voluntary Control of Motor output

The protocol implemented for the studies on voluntary control of motor output was performed though three subsequent phases: (1) pre-implant training with a virtual hand for standardizing the types of movements the subjects should voluntarily dispatch to the missing limb; (2) post-implant training to control output of tf-LIFE4s during the command to move the missing limb; (3) on-line prosthesis control designed to train the subject to control and standardise tf-LIFE4 output induced movement commands.

During phase (1), the subject practised sending three individual commands to the missing hand with the same speed/amplitude shown in dedicated videos by a virtual hand: (i) power grip; (ii) pinch grip; (iii) flexion of the little finger. These three actions were considered representative of the variety of movements controlled by the nerves under investigation: mostly median nerve fibres for the pinch, mostly ulnar nerve fibres for little finger flexion, and both for the power grip.

Following tf-LIFE4s implantation, phase (2) began, in which the same videos were used to trigger the subject's motor commands – without any activation of stump muscles – while recording neural signals. Videos showed alternating open-relaxed hand movements and were synchronised with the recording system. Signals from tf- LIFE4s and the EMG of, biceps and triceps were simultaneously recorded using a 48 kHz sampling rate, and were data-windowed in 1000 samples for mean rectified value calculation. Such recordings were acquired with the aim of eliminating eventual EMG contamination from tf-LIFE4 signals; contribution of EMG-derived control to the prosthesis was not an endpoint of the present study.

In phase (3), the ENG channels with the best signal-to-noise ratio were selected while analyzing the recordings from the previous phase. The online activities of the best channels, together with EMG activity, were shown to the subject, who was asked to modulate them while keeping the EMG silent in order to avoid EMG contamination of the tf-LIFE4 signals. This biofeedback approach was found to be the best training protocol among those tested (Tab. I). Audio EMG activity feedback, would reduce the associated EMG activity even further, but would also rapidly tire the subject.

Once a stable level of training was achieved, LIFE signals were translated into robotic hand actions and the subject had direct visual feedback on the correct/wrong execution of the intended movement. Each movement type was triggered by the signal level of a proper single channel. In order to exclude contamination by unwanted contractions from stump muscles or environmental noise, only rectified values greater than 3–8 microV in a time window ranging from 5 to 20 ms were used.

Channels were chosen depending on their signal-to-noise ratio and anatomical-functional location (i.e., channels from the median nerve for power or pinch grip, channels from the ulnar for little finger flexion). Whenever one type of action was classified, the robotic hand began and completed a movement after a time lag appropriate to a natural condition.

TABLE I

DIFFERENT OUTCOME OF TESTED FEEDBACK PROTOCOLS

Feedback Protocols		Outcome
Acoustic	Audio monitor connected to a single channel's activity	PP was mentally fatigued by audiomonitor sound
	Investigators verbally reporting the outcome; subject resting with closed eyes	PP experienced issues in focusing his attention
Tactile	Tf-LIFE electrical stimulation on the same nerve (but on a different electrode)	After 10 days it became impossible to elicit tactile sensation from tf-LIFEs' active sites
Visual	Virtual hand performing the same movement	No real feedback about PP's neural activity, it was used to restore some visual feedback of the missing hand
	Tf-LIFE channels activity directly showed to the subject together with EMG associated activity	Actual feedback about PP's neural and EMG activity (filtered and amplified). PP's performance improved quickly
	Real cybernetic hand prosthesis performing the same movement under subject's control	Both actual feedback and visual hand feedback, since the hand was controlled by PP's neural activity

III.III Bio-Feedback

To identify afferent fibres eliciting sensations, full mapping of all 32 contacts within the tested nerves was carried out. Rectangular cathode pulses of duration 10–300 micros and current intensity 10–100 microA were employed. To avoid electrode damage, all stimulation trials were below 75% of the maximum charge (4 nC), in the form of pulse trains at 10–500 Hz lasting 300–500 ms. The best active sites for sensation were characterised, beginning with short and low-current stimuli (10 microA, 10 micros) which were progressively increased in order to elicit different sensations; either the electrode's safety limits or subjective discomfort determined the maximal stimulus intensities.

To test the intraneural electrical stimulation as feed-back for motor control, a specific task was designed. P.P. was asked to produce a power grip every 5 s. In a set of trials, an operator triggered a stimulus train (0.3 s train of pulses, 10 microA, 10 micros at 70 Hz) after each burst of efferent activity recorded by tf-LIFE4s.

IV. EXPERIMENTAL RESULTS

IV.I Cortical Output

Intraneural tf-LIFEs recorded a significant amount of TMS-triggered signals triphasic in shape and of 4-8 msec in duration, grouped around post-stimulus 9 milliseconds (Fig. 6), which were selectively recordable only at specific contacts, while some contacts did not show propagated activity (Fig. 7).

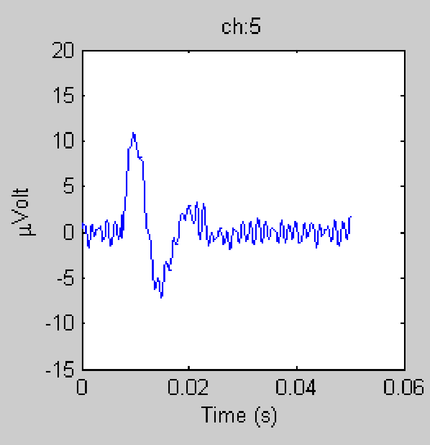

Figure 6. Example of motor action potential recorded from LIFEs, evoked from TMS stimulation of the motor cortex

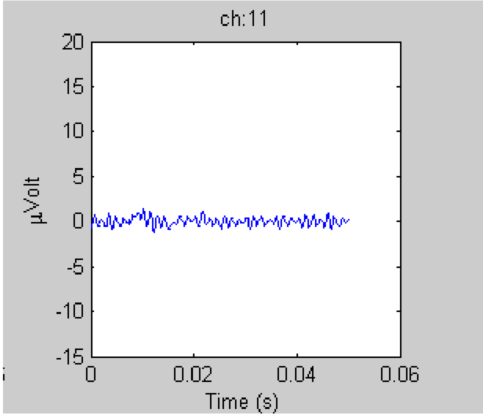

Figure 7. Example of silent channel during TMS stimulation of the motor cortex

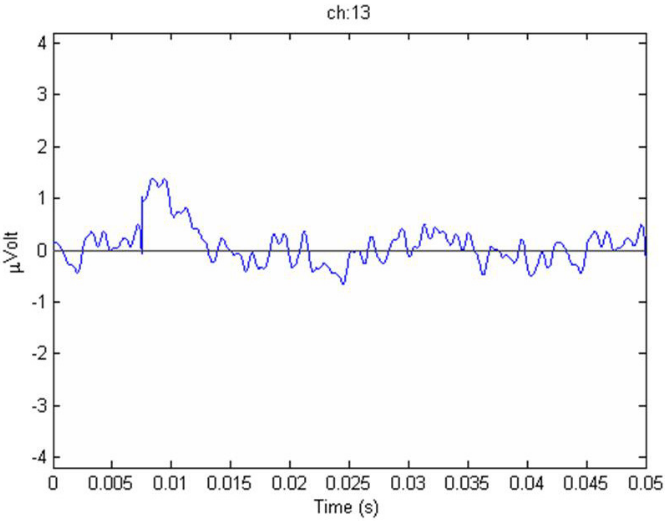

Figure 8. Silent EMG activity on the biceps recorded during sub threshold TMS stimulation.

In the sub-threshold conditions no responses could be recorded from muscles (Fig. 8), while signals were still present at specific recordings contact of tf-LIFEs within nerve fascicles (Fig. 9).

Progressively larger, reliable and reproducible responses were triggered in tf-LIFEs at threshold and supra-threshold conditions respectively (Fig. 10).

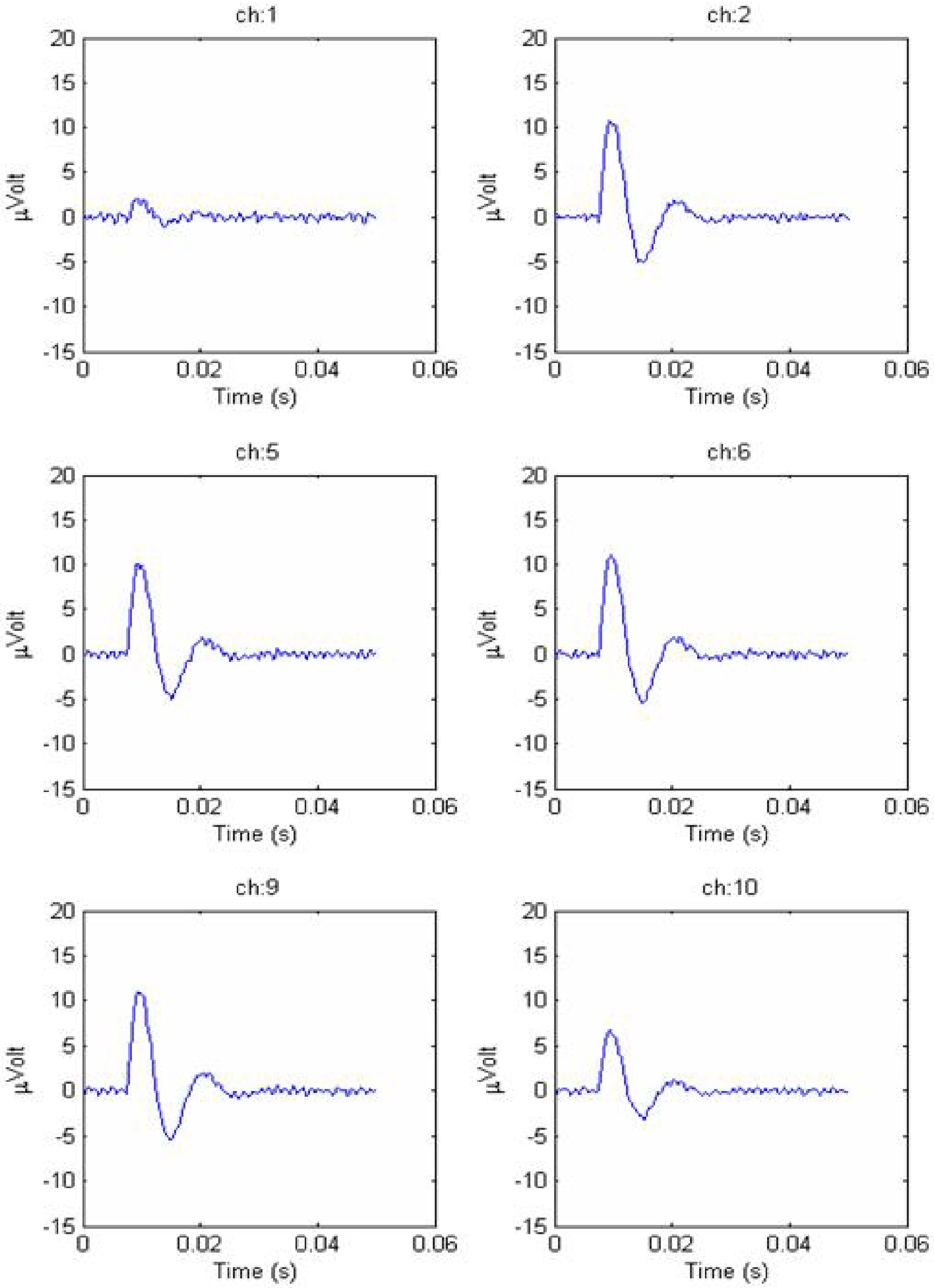

Figure 9. Peripheral neural activity at some of the working contacts during subthreshold TMS stimulation of the motor cortex. The first line represents the activity recorded from M1, the second line from M2, and the third from U1.

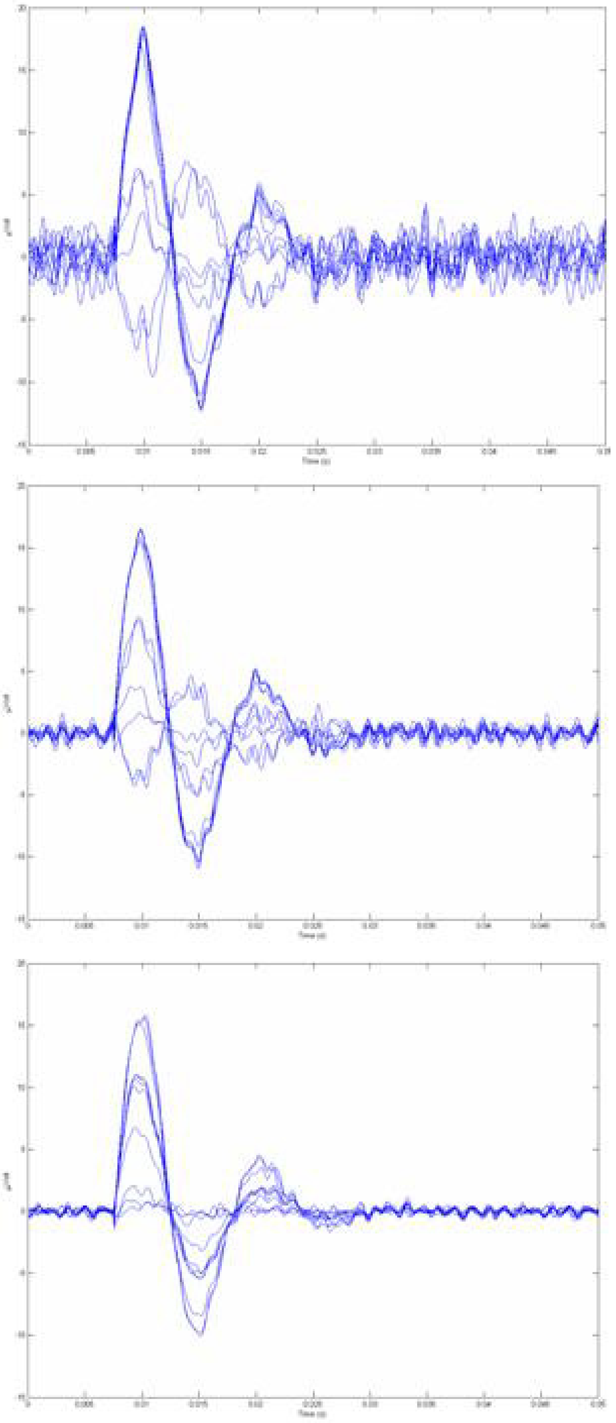

Figure 10. Overlapped evoked efferent activity recorded during: up) suprathreshold stimulation; middle) threshold stimulation, and; down) subthreshold stimulation.

IV.II Voluntary Control of Motor output

The electrodes and the channels whose activity shown more modulated activity during each one of P.P. mental tasks were selected for the three movements. The selected channels corresponded to the anatomical-functional location (i.e. channels from the median nerve were more active during power or pinch grip tasks, while channels from the ulnar nerve were more active during little finger flexion tasks) (Fig.11).

P.P. voluntary modulated his peripheral neural signals, which were successfully translated into robotic prosthesis actions. P.P. had to mentally focus to produce the same action with his missing limb. The online selection of the intended movement was triggered when the rectified value of the channel activity was greater than 3–8 microV in a time window ranging from 5 to 20 ms. Thanks to this threshold control architecture, LIFE signals were translated into robotic hand actions and the subject had direct visual feed-back on the correct/wrong execution of the intended movement. Whenever one type of action was classified, the robotic hand began and completed a movement after a time lag appropriate to a natural condition.

IV.III Bio-feedback

Discrete tactile sensations were elicited from different stimulating sites of three electrodes (i.e., from 4 sites of M1 and M2 in the median nerve and from 5 sites of U1 in the ulnar nerve) and referred in the fascicular projection territories of the corresponding nerves.

Stimulation was tested as feed-back during control motor task. P.P. was asked to produce a power grip every 5 s. In a set of trials, an operator triggered a stimulus train (0.3 s train of pulses, 10 microA, 10 micros at 70 Hz) after each burst of efferent activity recorded by tf-LIFE4s. As Fig. 12 shows, P.P. was able to reduce the motor activity approaching the correct frequency in less than one minute.

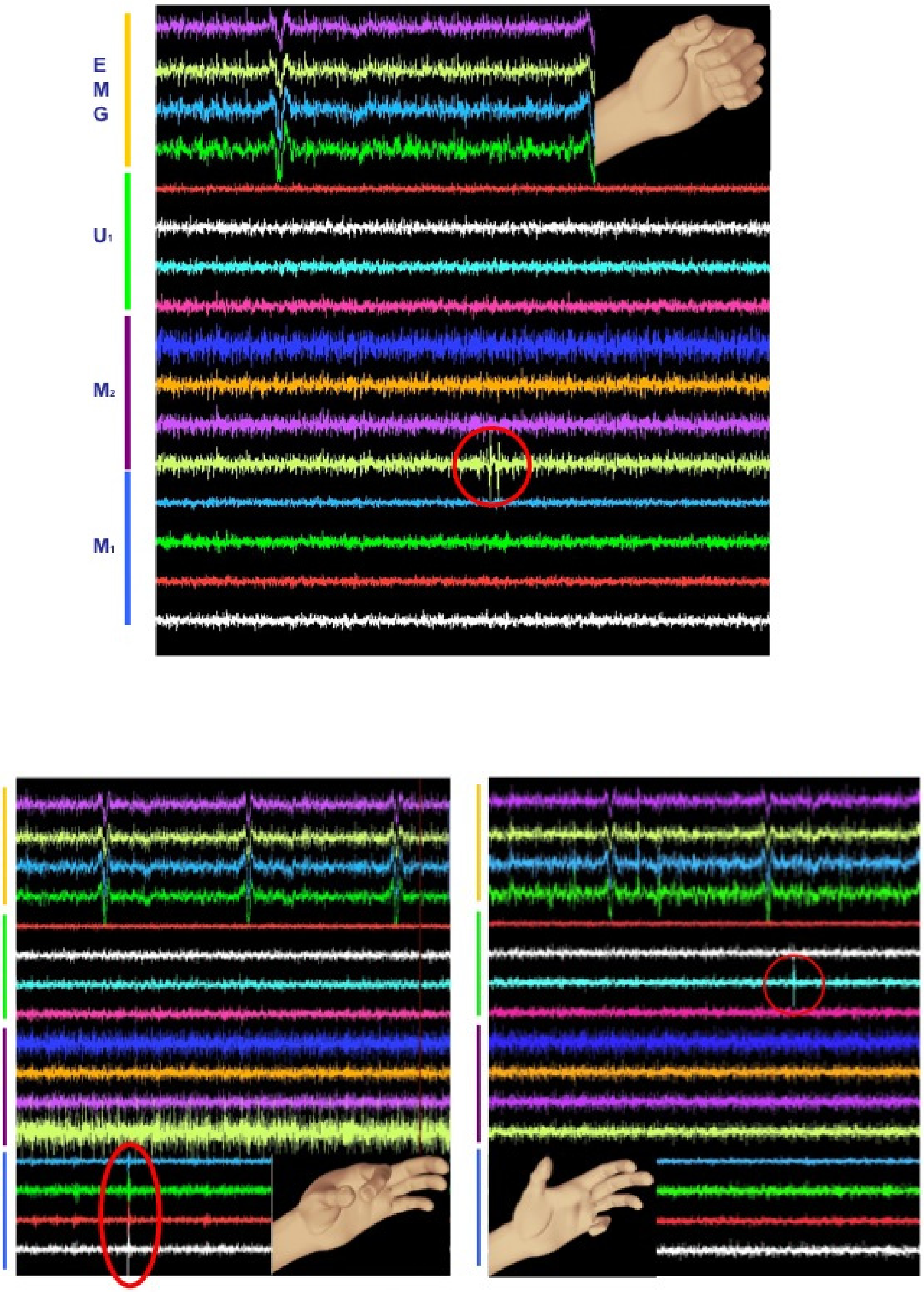

Figure 11. Voluntary modulation of efferent peripheral neural activity produced by P.P. while focusing on producing specific movements with the missing hand. M_1, M_2, U_1 respectively ENG activity from electrodes in the median and in the ulnar nerve.

The electrical charge necessary to elicit sensations (minimal threshold) increased during the first ten days from 0.1 to 1 nC, until no sensation was elicited through any of the three electrodes despite stimulation with the maximum allowed charge (~ 4 nC). In order to avoid irreversible electrochemical processes with the platinum electrode and possible contamination of motor signal recordings, stimulation procedures were halted.

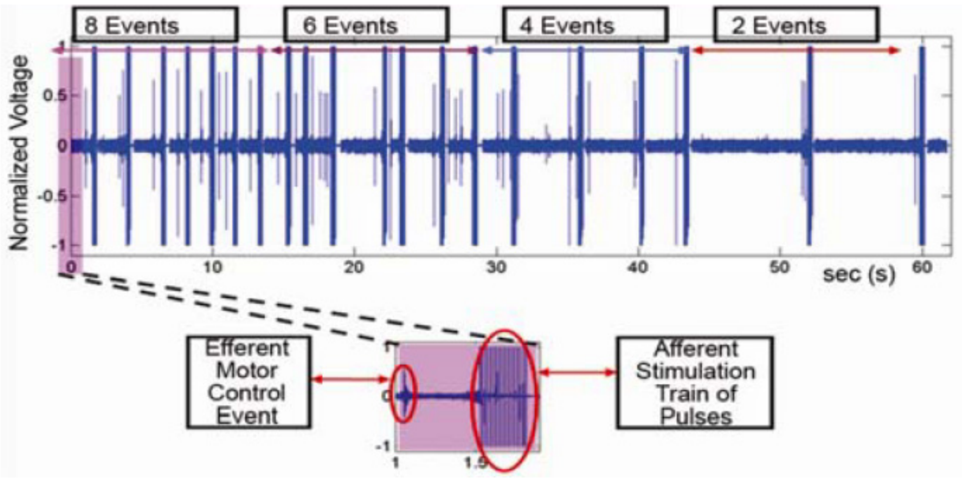

Figure 12. Efferent /Afferent signals during one minute trial. Each efferent movement control event was rewarded with a 0.3s train of 70Hz, 10mA, 10ms pulses. P.P. improved his control in less than one minute. From Rossini et al., 2009

V. CONCLUSIONS AND FUTURE WORK

The main aim of the study was to test the potentials of Neuroinspired Interfaces with the PNS for the bidirectional control of a robotic prosthetic hand. The bidirectional electrical interaction effectively made possible a first step towards an hybrid integration between user and prosthesis. In fact, the combined use of tf-LIFE4s and online signal processing/stimulation techniques has allowed discrimination of signal patterns for controlling three independent types of hand grip and allowed delivery of sensory feed-back in a completely natural fashion.

In particular, regarding the four "opened questions" aimed by the study, the results can be summarized as follows:

1. The cortical origin of the efferent neural activity recorded is supported by a number of evidences: the latency of the propagated action potential is appropriate for nervous conduction along the cortical spinal and peripheral nerve motor fibres, from cortex to the recording site; responses amplitude and representation in different fascicles of the nerves were intensity dependent; responses from tf-LIFE were recordable with the TMS intensities below threshold for triggering motor evoked potentials, therefore making nearly impossible a muscular contamination of the tf-LIFE recordings.
2. Training improved the control of motor output to the prosthesis; in particular, among all the different tested training protocols, the visual feedback provided by the robotic hand was the most effective; P.P. was able to online and naturally control three DOF of the robotic prosthetic hand; the three different actions were triggered by natural production of action planning towards the missing hand.
3. Tactile sensations were elicited and modulated by afferent stimulation. Frequency and pulse width concurred to modulate the sensations, which were referred in the fascicular projection territories of the corresponding nerves. Moreover, it was shown that the quality and selectivity of efferent signals was augmented by concomitant sensory feedback.

The future work on Neuroinspired Interfaces with the PNS will be aimed at the design and component optimization of fully integrated wearable robotic hand prosthesis for hand amputee. New stimulation and registration protocols, stemming from the promising results here presented, will be implemented.

CHAPTER FIVE

-

NEUROINSPIRED INTERFACES WITH ANTICIPATORY MOVEMENTS

-

ANTICIPATORY HEAD ROTATION

I. INTRODUCTION TO ANTICIPATORY INTERFACES

As seen in Chapter 1, the last level at which it is possible to extract information on user's intentions is at the intentions manifestation level, that is, where the user's cortical and peripheral activity convey to produce an action. All the current human-technology interfaces work at this level of information extraction, since they usually require users to operate the control interface with their hands (keyboard, joystick, mouse, etc) or with their feet (pedals, etc). Also speech recognition interfaces are action-level interfaces, since speech is produced by muscular contractions of the thorax and of the vocal chords. The scheme provided in Fig. 1 can be applied for any of the current commercial interface. Muscles contraction or limb movement can be both used by the user to operate the control interface, which translate user's action into commands for the technology while providing artificial feedback to the user.

The main difference between current commercial interfaces and Neuroinspired Interfaces is in the way the user operates the control interface. As seen in Chapter 1, Neuroinspired Interfaces are a subclass of Natural Interfaces. The characteristic feature of natural interfaces is the fact that they almost lack any physical control interface. Since the user is asked to behave "as he normally would" while trying to get the device to perform the desired action, he does not have to operate any physical interface-device interfacing him to the technology. The control interface in a natural interface monitors user's natural behaviours and detects those related with the technology interaction. The difference between Neuroinspired and Natural Interfaces in general is that user's intentions are extracted from physiological and involuntary events related with the natural action production.

If the involuntary movements monitored by the Neuroinspired Interface belong to the class of anticipatory movements, the interface may acquire predictive features. Anticipatory movements are involuntary movements that humans produce in anticipation of specific motor actions (Lan et al., 1999; Berthoz, 2000;

Johansson et al., 2001). A specific class of human-robot Neuroinspired Interfaces, defined Anticipatory Interfaces, is here proposed. Specific feature of these interfaces is the fact that in principle they can reduce the delay in commands actuation by monitoring user's unconscious anticipatory movements. Applications to robotics of such movements were proposed in terms of human manipulation mimicking (Pinpin et al., 2008). The long-term goal of the present study is to create a system able to understand users' intentions by monitoring involuntary natural anticipatory behaviours by which the interface can predict user's motor intentions.

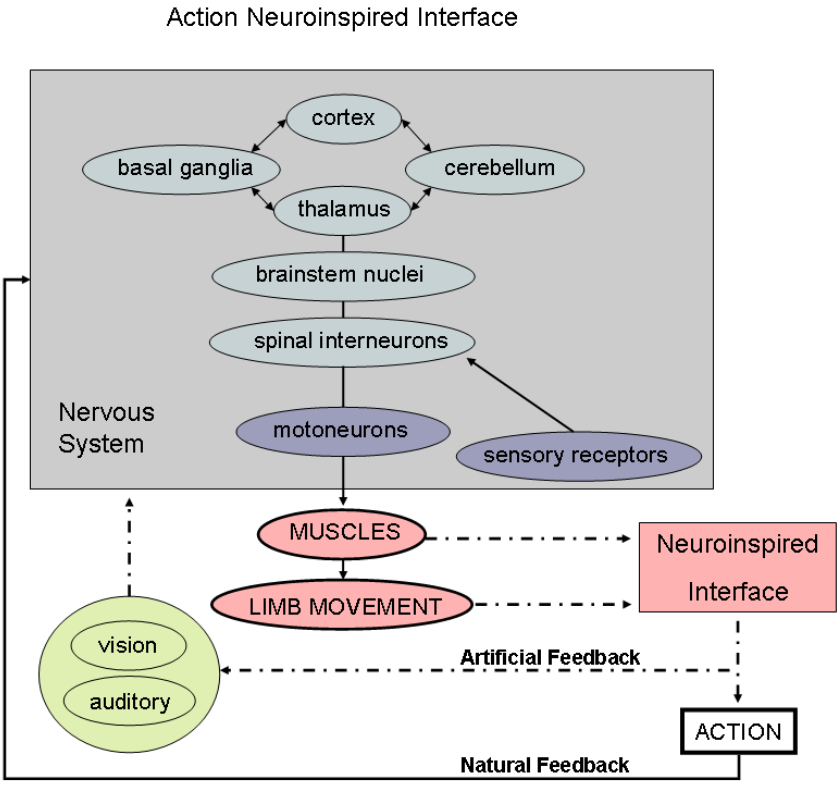

Figure 1. Information path that separates human's thoughts from actions in a action Neuroinspired Interface.

At the current state, the use of anticipatory movements to improve human-computer interfaces has been the subject of two main research efforts. In the first one, the mutual coordination between human gaze, head, and hand during manipulation tasks was exploited to make a robot-partner able to predict the movements of the human-partner, and to replicate them in real time and flawlessly (Laschi et al., 2007). The results of the second study are here presented. Anticipatory movements in subjects' navigating through a virtual environment or during teleoperation tasks, i.e. not moving actively, are discussed. It was found that the anticipation behaviour can be manifest with one second in advance of the virtual-steering action, and with up to 3 degrees of head rotation, which means sensible time for prediction and triggering movements wide enough to provide reliable information for an Anticipatory Interface (Rossini, Laschi and Guglielmelli, submitted).

I.I Definitions and General Properties

Generally, we define Anticipatory Interface as a control apparatus able to identify user's intention not by explicitly given commands, but by monitoring involuntary user's behaviours that are coupled with the intention and anticipating it (Fig. 2). In the standard path, the starting point is in the user's *motor planning,* which then voluntarily activates the *muscolo-skeletal system,* in order to operate the *interface* that controls the robot. Robot's actions are then received as a feedback by the user, which evaluates the correctness of the operations. If the *motor planning* determines some *involuntary motor commands* in anticipation to the *voluntary motor commands*, then an *Anticipatory Interface* can be used to detect the *involuntary anticipatory movements* and to traduce them in the intended actions, sent in form of *control commands* to the robot. Since the involuntary movements anticipate the planned actions, anticipatory interfaces could be able to predict user's intentions before they are executed. The fact that anticipatory movements are also involuntary movements, makes by definition Anticipatory Interfaces belonging to the group of Natural Interfaces.

There is a wide group of known involuntary movements that anticipate motor intentions (Grasso et al., 1998), such as gaze and head movements, which contain most of the information on human desired actions. They can be tracked by a multitude of devices such as gaze tracking systems, inertial measuring units, and optokinetic, photogrammetric, or ultrasound apparatus for movement analysis. By monitoring and decoding these anticipatory movements, Anticipatory Interfaces are in principle able to understand users' intention before any volitional control action is performed. Hence, among their unique properties, they have the potentials of reducing communication delays in teleoperation tasks. Also, since involuntary movements do not impose any cognitive load to users as they form an integral part of the related sensory-motor task, the operation of an Anticipatory Interface should require little training if any at all.

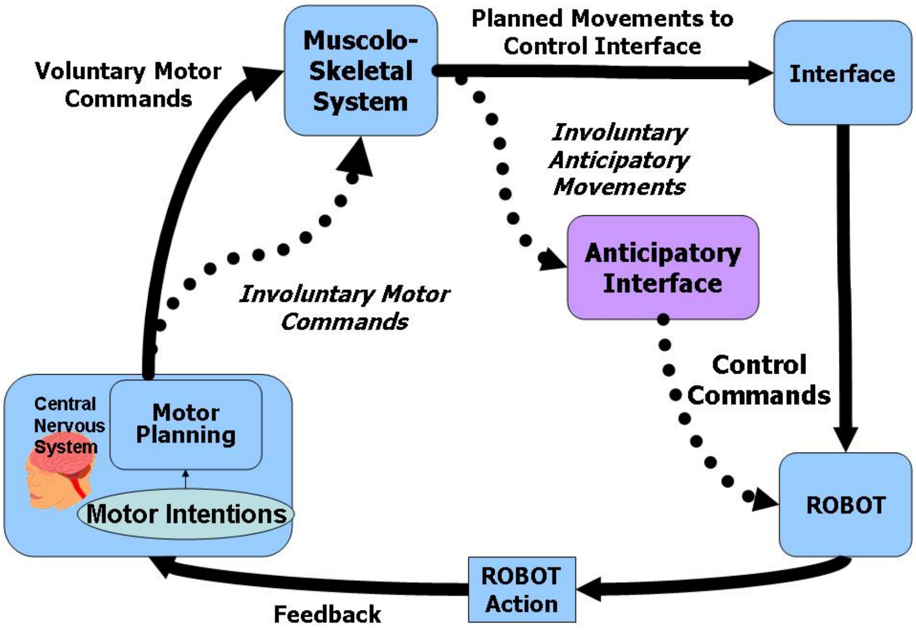

Figure 2. Differences in the thoughts-to-actions path between a standard interface (full arrows) and an Anticipatory Interface (dotted arrows).

II. ANTICIPATORY INTERFACE FOR TELEOPERATION

A well-known anticipatory movement is the head rotation that anticipates trajectory changes during human locomotion. It consists of a rotation of the head on the yaw plane (the plane parallel to the walking ground) and on the same direction of the planned turn. This anticipatory movement is in physiological tests characterized by a large anticipatory time (approx 1 s) and a wide rotation (approx. 25-30 degrees), as showed in Fig. 3 (adapted from Grasso et al., 1998). During the turn, the head rotates in the opposite direction, until it realigns with the trunk. The anticipation happens also at the end of the turn, with the head anticipating the return on the straight route and eventually realigning with the trunk again.

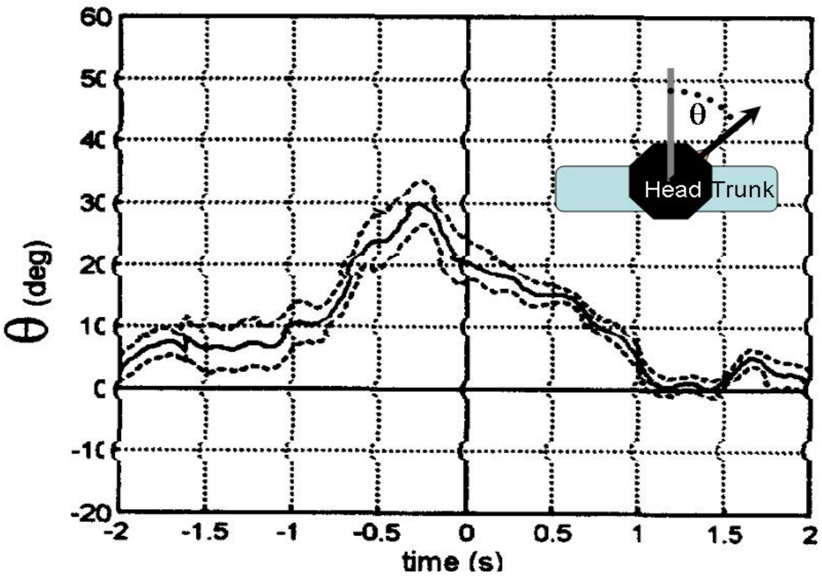

Figure 3. Head anticipatory movement during walking steering. Time is on the x-axis, where subject's steering begins at time 0. Head-trunk angle is on the y-axis. It is well visible how an anticipatory rotation starts one second before the steering, reaches his top immediately before the steering action, and comes back to zero during the steering. This second rotation is due to the re-alignment of the trunk rather than an actual rotation of the head. Adapted from Grasso et al., 1998

The neurophysiologic reason of the anticipatory behaviour can be found in human's locomotion neuro-controller, which is based on head's reference system. This means that before any turn during locomotion, head's reference system has to be aligned with the planned direction, in order to prepare the locomotion control system to maintain the new direction (Hicheur et al., 2005). It was found that the anticipatory behaviour always begins at the same distance from the turn (and not at the same time, as it was originally expected), and independently from locomotion speed. The head rotation amplitude is related with the amplitude of the incoming turn (Grasso et al., 2000). Interestingly, the anticipatory head rotation happens to be the same during locomotion in darkness or in blindness, and even during backward locomotion (with the head rotating in the opposite direction of the turning) (Grasso et al., 1998).

Before exploiting any physiological anticipatory movement into an Anticipatory Interface for teleoperation, it is necessary to prove the existence of such movements also during (non physiologic) teleoperation tasks. If anticipatory movements should persist, their features have to be characterized in order to extract important information regarding 1) how the anticipation time relates to tasks conditions; and 2) the physical dimensions of the anticipation movement that has to be automatically detected by the Anticipatory Interface.

III. MATERIALS AND METHODS

Head rotation measurements are usually obtained with optokinetic systems for movement reconstruction. These systems provide the best performances in terms of spatial and temporal resolution, though they are expensive and require a structured and dedicated environment, hence are best suited for applications that can be performed in small registration volumes. Inertial measuring units (IMUs), on the other side, allow measurements and registrations following User/Patient activities in his daily living environment, in open spaces and generally in unstructured environments. Compared to optokinetic systems, though, IMUs have lower spatial resolution and are prone to drift (Gal et al., 1997; Mayagoitia, Nene, and Veltink, 2002). Still, since of their small size, wearability, and easiness of use, together with not requiring structured environments(Laschi et al., 2007; Jang and Park, 2003), IMUs were targeted as the best candidates as motion monitoring systems in anticipatory interfaces.

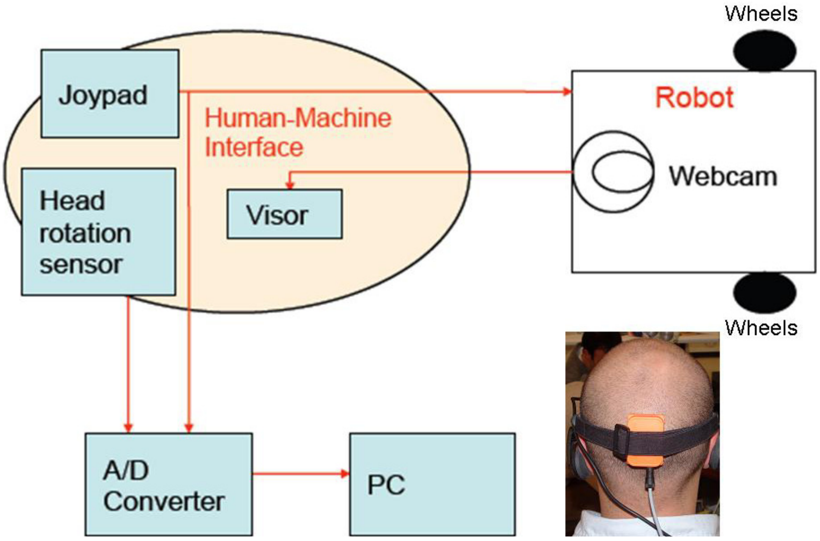

Figure 4. Experimental set-up and MTx inertial measuring unit placing on subject's head.

The teleoperation system is schematically composed as in Fig 4. A modular RoboDesigner® robot was assembled and optimized for the tele-operation task. Robot's movement was controlled with the left analogue stick of a common videogame joy-pad. The UP-DOWN movements on the stick controlled the fixed-velocity forward-backward movement, while the LEFT-RIGHT movements on the stick controlled the rotation. The robot was equipped with a webcam (which allows a max resolution of 640x480 and a fluid 30 fps frame rate). The full-screen version the video stream from the webcam was reproduced on an LCD wearable visor, integral with subject's head, and with a screen resolution of 642x480. Subjects' head orientation was measured and recorded with an Xsens MTx inertial measuring system, which is equipped with three accelerometer, three gyroscopes, and three magnetometers. Thanks to its sensors, the MTx can finely and continuously measure its absolute orientation in a 3D space. MTx was firmly placed on subjects' head as shown in Fig 4.

The two analogue signals (UP-DOWN; RIGHT-LEFT) produced by the joypad while controlling the robot were digitalized and recorded by a National Instruments PCI A/D. These signals, compared to those regarding head rotation angle on the yaw plane digitally acquired from the MTx, were used to measure the head anticipatory behaviour.

Three male subjects, mean age 30 and right hand, participated to the experiment. They were comfortably sitting on a chair, wearing the visor and the MTx, while holding the joy-pad with both hands.

Four teleoperation tasks were implemented: rally car race (virtual navigation in a videogame), and robot teleoperation at three different speeds. In the first one, the subject controls a virtual car in a car race videogame for 3 laps. Apart from the absence of the robot, the rest of the set-up remains as previously described. The other three tasks consisted in controlling the robot for 4 laps (two clockwise, and two counter clockwise) on an "eight-shaped" circuit with the same joy-pad. These three tasks were differentiated by the cruising speed (high: 50cm/s; medium: 30cm/s; low: and 4cm/s). Cruising speeds were kept fixed, which means that depending on the tasks, the robot could run always at a fixed speed.

After acquisition, head rotation angles on the yaw plane were band pass filtered in the range of 0.01-10Hz, while joy-pad signals were used as activity markers. Head rotations wider than 1/10 of degree and enduring longer than 100ms were analyzed and classified into two different behaviour events: single command events and global turn events.

Single command events are all the LEFT-RIGHT commands on the joy-pad tracks which determined any robot trajectory variations. The presence and the quality of head anticipatory rotations before each single command events were evaluated. Global turning events are the LEFT-RIGHT commands on the joypad tracks which determined a well defined turn after a straight fraction of the circuit. The presence and the quality of head anticipatory rotations before the opening and the closing of a global turn event were evaluated. In Anticipatory Interfaces implementations we are interested in the correlations between head anticipatory rotation and both single commands and the global trajectory planned by the subject.

IV. EXPERIMENTAL RESULTS

All of the three subjects showed homogeneous anticipatory head rotations before most (over 90%) of the single command and global turn events. The features of the anticipatory head rotations during teleoperation tasks were aligned with what previously reported in studies on human locomotion (Grasso et al., 1998). The teleoperation anticipatory head rotation is described in Fig. 5, and can be summarized in four steps:

1. the subject sees the approaching turn in the visor and elaborates a trajectory to overtake it;
2. a certain (and unknown) number of millisecond after 1), and a certain number of milliseconds (which depend on cruising speed) BEFORE executing the command to turn the robot, the subject performs an involuntary and anticipatory head rotation on the yaw plane;
3. differently from what found in physiological locomotion recordings (Prevost et al., 2002), the anticipatory movement does not end BEFORE the

turning phase, but stays for few milliseconds (around 20msec). This probably happens because of the misleading visual feedback (the scene in the visor does not rotate in accord with subject's head rotation as it would during physiological locomotion);

4. after the robot has reached a certain turning angle, subject's head starts a rotation in the opposite direction, anticipating the closing of the turn. In physiological conditions this second movement does not appear, since it is the trunk which comes back in line with the head, and not the opposite. This difference can be usefully exploited in Anticipatory Interfaces, since it can give the trigger for ending the "turn" command.

More than 50 control events where classified for the virtual navigation task and for the high and medium speed teleoperation tasks for each of the three subjects. For each event, the existence of an anticipatory head rotation, its anticipation time, and its rotation amplitude were characterized. Tab. I shows the mean and standard deviation values among the three subjects associated with each tasks, as well as the percentage of events which were anticipated by head rotation.

From the analysis of single command events emerged that turns coming after long period (>3 sec) of constant trajectory were associated with almost constant anticipation times and with wide anticipatory rotation amplitude (over one degree). As opposite, quick changes in trajectory (as during quick corrections while turning) were associated with non-homogeneous and unpredictable anticipatory movements. Also, anticipation time augments with slower navigation tasks, though below a certain speed, i.e. 5cm/s, no anticipatory movements appear anymore. Global turn events were classified only during the medium-speed task, where the fair difficulty level in controlling the vehicle allowed clean turns being executed. A total of 16 global turn events were classified among all the three subjects (Tab. II). Also, after each lap, a form of memorization of the route made the anticipatory time increasing (going from 100msec at the first turn to 1500 ms at the last one).

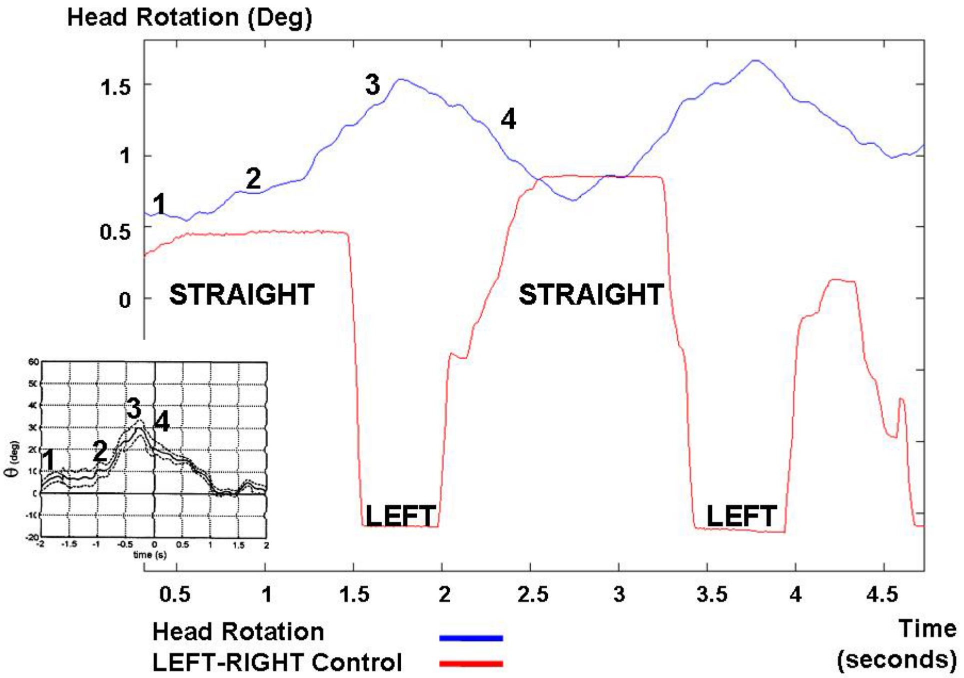

Figure 5. Anticipatory head rotation during teleoperation tasks compared with the anticipatory head rotation during physiological locomotion (small down-left, Grasso et al., 1998).

TABLE I
SINGLE COMMAND EVENTS RESULTS

	Head Rotation (deg)		Anticipation Time (ms)		Percentage
Task	Mean	SD	Mean	SD	%
Rally Car Race	0.57	0.42	300	152	91
Robot – High Speed	0.46	0.29	328	173	86
Robot – High Speed	0.53	0.42	415	230	90

Mean values and Standard Deviations of head rotation and anticipation time divided by tasks. Robot slow-speed task results are not reported since the task did not induce any anticipatory movement in any of the subjects. The percentage of control events which were preceded by an anticipatory movement is also reported.

Independently on the cruising speed, the strongest anticipatory behaviour (around 3 degrees of rotation) was associated with in-axe rotations (when the robot rotated on his central axe, without moving forward or backward).

TABLE II
GLOBAL TURN EVENTS RESULTS

	Head Rotation (deg)		Anticipation Time (ms)		Corrections
Subject	Turn Opening	Turn Closing	Turn Opening	Turn Closing	
1	0.25	0.33	843	892	3.2
2	1.3	0.37	624	384	2.8
3	0.42	0.61	544	580	1.6

Mean values of head rotation and anticipation time, those anticipating the beginning of a turn (*turn opening*) and those anticipating the end of the turn (*turn closing*). Results come only from the robot tele-navigation at medium-speed task. The mean number of corrections that happen during a whole turn event is also reported.

V. DISCUSSION

Anticipatory head rotation during teleoperation was found to have the same shape than what previously reported during physiological locomotion (Fig. 5), though anticipation times and rotation amplitudes where generally smaller than what recorded during locomotion. Anticipation time during teleoperation tasks maintained its inverse correlation with cruising speed previously reported during locomotion tests (Hicheur et al., 2005). These results show that the visual stimuli provided by the visor are enough to trigger the involuntary anticipatory behaviour during "virtual navigation" tasks as teleoperation, hence anticipatory head rotation can be exploited in Anticipatory Interfaces to anticipate users intentions with an anticipation time which can extend to 1.5s prior the actual command. An Anticipatory Interface properly designed could virtually reduce to zero communication lags happening within this anticipation time, i.e. allowing for "real-time like" control of a teleoperated device (Fig. 6). The operator would not control the rover with the joy-pad anymore, but his/her involuntary head movements would be detected by the interface and further decoded into the intended rover's actions.

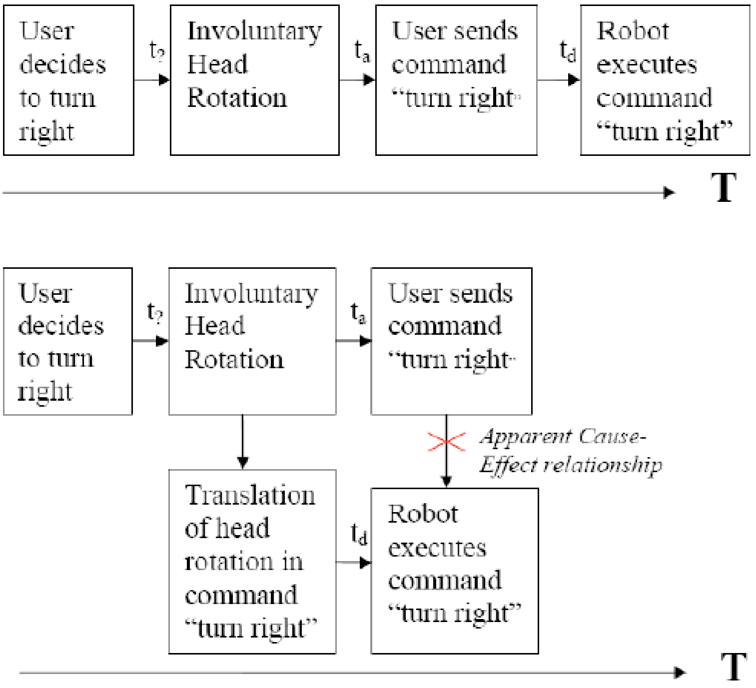

Figure 6. UP - Functioning timeline of a standard control interface with an intrinsic communication-execution delay present (t_d). The time elapsed from the user first intention to the execution of the command is: $t_? + t_a + t_d$; DOWN - Functioning timeline of an anticipatory interface with an intrinsic communication-execution delay present (t_d). The timeline has been shortened of the anticipation time. If the delay between the anticipatory movement and the execution of the command is set to be equal to that of natural anticipation (t_a), the user experiences an apparent cause-effect relationship between its interface operation and the corresponding command execution

The tasks at slow-speed showed that below a certain speed, i.e. at 5cm/s, anticipatory head rotation ceases to exist. This behaviour was never demonstrated with locomotion tests, since humans cannot walk so slowly still performing normal locomotion actions. Anticipatory Interfaces cannot be implemented for applications that require such slow cruising speeds. On the other side, the rally car race, the fast-speed and the medium-speed tasks showed that faster the cruise trigger shorter anticipation time. This means that the best-suited applications for Anticipatory Interfaces are those that require moderate cruising speeds, i.e. around 30cm/s, which maximize the anticipation time without ceasing it.

The large anticipatory rotation correlated with the single control events producing in-axe rotation is probably related with the more physiological nature of such rotation than the turning ones. In human locomotion head rotates with an angular speed that is much higher if compared with the walking speed. Human perception of head rotation while walking is, hence, a rotational one (as an in-axe rotation) rather than a curvilinear movement. During in-axis rotation, subjects' sensorimotor system faces a "quasi-physiological" movement, and reacts accordingly with the larger anticipatory rotation (of more than 3 degrees).

VI. FUTURE WORK

In the last decade, the studies on physiology of human perception revealed several motor patterns related with conscious actions, such as object manipulation or locomotion. These planned actions are anticipated by very characteristic involuntary motor actions that do not require any active cognitive control by the user himself in order to be performed. Since those involuntary motor actions precede planned actions by a considerable amount of time, they were called Anticipatory Movements.

These Anticipatory Movements represent a fascinating field of research for scientific purposes but also for technological applications. Since they are providing information in anticipation of the actually intended action, the intention can be read ahead. This anticipation time is precious as it allows for a shorter time lag in machine response. Additionally it could provide a local robot with the ability of predicting the user's intention and planning in advance the operation to be performed, waiting for the active control as a confirmation of the prediction, hence generating well planned and smooth actions (the importance of feed-forward control in robotics is well accepted). Here such interfaces are defined, due to these really particular features, Anticipatory Interfaces. The benefits of Anticipatory Interfaces for teleoperation applications can be significant, allowing users to naturally operate with a reduced communication delay during robots teleoperation.

Cruising speeds between 30 cm/s and 4 cm/s have to be tested in order to identify the range threshold of speed under which anticipatory behaviours stop to be expressed. Implementing a solution to simulate the rotation on site during head rotation could amplify the anticipatory behaviour. Giving the robot some autonomy in route planning may help users in producing more long-lasting anticipatory movements.

Once these questions are answered, it will be possible to fundamentally assess the potential usefulness of anticipatory interfaces and their potential benefits, in the design of future systems.

CHAPTER SIX

-

NEUROINSPIRED INTERFACES WITH ANTICIPATORY MOVEMENTS

-

UPPER LIMB MOVEMENT

I. INTRODUCTION TO MOTOR PRIMITIVES AND SUBMOVEMENTS

As seen in Chapter 5, when anticipatory involuntary movements are monitored by Neuroinspired Interfaces, the interfaces may acquire predictive features. These interfaces were named, accordingly, Anticipatory Interfaces: in principle they can reduce the delay in commands actuation by monitoring user's unconscious anticipatory movements. Here, the possibility of implementing a Neuroinspired Anticipatory Interface monitoring the wide class of upper limb movements during reaching tasks is considered. Differently to the head anticipatory rotation during locomotion considered in Chapter 5, a formally accepted model of human upper limb movement and control is still lacking. The question of how action is represented, planned and controlled in the brain remains in fact a fundamental problem. There is an emerging evidence that movements are made of combinations of motor primitives that can be flexibly combined to accomplish a variety of motor tasks. Bizzi and Mussa-Ivaldi (Bizzi and Mussa-Ivaldi, 2004) demonstrated that patterns of cortical and spinal output lead to specific combination of muscle synergies that can generate a broad repertoire of movement patterns. A complex movement, such as the manipulation of an object of arbitrary shape can be decomposed in a sequence of discrete units of motion, which are usually denoted as submovements (Rohrer and Hogan, 2003) (Fig. 1).

Studies on motion kinematics in adults (Flash & Henis, 1991; Abend et al., 1982), children (von Hofsten, 1979) and also stroke patients (Krebs et al., 1999) show that continuous movements can be regarded as composed of discrete units. Submovements seem to be quite evident during handwriting of cursive patterns (Teulings & Romero, 2003). Discrete submovements during slow finger movements of healthy subjects were reported (Vallbo & Wessberg, 1993), and recent studies confirmed the intermittent nature of motor outputs from motor areas in the brain during such movements (Gross et al., 2002).

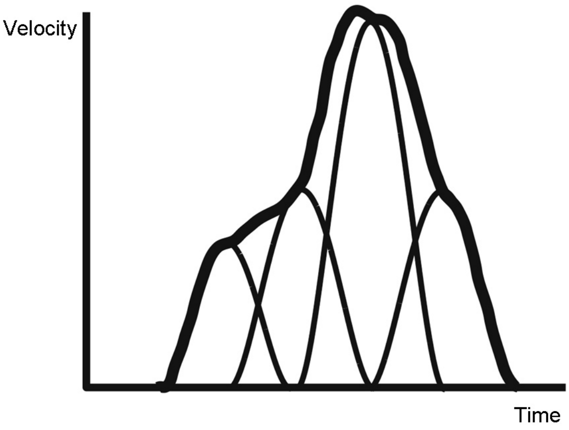

Figure 1. Example of complex movement represented as its velocity profile on a single axis. The overall movement (thick black line) can be expressed as the sum of underlying overlapping submovements (light lines). Adapted from Rohrer and Hogan, 2006.

II. HUMAN MOVEMENT DECOMPOSITION

Starting from the seminal work by Woodworth (1899), the existence of some invariance in the execution of upper limb pointing and reaching movement was revealed by several studies. Morasso (Morasso, 1981) instructed human subjects to point with one hand to different visual targets that were randomly activated. Motion analysis revealed that human arm movements during pointing tasks have two kinematic invariance: (i) the hand trajectories are approximately straight segments; (ii) the tangential hand velocity for different movements always appears to have a bell-shaped profile (that is to say that the time needed to accelerate the hand was approximately equal to the time needed to bring it back to rest). Interestingly, these invariance are present in the hand motion, but absent in the joints rotations (Abend, Bizzi, and Morasso, 1982).

Later, it was reported by several investigators that not-bell-shaped hand movement profiles could be actually seen as a composition of several bell-shaped velocity profiles occurring in sequence. The common assumption was that a primary, ballistic movement is produced to cover the major portion of the distance to the target. If the primary movement misses the target, secondary submovements are performed or after the end of the main movement (corrective submovements, Crossman and Goodeve 1983), or by overlapping the main movement (overlapping submovements – OSMs, Milner and Ijaz 1990; Flash and Henis 1991; Milner 1992; Berthier 1996; Lee et al. 1997; Novak et al. 2002, Fishbach et al., 2005) (Fig. 2).

Velocity profiles of the main movement and those of both corrective and overlapping submovements were considered to share a common shape, differing only in magnitude (peak velocity) and amplitude (velocity profile duration). The definition of the bell-shaped velocity profile, though, differed among different studies, i.e. it was analytically selected in order to satisfy the minimum-jerk constraint (Flash and Henis 1991; Berthier 1997; Lee et al. 1997), or determined empirically (Milner 1992; Krebs et al. 1999).

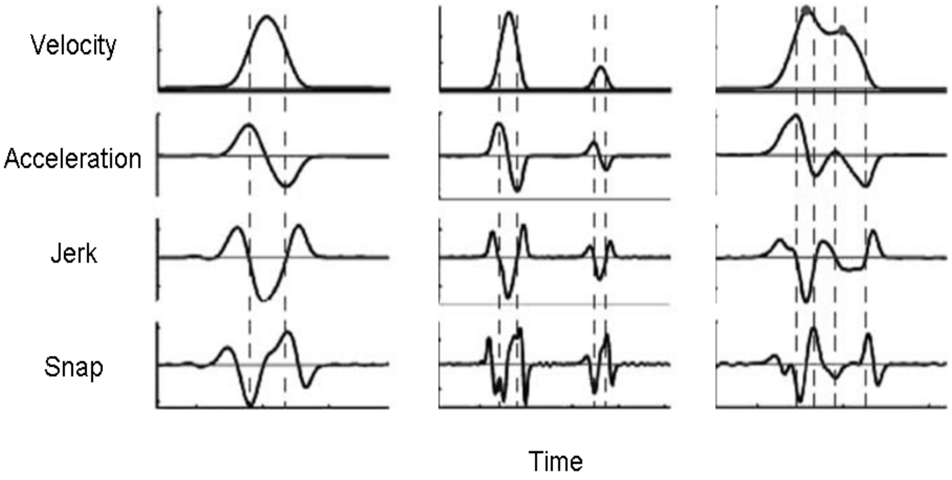

Figure 2. Upper limb movement. First line shows the velocity profile, second line the acceleration profile, third line the jerk profile and fourth line the snap profile. First column shows a single movement, second column shows a corrective submovement, and third column shows a complex movement composed of overlapping submovements. Adapted from Fishbach et al., 2005

Novak et al. (2000, 2002) left the restriction on common (velocity) profile and proposed an objective and automated algorithm to identify the existence and the timing of submovements that overlap the primary movement (before Novak's work the number and timing of the submovements were determined manually with guesses for initial parameters, as in the case of Lee et al. (1997)). His 'hard symmetry' submovements' extraction algorithm creates a unique symmetric bell-shaped velocity profile for the main movement and for each OSMs. Interestingly, even though with this algorithm the main movement and the OSMs are not constrained to match a common shape, they still appear to share many properties.

The assumption that the primary movement and the OSMs are strictly symmetric may be too restrictive, and the peak velocity of the obscured primary movement may not necessarily coincide with a local peak of the global movement velocity profile. The presence of an overlapping submovement, occurring while the previous submovement has not reached its velocity peak, can be identified by the velocity inflections. In a further study, Novak (Novak et al., 2002) partially applied these ideas. The primary movement peak velocity was defined in accordance with the first acceleration zero crossing after the global movement onset. Movement irregularities, thought to be due to corrective submovements, were detected as appreciable inflections in the acceleration after the time of the first zero crossing in the acceleration profile. These acceleration inflections were found by counting the zero-crossings of the first and second derivatives of acceleration (respectively jerk and snap). Regular movements, which are global movements that contain only the main movement with no overlapping submovements, show only a single jerk (deceleration minimum) and snap (deceleration inflection towards zero acceleration) zero crossing during the second half of the movement (after the first acceleration profile zero crossing). Irregular trials with overlapping submovements have instead more than one jerk or snap zero crossing (Fig. 7).

A similar approach can be found in (Teulings and Romero, 2003), where the velocity profile is segmented into primary and secondary submovements by the first zero crossing of the acceleration after the absolute peak velocity. Whatever happens before the first peak velocity is simply discarded as noise. In spite of introducing important novelties, in these approaches the main movement take into account everything happens before the first acceleration zero crossing, thus leading to extremely various velocity profiles not only between main and sub-movements, but also among different main movements recoded during several trials. Differences in submovements "emerging" from zero-crossings of the velocity profile in spite of acceleration or jerk profile were firstly categorized by Fradet (Fradet et al., 2008): movements parsed into submovements based on zero-crossings of velocity were tagged as type 1 submovements; submovements parsed from the zero-crossing of acceleration and jerk were respectively parsed as type 2 submovements. Unfortunately the characteristics of snap profile and zero-crossings were kept out from the analysis and categorization (Fig. 4).

A different approach was proposed by Selen (Selen et al., 2006): the duration of a single submovement was defined as the time between two successive local minima in the global velocity profile. The amplitude of a submovement was defined as the difference between a local maximum in the global velocity profile and the average value of the two nearest minima. The linear regression between submovement duration and submovement amplitude provided an intercept and a slope. The latter was interpreted as the error correction gain implemented by the neural controller. Finally, algorithmic and statistical optimizers were also applied to get "blind" movement decompositions (Rohrer and Hogan, 2003-2006; Dipietro et al., 2008) (Fig. 3).

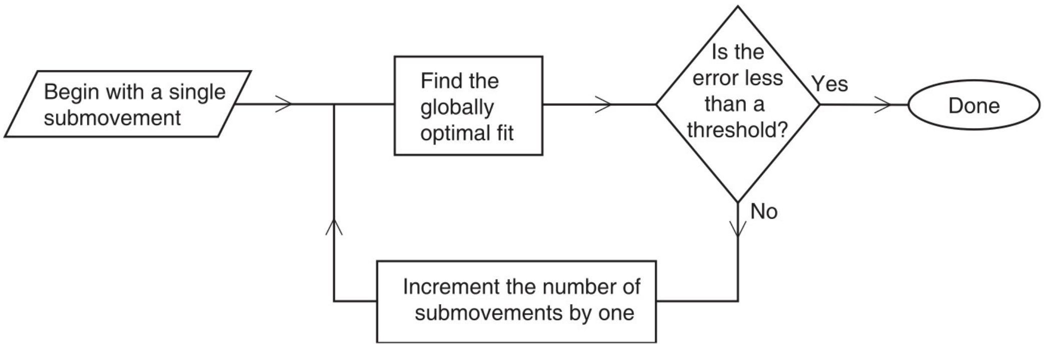

Figure 3. Iterative approache used by optimizers. From Rohrer and Hogan, 2003.

Dounskaia, Wisleder, and Johnson (2005) recently questioned the traditional interpretation of submovements: their results suggest non-homogenous origins and roles of OSMs. They proposed that during upper limb reaching tasks there are two definite subtasks which could require two distinct submovement types: a subtask for accurate target achievement and subtask for limb stabilization during motion termination. In fact, the arm needs to be actively arrested and stabilized at the target, which requires specific component of control. Motion termination is therefore a movement component that is necessary to perform in addition to motion deceleration to stop at the target, since acceleration needs to be nullified as soon as the target has been achieved. The existence of a stabilizing component of human limb movement control is not new in the literature: electromyographic studies interpreted the third phase of the triphasic pattern of muscle activity as responsible for limb stabilization (Berardelli et al., 1996).

The existence of stabilization submovements associated with motion termination was supported by Wisleder and Dounskaia (2007), who compared submovement incidence between discrete and cyclic movements.

Fradet, Lee and Dounskaia (2008) compared OSMs incidence between three different reaching movement tasks, chosen in order to separate the different subtasks. Discrete reaching task required the subject to reach the target and to stop over it; reciprocal reaching task did not require the subject to stop over the target, but to reach it and immediately move back to his original position; finally passing reaching task required the subject crossing the target and terminating motion after that. While discrete mode required arresting and stabilizing the arm at the target, in both the reciprocal and passing mode the stabilization of the arm at the target was not performed (Guiard, 1993; Meulenbroek & Thomassen, 1993; Meulenbroek, Vinter, & Desbiez, 1998). Quantitatively, the difference between the three modes was that both velocity and acceleration were nullified at the target during discrete movements, whereby reciprocal movements involved nullification of velocity only, while acceleration remained non-zero during the reversal, and in passing mode neither the velocity nor the acceleration were nullified. Each movement to the target was parsed in the primary and secondary submovement according to the method propose by Meyer et al. (1988), which indicates the initial smooth, half-bell-shaped portion of the velocity profile (that is, the velocity profile since movement beginning till the first velocity peak) defined as the main movement. The beginning of the secondary submovement was determined as the time instant of the deceleration phase at which one of the following events occurred: a zero-crossing from positive to negative value occurred in the signed velocity profile (type 1 submovement); the acceleration profile crossed zero from a negative to a positive value (type 2 submovement); the jerk profile crossed zero from a positive to a negative value (type 3 submovement). Examples of the three types of submovement during discrete movements are shown in Fig. 4.

The common inverse relationship between target size and submovement incidence was clearly found only in discrete mode tasks while in reciprocal mode tasks showed submovements mostly only with small target. This difference between the two modes suggests that in the discrete mode, submovements emerged not only due to decreases in target size but also due to motion termination. In passing mode tasks results reported a direct relationship between target size and submovements incidence, which is in contrast with Fitts Law (Fitts, 1954). While, on one side, this further supported motion termination as a source of submovements, on the other side challenged the interpretation of most of the extracted submovements as corrective adjustment.

The alternative interpretation proposed by Fradet, Lee and Dounskaia (2008) is that submovements may be motion fluctuations emerging during movements of high accuracy. The increase in muscle co-contraction during high accuracy movement (Gribble et al., 2003) was considered as one possible source of motion fluctuations, though the investigators clearly pointed towards low movement speed to be the main reason for motion fluctuation, with its dependence on target size being reduced to a mere by-product of speed-accuracy trade-off (Fitts, 1954). This hypothesis is also consistent with decreases in smoothness of movement trajectory with decreases in movement speed reported by Doeringer & Hogan, 1998.

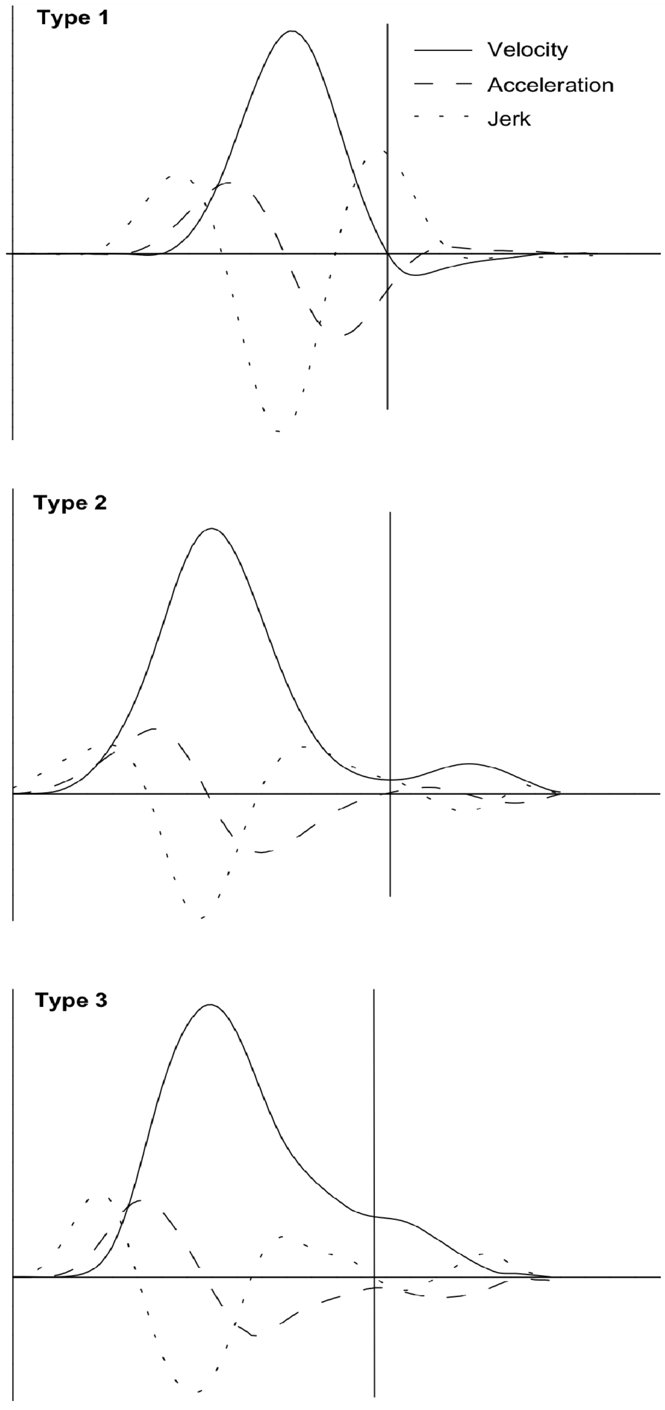

Figure 4. Complex upper limb movements. The vertical arrow crosses the x-axis at the overlapping submovement origin: velocity zero-crossing (type 1); acceleration zero-crossing (type 2); jerk zero-crossing (type 3). From Fradet, Gyusung and Dounskaia, 2008.

Wisleder and Dounskaia (2007) previously elaborated a similar hypothesis finding that incidence of submovements was independent of target size during cyclic movements of controlled frequency, and instead depended on cyclic frequency, that is, movement speed. Nevertheless, when cyclic frequency was self-paced, correlation of incidence of fine submovements with movement duration was rather low. Thus, it is possible that submovements represent motion fluctuations that emerge with decreases in movement speed.

Unsteady production of muscle force during slow movement and isometric production of low force levels can account for motion fluctuations, and could be a product of variability of the discharge rate of cortical and peripheral motor units (Moritz et al., 2005). Other mechanisms, such as motor unit synchronization, discharge rate, specific characteristics of low threshold motor units, and oscillation in excitatory drive, all features of neuromuscular noise (Todorov and Jordan 2002), have also been discussed as possible contributors to the variability of motor output (Taylor, Christou, & Enoka, 2003).

II.I Neuromuscular Noise and Submovement Origin

Neuromuscular noise seems to be dependent on movement's mean amplitude (Jones et al. 2002), and it could be the result of neural noise and non-linear recruitment of small motor units before large ones (Houk et al. 1970). According to this view, neuromuscular noise is a signal-dependent noise, which would explain a variety of phenomena in biological motor control. For example Meyer et al. (1988) demonstrated that a discrete controller that produces non-overlapping submovements would reproduce the classic logarithmic trade-off between the duration and precision of aimed movements, known as Fitts' law (1954). A different model of discrete controller producing overlapping submovements with signal-dependent neuromuscular noise was proposed to explain how adult behaviour can emerge from the jerky arm movements of infants (Burdet and Milner, 1998). Harris and Wolpert (1998) demonstrated that an optimal open-loop control system that tries to maximize end-position accuracy under conditions of signal-dependent noise might account for movement trajectories under a variety of experimental conditions.

Motion termination submovements may have a complete different origin. They could be a kinematic consequence of muscle activity that provides motion termination. This hypothesis, known as the active-origin hypothesis, explains motion termination submovements as the active result of the third phase of the triphasic muscle activation EMG pattern (Berardelli et al., 1996). Rather than centrally produced, motion termination submovements could be a product of spinal reflexes. Another possible origin of motion termination submovements, known as the passive-origin hypothesis, is that the oscillations of the limb during motion termination could be the passive result of the viscoelastic properties of the muscle–tendon complex. Both origins agree on the fact that motion termination submovements are not centrally programmed in response to pointing error or movement duration, but rather are a consequence of physical properties of the limbs and of control responsible for halting motion at the target (Fradet et al., 2008).

II.II Continuous vs. Discrete Motion Neuro-Controller

Most of the models of neuro-controllers responsible for controlling upper limb movements with signal-dependent neuromuscular noise are based on the hypothesis of a "discrete controller" (Woodworth 1899; Meyer et al. 1988; Flash and Henis 1991; Milner 1992; Berthier 1996; Lee et al. 1997; Novak et al. 2000, 2002; Fishbach et al. 2005). A discrete controller does not produce continuous corrections to the velocity profile, but it rather intermittently sends discrete corrections. However, some reports assert that submovements are actually the result of a single continuous neuro-controller (Kawato 1992; Shadmehr and Mussa-Ivaldi 1994; Bhushan and Shadmehr 1999).

It is quite implausible that a continuous control mechanism would produce velocity profiles that can be decomposed in sub-elements all equally shaped. Also, a continuous update would allow for smooth changes in the velocity profile that would keep the regularity of the movement (i.e. would not add inflection points). Another argument against the continuous-process interpretation of discrete corrections is that a continuous process predicts a relatively fixed correction latency, which is being determined by the sensorimotor delay (Saunders and Knill 2003). As recently demonstrated in monkeys by Fishback et al. (2005, 2006) there is not such fixed correction latency, but rather a wide range of correction latencies. The data reported by the literature so far seems to be more consistent with a mechanism of intermittent control, or a continuous control with a dead-zone (Hanneton et al. 1997), than with a continuous control process.

II.III The new theory of Rhythmic Neuro-controller based on composition of Quanta of Movements

The work here presented is addressed to test a new hypothesis of a rhythmic neuro-controller for human upper limb movement. While the existence of a discrete neuro-controller producing bell-shaped velocity profile submovements is already discussed in the literature, the new theory here presented is that a rhythmic neuro-controller works intermittently at a fixed frequency and producing common shape, common duration, and common interpeak distanced submovements differing solely in their velocity peak value (Fig. 5). Because of these invariant features, the concept of a "quantum of movement" is here proposed: a standard velocity pulse that is produced in series, with a fixed frequency, to control voluntary upper limb movement during reaching tasks.

In order to test the hypothesis, a modified version of the Branch&Bound decomposition algorithm proposed by Rohrer and Hogan, 2003, was developed in order to decompose human movements into sequences of submovements. A new model of movement composition, characterized by bell-shaped submovements having all the same duration and the same interpeak distance was implemented in the optimizer. In this algorithm, the number of submovements is calculated from the overall duration of the global movement, rather than incremented for every optimization (as in Rohrer and Hogan 2003, 2006).

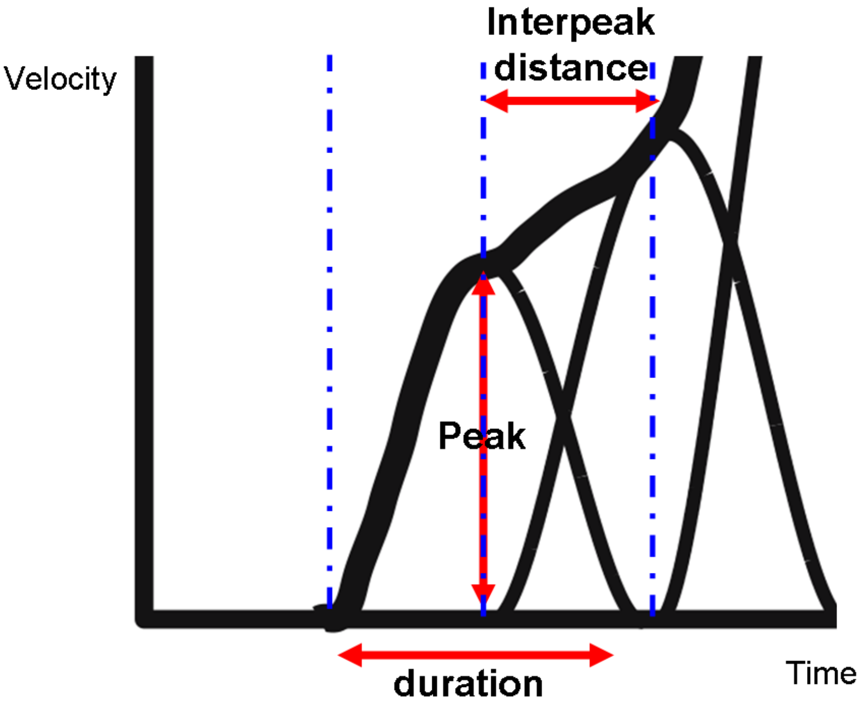

Figure 5. Main submovements feature as submovement duration, value at peak, and interpeak temporal distance. Adapted from Rohrer and Hogan, 2006.

While the Branch&Bound optimization algorithm is in principle capable of achieving the best combination of velocity amplitudes of submovements set in order to fit the original movement speed-profile, as any other optimization algorithm it needs very long execution times to produce acceptable solutions. Even if the modified Branch&Bound algorithm here proposed reduces the execution time by several orders of magnitude with respect to the original (Rohrerand Hogan, 2003), it is still slowed down severely when used to decompose long lasting movement recordings. Furthermore, as any other optimization algorithm, it works only on the complete movement profile, that is, it is not suitable for on-line decomposition during real-time upper limb movement recording sessions.

A completely new decomposition algorithm, the Predictive Decomposition algorithm, is here proposed. The Predictive Decomposition algorithm needs execution times remarkably inferior to the modified Branch&Bound optimization algorithm, and can perform movement decomposition without information on the overall movement profile. Because of these two peculiar features, the Predictive Decomposition algorithm is suitable to perform on-line during real-time acquisition of upper limb movement. The Predictive Decomposition algorithm provides also a predictive estimation of the velocity profile that anticipates the real movement for half of the submovement duration, and could hence be included in an Anticipatory Interface that relies on human upper-limb movement information.

The solutions provided by the two algorithms, the modified Branch&Bound and the Predictive Decomposition, are finally compared in terms of fitting error and composition.

III. MATERIALS AND METHODS

III.I Recording Set-Up

In order to record tremor-free upper limb movements from human subjects to be further decomposed with our algorithm, we used the MIT-Manus robot arm (see Fig. 6) as a support for the upper limb during motion. The MIT-Manus has the desirable feature of being a back driveable robot with null end-point inertia when moved by the subject, thus allowing to record clean data on the human motion. The MIT-Manus also appeared to be quite a common device for upper limb movement recordings in most of the literature we referred to. In addition to it, a magneto-inertial sensor was also used for kinematic recordings, i.e. the XSENS unit shown in Fig. 6.

Figure 6. MIT Manus robot arm and Xsens magneto-inertial unit

III.II Experimental Protocol

Acceleration data were recorded from five right-hand subjects (1 male, 1 female, in the range of 20-30 years of age). Subjects performed quick upper limb stretching movement (stretching the right arm frontally, moving the hand from the chest to a medium arm elongation, with shoulder-elbow joint control). The task had to be "quickly" performed, that is, as quick as possible still keeping control on the deceleration phase. Audio and video feedback was provided to the subjects.

III.III Analysis of acceleration data

The analysis of acceleration data has the goal of identifying the information on the "quantum of movement" needed by the modified Branch&Bound algorithm to test the proposed new model of rhythmic neuro-controller. By this model, any movement should start with a commonly shaped (apart from its velocity peak) submovement. Hence, it should be possible to identify a common shaped movement beginning. Nonetheless, if the insurgence of the second submovement can be intercepted, its temporal distance from movement beginning should be a constant (i.e., interpeak distance) among different trials. Finally, the movement shape between its beginning and the insurgence of the second submovement is due only to the first submovement. This information could be used to reconstruct the complete shape of the "quantum of movement".

The insurgence of the second submovement is searched in discrepancies in the acceleration, jerk, and snap profiles during the beginning of the reaching tasks (Fig. 4). The recorder acceleration data is smoothed with the Savitzky-Golay smoothing filter in order to reduce the high frequency sampling noise from spreading out after single and double differentiation. Firstly described in 1964 by Abraham Savitzky and Marcel J. E. Golay (Savitzky and Golay, 1964), this method essentially performs a local polynomial regression (in our case of fourth degree) on a series of values (in our case of 17) to determine the smoothed value for each point. The main advantage of this approach is that it tends to preserve features of the distribution such as relative maxima, minima and width, which are usually 'flattened' by other adjacent averaging techniques (like moving averages, for example).

Then the motion start and end coordinates are looked for in the data recorded. It is commonly assumed that the movement start can be identified by a local maximum in the snap profile (point s_1 in Fig. 7). That maximum, however, could be not much different from any other local maximum occurring in the snap profile, i.e. due to tremor. Hence a routine was implemented in the algorithm, which looks first at the global maximum in the acceleration profile, which usually corresponds to the first (positive) acceleration peak of the overall movement (point a_1 in Fig. 7). Having the global acceleration first max as a temporal limit, a second temporal limit is set at the maximum in the jerk profile from the beginning of the registration to the acceleration global maximum (point j_1 in Fig. 7). This point should be very close to the real beginning of the movement, which can be identified as the first local maximum in the snap profile immediately before this jerk maximum (point s_1 in Fig 7). The operator can tune this value afterwards. The end of the movement is set as the end of the event, and can be tuned by the operator afterwards.

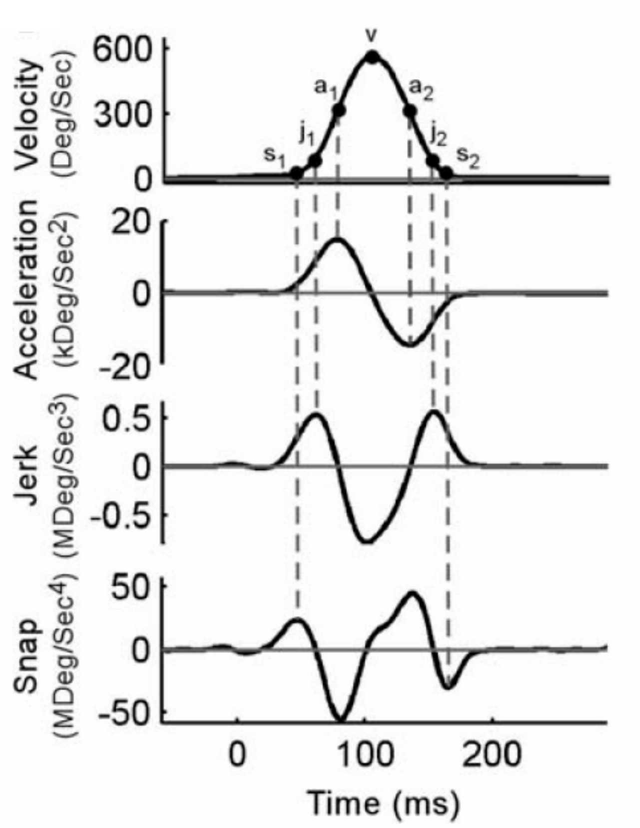

Figure 7. Single bell-shaped velocity profile submovement. The beginning of movement is identified by a local max in the snap (s_1), the first flex of the acceleration corresponds to a max of the jerk and a zero of the snap (j_1), and the first peak of the acceleration corresponds to a zero in the jerk and a min in the snap (a_1). The first peak in the velocity profile (v) corresponds to a zero in the acceleration, a min in the jerk, and a zero in the snap. From Fishbach et al., 2005.

Since for the hypothesis of the rhythmic neuro-controller any movement should start with a commonly shaped submovement, the main target of the acceleration profile analysis is to find a common shaped movement beginning and clues on the insurgence of the second submovement. It is here proposed to look for this kind of information in the discrepancies between the acceleration, jerk, and snap profile of the recorded movement, and those expected from a single submovement. For the proposed model, the first discrepancy holds two important information. First, it may indicate where a second submovement emerges. Second, the movement profile from its beginning to the first discrepancy should account of the sole first submovement, hence it may be a pure fragment of the quantum of movement. This information can then be used to reconstruct the complete shape of the "quantum of movement".

III.IV Modified Branch&Bound algorithm

The analysis of acceleration profile ultimately results in information regarding the candidate for "quantum of movement" (shape and duration) and the rhythmic neuro-controller activity frequency (the inverse of the constant distance between movement beginning and the insurgence of a second submovement). The same information is implemented in the modified Branch&Bound algorithm, which optimises the decomposition of the main movement into a series of velocity profiles having the quantum of movement shape and duration, at the frequency of the neuro-controller. The magnitude of the resulting error-function can be used as an indirect clue towards the existence of the rhythmic neuro-controller producing bell-shaped velocity profile motor commands at fixed frequency.

Since the error-function could vary also due to different bell-shaped velocity curve functions, two different curves were tested as submovement templates: the well known and largely used Minimum Jerk function, and the Support Bounded Lognormal Function LGNB, which proved to best fit the velocity profile of human upper limb movement (Plamondon, 1993; Rohrer and Hogan, 2006). The fitting algorithm is developed from the Branch&Bound algorithm for movement composition proposed by Rohrer and Hogan (2003). Minimum-jerk submovements can be uniquely described by three parameters – the amplitude of the peak A, the time at which the peak occurs t, and the duration of the movement w:

$$
\begin{aligned}
v(\tau) = \frac{A}{1.875}\Bigg(30\left(\frac{\tau - t + \frac{w}{2}}{w}\right)^2 - 60\left(\frac{\tau - t + \frac{w}{2}}{w}\right)^3\Bigg) \\
+ 30\left(\frac{\tau - t + \frac{w}{2}}{w}\right)^4\Bigg)\Bigg), t - \frac{w}{2} \leq \tau \leq t - \frac{w}{2} \\
= 0\ , \quad \text{otherwise}
\end{aligned}
$$

LGNB curve is a class of submovement shape that Plamondon (1992) found to fit point-to-point drawing movements better than any of the other 22 candidate functions (Plamondon et al. 1993). An LGNB curve is defined as a function B(t) such that:

$$
B(t) = \frac{D(T_1 - T_0)}{\sigma\sqrt{2\pi}(t - T_0)(T_1 - t)} \exp\left\{\left(\frac{-1}{2\sigma^2}\right)\left[\ln\left(\frac{t - T_0}{T_1 - t}\right) - \mu\right]^2\right\}
$$

for T0 ≤ t ≤ T1 , where D is the displacement resulting from the movement, T0 is the movement start time, T1 is the end time, μ controls the skewness (asymmetry), and σ determines the kurtosis ("fatness") of the curve. The five independent parameters that define LGNB submovements allow them to take on a wide range of submovement-like shapes.

In the presented model it is assumed that the bell shaped velocity profile submovements share all the same quantum-of-movement shape. Hence the values of all the parameters related with the curve shapes apart from their amplitude (submovement velocity peak) are set a priori. In the case of Minimum Jerk function, duration of single submovement and interpeak distance are predefined; in the case of LGNB function, also the value of σ and μ had to be set in order to define a common shape for the submovements. Also, the very nature of LGNB as a statistic function requires some additional tuning in its starting and ending point, as well as in its normalization, in order to obtain a curve which starts and ends with definite values and has a peak that corresponds to the velocity peak value. On the basis of the predefined values for the submovement shape and of the global movement duration, the algorithm makes an esteem of the total number of submovements required to compose the movement. The number of iterations in the Branch&Bound algorithm can be arbitrarily set by the operator, or can be automatically chosen by the algorithm in an inverse relationship with the number of submovements. This approach helps preventing to undergo into very long analysis time for movement composed by a very large number of submovements.

The outline of the original Branch&Bound algorithm as implemented in Rohrer and Hogan (2003) is as follows (refer to Fig. 8 for a step-by-step example in one dimension):

1. Bound the solution space (Fig. 8a). This requires finding upper and lower bounds for each element of fitting function p (the submovements-composed velocity profile function). These parameter bounds can be thought of as describing an M-dimensional hyperbox that contains all permissible values of the target function. Any given set of parameter values describes a point within the box and has a single value of the error function $E(p)$ associated with it. The goal of the algorithm is to find the point in the hyperbox for which $E(p)$ is at a minimum.
2. Break the solution space into a number of subspaces (Fig. 8b).
3. Evaluate $E(p_c)$ (the value of E at the centre of a subspace) for all subspaces (Fig. 8c).
4. Set $Elow = min(E(p_c))$ over all subspaces. $Elow$ is the lowest known error in the solution space (Fig. 8c).

5. Calculate a lower bound *L for E(p)* over each *s*ubspace *(*Fig. 8d,e).
6. Eliminate subspaces for which *L* > *Elow* since they cannot contain the solution (Fig. 8f).
7. Break remaining subspaces down into yet smaller subspaces.
8. Return to step 3 and repeat until a termination criterion is met.

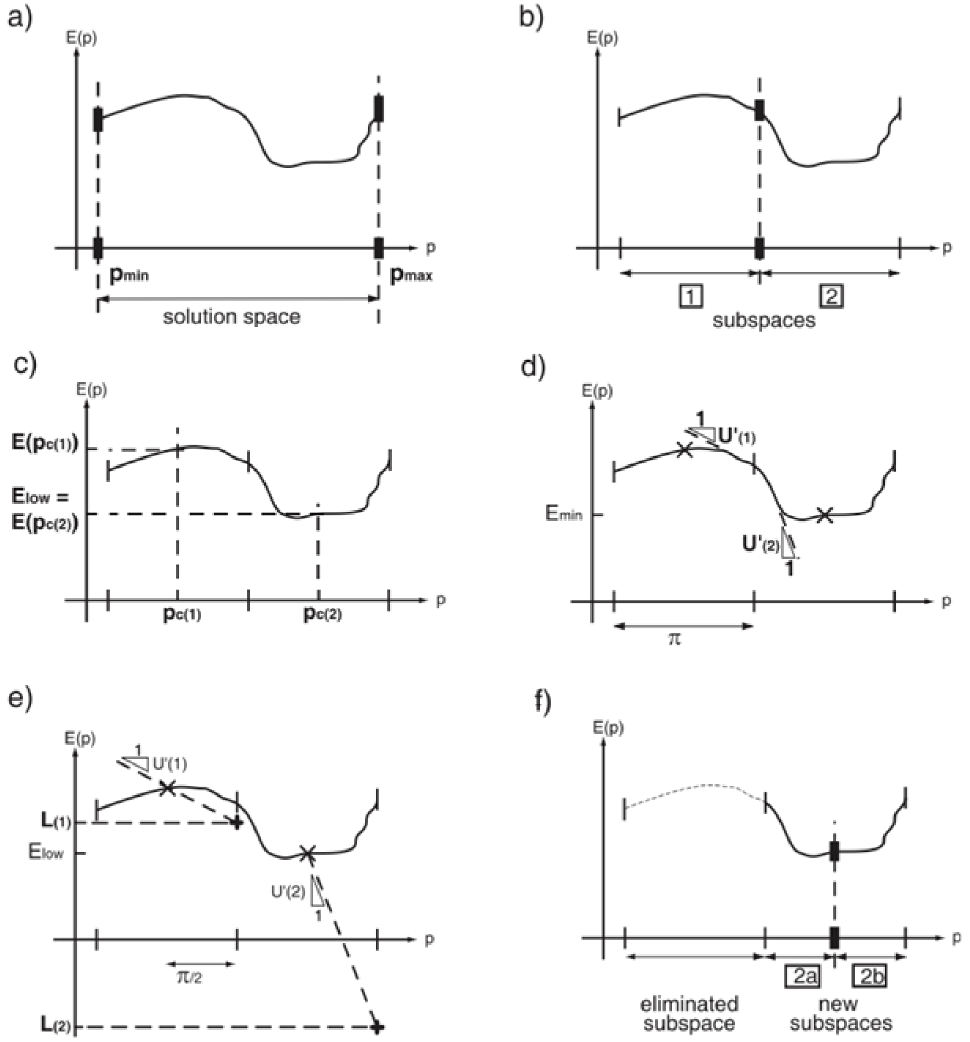

Figure 8. Step-by-step example in one dimension of the Branch&Bound Optimization Algorithm. From Rohrer and Hogan, 2003.

The modified version of the Branch&Bound algorithm for upper limb movement decomposition implemented in the present study is now explained. It starts by identifying the maxima in the subspaces of the submovements (Fig. 8b), in order to break the solution space in a number of possible submovements' velocity peaks combination. The maximum value taken by the velocity during the time in which a submovement exists is decomposed into two possible solutions, at its 1/2 and its 3/2 (Fig. 8c). This is done for each submovement; hence at the first cycle of the optimization algorithm each submovement has two possible velocity peak values. All the possible combinations of velocity peaks are calculated and sorted as several rows in the solution matrix.

Each one of the possible solutions (the rows in the solution matrix) is tested and its fitting error is evaluated (Fig. 8d). The latter is calculated as the integral of the point-to-point difference between the target function (the original velocity profile) and the fitting function (the velocity resulting from the composition of submovements). This permits the Branch&Bound algorithm to mathematically discard the subspaces in which it is impossible that there are better solutions than the best one founded.

One method for calculating a lower bound on E over a solution subspace is as follows:

1. Calculate an upper bound for $\frac{\partial E(p)}{\partial p_i}$ (call it U_i') over the subspace. The only parameter left free to change is the amplitude of the bell-shaped velocity profile, hence only $\frac{\partial E}{\partial A}$ bounding is necessary.

2. With both Minimum Jerk and the LGNB function, changes in A will either vacate area or occupy new area, but not both (Rohrer and Hogan, 2003). The area scales linearly with amplitude:

$$\Delta\mathscr{E} = \frac{\Delta A}{A}\ \text{(area under minimum-jerk curve)}$$

$$\Delta\mathscr{E} = \frac{\Delta A}{A}\left(\frac{wA}{1.875}\right)$$

$$\Delta\mathscr{E} = \frac{\Delta A w}{1.875}$$

$$\frac{\Delta\mathscr{E}}{\Delta A} = \frac{w}{1.875}$$

$$\frac{\partial\mathscr{E}}{\partial A} \le \frac{w_{MAX}}{1.875}$$

$$\Delta\mathscr{E} = \frac{\Delta A}{A}\text{(area under a lognormal curve)}$$

$$\Delta\mathscr{E} = \frac{\Delta A}{A}\left(A\sigma\sqrt{2\pi}e^{(\mu-\sigma^2/2)}\right)$$

$$\Delta\mathscr{E} = \left(\sigma\sqrt{2\pi}e^{(\mu-\sigma^2/2)}\right)\Delta A$$

$$\frac{\Delta\mathscr{E}}{\Delta A} = \sigma\sqrt{2\pi}e^{(\mu-\sigma^2/2)}$$

$$\frac{\partial\mathscr{E}}{\partial A} \le \sigma_{MAX}\sqrt{2\pi}e^{(\mu_{MAX}-\sigma^2_{MAX}/2)}$$

3. μ max and σ max in the proposed algorithm are the same as the fixed μ and σ. Define π_i (the span of parameter *i*) as $\pi_i = \max(p_i) - \min(p_i)$ over the subspace.

4. A lower bound, *L*, for *E(p)* over the subspace is given by $L = E(p_c) - \sum_i \frac{\pi_i}{2} U'_i$. This guarantees that $E(p) \ge L$ for all p in the current subspace (Fig 8d).

At this point the algorithm has as results both the velocity-peaks combination with the lowest fitting error, and the list of current solution subspaces with potential fitting error values lower than the current one. If the algorithm goes for another iteration, each one of these solution subspaces undergoes the branching procedure (Fig. 8c,d) and a new set of possible combination of submovements peak velocities is produced, tested, error evaluated, and pruned in a new set of good solution subspaces according to the new lowest fitting error value (Fig. 8e,f). The algorithm reiterates these steps until all the iterations are performed. At the last iteration, the solution subspace with the lowest fitting error is composed as a series of overlapping submovements and plotted for further analysis. Composed acceleration, jerk, and snap are also plotted for comparison with the ones evaluated during the acceleration profile analysis.

III.V Predictive Decomposition Algorithm

The Predictive Decomposition algorithm here presented relies on the proposed model of the rhythmic neuro-controller for human upper limb. It composes upper limb movement by producing submovements one after the other as the central rhythmic neuro-controller would do.

The Predictive Decomposition Algorithm requires solely information on the movement velocity profile at certain time epochs. Once the movement beginning is identified by the snap maximum, the Predictive Decomposition algorithm waits for a time equal to the half of the quantum of movement. At this time coordinate the algorithm gets the value of velocity, it assumes this value being the peak velocity of the first submovement, and composes the first submovement accordingly. After a time equal to the interpeak distance, the algorithm gets the new velocity value, subtracts it from the velocity value which would have been due to the previously composed submovement, assumes this pursued value as the velocity peak of the second submovement and composes the second submovement accordingly. After a time equal to the interpeak distance, the algorithm gets the new velocity value, subtracts it from the velocity value which would have been due to the two previously composed submovements, assumes this pursued value as the velocity peak of the third submovement and composes the third submovement accordingly. The Predictive Decomposition Algorithm goes on this way until the movement ceases.

Summarizing, the Predictive Decomposition algorithm gets values on the real velocity profile at the same frequency of submovements production, assumes the values due to the sum of the overlapped velocity profiles of the previously composed submovements and of the velocity peak of the submovement to be composed, evaluates the latter and uses this last value to compose the submovement. This iterative approach could partially resemble the behaviour of a rhythmic neuro-controller that produces submovements as peak-modulated velocity impulses.

IV. EXPERIMENTAL RESULTS

IV.I Rhythmic Neuro-Controller Characterization

The analysis of acceleration data has the goal of identifying shape and duration of the "quantum of movement", and to evaluate the frequency at which the rhythmic neuro-controller produces submovements. The analysis relies on the hypothesis that any movement should start with a commonly shaped (apart from its velocity peak) submovement. As any submovement, the profile should show some specific properties (Fig. 7):

a) the beginning of movement should be identified by a local max in the snap (i.e., the point marked as s_1 in Fig 7);

b) the first flex of the acceleration should correspond to a max of the jerk and a zero of the snap (i.e., the point marked as j_1 in Fig 7);

c) the first peak of the acceleration should correspond to a zero in the jerk and a minimum in the snap (i.e., the point marked as a_1 in Fig 7), and;

d) the first zero-crossing in the acceleration should correspond to a minimum in the jerk and a zero in the snap (i.e., the point marked as v in Fig 7).

The analysis of acceleration data evaluated these properties on all the trials comparing the results with the single bell-shaped velocity profile submovement model of Fig. 7.

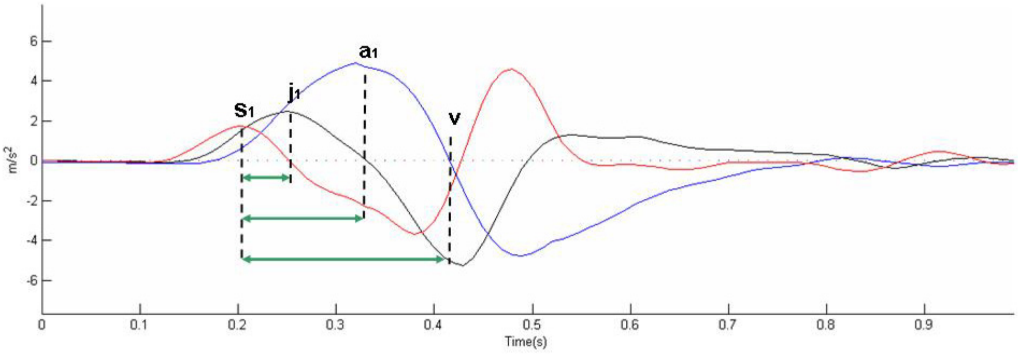

Figure 9. Recorded acceleration profile (blue), and scaled jerk (black) and snap (red) profiles. For a comparison with the single bell-shaped submovement shown in Fig. 7.

As shown in Fig. 9:

a) the beginning of movement is correctly identified by a maximum in the snap profile (the point marked as s_1 in Fig. 9);

b) the first flex of the acceleration corresponds to a max in the jerk profile and a zero in the snap profile,(the point marked as j_1 in Fig. 9);

c) the first peak of the acceleration corresponds to a zero in the jerk profile. However, this point does not always correspond to a minimum in the snap profile (the point marked as a_1 in Fig. 9);

d) the first zero in the acceleration does not exactly correspond to the a minimum in the jerk and a zero in the snap (the point marked as v in Fig. 9).

These results would indicate that the beginning of movement would present features very close to those of the bell-shaped velocity profile of Fig. 7.

TABLE I

Features Temporal Distances

Subject	S1-J1 (msec)				S1-A1 (msec)				S1-V (msec)			
	Mean	Min	Max	Std	Mean	Min	Max	Std	Mean	Min	Max	Std
1	49	40	60	8	116	100	130	12	209	190	230	14
2	35	30	40	5	83	70	100	9	181	150	200	16
3	38	30	40	4	94	80	100	7	256	230	300	25
4	36	30	40	5	77	70	90	6	141	120	180	17
5	37	30	40	5	86	70	100	8	261	180340	340	49

Intra-subject mean, max, min, and standard deviation of the temporal distances between the different features of Fig. 9.

The existence of one or more invariance would be an indirect clue on the existence of a commonly shaped quantum of movement, while the first discrepancy could indicate the beginning of the second submovement. To investigate the existence of invariance in these features, the temporal distances (arrows in Fig. 7) between the beginning of movement and the fist jerk peak (s_1-

j_1), the first acceleration peak (s_1-a_1) and the first velocity peak (correspondent to the first acceleration zero-crossing, s_1-v) were evaluated inter-subject (Tab. I). Inter-subject standard deviation progressively increases from s_1-j_1, to s_1-a_1, till s_1-v_1, which indicates that different trial recordings progressively diverge from each other.

In Fig. 10 the acceleration (blue) and scaled jerk (black) and snap (red) profiles of all the successive trials for one subject are shown. The lower image shows the three profiles normalized at their first peak (acceleration is normalized at a1, jerk at j1, and snap at s1). From this figure is clearly visible that the three profiles follow a common route almost until a1, after which they diverge sensibly.

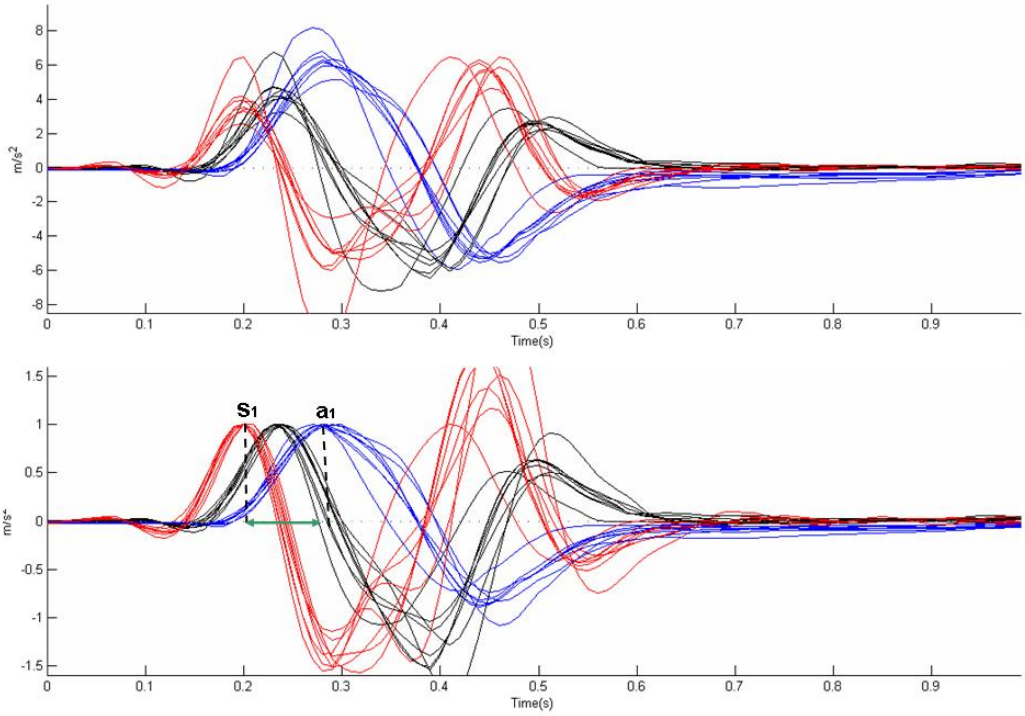

Figure 10. Up: acceleration (blue), jerk (black), and snap (red) profiles of all the recorded trials of subject RR. Down: Normalizing the data to each first peak, it seems that all the trials follow a common template up to a1.

These findings suggest that a bell-shaped movement with invariant features (apart from the velocity peak) untill the first acceleration peak is produced at the beginning of every movement. This is completely aligned with the hypothesis of the rhythmic neuro-controller producing bell-shaped quanta of movement.

Since a1 occurs at the first fourth of the submovement (Fig. 7), the temporal distance between s1 and a1 could be considered as one fourth of the quantum of movement. The duration of the quantum of movement can hence be evaluated for each subject as four times the mean s1-a1 duration (Tab. II).

Being close to the origin of first discrepancies, a1 is here considered to be the onset of the second overlapping submovement. In the hypothesis of a rhythmic neuro-controller, the temporal distance between movement onset and second submovement onset is equal to the temporal distance between the onset of all the overlapping submovements, and its inverse is equal to the neuro-controller control frequency (Table II).

TABLE II

EXTRACTED FEATURES

Subject	Quantum of Movement duration (msec)	Frequency of Submovement (Hz)
1	464	8.6
2	332	12
3	376	10
4	308	12
5	344	11

Quantum of movement duration and submovements production frequency evaluated for each subject.

IV.II Curve Function for Shaping Quantum of Movement

The information acquired from the analysis of acceleration showed the possible existence of a bell-shaped quantum of movement. Two different bell-shaped curve functions were tested as possible templates for the quantum: the well known and largely used Minimum Jerk function, and the Support Bounded Lognormal Function LGNB. These two curve functions are compared in Fig. 11.

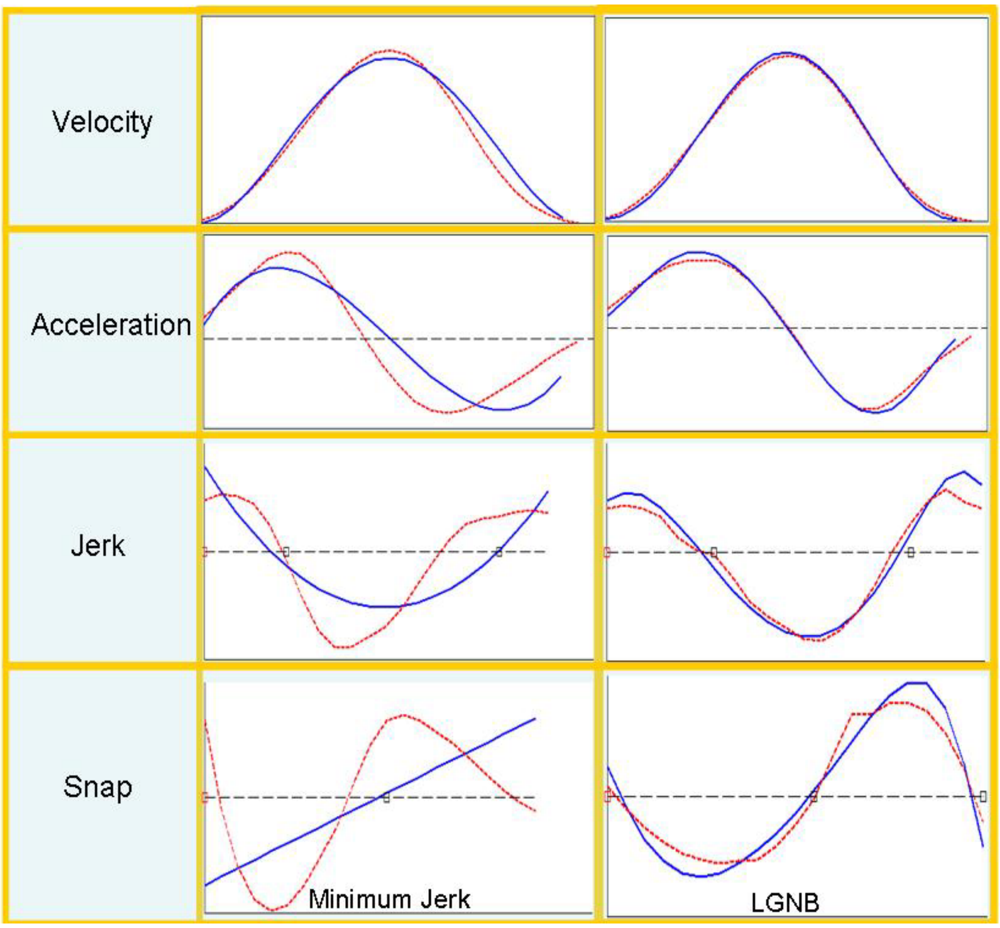

Figure 11. Comparison of Minimum Jerk and LGNB fitting curves is performed by evaluating the fitting for the velocity, acceleration, jerk, and snap profile. The physiological bell-shaped profile is the red dotted line.

In the case of the Minimum Jerk function, the reconstructed velocity profile fits very well a recorded bell-shaped velocity profile. This is aligned with the literature, which applies the minimum-jerk 4th grade polynomial function as the standard curve in velocity profile reconstruction. Also the acceleration profile fits quite well: the minimum-jerk 3rd grade polynomial function respects the zero crossing, maximum and minimum of the original acceleration, though it does not fit at the very beginning and at the very end of the movement. On the other hand, Minimum Jerk 2nd grade polynomial function fits badly with the original jerk: only the zero crossings and the sign of the original jerk are respected, but the shape is clearly different. Snaps fitting is even worse: the snap of the minimum-jerk function is a first grade polynomial function, which is a straight line. Even though it respects zero crossing and sign of the original snap, it is completely differently shaped.

LGNB curve function, on the other hand, fits well at all the four level of differentiation of the velocity profile. LGNB is not a polynomial function and, when derived, does not reduce its grade. It keeps "physiological" shape instead. This feature is particularly evident when analyzing jerk and snap, which have shapes very similar to the original ones.

IV.III Preliminary Experimental Results of the Modified Branch&Bound Algorithm

The modified Branch&Bound optimization algorithm was applied to test the rhythmic neuro-controller hypothesis. The quantum of movement was empirically set as a symmetric bell-shaped LGNB curve with a relatively large kurtosis (μ=0, σ=0.6). Quantum of movement duration and submovement production frequency were set as reported in Tab. II. An example of optimized decomposition is shown in Fig. 12.

The magnitude of the fitting error can be used as an indirect clue towards the existence of the rhythmic neuro-controller producing bell-shaped and peak-modulated quanta of movement with the duration and control frequency of Tab. II. Due to the long time required by the Branch&Bound algorithm to converge towards an acceptable solution, the data recorded from solely two subjects could be analyzed. In Tab. III, mean and standard deviation of the fitting mean square errors for the velocity and the acceleration profiles are reported. Four Branch&Bound iterations were performed for each fitting trial.

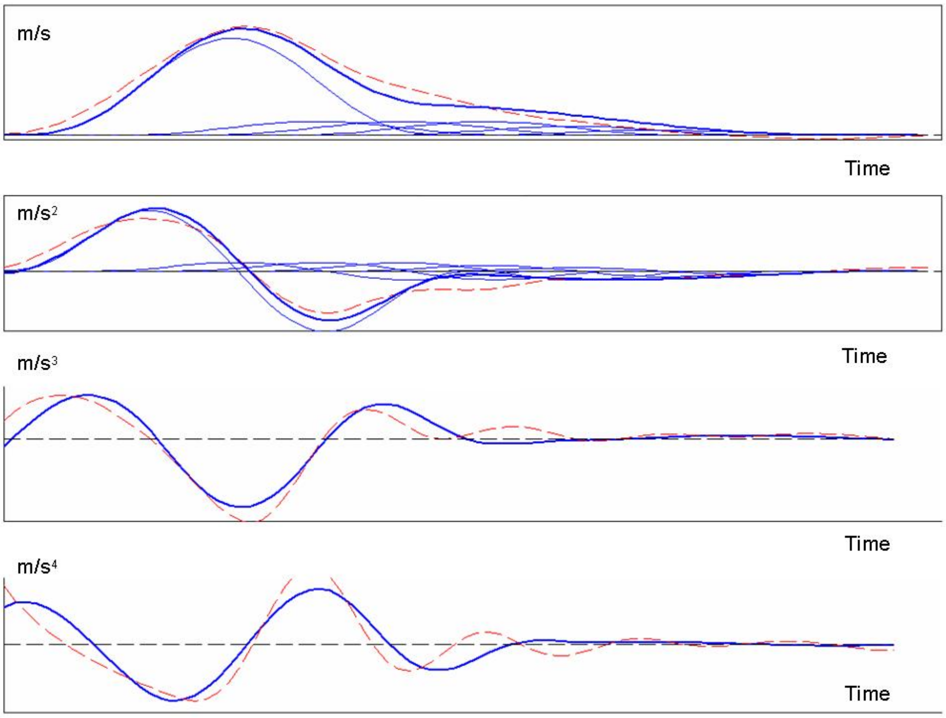

Figure 12. Example of optimized decomposition resulting from the modified Branch&Bound. From up to bottom, velocity, acceleration, jerk and snap profile. Red is the original profile, thick blue is the fitting function, while light blue curves in the velocity and acceleration plots are the single overlapping submovements.

TABLE III

MODIFIED B&B PERFORMANCE

Subject	Velocity Profile Fitting MSE (m/s)		Acceleration Profile Fitting MSE (m/s^2)	
	Mean	STD	Mean	STD
1	0.0030871	0.0018621	0.6096	0.314
2	0.0009761	0.0005161	0.5841	0.713

IV.IV Preliminary Experimental Results of the Predictive Decomposition Algorithm

The template of quantum of movement used in the Predictive Decomposition Algorithm is the same used in the modified Branch&Bound (μ=0, σ=0.6, duration and frequency from Tab. II). In Fig. 13 is shown s an example the resulting decomposition on the same trial showed in Fig. 12.

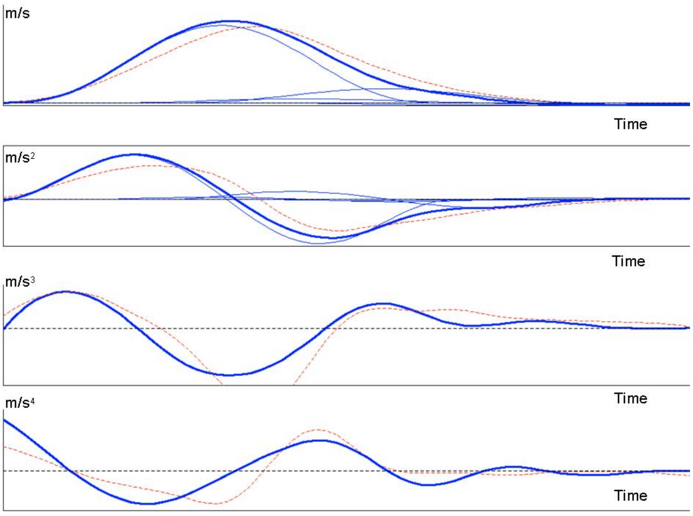

Figure 13. Example of movement Predictive Decomposition. From up to bottom, velocity, acceleration, jerk and snap profile. Red is the original profile, thick blue is the fitting function, while light blue curves in the velocity and acceleration plots are the single overlapping submovements.

In Fig. 14, the acceleration (blue) and scaled jerk (black) and snap (red) profiles of all the successive decomposed trials for one subject are shown. The lower image shows the three profiles normalized at their first peak (acceleration is normalized at a1, jerk at j1, and snap at s1). From this figure is clearly visible that the three profiles follow a common route almost until a1, after which they diverge sensibly, aligned with what shown in Fig. 10.

The magnitude of the fitting error of the Predictive Decomposition Algorithm can be used as an indirect clue towards the existence of the rhythmic neuro-controller. In Tab.IV, mean and standard deviation of the fitting mean square errors for the velocity and the acceleration profiles are reported for each subject.

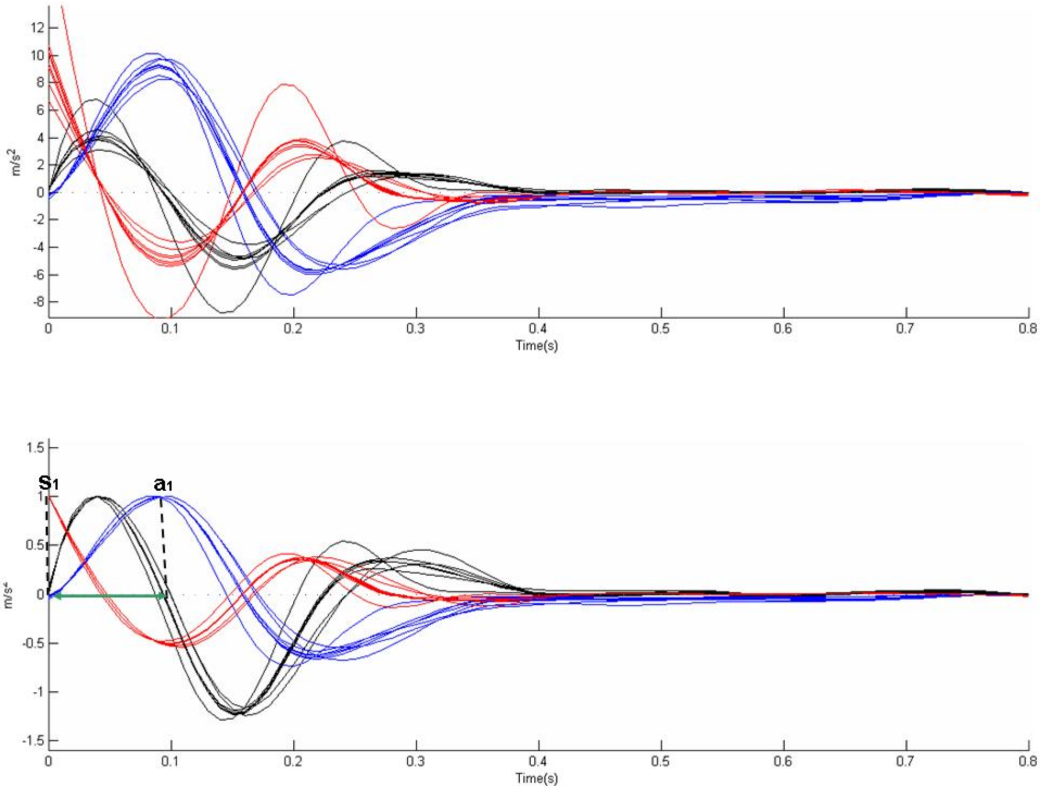

Figure 14. Up: acceleration (blue), jerk (black), and snap (red) profiles of all the decomposed trials of subject RR. Down: By normalizing the data to each first peak, it appears that after a1 the trials diverge from the template, aligned with Fig. 10.

TABLE IV

PREDICTIVE DECOMPOSITION ALGORITHM PERFORMANCE

Subject	Velocity Profile Fitting MSE (m/s)		Acceleration Profile Fitting MSE (m/s^2)	
	Mean	STD	Mean	STD
1	0.00473	0.00216	0.8358	0.2898
2	0.00251	0.00081	1.2363	0.2365
3	0.0012	0.00013	0.3982	0.0882
4	0.0027	0.00240	1.1398	0.8874
5	0.0013	0.00049	0.4697	0.3161

V. DISCUSSION

The preliminary results from the acceleration analysis suggest the existence of an invariant template of movement beginning that starts diverging at the first acceleration peak. Applying these results to the model of a rhythmic neuro-controller, a bell-shaped quantum of movement with empirically chosen duration and frequency was created. The quantum of movement durations ranged between 330-460 msec, a duration that is aligned with what was previously theoretically and experimentally suggested (Lee et al., 1997; Todorov and Jordan, 2002). The existence of discrepancies occurring between 80-120msec was previously reported in the literature as "early adjustments", that is, corrections occurring before velocity main peak (Messier and Kalaska 1999; Krakauer et al. 2002; Fishbach et al., 2005). The acceleration profile analysis suggests a control frequency of 8-12 Hz. Interestingly, this frequency overlaps with the well known frequency of upper limb tremor, which could indicate that the origin of tremor is somehow related to the rhythmic operation of the neuro-controller (McAuley, Rothwell, and Mardsen, 1997).

The fact that the peak of the acceleration (a_1) results as being the onset of the second submovement deserves a short dedicated discussion. If the second submovement starts after a_1, for example in v (at the half of the velocity peak), the acceleration due to the first submovement reaches its zero crossing before the onset of the second submovement. Since also the second submovement acceleration values at the same time zero (or almost zero), the resulting acceleration profile would be a set of dunes, which is very different from what is usually recorded during human motion (Fig. 15 UP). In order to get a composed velocity profile which, while fitting the original velocity profile, fits the acceleration profile as well, it is necessary to move the overlapping onset before v. The best compromise between overlapping onset reduction and minimized number of submovements is reached when the overlapping happens at a1 and, generalizing, at each fourth of the submovements (Fig. 15 DOWN). These points correspond to the minimum, the zero-crossing, and the maximum of the acceleration profile of each submovements.

The comparison between two fitting curve function reinforced the idea (Plamondon, 1993) that the Minimum Jerk function is not really a proper model of physiological movement, and should not be used for decomposition of movement into submovements. On the other hand, the results showed that LGNB is a much more physiological model for human upper limb movement, and this curve was afterwards used instead of the Minimum Jerk to shape the quantum of movement.

Preliminary results from the modified Branch&Bound algorithm are aligned with the hypothesis of the rhythmic neuro-controller producing LGNB-shaped quanta of movement having constant duration as four times the s1-a1 duration and control frequency equal to the inverse of the same duration. On the other hand, the Branch&Bound algorithm, as any other optimization algorithm, needs very long execution times to produce acceptable solutions, and it is not suited for on-line decomposition during real-time upper limb movement recording sessions.

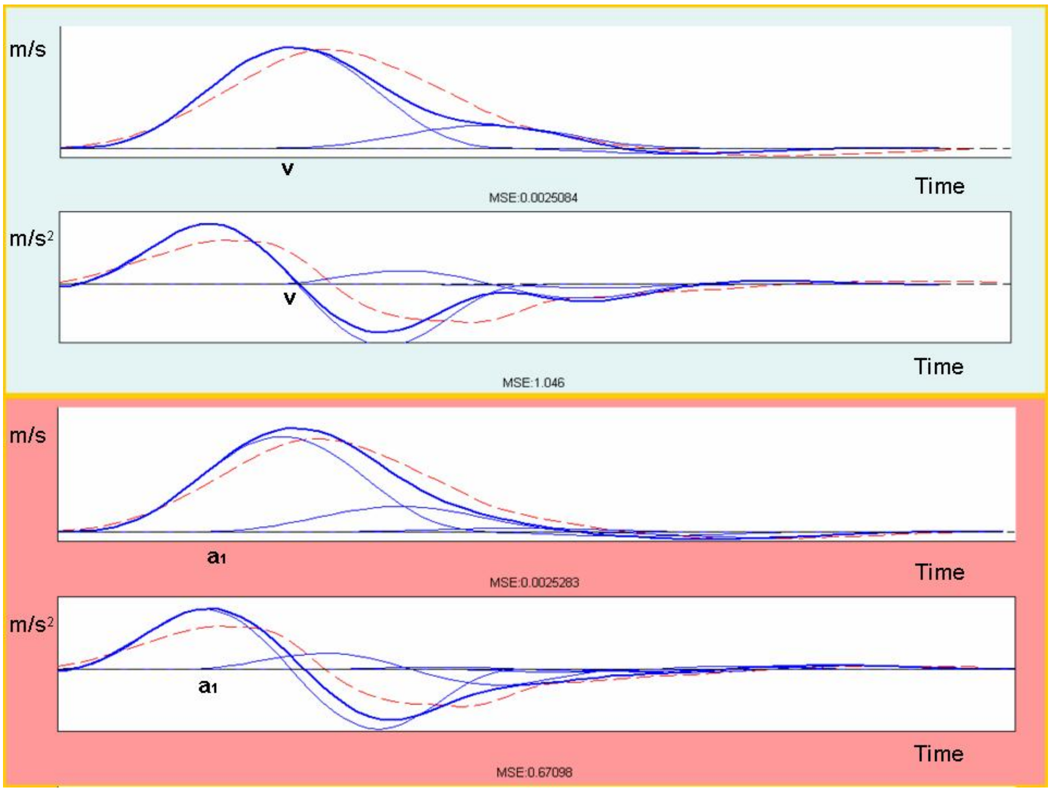

Figure 15. UP Decomposing with submovements starting at velocity peak, the rhythmic neuro-controller assumes an "hopping acceleration" behaviour. DOWN Decomposing with submovements starting at acceleration peak, the rhythmic neuro-controller assumes a physiological behaviour.

Since a Neuroinspired Anticipatory Interface relying on the decomposition of human upper limb movement in quanta of movements to predict user's intentions has to operate in real-time, a Predictive Decomposition Algorithm suited for online analysis of real-time recording sessions was proposed and compared with the performance of the modified Branch&Bound algorithm. The solutions provided by the two proposed algorithms are similar in terms of performance (velocity and acceleration profiles fitting error) and resulting decomposition (the submovements produced to fit the recorded data are similar). This suggests that the Predictive Decomposition algorithm could be based on a model that optimizes the submovement generation for upper limb movement composition.

The Predictive Decomposition algorithm mimics the behaviour of a rhythmic neuro-controller which produces submovements as peak-modulated velocity impulses. It gets values on the real velocity profile at the same frequency of submovements production, and assumes the values due to the sum of the overlapped velocity profiles of the already composed submovements and of the new submovement. It can, hence, anticipate the upper limb movement by the half of the quantum of movement. A Neuroinspired Anticipatory Interface relying on the Predictive Decomposition algorithm for upper limb movement monitoring could benefit of anticipation times between 150-230 msec.

It is possible that the quantum of movement and the submovement frequency are modulated in accordance with the intrinsic inertia and muscle recruitment method of the relative limb segment. The big and heavy segments of the upper limb (from shoulder to wrist), are characterized by wide muscle recruitment methods, that is even for slow and delicate movements almost all the fibres of dedicated muscles are recruited. Because of that, it is plausible that the quantum of movement for this body district is characterized by “long” (330-460 msec) bell-shaped velocity commands produced at a frequency around 8-12 Hz. For the same reasons, it can be hypothesized that the wrist, with its smaller inertia and more independent muscle activation capabilities, should be controlled with smaller parameters values, like shorter duration submovements with higher frequency (i.e., 200 msec duration at 20Hz; values extracted from the results with monkeys, Fishbach et al., 2005). The fingers should be controlled with the highest frequency and shortest duration time of submovements in the whole upper limb scheme (i.e., duration of 150 msec; value extracted from the results of Novak et al., 2003).

VI. FUTURE WORK

Even if at a preliminary stage, the obtained results on movement decomposition in submovements provided important and insightful information. Future efforts will be addressed to further validate the proposed model based on LGNB with more recordings and subjects. Moreover, possible presence of other constant parameters in submovements' features will be carefully analyzed. The study will focus on the classification of the invariance with respect to different level of task accuracy and discrepant sensorial feedback.

The extension of the approach to the analysis of wrist and fingers movement decomposition is planned. It is important to notice that despite there are wrist movement decomposition studies performed with monkeys, human data studies are still lacking.

The future work from this study are not only expected to pave the ground towards the design of an Anticipatory Interface with the upper limb movement, but also to improve knowledge on human motion generation and to provide new inputs to the design and development of motion controllers of artificial systems. In fact, recent findings in neuroscience represent a fundamental source of inspiration for the development of control architectures which feature the robust behaviour of biological systems in the presence of unstructured environments. A novel control paradigm for robot motion and interaction, which is based on the work on submovements here presented, is currently being implemented. Preliminary experimental results on a planar robotic arm seem to confirm the validity of the proposed rhythmic neuro-controller. Future efforts will be addressed to the development of an automatic and dynamic sequence generator module that on-line modifies features of submovements sequences based on sensory feedback..

Future work will be aimed at: 1) the first implementation of an Anticipatory Interface with the upper limb movement relying on the Predictive Algorithm ability to compose the recorded acceleration profile in real-time; 2) the extension of the human movement decomposition approach to wrist and fingers recordings; 3) the integration of the whole dataset coming from arm-wrist-fingers in a new robotic biomimetic controller for complex robotic systems, as robotic (prosthetic) hands.

CHAPTER SEVEN

-

THESIS CONCLUSIONS

Tesi di dottorato in Ingegneria Biomedica, di Luca Rossini,
discussa presso l’Università Campus Bio-Medico di Roma in data 16/04/2010.

I. SUMMARY

The main goal of the present Thesis was to prove the theoretical potentials of Neuroinspired Interfaces to extract meaningful information from all the three main levels of prospected human-interface connections (Chapter 1). The work followed the same "from thoughts to actions" path, exploring Neuroinspired Interfaces with the central nervous system (CNS – Chapter 2 and 3), the peripheral nervous system (PNS – Chapter 4), and the muscular action execution producing limb movements (Chapter 5 and 6).

The decision on where to extract the information makes a big difference on what kind of information can be extracted, how easily it can be accessed, and what can be separated from the multitude of information that human beings are constantly producing, elaborating, and conveying into actions.

II. CONNECTION LEVEL RESULTS

As seen in Chapter 2, Neuroinspired Interfaces with the central nervous system (CNS) belong to the class of Central Neural Interfaces, also known as brain-machine interfaces (BMIs) or brain-computer interfaces (BCIs). This class of Human-Technology interfaces can access the information at its higher level of production and abstraction, but it is currently limited in the temporal and spatial resolution at which the information can be discriminated. While this limit should be overtaken by future brain-imaging techniques and data analysis algorithms (Babiloni et al., 2001), any BMI will always access the information at a limited level of integration, which could jeopardize the effectiveness of the interfaces for some applications (i.e. controlling many degrees of freedom of robotic prosthesis). For those patients affected by severe paralysis, however, BMIs will remain an important (for some unique) communication mean.

Future BMIs could be appealing also for subjects whose sensorimotor performance are seriously affected by the particular working conditions, i.e., astronauts. In Chapter 3, information on the potential issues related with microgravity effects on brain activities were both indirectly extrapolated from studies related on specific changes in the cortical activity during orbital recordings, and generated with a new experiment performed during short-term (30 sec) human expositions to microgravity. The results suggest that it is possible for a subject with prior BMI experience to achieve stable performances of EEG modulation during short-time exposures to micro-gravity.

The sole level at which it is theoretically possible to access neural information in its fully integrated form is at the PNS. As seen in Chapter 1, the access to this kind of information is currently possible with invasive procedures (i.e. LIFE in Chapter 4). Despite the high level of invasiveness, Neuroinspired Interfaces with the PNS permit bidirectional control of complex devices, as a robotic prosthesis. In the very first attempt to connect a robotic prosthetic hand with the PNS via a Neuroinspired Interface, the control of three DOF plus one (rest state) was possible, which is already three times more than what it is currently possible with commercial hand prosthesis. The high level of invasiveness of Neuroinspired Interfaces with the PNS, however, makes this kind of technology an option only for particular users, as amputee or patients suffering paralysis not-related with the operations of the PNS (i.e. muscular degeneration).

For subjects who do not suffer from severe or localized paralysis, amputation, or any other severe reduction of sensorimotor performance, current Neuroinspired Interfaces with the CNS or PNS are yet not appealing. As seen in Chapter 1, one of the goals of the new human-technology interfaces is to reduce the “digital divide” and make the widest group of users able to naturally operate several devices. In order to address the widest group of users, Neuroinspired Interfaces must extract user's intentions information where the cortical and peripheral activities convey to produce an action, that is at the muscular or motion-limb level. While this is the level of information extraction at which all the current human-technology interfaces work, Neuroinspired Interfaces ask the user to behave "as he/she normally would". In the meantime user's intentions are extracted from physiological and involuntary events related with the natural action production.

III. NEW HUMAN-TECHNOLOGY INTERACTION PARADIGM - ANTICIPATORY INTERFACES

In the last decade, the studies on physiology of human perception revealed several motor patterns related with conscious actions, such as object manipulation or locomotion. Some of these planned actions are anticipated by characteristic involuntary motor actions which do not require any active cognitive control by the user himself in order to be performed. Since those involuntary motor actions precede planned actions by a considerable amount of time, they are called Anticipatory Movements.

As seen in Chapter 5, when anticipatory involuntary movements are monitored by Neuroinspired Interfaces, the interfaces may acquire predictive features. These interfaces were named, accordingly, Anticipatory Interfaces. Specific feature of these interfaces is the fact that in principle they can reduce the delay in commands actuation by monitoring user's unconscious anticipatory movements.

Two anticipatory movements were taken into consideration in two separate studies (Chapter 5 and 6). The first study demonstrated the persistence of anticipatory head rotation during teleoperation of a navigating robot. The exploitation of head-rotation anticipatory movements is discussed within the design of Anticipatory Interfaces as novel means to enable teleoperation with reduced command-signal delays.

The second study proposed and preliminary demonstrated the existence of an anticipatory rhythmic neuro-controller that controls human upper limb during reaching tasks. The activity of the rhythmic neuro-controller can be anticipated by using a Predictive Decomposition algorithm. Even if at a preliminary stage, the obtained results on movement decomposition in submovements provided important and insightful information.

IV. FUTURE WORK ON NEUROINSPIRED INTERFACES

Globally, from the results presented in this Thesis it emerges that Neuroinspired Interfaces may effectively extract information on user's intentions by monitoring and detecting user's natural and physiological behaviours and that this information can be translated into commands towards technological devices.

Current non-invasive Neuroinspired Interfaces with the CNS systems are useful solely to severely paralyzed patients, and are not directly applicable to human space exploration and exploitation activities. Future BMI systems for space applications should be able to operate continuously in reduced gravity conditions, allowing for multiple tasks to be performed concurrently with the BMI protocol execution. Hence, additional research driven by space requirements is necessary. Benchmark tests need to be implemented in order to assess the fitting level between systems and their target applications. Once the best BMI systems are identified, these would undergo long-term microgravity exposition tests, i.e. onboard the ISS. Apart from evaluating the effective usefulness of such systems in the accomplishment of specific astronauts' tasks, it remains very important to assess the effects of microgravity conditions on the use of BMIs after long-term neural adaptations.

With respect to Neuroinspired Interfaces with the PNS, future efforts will be aimed at designing and optimizing the first fully integrated wearable robotic hand prosthesis for amputee. New stimulation and registration protocols, stemming from the promising results presented in Chapter 4, are already under preparation.

As regards to the Neuroinspired Interfaces with Anticipatory Movements, their benefits can be significant, allowing users to naturally operate with a reduced communication delay.

The studies on Anticipatory Interfaces for teleoperation of cruising robots will firstly be focused on testing cruising speeds between 30 cm/s and 4 cm/s, in order to identify the range threshold of speed under which anticipatory behaviours stop to be expressed. Then the studies will try to identify solutions to simulate the rotation on site during head rotation, in order to amplify the anticipatory behaviour. Giving the robot some autonomy in route planning is expected to help users in producing more long-lasting anticipatory movements.

Finally future efforts on Anticipatory Interfaces with upper limb movement will be addressed to further validate the proposed model based on LGNB with more recordings and subjects. The study will try to classify the anticipatory behaviour with respect to different level of upper limb motor tasks accuracy and discrepant sensorial feedback. The extension of the approach to the analysis of wrist and fingers movement decomposition is planned as the subsequent step. The information coming from the studies on arm, wrist, and fingers will be finally used to conceive a complete rhythmic neuro-controller model. This model will permit the prediction of users' intentions by a new Anticipatory Interface. It is also expected to inspire new approaches to robot control for complex anthropomorphic robotic systems.

PUBLICATIONS AND RELEVANT ACTIVITIES

I. JOURNAL PAPERS

Rossini L., Laschi C., Guglielmelli E., Reducing Intrinsic Communication Delay in Tele-Navigation Operations by Predicting Human Motor Intentions from Anticipatory Movements, IEEE Robotics and Automation Magazine, Submitted 2009

Rossini P.M., Micera, S., Benvenuto A., Carpaneto J., Cavallo G., Citi L., Cipriani C., Denaro L., Denaro V., Di Pino G., Ferreri F., Guglielmelli E., Hoffmann K.P., Raspopovic S., Rigosa J., Rossini L., Tombini M., Dario P., Double Nerve Intraneural Interface Implant on a Human Amputee for Robotic Hand Control, Clinical Neurophysiology, In Press

Micera S., Citi L., Rigosa J., Carpaneto J., Raspopovic S., Di Pino G., Rossini L., Yoshida K., Dario P., Rossini P.M., Decoding sensory and motor information from neural signals recorded using intraneural electrodes: towards the development of a neurocontrolled hand prosthesis, Proceedings of the IEEE, Accepted 2009

Rossini P.M., Rossini L., Ferreri F., Transcranial Magnetic Stimulation: A Review, IEEE Engineering in Medicine and Biology Magazine, January February 2010

Tonet O. , M. Marinelli, L.Citi, P.M. Rossini, L. Rossini, G. Megali, P. Dario, "Defining brain–machine interface applications by matching interface performance with device requirements", Journal of Neuroscience Methods, 167, 91–104, 2008.

II. CONFERENCE PROCEEDINGS

Rossini L., Izzo D., Summerer L., "Brain Machine Interfaces for Space Applications", 31st annual international conference of the IEEE engineering in Medicine and Biology Society, Minneapolis Minnesota, August 2009

Micera S., Rigosa J., Carpaneto J., Citi L., Raspopovic S., Guglielmelli E., Benvenuto A., Rossini L., Di Pino G., Cavallo G., Carrozza M.C., Cipriani C., Hoffmann K.P., Dario P., Rossini P.M., "On the control of a robot hand by extracting neural signals from the PNS: preliminary results from a human implantation", 31st annual international conference of the IEEE engineering in Medicine and Biology Society, Minneapolis Minnesota, August 2009

Izzo D., Rossini L., Rucinski M., Ampatzis C., Healy G., Wilkins P., Smeaton A., Yazdani A., Ebrahimi T., "Curiosity Cloning: Neural Analysis of Scientific Knowledge", Proceedings of the International Joint Conference on Artificial Intelligence 2009, Workshop on Artificial Intelligence in Space, July 2009

Rossini L., T. Seidl, D. Izzo, L. Summerer, "Beyond astronaut's capabilities: a critical review", 58th International Astronautical Congress, Hyderabad, 2007

III. BOOK CHAPTERS

Summerer L., Izzo D., Rossini L., Why the BMIs Renaissance will affect Space Exploration, In L. Rossini, D. Izzo, L. Summerer (ED.), "Brain-Machine Interfaces for space applications: enhancing astronauts' capabilities", International Review of Neurobiology, vol. 86, 2009

Summerer L., Izzo D., Rossini L., BMIs and Space Exploration, Next and Far Future Roadmap, In L. Rossini, D. Izzo, L. Summerer (ED.), "Brain-Machine Interfaces for space applications: enhancing astronauts' capabilities", International Review of Neurobiology, vol. 86, 2009

IV. BOOK EDITED

Rossini, L., Izzo, D., Summerer, L., Brain-Machine Interfaces for space applications: enhancing astronauts' capabilities, International Review of Neurobiology, vol. 86, 2009

V. ACTIVITIES

- Stage at the Advanced Concepts Team of the European Space Agency from August 2006 to January 2007.
- Young Graduate Trainee on Bioengineering for Space Applications in the Advanced Concepts Team of the European Space Agency from June 2007 to June 2008.

- Consultant on Brain-Machine Interfaces for the Advanced Concepts Team of the European Space Agency, September 2008.
- Research Fellowship on *Non-invasive neural interfaces for the control of biomechatronics prosthesis*, from February 2009 to January 2011.
- Participation to the brain-machine interface experiments in microgravity condition at the December 2007 ESA's Parabolic Flight Campaign.
- Invited lecture on "Anticipatory Movements for Neuro-Inspired Interfaces" at the College de France, Physiology of Movement and Perception Lab, Prof. Alain Berthoz.
- Invited lecture at the Workshop on Brain Machine Interfaces for Space Applications in ESTEC-ESA, Noordvijk, 30 November 2009.
- Invited attendant expert to the results presentation of the ARIADNA project on Curiosity Cloning, 1st of December 2009.
- First Editor of the book *Brain Machine Interfaces for Space Application: Enhancing Astronaut's Capabilities* (Elsevier, "International Review of Neurobiology" series).
- Author of the internet pages on "Bioengineering for Space" in the ESA internet domain.
- International Congress on Robotics and Automation (ICRA) 2007, Rome, as IEEE Attendant Student.
- Neurobotics Summerschool 2007 on Brain Computer Interfaces.
- Introduction to Space System Engineering (2 days course chaired by Prof. Stephen Gabriel, University of Southampton).
- Co-Author of ARIADNA Call 2007 on Hybrid Controllers.
- Co-Author of ARIADNA Call 2008 on Curiosity Cloning.
- Scientific coordination of ASI's Call for Proposals on Biotechnology for Human Space Exploration: *MEG-BMI module for Space Exploration*..
- Scientific collaboration in Neurobotics FP7 project (2004-2008).
- Scientific collaboration in Brainhand CIR project (2008-2010).

- Scientific collaboration in the preparation of several national and European projects.
- Reviewer for several conferences and journals papers.

REFERENCES

Abend, W., Bizzi, E. & Morasso, P. (1982). Human arm trajectory formation. Brain: a journal of neurology, 105, 331-348.

Aggarwal, V., Chatterjee, A., Cho, Y., Rasmussen, R., Acharya, S., Thakor, N. V., 2006. Noninvasive cortical control of a prosthetic hand with local machine control and haptic feedback. In: Ann. Meeting of Biomedical Engineering Soc (BMES 2006). Chicago, USA.

Babiloni C., Pizzella V., Del Gratta C., Ferretti A., Romani G.L., "Fundamentals of electro-encephalography, magneto-encephalography, and functional magnetic resonance imaging", In L. Rossini et al. (ED.), "Brain Machine Interfaces for space applications: enhancing astronauts' capabilities", International Review of Neurobiology, 2009a, 86, 67-80

Babiloni F., Cincotti F., Carducci F., Rossigni P.M., Babiloni C., "Spatial enhancement of EEG data by surface Laplacian estimation: the use of magnetic resonance imaging-based head models", Clin Neurophysiol., 2001, 112, 5, 724-727

Babiloni, F., Cincotti1, F., Marciani, M., Salinari, S., Astolfi, L., Aloise, F., De Vico Fallani, F. Mattia, D., "On the use of brain computer interfaces outside scientific laboratories: toward an application in domotic environments", In L. Rossini et al. (ED.), "Brain Machine Interfaces for space applications: enhancing astronauts' capabilities", International Review of Neurobiology, 2009b, 86, 133-146

Bailey R.W., "Human performance engineering", ed. 2, Englewood Cliffs. N.J., 1989, Prentice Hall.

Bailey, N. R., Scerbo, M. W., Freeman, F. G., Mikulka, P. J., Scott, L. A., 2006. Comparison of a brain-based adaptive system and a manual adaptable system for invoking automation. Hum Factors 48 (4), 693–709

Barker A.T., C. W. Garnham, and I. L. Freeston, ''Magnetic nerve stimulation: The effect of waveform on efficiency, determination of neural membrane time constants and the measurement of stimulator output,'' Electroencephalogr. Clin. Neurophysiol., vol. 43, pp. 227–237, 1991

Barker A.T., R. Jalinous, and I. L. Freeston, ''Non-invasive stimulation of human motor cortex,'' Lancet, vol. 1, pp. 1106–1107, 1985

Berardelli, A., Hallett, M., Rothwell, J. C., Agostino, R., Manfredi, M., Thompson, P. D., et al. (1996). Single-joint rapid arm movements in normal subjects and in patients with motor disorders. Brain, 119, 661–674.

Berthier, N. (1996). Learning to Reach: A Mathematical Model.. Developmental Psychology, 32, 811-823.

Berthoz A:, Brain's sense of movement, Harvard University Press, June 2000.

Bhushan N, Shadmehr R (1999) Computational nature of human adaptive control during learning of reaching movements in force fields. Biol Cybern 81:39–60

Birbaumer, N., Kübler, A., Ghanayim, N., Hinterberger, T., Perelmouter, J., Kaiser, J., Iversen, I., Kotchoubey, B., Neumann, N., Flor, H., Jun 2000. The thought translation device (TTD) for completely paralyzed patients. IEEE Trans Rehabil Eng 8 (2), 190–193.

Birbaumer, N., Mar 2006. Brain-computer-interface research: coming of age. Clin Neurophysiol 117 (3), 479–483.

Birbaumer, N., Murguialday, A.R., Weber1, C., Montoya, P., "Neurofeedback and Brain-Computer-Interface (BCI): clinical applications", In L. Rossini et al. (ED.), "Brain Machine Interfaces for space applications: enhancing astronauts' capabilities", International Review of Neurobiology, 2009, 86, 107-117

Bizzi E, Mussa-Ivaldi FA, "Toward a neurobiology of coordinate transformations", In: The Cognitive Neurosciences III (Gazzaniga MS, ed), 2004, pp 413-474. Cambridge, MA: MIT Press

Blankertz, B., Muller, K.-R., Curio, G., Vaughan, T., Schalk, G., Wolpaw, J., Schlogl, A., Neuper, C., Pfurtscheller, G., Hinterberger, T., Schroder, M., Birbaumer, N., 2004. The BCI competition 2003: progress and perspectives in detection and discrimination of eeg single trials. Biomedical Engineering, IEEE Transactions on 51 (6), 1044–1051.

Bodeen C., "China space program reaches turning point with third manned mission featuring spacewalk", The China Post, 23 September 2008, 8 March 2009, http://www.chinapost.com.tw/china/national%20news/2008/09/23/175925/China-space.htm

Bokil, H. S., Pesaran, B., Andersen, R. A., Mitra, P. P., Aug 2006. A method for detection and classification of events in neural activity. IEEE Trans Biomed Eng 53 (8), 1678–1687.

Burdet E, Milner TE (1998) Quantization of human motions and learning of accurate movements. Biol Cybern 78:307–318

Buttfield, A., Ferrez, P., Millan, J. d. R., June 2006. Towards a robust bci: error potentials and online learning. Neural Systems and Rehabilitation Engineering, IEEE Transactions on [see also IEEE Trans. on Rehabilitation Engineering] 14 (2), 164–168.

Carmena, J. M., Lebedev, M. A., Crist, R. E., O'Doherty, J. E., Santucci, D. M., Dimitrov, D. F., Patil, P. G., Henriquez, C. S., Nicolelis, M. A. L., Nov 2003. Learning to control a brain-machine interface for reaching and grasping by primates. PLoS Biol 1 (2), E42.

Carpi F., De Rossi D., "EMG-based gaze-tracking-based man-machine interfaces", ", In L. Rossini et al. (ED.), "Brain- Machine Interfaces for space applications: enhancing astronauts' capabilities", International Review of Neurobiology, vol. 86, 2009, 3-21.

Chapin, J. K., Moxon, K. A., Markowitz, R. S., Nicolelis, M. A., Jul 1999. Real-time control of a robot arm using simultaneously recorded neurons in the motor cortex. Nat Neurosci 2 (7), 664–670.

Cheng, M., Gao, X., Gao, S., Xu, D., 2002. Design and implementation of a brain-computer interface with high transfer rates. IEEE Trans Biomed Eng 49 (10), 1181–1186.

Cheron G., A.M. Cebolla, M. Petieau, A. Bengoetxea, E. Palmero- Soler, A. Leroy, B. Dan, "Adaptive changes of rhythmic EEG oscillations in space: implications for brain machine interface applications", In L. Rossini, D. Izzo, L. Summerer (ED.), "Brain- Machine Interfaces for space applications: enhancing astronauts' capabilities", International Review of Neurobiology, vol. 86, 2009.

Cincotti, F., Aloise, F., Babiloni, F., Marciani, M., Morelli, D., Paolucci, S., Oriolo, G., Cherubini, A., Bruscino, S., Sciarra, F., Mangiola, F., Melpignano, A., Davide, F., Mattia, D., February 20-22, 2006. Brain-operated assistive devices: the aspice project. In: Biomedical Robotics and Biomechatronics, 2006. BioRob 2006. The First IEEE/RAS-EMBS International Conference on. pp. 817–822.

Citi L., O. Tonet, M. Marinelli, "Matching brain-machine interface performance to space applications", In L. Rossini, D. Izzo, L. Summerer (ED.), "Brain-Machine Interfaces for space applications: enhancing astronauts' capabilities", International Review of Neurobiology, vol. 86, 2009.

Clement G., "Fundamentals of space medicine", Kluwer Academic Publishers, The Netherlands, 2003.

Cook A.M., Hussey S.M., "Assistive Technologies: principles and practice", "nd Ed., 2002, Mosby Inc., St. Louis, Missouri

Coyle, S., Ward, T., Markham, C., McDarby, G., 2004a. On the suitability of near-infrared (NIR) systems for next-generation Brain-Computer Interfaces. Physiological Measurement 25 (4), 815–22.

Coyle, S., Ward, T., Markham, C., McDarby, G., Aug 2004b. On the suitability of near-infrared (NIR) systems for next-generation brain-computer interfaces. Physiol Meas 25 (4), 815–822.

Crossman, E. & Goodeve, P. (1983). Feedback control of hand-movement and Fitts'law. The Quarterly Journal of Experimental Psychology Section A, 35, 251-278.

Curran, E. A., Stokes, M. J., Apr 2003. Learning to control brain activity: a review of the production and control of EEG components for driving brain-computer interface (BCI) systems. Brain Cogn 51 (3), 326–336.

Dhillon G. and K. Horch, "Direct neural sensory feedback and control of a prosthetic arm," IEEE Trans. Neural Syst. Rehabil. Eng., vol. 13, no. 4, pp. 468–472, Dec. 2005.

Dhillon G., S. Lawrence, D. Hutchinson, and K. Horch, “Residual function in peripheral nerve stumps of amputees: Implications for neural control of artificial limbs,” J. Hand Surg., vol. 29A, no. 4, pp. 605–615, 2004.

Dipietro L., Krebs H.I., Fasoli S.E., Volpe B.T., and Hogan N., Submovement changes characterize generalization of motor recovery after stroke, Cortex (2008), doi:10.1016/j.cortex.2008.02.008

Doeringer, J. A., & Hogan, N. (1998). Intermittency in preplanned elbow movements persists in the absence of visual feedback. Journal of Neuroscience, 80, 1787–1799.

Donoghue, J. P., Nov 2002. Connecting cortex to machines: recent advances in brain interfaces. Nat Neurosci 5 Suppl, 1085–1088.

Dornhege, G., Blankertz, B., Curio, G., Müller, K.-R., 2004. Increase information transfer rates in BCI by CSP extension to multi-class. In: Thrun, S., Saul, L., Schölkopf, B. (Eds.), Advances in Neural Information Processing Systems 16. MIT Press, Cambridge, MA.

Dounskaia, N., Wisleder, D., & Johnson, T. (2005). Influence of biomechanical factors on substructure of pointing movements. Experimental Brain Research, 164(4), 505–516.

Elbert T., Pantev C., Wienbruch C., Rockstroh B., Taub E., “Increased cortical representation of the fingers of the left hand in string players”, Science, 1995, 270, 305-307.

ELIPS, “European programme for Life and Physical sciences and applications utilising the International Space Station (ELIPS)”, European Space Agency, 2004, 8 March 2009, http://www.spaceflight.esa.int/users/index.cfm?act=default.page&level=16&page=453

Fabiani, G., McFarland, D., Wolpaw, J., Pfurtscheller, G., Sept. 2004. Conversion of EEG activity into cursor movement by a brain-computer interface (BCI). Neural Systems and Rehabilitation Engineering, IEEE Transactions on [see also IEEE Trans. on Rehabilitation Engineering] 12 (3), 331–338.

Fagg A.H., Hatsopoulos N.G., de Lafuente V., Moxon K.A., Niemati S., Rebesco J.M., Romo R., Solla S.A., Reimer J., Tkach D., Pohlmeyer E.A., Miller L.E., “Biomimetic brain machine interface for the control of movement”, Journal of Neuroscience, 2007, 27, 44, 11842-11856.

Farwell, L. A., Donchin, E., Dec 1988. Talking off the top of your head: toward a mental prosthesis utilizing event-related brain potentials. Electroencephalogr Clin Neurophysiol 70 (6), 510–523.

Ferraina S., Battaglia-Mayer A., Genovesio A., Archambault P., Caminiti R., “Parietal enconding of action in depth”, Neuropsychologia, 2009, 47, 6, 1409-1420.

Fetz E.E., “Volitional control of neural activity: Implications for brain-machine interfaces”, Journal of Physiology, 2007, 579, 3, 571-579.

Fetz, E. E., 1969. Operant conditioning of cortical unit activity. Science 163 (870), 955–958.

Fishbach A., Roy S.A., Bastianen C., Miller L.E., Houk J.C., “Deciding when and how to correct a movement: discrete submovements as a decision making process”, Exp. Brain Res., 2006

Fishbach A., Roy S.A., Bastianen C., Miller L.E., Houk J.C., Kinematic properties of on-line error corrections in the monkey, Exp Brain Res, 2005, 164: 442–457

Fitts, P. M. (1954). The information capacity of the human motor system in controlling the amplitude of movement. Journal of Experimental Psychology, 47(6), 381–391.

Flash, T. & Henis, E. (1991). Arm trajectory modifications during reaching towards visual targets. Journal of cognitive neuroscience, 3, 220-230.

Fradet L., Lee G., Dounskaia N., Origins of submovements during pointing movements, Acta Psychologica 129 (2008) 91–100

Gal J., W. Herzog, G. Kawchuk, P. Conway, and Y-T Zhang, "Measurements of vertebral translations using bone pins, surface markers and accelerometers", Clin. Biomech., Vol. 12 No. 5, 1997, pp. 337- 340.

Gao, X., Xu, D., Cheng, M., Gao, S., June 2003. A bci-based environmental controller for the motion-disabled. Neural Systems and Rehabilitation Engineering, IEEE Transactions on [see also IEEE Trans. on Rehabilitation Engineering] 11 (2), 137–140.

Geng, T., Gan, J. Q., Dyson, M., Tsui, C. S., Sepulveda, F., 2006. EEG-based synchronous parallel bci. In: Proc. MAIA Workshop on Brain Computer Interfaces.

Georgopoulos, A., Langheim, F., Leuthold, A., Merkle, A., Jul 2005. Magnetoencephalographic signals predict movement trajectory in space. Exp Brain Res, 1–4.

Gordon J., Ghilardi M.F., Ghez C., "Impairments of reaching movements in patients without proprioception I. Spatial errors", Journal of Neurophysiol., 1995, 73(1), 347

Graimann, B., Huggins, J. E., Levine, S. P., Pfurtscheller, G., Jun 2004. Toward a direct brain interface based on human subdural recordings and wavelet-packet analysis. IEEE Trans Biomed Eng 51 (6), 954–962.

Graimann, B., Huggins, J. E., Schlögl, A., Levine, S. P., Pfurtscheller, G., Sep 2003. Detection of movement-related desynchronization patterns in ongoing single-channel electrocorticogram. IEEE Trans Neural Syst Rehabil Eng 11 (3), 276–281.

Grandori F. and P. Ravazzani, ''Magnetic stimulation of the motor cortex— Theoretical considerations,'' IEEE Trans. Biomed. Eng., vol. 38, pp. 180–191, 1991

Grasso R., C. Assiante, P. Prevost, and A. Berthoz, "Development of anticipatory orienting strategies during locomotor tasks in children," Neuroscience and Biobehavioral Reviews, Vol. 22, No. 4, 1998, pp. 533–539.

Grasso R., P. Prevost, Y. Ivanenko, and A. Berthoz, "Eye-Head coordination for the steering of locomotion in humans: an anticipatory synergy", Neuroscience Letters , Vol. 253, No. 2, 1998, pp. 115–118.

Grasso R., Y.P. Ivanenko, J. McIntyre, I. ViaudDelmon, and A. Berthoz, "Spatial, not temporal cues drive predictive orienting movements during navigation: a virtual reality study", NeuroReport, vol. 11, n. 4, 2000, pp. 775–778.

Gribble, P. L., Mullin, L. I., Cothros, N., & Mattar, A. (2003). Role of cocontraction in arm movement accuracy. Journal of Neurophysiology, 89(5), 2396–2405.

Gross, J., Timmermann, L., Kujala, J., Dirks, M., Schmitz, F., Salmelin, R. & Schnitzler, A. (2002). The neural basis of intermittent motor control in humans. Proc Natl Acad Sci US A, 99, 2299-2302.

Guger, C., Harkam, W., Hertnaes, C., Pfurtscheller, G., 1999. Prosthetic control by an EEG-based brain-computer interface (BCI). In: Proceedings of AAATE 5th European Conference for the Advancement of Assistive Technology. Düsseldorf, Germany.

Guiard, Y. (1993). On Fitts's and Hooke's laws: Simple harmonic movement in upper-limb cyclical aiming. Acta Psychologica, 82(1–3), 139–159.

Hanneton S, Berthoz A, Droulez J, Slotine JJ (1997) Does the brain use sliding variables for the control of movements? Biol Cybern 77:381–393

Harris CM, Wolpert DM (1998) Signal-dependent noise determines motor planning. Nature 394:780–784

Heller L. and D. B. van Hulsteyn, ''Brain stimulation using electromagnetic sources: Theoretical aspects,'' Biophys. J., vol. 63, pp. 129–138, 1992

Henneman, E., Clamann, H.P., Gillies, J.D., Skinner, R.D. (1974). Rank order of motoneurons within a pool: law of combination. J. Neurophysiol. 37, 1338-1349.

Hicheur H., S. Vieilledent, M.J.E. Richardson, T. Flash, and A. Berthoz, "Velocity and curvature in human locomotion along complex curved paths: a comparison with hand movements", Exp. Brain Res., vol. 162, 2005, pp. 145–154.

Hochberg, L. R., Serruya, M. D., Friehs, G. M., Mukand, J. A., Saleh, M., Caplan, A. H., Branner, A., Chen, D., Penn, R. D., Donoghue, J. P., Jul 2006. Neuronal ensemble control of prosthetic devices by a human with tetraplegia. Nature 442 (7099), 164–171.

Houk JC, Singer JJ, Goldman MR (1970) An evaluation of length and force feedback to soleus muscles of decerebrate cats. J Neurophysiol 33:784–811

Humphrey, D. R., Schmidt, E. M., Thompson, W. D., 1970. Predicting measures of motor performance from multiple cortical spike trains. Science 170 (959), 758–762.

Hruby T., Marsalek P., "Event-related potentials-the P3 wave", Acta Neurobiologiae Experimentalis, 63(1):55–63, 2002.

Izzo D., Rossini L., Rucinski M., Ampatzis C., Healy G., Wilkins P., Smeaton A., Yazdani A., Ebrahimi T., "Curiosity Cloning`: Neural Analysis of Scientific Knowledge", Proceedings of the International Joint Conference on Artificial

JangI.J., and W.B. Park, "Signal Processing of the Accelerometer for Gesture Awareness on Handlheld Devices", Proceedings of the 2003 IEEE International Workshop on Robot and Human Interactive Communication, Millbrae, California, USA, 2003.

Jerbi, K., Freyermuth, S., Minotti, L., Kahane, P., Berthoz, A., Lachaux, J.P., "Watching Brain TV and Playing Brain Ball: Exploring novel BCI strategies using real-time analysis of human intracranial data", In L. Rossini et al. (ED.), "Brain Machine Interfaces for space applications: enhancing astronauts' capabilities", International Review of Neurobiology, 2009, 159-168

Johansson R., G. Westling, A. Backstorm, and J. Flanagan, "Eye-Hand coordination in object manipulation", Journal of Neuroscience , Vol. 21, 2001, pp. 6917–6932.

Jones KE, Hamilton AF, Wolpert DM (2002) Sources of signal- dependent noise during isometric force production. J Neurophysiol 88:1533–1544

Kahane, P., Minotti, L., Hoffmann, D., Lachaux, J-P., and Ryvlin, P., "Invasive EEG in the definition of the seizure onset zone: depth electrodes", In: Handbook of Clinical Neurophysiology. Pre-surgical assessment of the epilepsies with clinical neurophysiology and functional neuroimaging. (F. Rosenow, HO, Lüders, Ed.) Elsevier Science, 2004

Kauhanen, L., Nykopp, T., Lehtonen, J., Jylänki, P., Heikkonen, J., Rantanen, P., Alaranta, H., Sams, M., Jun 2006. EEG and MEG brain-computer interface for tetraplegic patients. IEEE Trans Neural Syst Rehabil Eng 14 (2), 190–193.

Kawato M (1992) Optimization and learning in neural networks for formation and control of coordinated movement. In: Meyer DE, Kornblum S (eds) Attention and performance, vol XIV. MIT Press, Cambridge, MA, pp 821–849

Kelly, S., Lalor, E., Finucane, C., McDarby, G., Reilly, R., 2005a. Visual spatial attention control in an independent brain-computer interface. IEEE Trans Biomed Eng 52 (9), 1588–1596.

Kelly, S., Lalor, E., Reilly, R., Foxe, J., 2005b. Visual spatial attention tracking using high-density SSVEP data for independent brain-computer communication. IEEE Transactions on Neural System and Rehabilitation Engineering 13 (2), 172–178.

Kennedy, P. R., Bakay, R. A., Jun 1998. Restoration of neural output from a paralyzed patient by a direct brain connection. Neuroreport 9 (8), 1707–1711.

Kennedy, P. R., Sep 1989. The cone electrode: a long-term electrode that records from neurites grown onto its recording surface. J Neurosci Methods 29 (3), 181–193.

Kennedy, P., Adams, K., Bakay, R., Goldthwaite, J., Montgomery, G., and Moore, M., "Direct control of a computer from human central nervous system," IEEE Transactions on Rehabilitation Engineering, Vol. 8, 2000, pp. 198–202.

Kostov, A., Polak, M., Jun 2000. Parallel man-machine training in development of EEG-based cursor control. IEEE Trans Rehabil Eng 8 (2), 203–205.

Krakauer JW, Gordon J, Veytsman M, Ghez C (2002) Contributions of planning and updating to accuracy of reaching movements in normals and stroke. In: Society for Neuroscience, vol Program No. 169.4

Krebs, H., Aisen, M., Volpe, B. & Hogan, N. (1999). Quantization of continuous arm movements in humans with brain injury. Proceedings of the National Academy of Sciences, 96, 4645.

Kriggs T., B. R. Buchbinder, W. E. Butler, K. H. Chiappa, H. J. Jiang, B. R. Rosen, and G. R. Cosgrove, ''Stereotactic transcranial magnetic stimulation: Correlation with direct electrical cortical stimulation,'' Neurosurgery, vol. 41, pp. 1319–1325, 1997

Krusienski, D.J., Wolpaw, J.R., "Brain-Computer Interface Research at the Wadsworth Center: Developments in Noninvasive Communication and Control", In L. Rossini et al. (ED.), "Brain Machine Interfaces for space applications: enhancing astronauts' capabilities", International Review of Neurobiology, 2009, 86, 147-157

Kübler, A., Kotchoubey, B., Hinterberger, T., Ghanayim, N., Perelmouter, J., Schauer, M., Fritsch, C., Taub, E., Birbaumer, N., Jan 1999. The thought translation device: a neurophysiological approach to communication in total motor paralysis. Exp Brain Res 124 (2), 223–232.

Land M., N. Mennie, and J. Rusted, "The roles of vision and eye movements in the control of activities of daily living", Perception , Vol. 28, No. 11, 1999, pp. 1311–1328.

Laschi C., E. S. Maini, F. Patanè, L. Ascari, G. Ciaravella, U. Bertocchi, C. Stefanini, P. Dario, "A vestibular interface for natural control of steering locomotion of robotic artifacts: preliminary experiments with a robotic endoscope", in Robotics Research, The 12th International Symposium, S. Thrun, H. Durrant-Whyte, R. Brooks (Ed.s), Springer Tracts on Advanced Robotics (STAR Series), Vol. 28, 2007, pp.537-551.

Laubach, M., Wessberg, J., Nicolelis, M. A., Jun 2000. Cortical ensemble activity increasingly predicts behaviour outcomes during learning of a motor task. Nature 405 (6786), 567–571.

Lebedev, M. A., Nicolelis, M. A., 2006. Brain-machine interfaces: past, present and future. Trends Neurosci 29 (9), 536–46.

Lee K.S., Thomas D.J., "Control of computer-based technology for people with physical disabilities: an assessment manual, Toronto, 1990, University of Toronto Press.

Lee D., Port N.L., Georgopoulos A.P., "Manual interception of moving targets. II. Online control of overlapping submovements", Exp Brain Res, 1997, 116, 421-433.

Lehtonen, J., 2002. EEG-based brain computer interfaces. Master's thesis, Helsinki Univesrsity of Technology, Dept. of Electrical and Comm. Eng.

Leroy A., C. De Saedeleer, A. Bengoetxea, A. Cebolla, F. Leurs, B. Dan, A. Berthoz, J. Mcintyre, G. Cheron, "Mu and alpha rhythmsduring the arrest reaction in microgravity", Microgravity Science and Technology, Vol. 19, pp. 45-50, 2007.

Leuthardt, E. C., Schalk, G., Wolpaw, J. R., Ojemann, J. G., Moran, D. W., Jun 2004. A brain-computer interface using electrocorticographic signals in humans. J Neural Eng 1 (2), 63–71.

Marg, E., Adams, J. E., Sep 1967. Indwelling multiple micro-electrodes in the brain. Electroencephalogr Clin Neurophysiol 23 (3), 277–280.

Mason, S. G., 2005. Dry electrode technology: What exists and what is under development? Tech. rep., Neil Squire Society.

Mayagoitia R.E., A. V. Nene, and P. H. Veltink, "Accelerometer and rate gyroscope measurement of kinematics: An inexpensive alternative to optical motion analysis systems", J. Biomech., vol. 35, pp. 537–542, 2002.

Maynard, E. M., Nordhausen, C. T., Normann, R. A., Mar 1997. The Utah intracortical Electrode Array: a recording structure for potential brain-computer interfaces. Electroencephalogr Clin Neurophysiol 102 (3), 228–239.

McAuley J.H., Rothwell J.C., Marsden C.D., "Frequency peaks of tremor, muscle vibration and electromyographic activity at 10 Hz, 20 Hz and 40 Hz during human finger muscle contraction may reflect rhythmicities of central neural firing", Exp Brain Res, 1997, 114, 525-541

McFarland, D. J., Sarnacki, W. A., Wolpaw, J. R., Jul 2003. Brain-computer interface (BCI) operation: optimizing information transfer rates. Biol Psychol 63 (3), 237–251.

Menon C., C. de Negueruela, J.d.R. Millan, O. Tonet, F. Carpi, M. Broschart, P. Ferrez, A. Buttfield, F. Tecchio, F. Sepulveda, L. Citi,C. Laschi, M. Tombini, P. Dario, P.M. Rossini, and D. De Rossi, "Prospects of brain machine interfaces for space system control", Acta Astronautica, 2008.

Messier J, Kalaska JF (1999) Comparison of variability of initial kinematics and endpoints of reaching movements. Exp Brain Res 125:139–152

Meulenbroek, R. G., & Thomassen, A. J. (1993). Exploitation of elasticity as a biomechanical property in the production of graphic stroke sequences. Acta Psychologica, 82(1–3), 313–327.

Meulenbroek, R. G., Vinter, A., & Desbiez, D. (1998). Exploitation of elasticity in copying geometrical patterns: The role of age, movement amplitude, and limb- segment involvement. Acta Psychologica, 99(3), 329–345.

Meyer DE, Abrams RA, Kornblum S, Wright CE, Smith JE (1988) Optimality in human motor performance: ideal control of rapid aimed movements. Psychol Rev 95:340–370

Meyer, D. E., Abrams, R. A., Kornblum, S., Wright, C. E., & Smith, K. J. E. (1988). Optimality in human motor performance: Ideal control of rapid aimed movements. Psychological Review, 95, 340–370.

Micera S., Navarro X., "Bidirectional Interfaces with the Peripheral Nervous System", In L. Rossini et al. (ED.), "Brain Machine Interfaces for space applications: enhancing astronauts' capabilities", International Review of Neurobiology, 2009, 86, 23-38.

Micera, S., Carrozza, M., Beccai, L., Vecchi, F., Dario, P., 2006. Hybrid bionic systems for the replacement of hand function. Proc IEEE 94 (9), 1752–1762.

Micera S., Citi L., Rigosa J., Carpaneto J., Raspopovic S., Di Pino G., Rossini L., Yoshida K., Dario P., Rossini P.M., "Decoding sensory and motor information from neural signals recorded using intraneural electrodes: towards the development of a neurocontrolled hand prosthesis", Proceedings of the IEEE, Accepted 2009

Micera S., Rigosa J., Carpaneto J., Citi L., Raspopovic S., Guglielmelli E., Benvenuto A., Rossini L., Di Pino G., Cavallo G., Carrozza M.C., Cipriani C., Hoffmann K.P., Dario P., Rossini P.M., "On the control of a robot hand by extracting neural signals from the PNS: preliminary results from a human implantation", 31st annual international conference of the IEEE engineering in Medicine and Biology Society, Minneapolis Minnesota, August 2009

Middendorf, M., McMillan, G., Calhoun, G., Jones, K. S., 2000. Brain-computer interfaces based on the steady-state visual-evoked response. IEEE Trans Rehabil Eng 8 (2), 211–214.

Millán J.R., P.W. Ferrez, T. Seidl, "Validation of Brain-Machine Interfaces during Parabolic Flight", In In L. Rossini, D. Izzo, L. Summerer (ED.), "Brain-Machine Interfaces for space applications: enhancing astronauts' capabilities", International Review of Neurobiology, vol. 86, 2009.

Millán, J. d. R., Mouriño, J., 2003. Asynchronous BCI and local neural classifiers: An overview of the Adaptive Brain Interface project. Neural Systems and Rehabilitation Engineering, IEEE Transactions on 11 (2), 159–161.

Millán, J. d. R., Renkens, F., Mouriño, J., Gerstner, W., Jun 2004. Noninvasive brain-actuated control of a mobile robot by human EEG. IEEE Trans Biomed Eng 51 (6), 1026–1033.

Milner TE and Ijaz MM. The effect of accuracy constraints on three dimensional movement kinematics. Neuroscience 35: 365–374, 1990.

Milner, T. (1992). A model for the generation of movements requiring endpoint precision. Neuroscience, 49, 487-496.

Moran, D. W., 2003. Electrocorticographic (ECoG) control of brain-computer interfaces. In: Proc. WTEC Brain-Computer Interface Workshop. pp. 21–25.

Morasso P., Penso M., suetta G.P., Tagliasco V., "Towards standardization of communication and control systems for motor impaired people", Med Biol Eng Comput, 1979, 17, 481-488

Morasso, P. (1981). Spatial control of arm movements. Experimental Brain Research, 42, 223-227.

Moritz, C. T., Barry, B. K., Pascoe, M. A., & Enoka, R. M. (2005). Discharge rate variability influences the variation in force fluctuations across the working range of a hand muscle. Journal of Neurophysiology, 93(5), 2449–2459.

Müller-Putz, G. R., Scherer, R., Pfurtscheller, G., Rupp, R., 2005. EEG-based neuroprosthesis control: a step towards clinical practice. Neurosci Lett 382 (1-2), 169–174.

Mussa-Ivaldi, F. A., Miller, L. E., Jun 2003. Brain-machine interfaces: computational demands and clinical needs meet basic neuroscience. Trends Neurosci 26 (6), 329–334.

NASA, "NASA 101 - From Vision to Reality", NP-2008-02-498-HQ, 2008, 8 March 2009, http://www.nasa.gov/externalflash/nasa101/index.html

Neumann, N., Kubler, A., Kaiser, J., Hinterberger, T., Birbaumer, N., "Conscious perception of brain states: mental strategies for brain-computer communication", Neurophysiologia, 2003, 41, 1028-1036

Nicolelis, M., "Actions from Thoughts," Nature, Vol. 409, 2001, pp. 403–407.

Nicolelis, M., "Brain-Machine interfaces to restore motor function and probe neural circuits," Nature, Vol. 4, 2003, pp. 417–422.

Novak KE, Miller LE, Houk JC (2000) Kinematics of rapid hand movements in a knob-turning task. Exp Brain Res 132:419– 433.

Novak, K. E., Miller, L. E., & Houk, J. C. (2002). The use of overlapping submovements in the control of rapid hand movements. Experimental Brain Research, 144(3), 351–364.

Novak, K., Miller, L. & Houk, J. (2003). Features of motor performance that drive adaptation in rapid hand movements. Experimental Brain Research, 148, 388-400.

Nykopp, T., 2001. Statistical modelling issues for the adaptive brain interface. Master's thesis, Helsinki Univesrsity of Technology, Dept. of Electrical and Comm. Eng.

Obermaier, B., Neuper, C., Guger, C., Pfurtscheller, G., Sep 2001. Information transfer rate in a five-classes brain-computer interface. IEEE Trans Neural Syst Rehabil Eng 9 (3), 283–288.

Olsen D., and M. Goodrich, "Metrics for evaluating human-robot interactions," Proc. NIST Performance Metrics for Intelligent Systems Workshop , 2003.

Payette J., "Advanced human-computer interface voice processing applications in space," Human Language Technology Conference Proceedings of the workshop on Human Language Technology, Plainsboro, NJ, pp. 416– 420, 1994.

Perzanowski D., A. Schultz, W. Adams, E. Marsh, and M. Bugajska, "Building a Multimodal Human-Robot Interface", IEEE Intelligent Systems, Vol. 16, No. 1, pp. 16–21, 2001.

Pfurtscheller, G., Flotzinger, D., Kalcher, J., 1993. Brain-computer interface: a new communication device for handicapped persons. J Microcomputer App 16 (3), 293–299.

Pfurtscheller, G., Guger, C., Müller, G., Krausz, G., Neuper, C., Oct 2000. Brain oscillations control hand orthosis in a tetraplegic. Neurosci Lett 292 (3), 211–214.

Pinpin L.K., R.S. Johansson, C. Laschi, P. Dario, "Gaze Interface: Utilizing Human Predictive Gaze Movements for Controlling a HBS", IEEE RAS/EMBS International Conference on Biomedical Robotics and Biomechatronics, Scottsdale, AZ, USA, October 20-22, 2008.

Plamondon R (1992) A theory of rapid movements. In: Stelmach GE, Requin J (eds) Tutorials in motor behavior II. Elsevier, Amsterdam, pp 55–69

Plamondon R, Alimi AM, Yergeau P, Leclerc F (1993) Modeling velocity profiles of rapid movements: a comparative study. Biol Cybern 69:119–128

Pletser V., and O. Quadens, "Degraded EEG response of the human brain in function of gravity levels by the method of chaotic attractor", Acta Astronautica, 52:581–589, 2003.

Plonsey R,, Biomagnetic Phenomena. New York: McGraw-Hill, 1969.

Prevost P., Ivanenko Y., Grasso A., Berthoz A., "Spatial invariance in anticipatory orienting behaviour during human navigation", Neuroscience Letters, 2002, 339, 243-247

Rauterberg M., Steiger P., "Pattern recognition as a key technology for the next generation of user interfaces", IEEE International Conference on Systems, Man and Cybernetics, Beijing, China, October 14-17, 1996, 4, 2805-2810

Rickert, J., de Oliveira, S. C., Vaadia, E., Aertsen, A., Rotter, S., Mehring, C., Sep 2005. Encoding of movement direction in different frequency ranges of motor cortical local field potentials. J Neurosci 25 (39), 8815–8824.

Rohrer B, Hogan N (2003) Avoiding spurious submovement decompositions: a globally optimal algorithm. Biol Cybern 89:190–199

Rohrer, B. & Hogan, N. (2006). Avoiding Spurious Submovement Decompositions II: A Scattershot Algorithm. Biological Cybernetics, 94, 409-414.

Rossini L., T. Seidl, D. Izzo, L. Summerer, "Beyond astronaut's capabilities: a critical review", 58th International Astronautical Congress, Hyderabad, 2007

Rossini L., Izzo D., Summerer L. (Eds.), "Brain Machine interfaces for space applications: enhancing astronaut capabilities", International Review of Neurobiology, 86, Elsevier, New York, NY, 2009a.

Rossini L., Izzo D., Summerer L., "Brain-Machine interfaces for space applications", IEEE 31st Annual International Conference of the IEEE Engineering in Medicine and Biology Society, 2009b.

Rossini L., Laschi C., Guglielmelli E., "Reducing Intrinsic Communication Delay in Tele-Navigation Operations by Predicting Human Motor Intentions from Anticipatory Movements", IEEE Robotics and Automation Magazine, Submitted

Rossini P.M., Micera S., Benvenuto A., Carpaneto J., Cavallo G., Citi L., Cipriani C., Denaro L., Denaro V., Di Pino G., Ferreri F., Guglielmelli E., Hoffmann K.P., Raspopovic S., Rigosa J., Rossini L., Tombini M., Dario P., "Double nerve intraneural interface implant on a human amputee for robotic hand control", Clinical Neurophysiology, In Press, 2009.

Rossini P.M., "Implications of Brain Plasticity to Brain Machine Interfaces operation: a potential paradox?" , In L. Rossini, D. Izzo, L. Summerer (ED.), "Brain-Machine Interfaces for space applications: enhancing astronauts' capabilities", International Review of Neurobiology, vol. 86, 2009.

Rossini P.M., M. G. Marciani, M. Caramia, V. Roma, and F. Zarola, ''Nervous propagation along ''central'' motor pathways in intact man: Characteristics of motor responses to ''bifocal'' and ‘‘unifocal’’ spine and scalp non-invasive stimulation,’’ Electroencephalogr. Clin. Neurophysiol., vol. 61, pp. 272–286, 1985

Rossini P.M., Rossini L., Ferreri F., “Transcranial Magnetic Stimulation: a Review”, IEEE Engineering in Medicine and Biology Magazine, January/February, 2010

Rossini PM, Barker AT, Berardelli A, Caramia MD, Caruso G, Cracco RQ, et al. Non-invasive electrical and magnetic stimulation of the brain, spinal cord and roots: basic principles and procedures for routine clinical application. Report of an IFCN committee. Electroencephalogr Clin Neurophysiol 1994; 91: 79-92.

Rossini, P. M., Barker, A. T., Berardelli, A., Caramia, M. D., Caruso, G., Cracco, R. Q., Dimitrijevic´, M. R., Hallett, M., Katayama, Y., Lücking, C. H., 1994. Non-invasive electrical and magnetic stimulation of the brain, spinal cord and roots: basic principles and procedures for routine clinical application. report of an IFCN committee. Electroencephalogr Clin Neurophysiol 91 (2), 79–92.

Rossini, P. M., Rossi, S., Feb 2007. Transcranial magnetic stimulation: diagnostic, therapeutic, and research potential. Neurology 68 (7), 484–488.

Rothwell J., “Meet the brain: neurophysiology”, In L. Rossini et al. (ED.), “Brain Machine Interfaces for space applications: enhancing astronauts’ capabilities”, International Review of Neurobiology, 2009, 86, 51-65, 119-131

Santhanam, G., Ryu, S., Yu, B., Afshar, A., Shenoy, K., March 16-19, 2005. A high performance neurally-controlled cursor positioning system. In: Neural Engineering, 2005. Conference Proceedings. 2nd International IEEE EMBS Conference on. pp. 494–500.

Saunders JA, Knill DC (2003) Humans use continuous visual feedback from the hand to control fast reaching movements. Exp Brain Res 152:341–352

Savitzky, A.; Golay, M.J.E. (1964). "Smoothing and Differentiation of Data by Simplified Least Squares Procedures". Analytical Chemistry 36 (8): 1627–1639

Scherer, R., Müller-Putz, G.R., Pfurtscheller, G., "Flexibility and practicality: Graz Brain-Computer Interface approach", In L. Rossini et al. (ED.), “Brain Machine Interfaces for space applications: enhancing astronauts’ capabilities”, International Review of Neurobiology, 2009, 86, 119-131

Schwartz, A.B., "Useful signal from motor cortex", 2007, J. Physiol, 2007, 579, 3, 581-601

Selen L.P.J., van Dieen J.H., and Beek P.J., Impedance Modulation and Feedback Corrections in Tracking Targets of Variable Size and Frequency, J Neurophysiol 96: 2750–2759, 2006.

Sellers, E. W., Kübler, A., Donchin, E., 2006. Brain-computer interface research at the university of south florida cognitive psychophysiology laboratory: the P300 speller. IEEE Trans Neural Syst Rehabil Eng 14 (2), 221–224.

Serruya, M. D., Hatsopoulos, N. G., Paninski, L., Fellows, M. R., Donoghue, J. P., Mar 2002. Instant neural control of a movement signal. Nature 416 (6877), 141–142.

Shadmehr R, Mussa-Ivaldi FA (1994) Adaptive representation of dynamics during learning of a motor task. J Neurosci 14:3208– 3224

Siciliano, B., and Villani, L., 1999, "Robot Force Control", Kluwer Academic Publishers, Boston, MA.

Solov'yev V., "Problems of human-machine interaction on Space Flight," Humans and Machines in Space, Proceedings of the 29th Goddard Memorial Symposium, edited by M. &. K. Johnson, Univelt publisher, pp. 73–77, 1991.

Souvestre P., and C. Landrock, "Biomedical performance monitoring and assessment of astronauts by means of ocular-vestibular monitoring system," Acta Astronautica, Vol. 60 pp. 313–321, 2007.

Space Adventures Home Page, Space Adventures Ltd., 8 March 2009, http://www.spaceadventures.com/index.cfm

Summerer L., D. Izzo, and L. Rossini, "Prefance – Why the BMI "renaissance" could affect the future of space exploration", ", In L. Rossini, D. Izzo, L. Summerer (ED.), "Brain-Machine Interfaces for space applications: enhancing astronauts' capabilities", International Review of Neurobiology, vol. 86, 2009a.

Summerer L., D. Izzo, and L. Rossini, "Brain-Machine interfaces for space applications: Research, Technological Development and Opportunities", ", In L. Rossini, D. Izzo, L. Summerer (ED.), "Brain-Machine Interfaces for space applications: enhancing astronauts' capabilities", International Review of Neurobiology, vol. 86, 2009b.

Sutter, E. E., 1992. The brain response interface: communication through visually-induced electrical brain responses. J Microcomputer App 15 (1), 31–45.

Tanaka, K., Matsunaga, K., Wang, H., Aug. 2005. Electroencephalogram-based control of an electric wheelchair. Robotics, IEEE Transactions on [see also Robotics and Automation, IEEE Transactions on] 21 (4), 762–766.

Taylor, A. M., Christou, E. A., & Enoka, R. M. (2003). Multiple features of motor-unit activity influence force fluctuations during isometric contractions. Journal of Neurophysiology, 90(2), 1350–1361.

Taylor, D. M., Tillery, S. I. H., Schwartz, A. B., Jun 2002. Direct cortical control of 3D neuroprosthetic devices. Science 296 (5574), 1829–1832.

Taylor, D., Tillery, S., Schwartz, A., June 2003. Information conveyed through brain-control: cursor versus robot. Neural Systems and Rehabilitation Engineering, IEEE Transactions on [see also IEEE Trans. on Rehabilitation Engineering] 11 (2), 195–199.

Tecchio, F., Rossini, P. M., Pizzella, V., Cassetta, E., Romani, G. L., Aug 1997. Spatial properties and interhemispheric differences of the sensory hand cortical representation: a neuromagnetic study. Brain Res 767 (1), 100–108.

Teulings, H. & Romero, D. (2003). Submovement Analysis in Learning Cursive Handwriting or Block Print. Proceedings of the 11th Conference of the International Graphonomics Society (IGS2003), , 107-110.

Todorov E., and Jordan M.I., Optimal feedback control as a theory of motor coordination, Nature Neuroscience, vol. 5, n. 11, 1226:1235, 2002

Tonet O. , M. Marinelli, L.Citi, P.M. Rossini, L. Rossini, G. Megali, P. Dario, "Defining brain–machine interface applications by matching interface performance with device requirements", Journal of Neuroscience Methods, 167, 91–104, 2008.

Truccolo W, Friehs GM, Donoghue JP, Hochberg LR., "Primary motor cortex tuning to intended movement kinematics in humans with tetraplegia.", J Neurosci., 2008, 28, 5, 1163-78

Vallbo, A. & Wessberg, J. (1993). Organization of motor output in slow finger movements in man. The Journal of Physiology, 469, 673-691.

Velliste, M., Perel, S., Spalding, M.C., Whittford, A.S., Schwartz, A.B., "Cortical control of a prosthetic arm for self-feeding", Nature, 2008, 453, 1098-1101

Vidal M., M. Lipshits, J. McIntyre, A. Berthoz, "Gravity and spatial orientation in virtual 3D-mazes", J. Vestib. Res. 13, 273-286, 2003.

von Hofsten, C. (1979). Development of visually guided reaching: The approach phase. Journal of Human Movement Studies, 5, 160-178.

Vuckovic, A., Sepulveda, F., 2006. EEG gamma band information in cue–based single trial classification of four movements about right wrist. In: Proc. MAIA Workshop on Brain Computer Interfaces.

Wang, C., Guan, C., Zhang, H., 2005. P300 brain-computer interface design for communication and control applications. Conf Proc IEEE Eng Med Biol Soc 5, 5400–5403.

Wang, Y., Wang, R., Gao, X., Hong, B., Gao, S., Jun 2006. A practical vep-based brain-computer interface. IEEE Trans Neural Syst Rehabil Eng 14 (2), 234–239.

Weiskopf, N., Mathiak, K., Bock, S. W., Scharnowski, F., Veit, R., Grodd, W., Goebel, R., Birbaumer, N., Jun 2004. Principles of a brain-computer interface (BCI) based on real-time functional magnetic resonance imaging (fMRI). IEEE Transactions on Biomedical Engineering 51 (6), 966–970.

Wesseberg, J., Stambaugh, C., Kralik, J., Beck, P., Laubach, M., Chapin, J., Kim, J., Biggs, J., Srinivasan, M., and Nicolelis, M., "Real-time prediction of hand trajectory by ensemble of cortical neurons in primate," Nature, Vol. 408, 2000, pp. 361–365.

Will B., Dalrymplr-Alford J,m Wolff M., Cassel J.C., "The concept of brain plasticity-Paillard's systemic analysis and emphasis on structure and function (followed by the translation of a seminal paper by Paillard on plasticity)", Behav Brain Res., 2008, 192, 1, 2-7

Wilson, J. A., Felton, E. A., Garell, P. C., Schalk, G., Williams, J. C., Jun 2006. Ecog factors underlying multimodal control of a brain-computer interface. IEEE Trans Neural Syst Rehabil Eng 14 (2), 246–250.

Wisleder, D., & Dounskaia, N. (2007). The role of different submovement types during pointing to a target. Experimental Brain Research, 176(1), 132–149.

Wolpaw, J., "Brain-computer interfaces as new brain output pathways," Journal of Physiology, Vol. 579, 2007, pp. 613–619.

Wolpaw, J., Birbaumer, N., McFarland, D., Pfurtscheller, G., and Vaughan, T., "Brain-Computer interfaces for communication and control," Journal of Clinical Neurophysiology, Vol. 113, 2002, pp. 767–791.

Wolpaw, J. R., McFarland, D. J., Dec 2004. Control of a two-dimensional movement signal by a noninvasive brain-computer interface in humans. Proc Natl Acad Sci U S A 101 (51), 17849–17854.

Wolpaw, J. R., McFarland, D. J., Neat, G. W., Forneris, C. A., Mar 1991. An EEG-based brain-computer interface for cursor control. Electroencephalogr Clin Neurophysiol 78 (3), 252–259.

Woodworth, R. S. (1899). The accuracy of voluntary movement. Pycbologcal Review, 3, (Monograph Supplement), 1-119. Date of accptance: October 7, 1998

Yoo, S.-S., Fairneny, T., Chen, N.-K., Choo, S.-E., Panych, L. P., Park, H., Lee, S.-Y., Jolesz, F. A., Jul 2004. Brain-computer interface using fmri: spatial navigation by thoughts. Neuroreport 15 (10), 1591–1595.

Luca Rossini