New proposals for EEG and fMRI based Brain Computer Interface technology

Contents

CHAPTER 1

INTRODUCTION

One of most important characteristic of humans resides in the ability of communicate mainly through speech, gesturing, or writing. Moreover, in the history of mankind people have been successful in finding other ways of expression like music, painting, sculptures, photography, film, etc. We are living the century of the progress, that changed totally our way to live and to communicate. In particular, recent advances in technology allows also to probe and monitor physiological processes inside the human body, like the blood pressure, the heart rate variability, the muscular activity, and the brain electrical activity in efficient and non invasive ways. Such activities have been already used as information in new communication channels.

The brain computer interface (BCI) technology can be considered a new communication method that provides a direct connection between the brain and an external device. More specifically, the idea underlying BCIs is to detect patterns of brain activity and to link these patterns to commands executed by a computer or other devices. In 2000 Wolpaw et al. defined a BCI as a communication system that does not depend on the normal output pathways of peripheral nerves and muscles [1]. Thus, BCI communication could substantially improve quality of life for people with very little voluntary muscle control or affected by locked-in syndrome. The locked-in syndrome is a condition in which patients are fully conscious and aware of what is happening in their environment but are not able to communicate or move. A disease that is known to lead to the locked-in syndrome is amyotrophic lateral sclerosis (ALS) that is a progressive, neurodegenerative disease and is characterized by the death of motor neurons which in turn leads to the loss of control over voluntary muscles. Also multiple sclerosis, stroke or other cerebral incidents leading to the infarction or degeneration of parts of the brain can cause the locked-in syndrome. BCI is a promising means to give back basic communication abilities and a small degree of autonomy to people with severe motor disabilities. Prototype systems allow, for example, to choose symbols from an alphabet by concentrating on specific mental tasks or to move artificial limbs, solely by imagining movements[2].

Since the first experiments of electroencephalography (EEG) by Hans Berger in 1929 [3], the idea that brain signals could be used as a communication channel has rapidly emerged. The EEG discovery has enabled researchers to measure the human's brain activity and to start trying to decode this activity. However, it is only in 1973 that the first prototype of a BCI came out, in the laboratory of Dr. Vidal [4]. To date, the modern EEG acquisition devices are relatively inexpensive and easily transportable, and for these reasons and because the setup of recording sessions takes only little time, the EEG is used in many BCI systems.

The first step of the process involved in the development of a BCI system is to measure the signals on the scalp of a subject. The brain signals are then processed according to the particular cerebral waves that the system use (μ, β rhythm, sensory motor rhythms, slow cortical potential, event related potential). Then, a translation algorithm is necessary to convert the brain features extracted into control commands using linear or nonlinear equations. During this step the adaptation of specific parameters is performed with relation to the output device that will be controlled (cursor movement, letter or icon selection, external device control). Furthermore, the BCI system has to provide a feedback for the user that can be visual, haptic or auditory.

An EEG-based BCI has been used in this thesis to evaluate a new method for feature extraction, in particular a new approach based on non linear time series analysis is proposed. The recent progresses in the theory of nonlinear dynamics and complex systems mathematics provide new methods for the study of brain signals [5]. Nonlinearity as a necessary condition for chaotic behaviour is present in many dynamical systems found in nature, including the brain at the cellular level, since the dynamics of individual neurons are governed by threshold and saturation phenomena [6].

Nowadays, about one-third of BCI designs have used power-spectral features, so linear methods, because of their ease of application, computational speed and direct interpretation of the results. The goal of my research activity is to improve the potentiality of the classical feature extraction method using a non linear parameter, the Lyapunov exponent, using a fast algorithm proposed by Bucolo et al.[7], particularly suitable for real time processes, thus also for BCI.

Brain computer interface can improve the quality of life not only for people with motor impairment but indirectly also for other categories because BCI are also used for the treatments of medical disorders. A lot of research group use the BCI technology with the purpose to investigate the brain behaviour. For example, patients with attention-deficit and hyperactivity disorder (ADHD) [8] were treated with self regulation of 12–15 Hz EEG brain activity. Epilepsy patients were trained to suppress epileptic activity by self-regulation of slow cortical potentials (SCP) [9]. If the neurobiological basis of the disorder is known in terms of abnormal activity in a certain region of the brain, functional magnetic resonance image (fMRI) based BCI can be targeted to those regions with greater specificity for treatment. Many types of disorders, namely, memory disorders, chronic pain, motor disorders, psychopathy, social phobia, depression, emotional disturbances, anxiety, and posttraumatic disorder might be treated with fMRI based BCI.

FMRI based BCI is a general system employing real-time fMRI technology that enables various applications including training to self-regulate activity in precisely specified regions of the brain to study plasticity and functional reorganization, application of the knowledge so derived in psychophysiologic treatement, quality assurance of neuroimaging data, presurgical patient assessment and teaching of brain imaging methods [10]. In the context of a self regulation experiment, fMRI based BCI can extract BOLD activity from voxels in one or more regions of interest (ROIs) in the brain to compute average activity in the ROIs, or correlation coefficient of activity between ROIs, or any other function that could be used to provide feedback to the participant. However, fMRI based BCI need not necessarily function based on self-regulation of brain activity alone. There has recently been much progress in the detection and discrimination of mental states using fMRI data [11].

In recent years, many imaging studies have focused on defining a network of brain structures involved in the processing of pain. Additionally, it has been shown that stimulus-evoked pain, which is a frequent symptom of neuropathic pain, cause distinct patterns of brain activation [25]. In the present study, an fMRI experimental protocol is analyzed with the purpose to demonstrate that in response to painful stimulation it is possible to regulate activation in the so called pain processing areas, contributing to the research about the cure of patients that suffer of chronic pain.
In this thesis also different EEG-based BCI applications are introduced. The main aim is to provide to people with motor impairment a new way for expressing their feelings. Many of the applications proposed allow to a user to create artistic representation or to compose music.
Some laboratories have already begun to develop BCI systems that provide people with severe motor disabilities an alternative way to express their creativity, thus improving their quality of life. Kübler et al. [12], for example, developed a BCI application that allows screen painting using event related potential (ERP). Another example that shows the possibility of

creating recreational and therapeutic devices is proposed by Miranda et al.[13], who introduce an EEG-based BCI to compose and perform music.

This thesis is organized into four chapters. Chapter 2 contains background material, Chapter 3 describes two experimental BCI protocols and the new methods used to analyze the brain signals acquired during an EEG and an fMRI task, Chapter 4 introduce different BCI applications designed and realized in laboratory, and Chapter 5 contains a summary and an outlook on future work. In Chapter 2, a general introduction to the field of BCI research is given. Topics reviewed include different methods for measuring brain activity, the types of neurophysiologic signals that can be used in BCI systems, algorithms for extracting useful features from neurophysiologic signals, and BCI applications. This chapter provides an overview particularly on those methods that mainly are relevant in the context of the thesis. In section 2.3, electroencephalogram (EEG) and functional magnetic resonance imaging (fMRI) techniques for brain signals acquisition are introduced more in detail respect to the other techniques like electrocorticogram (ECoG), magnetoencephalogram (MEG) or magnetic resonance imaging (MRI). Section 2.4 deals with two different approach for the discrimination of neurophysiologic signals. The first approach concerns the changes in brain signals resulting from perception and processing of stimuli. In the second one users control their brain activity by concentrating on a specific mental task, for example imagination of hand movement can be used to modify activity in the motor cortex. In BCIs after the data acquisition phase, the features extraction module allows to transform raw neurophysiologic signals into control commands for different kind of applications. For this purpose the temporal, frequency and spatial domain processing methods for features extraction in BCIs are discussed in section 2.5, with particular attention on non linear methods like Lyapunov exponent extraction.

In Chapter 3, two experimental configurations are introduced. For the first protocol the user performs a sensory motor task imaging to move the left or right hand in relation to an arrow displayed on a screen. A new approach based on nonlinear time series analysis to extract EEG signals features is proposed. In particular a fast algorithm that computes the largest Lyapunov exponent was used. The results obtained reveal the capability and the potentiality of this method in respect to the classical approach. The second configuration is related to an fMRI based BCI protocol. The oxygenation level-dependent (BOLD) effects in pain processing areas in response to painful stimulation is investigated . Functional connectivity between spatially remote brain signals is computed with the aim to demonstrate the possibility for a subject to regulate the BOLD trend.

In Chapter 4, three different kinds of applications designed are described in details. For the first one the experimental setup of a BCI system that allows to a user to control a robotic hand using event related potentials and sensory motor rhythms is introduced. The second application consists on an interactive system that allows to create luminous artistic representation. In particular the images shown refer to the paths of light that the user creates controlling two twin robots through his sensory motor rhythms. Finally, three applications that provide alternative form of communication for people with motor disabilities are described. The setup and configuration of the music composer, painting and writing application are documented separately.

In Chapter 5 the contributions of this thesis are summarized and an outlook on possible extensions of the presented work is provided.

CHAPTER 2

BRAIN COMPUTER INTERFACE

2.1 DEFINITION

In the last decades the analysis of the brain signals, as a valid diagnostic approach in neurology, has roused a growing interest. Particularly in the eighties for the first time the analysis of cerebral waves has been used in a research contexts for the design of human machine interfaces (HMI). Among these it is included the brain computer interface (BCI) [1] that provides a direct connection between the brain and an external device, through the analysis of brain signals acquired from multiple electrodes placed on the scalp of a subject.

In 2000 Wolpaw et al. defined a brain-computer interface as a communication system that does not depend on the normal output pathways of peripheral nerves and muscles [14]. In other words a BCI can be an alternative method, specially for subjects affected by particular diseases, for acting on the world. The principal reason for interest in BCI development is the possibilities it can offers for providing new augmentative communication technology to those who are paralyzed or have severe motor disabilities. With this aim, over the past three decade, many laboratories have begun to design BCI application. The firsts implemented brain wave controlled tasks as the spelling [15], allowing to a subject to select letters of the alphabet, and cursor movement control [16], have increased the attention toward this technology. Some significant examples are controlling a wheelchair on established paths using thought [17] or applications in home automation and domotics [18]-[19]. To date a wide range of BCI systems have been designed also for other purposes like the development of interactive platform used on video game console [20].

The BCI technology can be classified in two categories, independent and dependent. Independent BCIs provide the brain with wholly new output pathways without using the normal pathways of peripheral nerves and muscles. Dependent BCIs are of lower theoretical interest than independent one because normal channel of communication like extra ocular muscles and cranial nerves are also used. Thus, for people with the most severe neuromuscular disabilities, who may lack all normal output channels, independent BCIs are likely to be more useful.

Successful BCI operation requires that the user develop and maintain a new strategy of communication, a strategy that consists not of proper muscle control but rather of proper control of specific electrophysiological signals, and it also requires that the BCI translate that control into output that accomplishes the user's intent.

Detailed reports about the work in many BCI laboratories around the world can be found in the 2006 BCI special issue of IEEE Transactions on Neural Systems and Rehabilitation

Engineering [21]. Other reviews can be found in the articles of Wolpaw et al. [14], Lebedev and Nicolelis [22], Birbaumer and Cohen [23], and Mason et al. [24].

2.2 BCI ARCHITECTURE

A control system has input, output, components that translate input into output, and a protocol that determines the onset, offset, and timing of operation. In the case of a BCI the input are the brain signals that are recorded, processed in real-time and translated into control commands, the output, that operate external devices or a computer display. Figure 1 shows these elements and their principal interactions.

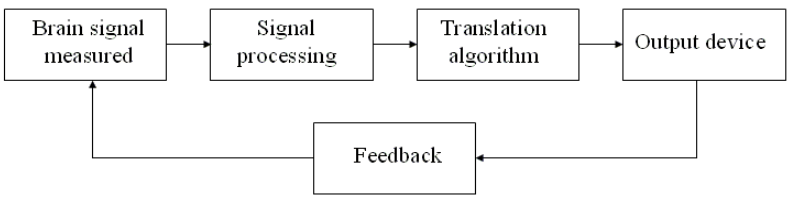

Figure 1 - Building blocks of a BCI. A subject performs a specific cognitive task or concentrates on a specific stimulus. Brain signals are acquired and then processed with signal processing and translation algorithms. The outcome of the translation is fed into an application, for example a spelling device, or an external device. The application generates feedback to inform the subject about the outcome of translation.

Research areas include evaluation of all blocks. For the brain signals acquisitions, different aspects and methods have been investigated: invasive and non invasive technologies, different types of electrodes, the sampling rate, the methods for measuring brain activity. In particular, in this thesis we focus on non invasive EEG and fMRI as the measurement technologies. A preprocessing is needed for cleaning and denoising input data in order to enhance the relevant information embedded in the signals [28]. Feature extraction and translation are processes that can be performed by using different linear or nonlinear signals processing and classification methods [1]. The classification step assigns a class to a set of features extracted from the signals [29]. This class corresponds to the kind of mental state identified. In addition, being the brain signals unique for each subject, an adaptation algorithm is needed to optimize the performance of BCI processes in relation to each user. Once the mental state is identified, a command is associated to this mental state in order to control a given application such as a speller or a robot [27]. Then, as for the brain's normal neuromuscular output channels, a BCI depends on feedback and on adaptation of brain activity based on that feedback, which can be visual, haptic, or auditory.

EEG signals are highly subject-specific and for this reason BCI systems must be calibrated and adapted to each user. A considerable calibration work is necessary to have an efficient BCI system. This work is generally done offline and aims at calibrating the classification algorithm, calibrating and selecting the optimal features, selecting the relevant sensors, etc. In order to do so, a training data set must have been recorded previously while the user perform each mental task of interest several times, according to given instructions. The recorded EEG signals will be used as mental state examples in order to find the best calibration parameters for this subject.

Thus, the BCI operation depends on the interaction of two adaptive controllers: the user's brain, which produces the signals measured by the BCI; and the BCI itself, which translates these signals into specific commands.

2.3 SIGNAL ACQUISITION

Different methods to measure brain activity can be used in a BCI. In 1929 the neuropsychiatric Hans Berger recorded for the first time the brain's spontaneous electrical activity [3]. Since then the development of the electroencephalography (EEG) led to the birth of other important methods for acquiring brain signals/imaging like the magnetoencephalography (MEG), that is the technique for measuring the magnetic fields produced by electrical activity in the brain; the functional magnetic resonance imaging (fMRI); or tomographic imaging technique like SPECT and PET. Each method has its own advantages and disadvantages. Depending on the needs and on the willingness of the user one of the methods will be choose for acquiring the brain signal for designing a BCI. Clearly, the development of new methods for measuring brain activity has the potential to yield advanced BCI systems.

In the following paragraphs an overview of EEG and fMRI technique is presented.

2.3.1 Electroencephalogram

The most widely used non invasive techniques for measuring electrical brain activity is probably the electroencephalogram (EEG). Since its discovery the EEG has been employed to answer many different questions about the functioning of the human brain and has served as a diagnostic tool in clinical practice.

The EEG technique consists in the measure of the potentials on the scalp surface caused by the extracellular currents that flow towards the region of the synapse [30].

The EEG signal acquisition method give a best temporal resolution compared to the other neuroimaging techniques like fMRI, SPECT and PET. Moreover the devices required to the EEG are less unmanageable with respect to the other methods

(MEG, fMRI, SPECT, PET), that typically monopolize a whole room. The EEG required devices are simple and cheap and the preparation of measurements takes only a small amount of time. EEG signals are recorded with small silver/silver chloride electrodes with a radius of about 5mm, placed on the scalp at standardized positions, like the 10-20 international system (see Fig. 2). Conductive gel or saltwater is used to improve the conductivity between scalp and electrodes. To affix the electrodes to the scalp, often an electrode cap is used. EEG signals are always recorded with respect to reference electrodes, i.e. EEG signals are small potential differences (0 - 100 μV) between electrodes placed at different positions on the scalp. The reference is needed because provides a baseline against which the activity at each of the other electrodes can compared. The reference electrode must not cover muscles, because its contractions are induced by electrical signals, for this reason usually is placed at the mastoid bone which is located behind the ear. The other electrodes are placed following a standardized system. Over the right hemisphere electrodes are labeled with even numbers. Odd numbers are used for those on the left hemisphere. Those on the midline are labeled with a z. The capital letters stands for the location of the electrode (C=central, F=frontal, Fp= frontal pole, O= occipital, P= parietal and T= temporal).

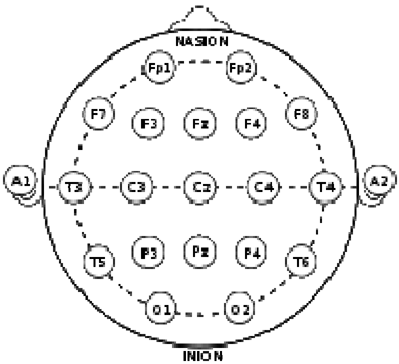

Figure 2 - Electrode placement according to the 10-20 international system. Odd numbers indicate electrodes located on the left side of the head. Even numbers indicate electrodes located on the right side of the head. Capital letters are used to reference each cortical zone, namely frontal (F), central (C), parietal (P), temporal (T), and occipital (O). Fp and A stand for frontal pole and auricular. The designation 10-20 comes from the percentage ratio of the inter-electrode distances with respect to the nasion-inion distance.

When all the electrodes are placed at the right position the electrical potential can be measured. According to a person's state the frequency and the shape of the EEG signal change. If a person is awake beta activity can be recognized, which means that the frequency is relatively fast. The alpha activity, which have a slower frequency, can be noted before that a person falls asleep. The slowest frequencies are called delta activity, which occur during sleep.

An important aspect of an EEG based BCI is the presence of artifacts that can invalidate the information deriving from the brain signals. Artefacts often have much larger amplitude than the signals of interest, thus the artefacts removal and filtering procedures have to be applied online before an analysis of EEG signals can be attempted. Artefacts can be due to physiological or non physiologic sources. Physiological sources for artefacts include eye movements and eye blinks, muscle activity, heart activity, and slow potential drifts due to transpiration. Non physiologic sources for artefacts include power supply line noise (at 50 Hz or 60 Hz), noise generated by the EEG amplifier, and noise generated by sudden changes in the properties of the electrode-scalp interface.

EEG is used in many BCI systems because modern acquisition devices are relatively inexpensive and easily transportable and because the setup of recording sessions takes only little time.

Moreover EEG method allows to measure electric potentials of the brain at a temporal resolution on the order of milliseconds.

2.3.2 Functional magnetic resonance imaging and other methods for signal acquisition

The functional magnetic resonance (fMRI) imaging is a non invasive test that measure the metabolic changes that take place in an active part of the brain, in other words this method allows to detect the brain areas which are involved in a task, a process or an emotion. This method is a MRI-based neuroimaging technique. MRI is based on a physics phenomenon, called nuclear magnetic resonance (NMR), which was discovered in1930s by Felix Bloch (working at Stanford University) and Edward Purcell (from Harvard University). In this resonance, magnetic fields and radio waves cause atoms to give off tiny radio signals.

The fMRI brain mapping is done by setting up an MRI scanner in a special way so that the increased blood flow to the activated areas of the brain shows up on functional MRI scans.

The first MRI equipment in health were available at the beginning of the 1980s. In 2002, approximately 22000 MRI scanners were in use worldwide, and more than 60 million MRI examinations were performed. MRI uses a powerful magnetic field, radio frequency pulses and a computer to produce detailed pictures of organs, soft tissues, bone and virtually all other internal body structures. The images can then be examined on a computer monitor. Detailed MR images allow physicians to better evaluate various parts of the body and determine the presence of certain diseases that may not be assessed adequately with other imaging methods such as x-ray, ultrasound or computed tomography.

The fMRI cannot detect absolute activity of brain regions. It can only detect difference of brain activity between several conditions. Functional MRI allows to noninvasively measure the so called blood oxygen level dependent (BOLD) signal. The BOLD signal does not directly represent neuronal activation but rather depends on the level of oxygenated and deoxygenated hemoglobin and on the hemodynamic response to neuronal activation. The peak of the BOLD signal is typically very broad and observed four to five seconds after the neuronal activation (Fig.3). Compared to MRI, fMRI does not depend on contrast agents although contrast agents enable far greater detection sensitivity than BOLD signal. Higher BOLD signal intensities arise from decreases in the concentration of deoxygenated hemoglobin.

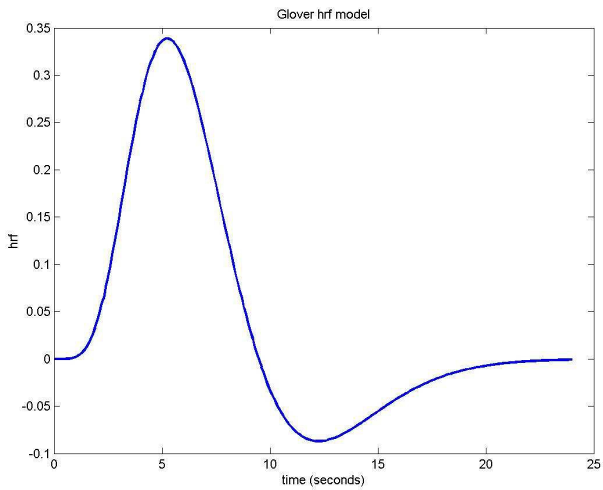

Figure 3 - Simulated neural response to a single stimulus.

During the fMRI acquisitions the patient is asked to alternatively perform several tasks or is stimulated to trigger several processes or emotions. Each of these conditions is repeated several times and can be separated by rest periods. The combination of these conditions is called a functional MRI paradigm. The stimuli are usually audio-visual but can involve more complex systems (odors, tastes, etc.). An fMRI experiment usually lasts 1-2 hours. The subject will lie in the magnet and a particular form of stimulation will be set up and MRI images of the subject's brain are taken. In the first step a high resolution single scan is taken. This is used later as a background for highlighting the brain areas which were activated by the stimulus. In the next step a series of low resolution scans are taken over time, for example, 150 scans, one every 5 seconds. For some of these scans, the stimulus will be presented, and for some of the scans, the stimulus will be absent. The brain images in the two cases can be compared, to see which parts of the brain were activated by the stimulus. The analysis is done using a series of tools which correct distortions in the images, remove the effect of the subject moving their head during the experiment. Then to generate a functional map from fMRI data set, signal intensities of images obtained during control and stimulation periods are compared on a voxel-by-voxel basis. Voxels passing a statistical

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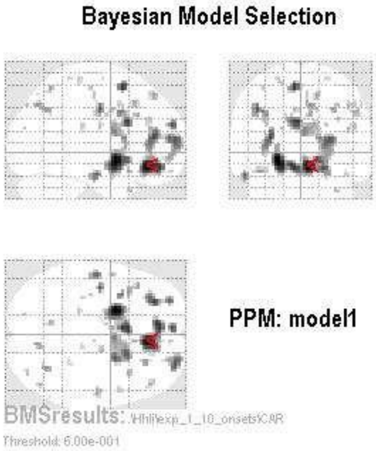


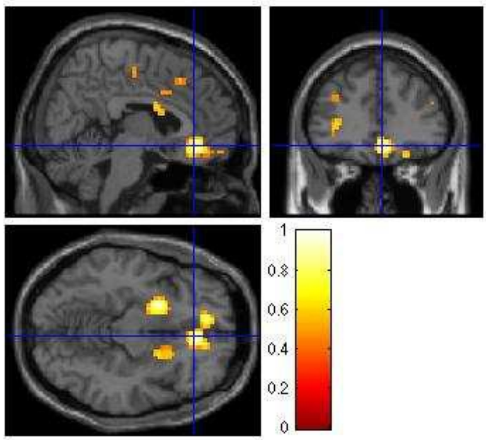


Figure 4 - Examples of the activation maps produced by the software package SPM[31]. The colour scale (from red to yellow) represents the percentage signal change observed in that region.

Functional MRI is becoming the diagnostic method of choice for learning how a normal, diseased or injured brain is working, as well as for assessing the potential risks of surgery or other invasive treatments of the brain. In BCI research fMRI has been used in basic proof of concept systems [32]-[33] and to elucidate the brain mechanisms underlying successful self regulation of brain activity [34] To date, the use in practical BCI systems is not so diffused because fMRI devices are technically demanding, expensive and cannot be easily moved from one place to another.

The spatial resolution of fMRI is very good, structures of the size of a few millimetres can be localized with the fMRI. In addition, signals can be acquired from the whole brain and not only from the cortex, as for example with the EEG. The temporal resolution is relatively low when compared to methods that directly measure electrical brain activity. Therefore, some research groups are working around this issue by combining fMRI with data collection techniques such as EEG or magnetoencephalography (MEG), which have much higher temporal resolution but rather poorer spatial resolution.

2.4 NEUROPHYSIOLOGIC SIGNALS

The goal of an ideal BCI system is to directly detect every wish or intention of its user and perform the corresponding action. However, it is very difficult to clearly define how wishes or intentions are related to neurophysiologic signals. The users have to acquire conscious control over their brain, in some cases learning to focus the attention in particular events like the presence of some stimuli and in other cases performing training sessions. Consequently, some features of particular neurophysiologic signals are used to interpret the intentions of a subject. In BCI systems two fundamentally different approaches exist to achieve the goal of translating wishes in action . In the first approach subjects perceive a set of stimuli displayed by the BCI system and can control their brain activity by focusing onto one specific stimulus. The changes in neurophysiologic signals resulting from perception and processing of stimuli are termed event-related potentials (ERPs). In the second approach users control their brain activity by concentrating on a specific mental task, for example

imagination of hand movement can be used to modify activity in the motor cortex. In this approach feedback signals are often used to let subjects learn the production of easily detectable patterns of neurophysiologic signals. The types of signals resulting from concentration on mental tasks together with the corresponding BCI paradigms are called oscillatory activity that can be classified depending on the frequency bands. The most commonly oscillatory activity involved in BCI are the sensory motor rhythm (SMR) that occur during motor tasks and even motor imagery in the frequency range of 8–32 Hz.
In the following paragraphs the attention is focused mainly on a wave named P300, a positive deflection in the EEG that appears approximately 300 ms after the presentation of a stimulus, and on the oscillatory activity that occur during motor imagery task, the SMR.

2.4.1 Event-Related Potentials

Event-related potentials are voltage fluctuations that are associated in time with some physical or mental occurrence, for example after the presentation of a stimulus, before execution of a movement, or after the detection of a novel stimulus. These potentials can be recorded from the human scalp and extracted from the ongoing electroencephalogram by means of filtering and signal averaging. Because the temporal resolution of these measurements is on the order of milliseconds, ERPs can accurately measure when processing activities take place in the human brain. Traditionally, ERPs are recorded with the EEG and have been used in neuroscience for studying the different stages of perception, cognition, and action. Event-related potentials can be divided into two classes. Exogenous ERPs are the result of early, automatic processing of stimuli and the features of this signals depends mainly on the physical stimulus characteristics. The motor-related potentials (MRPs) are exogenous ERPS and are independent of the perception or processing of stimuli. The events to which MRPs are related are the preparation or imagination of movements. MRPs are slow negative potentials, observable over the sensorimotor cortex before movement onset or during movement imagination. MRPs have been also used in combination with sensorimotor rhythms in a BCI based on motor imagery [35].

Endogenous ERPs are the result of later, more conscious processing of stimuli and have characteristics that depend mainly on the stimulus context, i.e. on the task the subject was given and on the attention the subject pays to the stimuli. The P300 is an endogenous ERP that has gained much attention in the neuroscientific and medical research. The name of this particular signal denotes the positive deflection in the EEG, appearing approximately 300 ms after the presentation of rare or surprising, task-relevant stimuli [36]. Furthermore, different components of ERPs can be observed, for example positive deflection after 200 ms and negative one after 100 ms, as shown in figure 5. The P300 reflects high-level processing of stimuli and for this reason in BCI systems is favorite respect to the other ERP components that reflect low-level, automatic processing of stimuli.

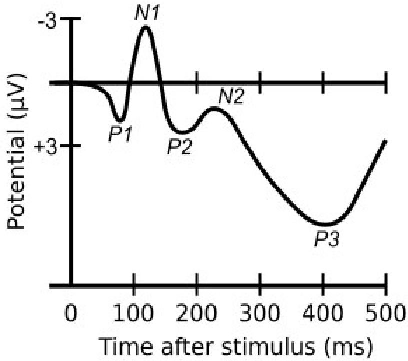


Figure 5 - Typical P300 wave. The P300 (or P3) is a positive deflection in the EEG, which appears approximately 300 ms after the presentation of a rare or surprising stimulus. A series of negative and positive components (N1, P2, N2) precedes the P3. While the P3 reflects high-level processing of stimuli, the earlier components reflect low-level, automatic processing of stimuli.

To evoke the P300, subjects are asked to observe a random sequence of two types of stimuli. One stimulus type (the oddball or target stimulus) appears only rarely in the sequence, while the other stimulus type (the normal or nontarget stimulus) appears more often. Farwell and Donchin on 1988 for the first time exploited the P300, observed after visual stimulations, in a BCI system [37]. They described the P300 speller which allows to a subject to select desired letter just observing a matrix containing symbols from the alphabet displayed on a screen. Rows and columns of the matrix are flashed in random order, and flashes of the row or column containing the desired symbol constitute the oddball stimulus, while all other flashes constitute non target stimuli.

The use of ERPs is particularly suitable for subjects with concentration problems or for subjects not willing to go through a long training phase because no user training is necessary. Indeed, ERPs occur as a natural response of the brain to stimulation, and this is an important advantage. A disadvantage is that communication depends on the presentation and perception of stimuli. Subjects are thus required to have remaining cognitive abilities. Moreover, BCI systems based on ERPs have only limited application scenarios because a device to present stimuli is needed and because users need to pay attention to stimuli, even in the presence of other unrelated, distracting stimuli.

In the present thesis the P300 waves are used for designing some application described in chapter 4.

2.4.2 Oscillatory activity

Sinusoid like oscillatory brain activity occurs in many regions of the brain and changes according to the state of subjects. Oscillation in particular frequency bands could play a key role in the emergence of memories, emotions, thoughts, and actions. Typically observable oscillatory activity in the EEG are the delta (1 - 4 Hz), theta (4 -8 Hz), alpha and mu (8 - 13 Hz)1, beta (13 - 25 Hz), and gamma (25 - 40 Hz) rhythms. The changes in power of specific bandwidths is used as control signals for BCI systems. In particular, sensorimotor rhythms (SMR) are specific oscillations in the frequency range of 8–32 Hz that occur during motor tasks and even motor imagery and can be observed over the sensorimotor cortex also when a subject does not perform movements. These oscillations are decreased in amplitude when movements of body parts are imagined or performed. Imagination of movement of the left hand corresponds to a decrease in SMR amplitude over the right sensorimotor cortex, whereas imagination of movement of the right hand corresponds to a decrease in amplitude over the left sensorimotor cortex. Figure 6 shows the activated brain regions during a motor imagery task.

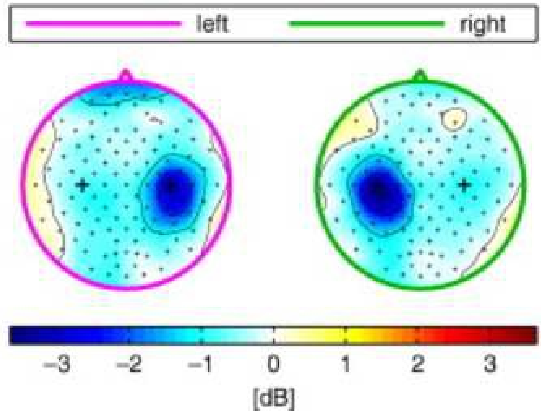


Figure 6- Brain areas that are active during a motor imagery task. If the user thinks to move the left hand a decrease in SMR amplitude can be noticed over the right sensorimotor cortex and the contrary for the imagination of the right hand movement.

Feedback training has to be used to let users acquire control over sensorimotor rhythms because the changes in SMR occurring in untrained users are usually not strong enough to be detected by a classification algorithm. Thus the training that subjects have to perform is a disadvantage also because it can take several weeks before users are able to reliably control a BCI. Therefore, BCI systems based on oscillatory activity might be less suited for subjects with concentration problems or for subjects who are not willing to go through a long training phase. But if oscillatory activity are used, more flexible BCI systems can be imagined, in respect to the systems that use the ERP, because no computer screen or other device is needed to present stimuli. The research group of Pfurtscheller in Austria [38] introduced important studies about BCI systems employing imagined movements of hands, feet, or tongue. The group of Wolpaw in the United States has also worked on such systems, and an impressive sensorimotor rhythm BCI allowing for fast control of a 2D cursor has been described by Wolpaw and McFarland [16]. Many other groups have performed research on testing sensorimotor rhythm interfaces with severely handicapped subjects [39].

2.5 FEATURES EXTRACTION

In the previous section we have discussed paradigms that let users control their brain activity. In a BCI the neurophysiologic signals are acquired and translated into control command. To allow the control of external devices the brain waves have to be classified for the discrimination of different classes of signals. In many cases the first step for classification of neurophysiologic signals is to acquire labeled training data. Thus, the subject has to perform prescribed actions, while neurophysiologic signals are recorded and afterwards analyzed to learn the desired mapping from signals to classes.

After the data acquisition phase, significant features are extracted from the raw brain signals with the aim to transform the neurophysiologic signals into a representation that makes classification easy. In other words, the goal of feature extraction is to remove noise and other unnecessary information from the input signals, while at the same time retaining information that is important to discriminate different classes of signals. Another, related, goal of feature extraction is to reduce the dimensionality of the data that has to be classified.

In this section we only review some methods for feature extraction in BCIs. To achieve the goals of feature extraction, neurophysiologic a priori knowledge about the characteristics of the signals in the temporal, the frequency, and the spatial domain is necessary. Depending on the type of signals to be classified this knowledge can take many different forms. A more exhaustive review of feature extraction methods for BCIs can be found in [28]. To date, nonlinear methods for signals analysis are also used in many research context and in this thesis the extraction of a nonlinear parameter is proposed for BCI.

2.5.1 Time Domain

The presentation of particular stimuli or the actions of the user of a BCI system cause changes in the amplitude of neurophysiologic signals in the time domain, at specific time interval. P300 and MRPs are signals that can be characterized with the help of time domain features. A strategy that is often used to separate these signals from background activity and noise is lowpass or bandpass filtering, optionally followed by downsampling. Indeed, most of the energy of the P300, SCPs, and MRPs is concentrated at low frequencies. Lowpass filtering, together with downsampling thus allows to remove unimportant information from high frequency bands. In addition, the dimensionality of the signals is reduced. Examples for systems in which filtering and downsampling have been employed are the P300 BCI described by Sellers and Donchin [40] and the system for classification of MRPs described by Blankertz *et al.* [41].

An alternative to filtering is to use the wavelet transform of the signals. Systems based on the discrete wavelet transform (DWT), as well as systems based on the continuous wavelet transform (CWT) have been described in the literature. An example for the use of the DWT is the P300-based BCI system described by Donchin *et al.* [42].

Besides the use for the EEG signals P300 and MRP, time domain features are also used in BCI systems based on microelectrode arrays, that is an invasive technique for recording activity from single neurons or from small groups of neurons.

2.5.2 Frequency domain

Frequency domain features are related to changes in oscillatory activity. Such changes can be evoked by presentation of stimuli or by concentration of the user on a specific mental task. Since the phase of oscillatory activity is usually not time-locked to the presentation of stimuli or to actions of the user, time domain feature extraction techniques cannot be used. Instead, feature extraction techniques that are invariant to the exact temporal evolution of signals have to be used. The most commonly used frequency domain features are related to changes in the amplitude of oscillatory activity. For example in systems based on motor imagery, the band power in the mu and beta frequency bands at electrodes located over the sensorimotor cortex is used as a feature.

During specific tasks the synchronization between signals from different brain regions can occur and might indicate that these regions communicate. This characteristic can be considered a second type of frequency domain features. The communication between the brain regions permits to discriminate different signals features for different cognitive tasks. The use of synchronization features in combination with band power features was explored by Gysels and Celka [43] in a BCI based on the cognitive tasks like the left and right hand movement or the composition of words. Also Brunner *et al.* [44] used synchronization features in combination with band power features in BCI based on other cognitive tasks. In both studies the combining synchronization and band power features led to classification accuracy that was superior to that obtained with only synchronization or band power.

2.5.3 Spatial domain

Generally the feature extraction techniques described above use data from only one electrode, the synchronization features are an exception that are extracted from bivariate time series. In many systems however, data from more than one electrode is available. The goal of spatial feature extraction methods is to find efficient combinations of features from more than one electrode.

When a user perform a cognitive task some changes occur in specific brain regions. The changes in band power, P300 peaks, or other features are usually stronger at electrodes over brain regions that are related to specific cognitive task. Thus, for performing spatial feature extraction method only electrodes that carry useful information for a particular task is used.

A spatial feature extraction consists in applying spatial filtering algorithms before further processing takes place. Spatial filtering corresponds to building linear combinations of the signals measured at several electrodes. Denoting by $s(t) \in R^E$ the signal from E electrodes at time t, spatial filtering can be expressed as $\hat{s}(t) = Cs(t)$. Here the $F \times E$ matrix C contains the coefficients for F spatial filters and the vector $\hat{s}(t) \in R^F$ contains the spatially filtered signals at time t.

To determine the filter coefficients different methods can be used. For example for motor imagery based BCIs, it has been shown that spatial filtering with a Laplacian filter can increase performance [45]. Simple Laplacian filters can be built by subtracting the mean signal of the surrounding electrodes from the signal of each electrode. Applying a Laplacian filter corresponds to spatial high-pass filtering, focal activity which is characteristic for motor imagery tasks is thus enhanced.

In other methods for spatial feature extraction, filter coefficients are computed from a set of training data. An algorithm which is very popular in the area of motor imagery based BCI systems is the common spatial patterns (CSP) algorithm [46]. The CSP algorithm determines spatial filters that maximize the temporal variance of data recorded under one condition and minimize the temporal variance of data recorded under a second condition.

Another method for computing the coefficients of spatial filters from training data is independent component analysis (ICA). In ICA algorithms it is assumed that a set of multichannel signals s(t) is generated by linearly mixing a set of source signals x(t):

$s(t) = Mx(t)$.

The goal is to compute a matrix F that allows one to reconstruct the source signals x by multiplying s with F. To achieve this without having information about M, one assumes that the source signals are statistically independent. The ICA algorithm thus computes F such that the signals s(t) multiplied with F are maximally independent. In the case of EEG signals, the idea underlying the application of ICA is that the signals measured on the scalp are a linear and instantaneous mixture of signals from independent sources in the cortex, deeper brain structures, and noise [47]. ICA has been mainly used in P300-based BCIs as a feature extraction method. In such systems ICA is used to separate multichannel EEG into several components, corresponding to sources in the brain or noise, for example from eye blinks. By retaining only components that have a P300 like spatial distribution or show P300 like waveforms, the signal to noise ratio can be improved.

2.5.4 Nonlinear methods

Nonlinear time series analysis focuses on methodologies that distinguish chaotic signals from noise, and how properties of chaos can be used to model and classify dynamical systems [48]. The analysis of nonlinear dynamics has a fundamental role for studying magnetoencephalography (MEG), electroencephalography (EEG) and other brain signals with the purpose of characterizing, for example, normal resting activity

[49] and pathological states [50]-[51]. Different nonlinear parameters are investigate in literature like the maximum Lyapunov exponent, the asymptotic distance, the entropy, the Higuchi dimension, the detrended fluctuation analysis.

To date, the Lyapunov exponent calculation (λ) have been applied to a wide range of biological and biomedical phenomena. One of the biggest areas of interest has been in analyzing functional brain activity (i.e., EEG or MEG) with the aim to detect early the disease onset. Stam, for instance, suggests that the most promising potential clinical applications appear to be in identifying and predicting epileptic seizures and sleep disorders [51]. Another area where Lyapunov exponent calculations have been applied extensively is in analyzing the heart rate variability, so in the electrocardiography (ECG) analysis. In this area Perkiomaki presented an interesting review [52].

The nonlinear behaviour of time series is characterized by successive phenomena of stretching and folding. It is important to note that, while λ is only sensitive to the stretching mechanism, another non linear parameters, the asymptotic distance, is sensitive to both the stretching and the folding mechanisms. Also the evolution of the asymptotic distance d_{∞} [53]-[54] has been studied in literature for characterizing nonlinear dynamics in the six experimental datasets. One of the method for evaluating d_{∞} is the implementation introduced by Sapuppo that is computationally less onerous then the conventional methods [48].

Another important indicator used for non linear analyses is the entropy. It has been introduced by Pincus to quantify the regularity of a sequence [55]. He demonstrates that a larger value of entropy correspond to more irregularity in the data. Hornero suggests that nonlinear analysis techniques could be useful in Alzheimer's disease diagnosis [50]. The results of his work show that EEG and MEG background activities in Alzheimer's disease patients are less complex and more regular than in healthy control subjects.

The fractal dimension is a nonlinear parameter that quantify the complexity and the self similarity of a time series. This indicator can be computed using various algorithms for example that proposed by Higuchi [56].

In recent year also the detrended fluctuation analysis (DFA) method [57] has become a widely-used technique for providing a simple quantitative parameter to represent the correlation properties of a signal [58]-[59]. In the biomedical context, it has successfully been applied to diverse fields such as DNA sequences, neuron spiking, human gait, and heart rate dynamics [57]-[60]-[61]

Since the first nonlinear EEG studies [5] several steps forward have been done, and the nonlinear analysis of EEG has been widely used for diagnosis of neurovegetative pathologies. For example in Alzheimer's Disease a lower value of correlation dimension, maximum Lyapunov exponent and sample entropy, than in healthy control subjects have been found. In addition, Daly analyzed the performance of the Wackermann parameters in the classification of single-trial ERP responses [62] for BCI. In this thesis the Lyapunov exponent has been extracted from brain signals acquired during a motor imagery task in a BCI system.

In mathematics the Lyapunov exponent or Lyapunov characteristic exponent of a dynamical system is a quantity that characterizes the rate of separation of infinitesimally close trajectories, thus quantize the sensitivity to initial conditions.

Given a chaotic system, two trajectories starting from very close randomly chosen initial conditions will diverge exponentially at a rate given by the largest Lyapunov exponent [63]-[64]. Thus, the largest Lyapunov exponent can be defined using the following equation where $\delta(t)$ is the average divergence at time *t* and *C* is a constant that normalizes the initial separation:

$$\delta(t) = Ce^{\lambda_1 t} \tag{1}$$

When plotting $ln|\delta(t)|$ versus t, the result is a curve that is close to a straight line with a positive slope of λ, indeed:

$$\ln|\delta(t)| = \ln C + \lambda_1 t \tag{2}$$

The curve is never exactly straight. It has wiggles because the strength of the exponential divergence varies somewhat along the attractor. The exponential divergence must stop when the separation is comparable to the "diameter" of the attractor – the trajectories obviously can't get any farther apart than that. This explains the leveling off or saturation of the curve in Figure 7. The value of saturation is the parameter d_∞.

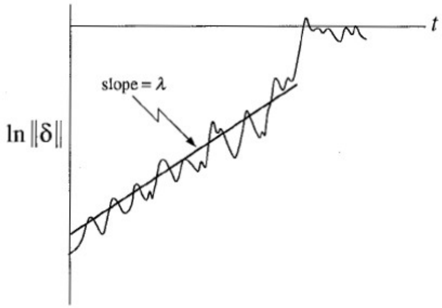


Figure 7 - Example of divergence curve.

The number λ is often called the Lyapunov Exponent although actually *n* different Lyapunov exponents exist for a n-dimensional system. This value coincided with the largest Lyapunov exponent. Moreover λ depends on which trajectory is studied, thus the true value of λ is obtained by averaging over many different points on the same trajectory.

Given a time series a direct method to calculate the largest Lyapunov exponent λ_{max} is thought the formula of the prediction error between very close trajectory [5]. Here it is reported the formula used in the TISEAN software for the calculation of λ_{max} [65]-[5]:

$$\lambda_{max} = \left\langle \frac{1}{Nt_s} \sum_{n=1}^{N} \ln \left(\frac{\left\| y^{n+k} - y^{nn+k} \right\|}{\left\| y^{n} - y^{nn} \right\|} \right) \right\rangle \qquad (3)$$

where y^{nn} is the nearest neighbour of y^{n}, t_s is the sampling time and N is the time series length. The Lyapunov exponents are fully representative of the sensitivity to initial condition (stretching phase) of a given nonlinear dynamical system, being positive for chaotic behaviours [66]. Often it is sufficient to establish the existence of at least one positive Lyapunov exponent to define chaotic dynamics [26].

CHAPTER 3

EXPERIMENTAL PROTOCOLS AND RESULTS ANALYSIS

3.1 EEG EXPERIMENTAL PROTOCOL

Signal processing and classification methods are essential tools in the improvement of Brain Computer Interface technology. In this thesis a new approach based on nonlinear time series analysis to extract EEG signals features is proposed. In particular a fast algorithm that computes the largest Lyapunov exponent was used. This signal processing approach was tested offline considering three sessions of imaginary motor tasks. The results obtained reveal the capability and the potentiality of this method in respect to the classical approach [77].

Dataset1 -14 electrodes	Dataset2 -16 electrodes	Dataset3 -16 electrodes
1-Training session 60s	1-Training session 60s	1-Training session 60s
2-Training session 60s	2-Training session 60s	2-Training session 60s
3-Training session 60s	3-Training session 60s	3-Training session 60s

Table 1 - Experimental data sets over a three-day time period.

For our experiment the user, without any muscular involvement, modifies his neuronal activity in the primary sensory-motor areas performing a motor imagery task. During the training session, the computer screen is either blank, or displaying an arrow pointing left or right. The two different stimuli appear for several times in a random sequence. Depending on the direction of the arrow, the subject is instructed to imagine a movement of the left hand or of the right hand. If the screen was blank the user is instructed to have a rest. The same task was performed three times in three different days by an healthy right-handed subject (female, aged 28 years) who wore a EEG cap with integrated electrodes. The EEG potentials were recorded using two channels configuration: for the first session the signals was acquired at 14 locations (FC5, FC1, FC2, FC6, C3, Cz, C4, CP5, CP1, CP2, CP6, T7, Pz and T8) and for the second and third sessions at 16 locations (replacing T7 and T8 with P3, P4, F3 and F4) sites in the standard 10-20 System and digitized at 2000 Hz. This change has been decided to have augmentative information after a first view of the results obtained for the first trial.

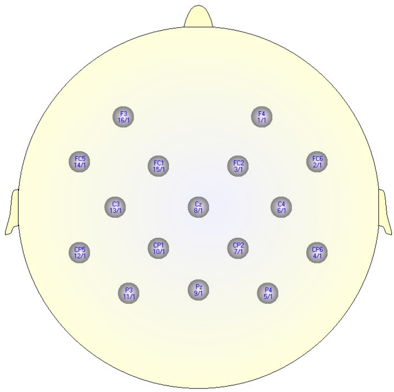


Figure 8 - Electrodes configuration used for the experiment. 16 channels positioned according to the international 10-20 system.

3.1.1 Analysis strategy

For this thesis different tools have been used to analyze the brain signal acquired from the user that performs an imagery movement protocol. The BCI2000 software has been used for data acquisition, stimulus presentation and brain monitoring applications. Moreover, BCI2000 allows us to convert the measured brain signals in a format suitable for MATLAB analysis. The BCI2000 software tool has been implemented by

Schalk et al. [66] with the purpose to facilitate the research and the applications on brain computer interaction. The BCI2000 is a general-purpose system for brain-computer interface and it is available for free for non-profit research and educational purposes. It consists of four modules that communicate with each other: source (data acquisition and storage), signal processing, user application, and operator interface. The modules communicate through a protocol based on TCP/IP, thus each one can be written in any programming language and can be run on any machine.

The brain signal recorded using the BCI2000 have been then elaborated with MATLAB software. The MATLAB language has been used for programming the algorithm that allowed us to obtain the results discussed in section 3.1.3. The signals acquired during all the training sessions were filtered in six different bands: delta (1-4 Hz), theta (4-8 Hz), alpha (8-12 Hz), beta I (12-16 Hz), beta II (16-20 Hz), and gamma (20-49 Hz. In each band and for all the channels the power and the Lyapunov exponent (λ) were computed. The DivA algorithm introduced by Bucolo et al. has been used for computing the λ parameter. Different set of data were extracted depending on the stimulus:

the imagination of the right hand, the imagination of the left hand or the resting phase. Then, the correlation coefficient V [67] associated with the two conditions, Left (LA) and Right (RA) arms imaginary movement versus rest phase (RP) were evaluated The total variance was calculated according to the following expression:

$$V = \frac{1}{n}\sum_{x=1}^{n}(x - \propto)^2 \tag{4}$$

where *x* and m are the amplitude and the average value of the EEG signal for a specific channel and *n* is the number of samples (in our experiments, *n* = 200). This measure provides a way to select the frequency band and locations where the EEG signals are more influenced by the task (left and right arm imagery).

3.1.2 Lyapunov exponent extraction: algorithm implementation

For our experiment DivA, an alternative methodology for the extraction of the asymptotic distance and of the Lyapunov exponent λ was used [7]. This implementation results to be computationally less onerous than the conventional ones, since it is not based on the time-delay embedding concept and also no intermediate computational steps are needed to obtain the final result being particularly suitable for real time analysis. Let us assume that x denotes a k-dimensional vector, and consider the dynamical system specified by the discrete map:

$$x_{n+1} = G(x_n) \tag{5}$$

Let us consider N couples of trajectories starting from two nearby points separated by a small distance h_0, $\left|x_0^{(i)} - x'^{i}_0\right| \leq h_0$;

$$x_j^{(i)} = G_n(x_0^{(i)}) \qquad x'^{(i)}_j = G_n(x'^{(i)}_0) \tag{6}$$

Averaging the N couples of trajectories, the mean distance between trajectories after j iteration can be defined as:

$$d_j = \frac{1}{N}\sum_{i=1}^{N}\left| x_j^{(i)} - x'^{(i)}_j \right| \qquad (7)$$

where the |•| operator denotes the usual norm. The d_j asymptotic value is defined as:

$$d_\infty = \lim_{n\to\infty}\frac{1}{n}\sum_{j=1}^{n} d_j \qquad (8)$$

It is well known that, after n iterations, the map of the time diverging distance can be expressed as:

$$d_{n+1} = e^{n\lambda} d_0 = e^{\lambda} d_n = \Lambda d_n \qquad (9)$$

where λ is the Lyapunov exponent of system. After a sufficiently large number of iterations, the folding process takes place to keep the trajectories bound in the phase space. To take this phenomenon into account, the (9) can be considered as a first order expansion of d_∞ and, in the hypothesis that $d_n<1$ for any n, it includes a second order correction term representing the folding action:

$$d_{n+1} = \Lambda d_n - \Gamma d_n^2 \qquad (10)$$

The fixed points of (10) are:

$$d^{*} = 0 \text{ and } d^{**} = d_{\infty} = \frac{\Lambda - 1}{\Gamma} \qquad (11)$$

The characteristic values describing the evolution of nearby trajectories are Λ, Γ, and d_{∞}, although only two of these are actually needed because of the relationship (11).

The aim of DivA algorithm, given a signal *s(t)* (i.e. given a time series), is to compute the divergence (d_j) among trajectories x_i.

The algorithm starts with the choice by the operator of an initial condition $x_0^{(0)}$ and a distance h_0, which identifies a small range $[(x_0 - h_0/2), (x_0 + h_0/2)]$ that generally depends on the resolution of the signal *s(t)* and on the number of trajectories found. Then, points whose y-coordinate belongs to the range $[(x_0 - h_0/2), (x_0 + h_0/2)]$, are extracted; these points represent a set of candidate to become *starting points* of the algorithm in relation to the equation (6). The first *starting point* found is assumed to be $x^{*} \equiv x_0^{(0)}$, this point will be used as reference point for the following steps.

The algorithm proceeds with the computing of the first derivate in x^*. Among the points in the set of the candidate starting points, only those whose derivative meets constrain (12) will represent the final set of *starting points* from which trajectories will be calculated.

$$\left|\dot{x}_0^{(0)} - \dot{x}_0^{(i)}\right| = p \cdot \mathrm{var}(s^{'}(t)) \qquad (12)$$

Parameter *p* in (12) is the *slope ratio* and is chosen, by user empirically, small enough so that pairs of trajectories that have a different initial slope are discarded, thus decreasing the number of trajectories for the calculation of the d_j, but not too strict so that a sufficient number of trajectories, respecting the requirement on the range and the initial slope, can be extracted. The term *var(s')* represents the variance of the derivative of signal *s(t)*. The constrain on the slope has been introduced in order to collect all points having the same properties in the zero order and first order dynamics.

By means of the above described steps, set of starting points is found: $X=(x_0^{(i)}, i=0,\ldots n)$. Each point $x_0^{(i)}$ identifies a trajectory made up of all the samples in the range: $[x_0^{(i)},(x_0^{(i)}+lenght\_trj1)]$, where *length_trj* is the length of the trajectories chosen in a way that, when the distance between them is computed, both the stretching and the folding effects are taken into account, and the asymptotic behaviour of the system can be studied. Moreover, all the combinations among points $x_0^{(i)}$ will be considered, discarding those couples whose distance (in samples) is inferior to the parameter m*inimum trajectories delay* (td_{min}), and their differences will be computed thus obtaining d_j.

The d_∞, representing the asymptotic value of d_j, is then extracted and used as a parameter for characterizing the nonlinear dynamics of the system. Moreover, from the computed curve d_j, the maximum Lyapunov exponent can be extracted as the initial slope of the curve. This extraction can be computed in different ways, polynomial fit, custom equation fit or in empiric way. This last method is the one used in this thesis. The slope is simply computed considering the straight line joining the first occurrence of the lowest value with the first value settle around the asymptotic value of d_j.

3.1.3 Results and discussions

The signals acquired during all the training sessions were filtered and the power and λ were computed. Then, the correlation coefficients associated with the two conditions, Left (LA) and Right (RA) arms imaginary movement versus rest phase(RP) were evaluated.

As it is expected from previous well-known results, according to the International 10-20 System, the evolution of the power in gamma band, reveals that imagination of hands or arms movement cause a radial current flow in the sensory-motor area close to the positions C3 or C4, respectively associated with the right and the left arms [68] (see Fig.11). Figure 9 plots the space-frequency map of the correlation coefficient (r) for λ, it is possible to distinguish in the gamma-band a higher level of sensitivity during the LA imaginary activity in the electrode C4 (6) and during the RA in C3 (13).

The same conclusion can be drawn considering Fig.10 where for each dataset the r-value for both power (blue line) and λ (red line) in gamma band versus the channels have been taken into account. In addition Fig. 11 shows for both parameters the head maps of the r-value averaging the dataset 2 and 3. The first row of pictures is referred to the LA activity and the second to the RA.

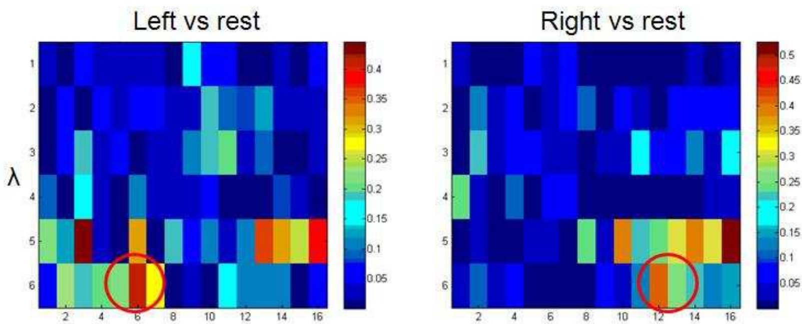


Figure 9: Space-frequency map of the correlation coefficient for λ, the first image on the left reports the LA versus rest and the second image on the right the RA versus rest.

These results could lead to investigate on the potentiality of this new parameter to drive a BCI system. In this direction first of all a series of statistical comparisons were performed, to confirm the attitude of this feature to characterize LA-RA activity:

-between λ in C4 during LA and RA ($n1 = n2 = 45$, $t = 4{,}1$ and $p = 0{,}0071\%$);

-between λ in C3 during LA and RA ($n1 = n2 = 45$, $t = -2,9$ and $p = 0,42\%$);
-between λ in C4 and in all the other channels during the LA ($n1 = 45$, $n2 = 645$, $t = 3,8$ and $p = 0,012\%$);
-between λ in C3 and in all the other channels during the RA ($n1 = 45$, $n2 = 645$, $t = 1,7$ and $p = 8\%$);
where t=t-test value, n1 and n2=samples size, and p=probability of observing a value as extreme or more extreme than the obtained t-value. The rejection of the null hypothesis at the 5% significance level has been confirmed in the first three cases, meanwhile in the last comparison is required the 8%. In this contest considering the size of the sample n1 and n2 a power of about 60% can be assumed.

From these results it is possible to confirm the previous analysis and further more can be enhanced the attitudes of the subject investigated to an higher level of brain wave control during the LA than the RA. For both tests involving channel C4 bigger t values were obtained.

To point out on the parameter sensitivity the indicator D=maxleft-maxright has been evaluated, where maxleft and maxright are the maximum r value of the signal recorded from the electrodes that cover respectively the left and right motor cortex area. Figure 12 shows that the value of D for λ is higher than for the power or at least comparable. This results highlight the potentiality of λ to be used as more robust feature for BCI. In future encouraged from these preliminary results an extended case study will be designed taking into account more subjects, and higher precision methods for classification will be applied. Once the valence of this approach will be proved, to move toward the on-line implementation another important aspect that has to be faced is the algorithmic complexity. Up to now the proposed algorithm for the evaluation of the lambda has not been fully-optimized but the low computational time of about 30sec involved in the process one complete dataset (on a Quad 1.58 GHz PC) is a promising beginning.

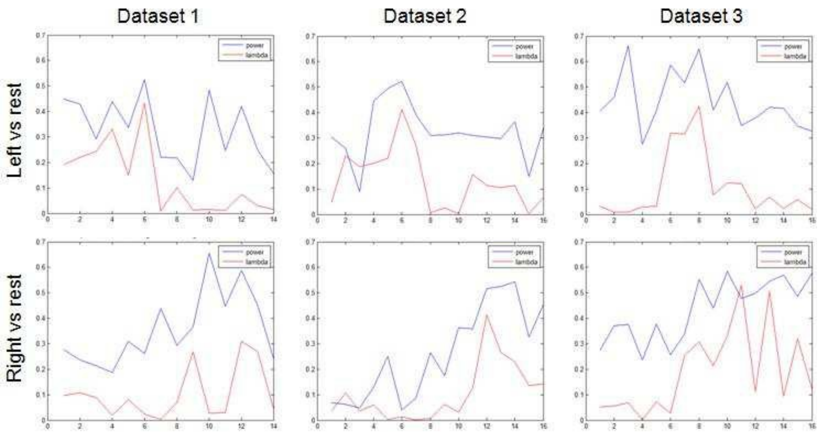


Figure 10 - the correlation coefficient for power(blue line) and λ (red line) in the gamma band for each experimental datasets. Channels from 1 to 7 are related to the right hemisphere and channels from 10 to 16 to the left hemisphere.

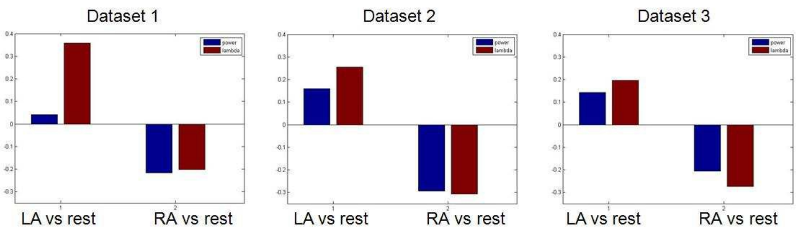


Figure 12 - D value computed for the power(blue) and λ (red) during LA and RA for all the dataset.

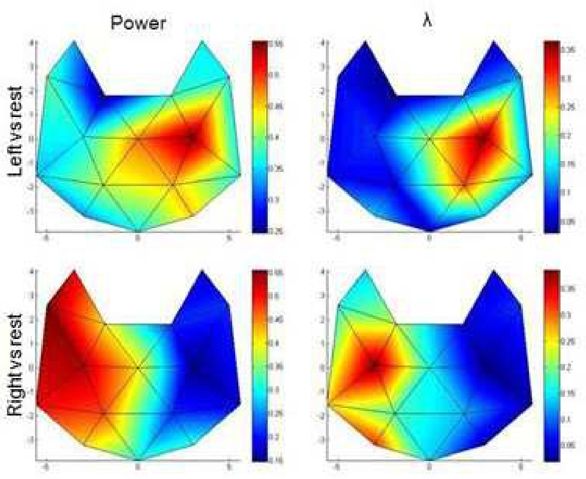


Figure 11 - Head map distribution of the r value for the second and third dataset.

3.2 FMRI EXPERIMENTAL PROTOCOL

An operant conditioning paradigm has been established by the central institute of mental health, Heidelberg University, Mannheim [69], with subjects learning to differentially regulate the blood oxygenation level-dependent (BOLD) effects in the anterior cingulate cortex (ACC) and the posterior Insula (pIns). The use of fMRI technique offers the possibility of uncovering the cerebral processing of the human pain experience. In recent years, many imaging studies have focused on defining a network of brain structures involved in the processing of normal pain. These brain areas are often referred as the matrix of pain [68].

The aim of our analysis was to investigate whether it is possible to regulate activation in these pain processing areas in response to painful stimulation in a way that uncouples the response in these functionally related areas.

One healthy male subject aged 25 years has been selected for performing the fMRI paradigm. In the first localizing session (LOC) painful electrical stimuli (approximately 70% above pain threshold) to the base of the third digit (left hand) have been applied for every subject both for localizing the activated brain regions and for establishing the individual pain threshold. During this stimulation a clearly online localizable BOLD change in both the ACC and the pIns has been noticed (Fig. 1). No feedback was given during the baseline section. The localizer allowed to pinpoint the exact locations of the individual Regions Of Interest (ROI) in the ACC and pIns. Seven days after the LOC, on four consecutive days, the subjects performed six feedback sessions, each lasting 7.5 minutes for the four conditions (24 sessions total, 6 sessions per condition), see Table 1. For conditions 1 and 3 feedback was computed by subtracting BOLD signal changes in the ACC from signal changes in the pIns, for conditions 2 and 4 this was reversed.

	Calculation for feedback	**Instruction for subjects**
Condition 1	**BOLD response in ACC – BOLD response in pIns**	**Ball direction up, i.e. positive difference (ACC > pIns)**
Condition 2	**BOLD response in pIns – BOLD response in ACC**	**Ball direction up, i.e. positive difference (pIns > ACC)**
Condition 3	**BOLD response in ACC – BOLD response in pIns**	**Ball direction down, i.e. negative difference (ACC < pIns)**

Condition 4	**BOLD response in pIns – BOLD response in ACC**	**Ball direction down, i.e. negative difference (pIns < ACC)**

Table 1 - Conditions and rules for feedback calculation

Visual feedback was given in the form of a blue or yellow ball indicating the condition (1 and 3 or 2 and 4), its movement indicating magnitude and direction of difference in BOLD activation in the ACC and pIns during the painful stimulation. Of the 4 conditions, 2 conditions were identical, i.e. positive feedback was given due to the same direction of difference in BOLD response in the ROI, different only in ball-color and direction of the arrow. On-line data-preprocessing was done with Turbo-Brainvoyager. Visual feedback of activation data was done with Presentation according to [70].

In each session subjects were first instructed to move the ball up or down during 6 painful stimulation blocks lasting 30s in the direction of an arrow that appeared next to the ball during stimulation. In the 20s between each stimulation block subjects performed mental arithmetic.

After the session subjects had to rate the individual perception of pain intensity and unpleasantness of the stimulus as well as report on the strategy they used to move the ball and rate their individual ability to control the ball.

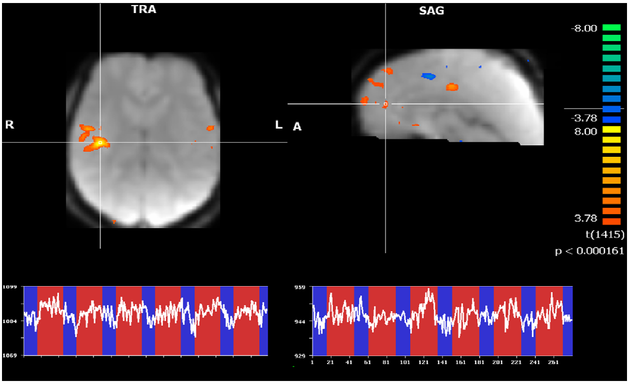


Figure 12 - Blood oxygenation level-dependent (BOLD) effect in the first localizer session in subject 9. Upper panel: Statistical parametric map. Lower panel: Time course of BOLD signal in the posterior Insula (pIns,left) and in the anterior cingulate cortex (ACC, right).

3.2.1 Functional connectivity between spatially remote brain signal acquired during BCI protocol

Functional neuroimaging studies in humans have shown that physiologic pain stimuli elicit activity in a wide network of cortical areas commonly labeled as the ‘pain matrix’ and thought to be preferentially involved in the perception of pain. The a priori information about how pain is processed in several areas in the brain, led us to choose the so called pain matrix as region of interest (ROI). Then, the images acquired during the discussed protocol have been elaborated using specific tools for reconstruct the temporal trend of the signals for every ROI.
The ROIs that have been selected are: anterior cingulate cortex (ACC), left and right posterior insula (pInsL, pInsR), left anterior insula (aInsL), medial cingulate cortex (MCC), left primary somatosensory area (SI_L), left second somatosensory area (SII_L), right second somatosensory area (SII_R). Moreover, the signal extracted from a region that have no correlation with the pain matrix has been evaluated.

In this thesis the estimation of the connectivity between the ROIs listed above is presented. The functional connectivity has been evaluated by computing the direct transfer function (DTF) technique [71] that is a full multivariate spectral measure used to determine directional influences between any given pair of signals in a multivariate dataset. It is computed on a multivariate autoregressive model (MVAR) that simultaneously models the whole set of signals. DTF has been demonstrated [72] to be based on the concept of Granger causality, according to which an observed time series $s_1(n)$ can be said to cause another time series $s_2(n)$ if the prediction error for $s_2(n)$ at the present time is reduced by the knowledge of the past measurements of $s_1(n)$. This kind of relation is not reciprocal, thus allowing to determine the direction of information flow between the time series.

The DTF technique was applied to the dataset $X(t)=X_1(t)+X_2(t)+\ldots+X_k(t)$ obtained for the nine ROIs considered. The MVAR model for this signal can be expressed as:

$$X(t) = \sum_{i}^{p} A(i)X(t-i) + E(t) \qquad (13)$$

where X(t) is the data vector in the time t, E(t) is the vector of white noise values, A(i) are the model coefficients and p is the model order. Then, equation (13) is transformed to the frequency domain, in order to investigate the spectral properties of the examined process:

$$X(f) = A^{-1}(f)E(f) = H(f)E(f) \qquad (14)$$

H(f) is the transfer matrix of the system, whose element H_{ij} represents the connection between the *j*th input and the *i*th output of the system. With these definitions, the causal influence of the cortical waveform estimated in the *j*th ROI on that estimated in the *i*th ROI. The directed transfer function $\theta_{ij}^2(f)$ is defined as:

$$\theta_{ij}^2(f) = \left|H_{ij}(f)\right|^2 \qquad (15)$$

In order to be able to compare the results obtained for cortical waveforms with different power spectra, a normalization was performed by dividing each estimated DTF by the squared sums of all elements of the relevant row, thus obtaining the so called normalized DTF [71]:

$$\gamma_{ij}^2(f) = \frac{\left|H_{ij}(f)\right|^2}{\sum_{m=1}^{k}\left|H_{im}(f)\right|^2} \tag{16}$$

$\gamma_{ij}(f)$ expresses the ratio of influence of the cortical waveform
estimated in the *j*th ROI on the cortical waveform estimated on the *i*th ROI with respect to the influence of all the estimated cortical waveforms. Normalized DTF values are in the interval [0,1] when the normalization condition:

$$\sum_{n=1}^{k}\gamma_{in}^2(f) = 1 \tag{17}$$

is applied. The matrix $\gamma_{ij}(f)$ is then visualized in a graph that shows the correlation between the different regions of the brain using some arrows that elicit also the direction of the connection. In the following paragraph the results are shown using two explicative figure.

3.2.2 Results and discussions

The connectivity patterns between the ROIs have been represented by arrows pointing from one brain area toward another one. MATLAB functions have been used with the aim to represent the resulting dependencies estimated in the DTF matrix. A threshold has been choose to visualize just the stronger connection, in our case we decide to set the threshold to 0.8.

Figure 13 and 14 show the link between the ROIs for two different trials. The first one is related to the first localizing session, so no feedback was given and the user was ask, during the stimulation, to focus his attention on the pain. Figure ? is related to the 6 th trial, that is the last performed by the user, recorded when the feedback was computed by subtracting BOLD signal changes in the ACC from signal changes in the pIns.

Figure 1 shows the correlations between pInsL, pInsR and ACC regions, more strongly connected in respect to the other ROIs, because strictly involved in the perception of pain.

Instead, after five training sessions the connections between ACC, pInsR and pInsL decrease considerably and in Figure 2 the correlations disappear because lower than 0.8. These results suggest that the user is able to modulate his brain signals and in this particular case has disconnect the activation in the ACC and in the pIns.

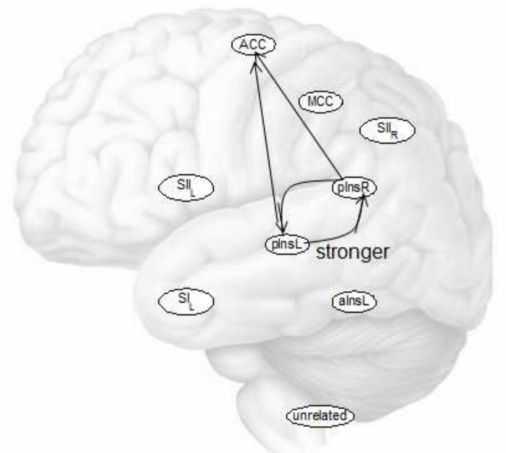


Figure 13- Functional connectivity between the signals recorded in nine regions of interest during the baseline condition. In this task the user is asked to focus the attention on the pain. No feedback was provided.

If an individual can learn to directly control activation of localized regions within the brain, this approach might provide control over the neurophysiologic mechanism that mediate behaviour and cognition and could potentially provide a different route for treating disease.

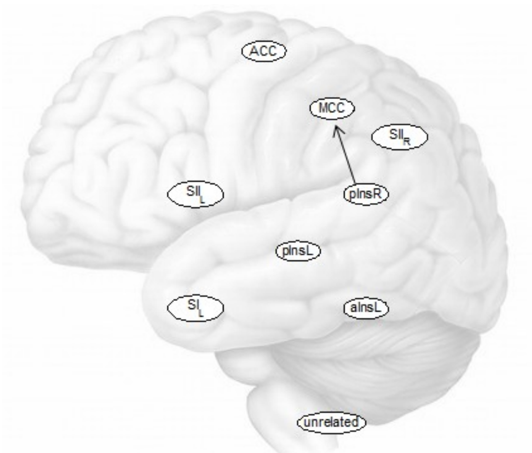


Figure 14 - Functional connectivity between the signals recorded in nine regions of interest. During this task the visual feedback was given in the form of a blue ball indicating the condition 1, its movement indicating magnitude and direction of difference in BOLD activation in the ACC and pIns during the painful stimulation.

Another consideration can be done in relation to the role of the medial cingulate cortex in the process of pain perception. Figure 14 shows clearly that the connectivity between the pInsR and the MCC increases in the last trial, thus after the performance of five trials. It could be interesting to better investigate the causal influence of the cortical waveform estimated in the pInsR on that estimated in the MCC. Understanding these modulatory mechanisms in health and in disease could be useful for developing effective therapies for the treatment of clinical pain conditions.

CHAPTER 4

DESIGN OF BCI APPLICATIONS

4.1 ARTISTIC PATTERN GENERATION USING BRAIN SIGNAL

In this work, a creative BCI application based on SMR is presented. The proposed interactive BCI system allows communication between two coordinated robots and a user [76]. The twin robots are equipped with light-emitting diodes (LEDs) so that the user can create a desired artistic representation by controlling their trajectories. The twin robots in motion generate luminous paths and a camera takes pictures of these light trajectories that represent the user's "canvas."

The BCI-based interactive system used in this work consists of an EEG system, a personal computer, twin robots, and a camera (Figure 15). The signals acquired through the EEG system are digitalized and elaborated through the BCI2000 platform running on a PC.

During the signal processing procedure, a series of spatial and temporal filters are applied and specific features extracted from the EEG signals are translated into robot control commands. Afterward, the control signal is sent at the same time to two robots that will perform the same movements and generate a luminous artistic pattern. Thus, the trajectories that the robots follow depend on the will of the user.

The interactive BCI platform designed allows two coordinated robots and the user to communicate by modulation of the user's SMRs. Our application has been tested exploiting the modules of the BCI2000 software [66].

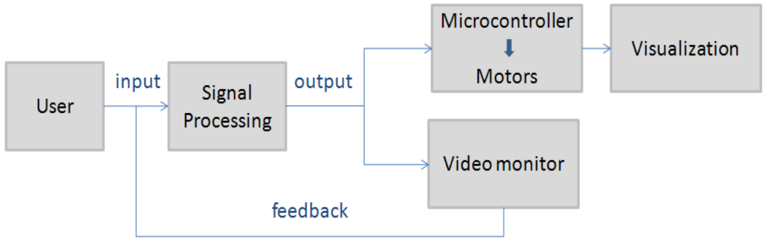


Figure 15. Block diagram of the designed interactive platform.

In the establishment of a BCI task, the training session has a fundamental role for two main reasons. First, it is essential for a subject to learn how to control the amplitude of his or her SMR by imagination or movement of the limbs or hands. Second, because the features of EEG signals differ from subject to subject, training is mandatory to determine the best channel location and most suitable frequency band (i.e., to determine which signals are the most suitable for the task and which frequency band is the most sensitive to changes).

The designed technological platform consists also of two robots. The robots basic structure, shown in Figure 16 and 17, is the classic differential-drive, consisting of two actuated wheels and two smaller passive caster wheels whose function is to keep the robot statically balanced. The velocities of the two motors (*MA* and *MB*) are indicated respectively as *VMA* and *VMB*. Each robot is equipped with an arm on which an electronic device to generate time-varying light patterns is mounted. The arm is actuated by a third motor, which turns faster than the other two motors. The electronic device mounted on the arm consists of an array of 16 red, green, and blue (RGB) LEDs and an autonomous microcontroller. Several parameters such as colour, brightness, frequency, and intermittence of lights can be set, thus generating different luminous patterns. The kinematic structure of the robots was created using the LEGO MINDSTORMS robotic kit due to its simplicity and reconfigurability [73].

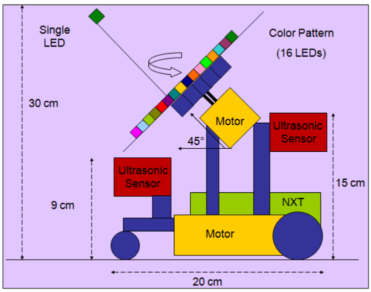


Figure 16 - Side view of the robots structure.

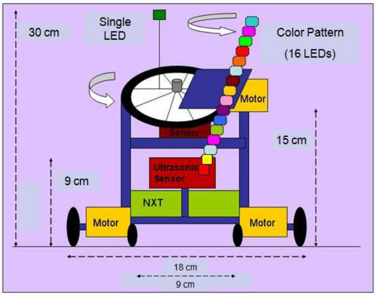
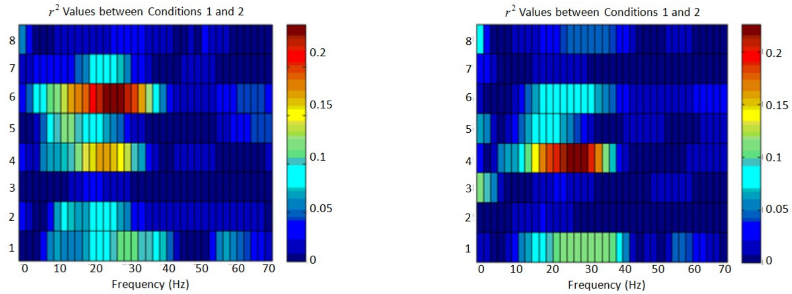


Figure 17 - Front view of the robots structure.

Real-time analysis of SMRs is at the basis of the communication between the user and the robots. The user, without any muscular involvement, modifies his or her neuronal activity in the primary sensory-motor areas by performing a motor imagery task. The task was performed by a healthy right-handed subject (female, aged 27 years) who wore an EEG cap with integrated electrodes. The EEG potentials were recorded at eight locations (F3, F4, T7, C3, Cz, C4, T8, and Pz) according to the International 10-20 System [74] and digitized at 2000 Hz. The locations of the EEG electrodes have been assembled over the motor and somatosensory areas.

Movement and imagination of hand or arm movement cause a radial current flow in the sensory-motor area close to the positions C3 or C4, respectively associated with the right and the left arms [75]. During the training session, the total variance V of the brain signals was calculated for all eight channels in the 0 to 70 Hz frequency range. The variance was calculated according to the equation (4). This measure provides a way to select the frequency band and locations where the EEG signals are more influenced by the task (left and right arm imagery). In fact, in Figure 18, the color maps of the variance related to training on the right (a) and left (b) arm movement for an imagery task show an increase of the variance value occurring for the motor imagery of the right arm on the electrode 4 (C3) around the frequency of 16 Hz, and for the motor imagery of the left arm on the electrode 6 (C4) around the frequency of 16 Hz. For this reason, the control law implemented has been based on information from such signals.



(a) (b)

Figure 18. Variance values of the brain signals measured on eight channels: (a) while the subject thinks about moving the right arm and (b) while the subject thinks about moving the left arm.

The two EEG signals have been filtered and then translated into an output signal *Cv* using the following equation:

$$C_v = w_r \cdot A_r + w_l \cdot A_l \qquad (18)$$

where *Ar* and *Al* are the time-varying variances of one left-side (C3) and one right-side (C4) channel, respectively. The weights *wr* and *wl* are determined by the offline inspection of the brain waves according to the values of *Ar* and *Al*. Indeed for some subjects, the variances produced by imagining left and right movement have different intensity. If $Ar > Al$, it is convenient to set $wl > wr$ and vice versa; if $Al > Ar$, it is convenient to set $wr > wl$. The command signal Cv is used both to control the robots' movement and the position of a cursor on the video screen as visual feedback for the user. Concerning visual feedback, the screen displays a cursor on the left edge that begins to move horizontally toward the right edge of the screen. The cursor's vertical position depends on the value of Cv that represents the angular coefficient of the tangent to the cursor trajectory. Concerning commands to robots, the BCI2000 processes in real time the brain signal measured on the user's scalp and sends nine parameters to the MATLAB software. For our experiments only the value of Cv is used, but the system is general enough so that other parameters could be used for future applications. The User Datagram Protocol (UDP) has been used for communication between BCI2000 and MATLAB. The angular coefficient is converted in control signals for driving the robots using the following paradigm:

- if $Cv < -1$, the robots turn right quickly (VMA=80, VMB= 0);
- if $-1 < Cv < 0$, the robots turn right slowly (VMA=60, VMB=30);

- if $0 < Cv < 1$, the robots turn left slowly (*VMA*=30, *VMB*=60);
- if $Cv > 1$, the robots turn left quickly (*VMA*=0, *VMB*=80).

The robots can move in all directions within an arena 190 cm long and 245 cm wide. The scenario is totally dark. Initially, the light is turned off so that the spectator can see just the effects produced by the luminous pattern mounted on each robot. A camera is located in a strategic point to take pictures of the whole arena every 10, 15, or 20 seconds. The camera sends the pictures that it takes to a slide projector. The images produced can be used to provide feedback to the user. This visual feedback helps the user learn to control his or her EEG activity.

The user controlling the robots, which when moving produce light patterns, can create a wide variety of images that are then taken by the camera. Indeed, every image generated in this manner is unique, since several variables continually change. Examples of variables include the starting point of a robot with respect to the other; the intermittence and color of the luminous pattern; the presence of obstacles and the trajectory followed during the data capture process; and the exposure time of the camera lens.

Some pictures of the trajectories observed during the motion of the twin robots are now reported. Figure 19 refers to the motion of the robots during a time interval of 10 seconds, while Figures 20 and 21 refer to an exposure time of the camera lens of 15 and 20 seconds, respectively. In particular, in Figure 21 we can clearly recognize the identical trajectories of the twin robots. A1 and A2 indicate the starting points of the two robots. In this case, the user has thought to move the right arm and consequently the robots turned right. Then, the user again imagined a right arm movement and another change of direction (points B1 and B2) was observed in the robot trajectory. The points where the robots stopped their motion are C1 and C2.

Figure 19 - Picture obtained by the user controlling the two robots modulating her brain signals. The time exposure of the camera lens is 10 seconds.

Figure 20 - Picture obtained by the user controlling the two robots modulating her brain signals. The time exposure of the camera lens is 15 seconds.

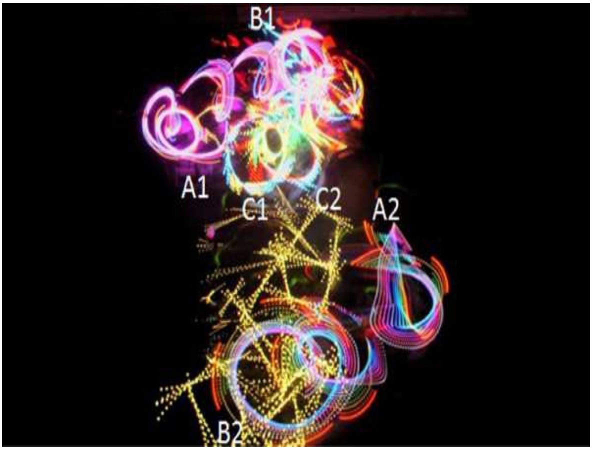


Figure 21 - Picture obtained by the user controlling the two robots modulating her brain signals. The time exposure of the camera lens is 20 seconds.

4.2 CONTROLLING A ROBOTIC HAND USING SMR AND ERP

An EEG based BCI application has been designed with the purpose to control a robotic hand through both sensory motor rhythms and event related potential.

The signals measured from the user's scalp are digitalized, elaborated and sent to the external device exploiting the BCI2000 [66] and the MATLAB software. During the signal processing procedure, a series of spatial and temporal filters are applied and specific features are extracted from the EEG signals and translated into control command for the robotic hand (Fig.22). The same signal processing and translation algorithm techniques of the previous application have been used.

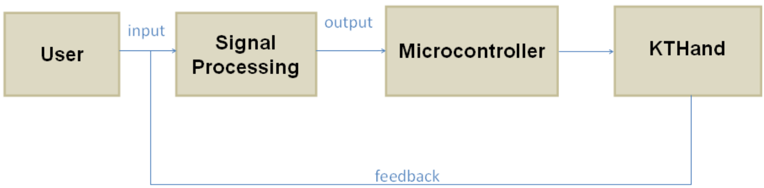


Figure 22 - Block diagram of the designed BCI application.

The designed application have two configuration. In the first one the neurophysiologic signals used are the sensory motor rhythms. The trained user is instructed to imagine a movement of the left or of the right hand for respectively closing or opening the robotic hand. For the second approach the event related potential are the neurophysiologic signals extracted and translated for controlling the device. In this case the subject is seated in front of a screen that displays a matrix of words as shown in Figure 23. These words are intensified in rows and columns in a random order according to the row/column paradigm implemented for the first time by Farwell and Donchin in 1988 [37]. The intersection of the target row and column creates the P300 in EEG signals and, therefore, detection of the target word. Due to very low amplitude of the P300 in EEG, the classification of the P300 requires a minimum numbers of flashes to achieve high accuracy, thus the disadvantage of the use of ERP respect to the use of SMR is the longer interval of time for distinguishing the will of the subject.

The robotic hand used to design the current application has been assembled for the first time by the KTH Royal Institute of Technology. The KTHand robot hand is a three fingered under-actuated hand of anthropomorphic design. All drawings, the bill of material, and assembly instructions are freely available on the web at the address: www.md.kth.se/kthand. Each finger is controlled by a direct current motor which rotates a pulley upon which a tendon is wound up. Shortening the tendon flexes the finger. A leaf spring runs along the finger and acts as abductor but is also an integral part of the joint design. The position of the pulley is measured by an magnetic absolute position encoder (see Fig. 24).

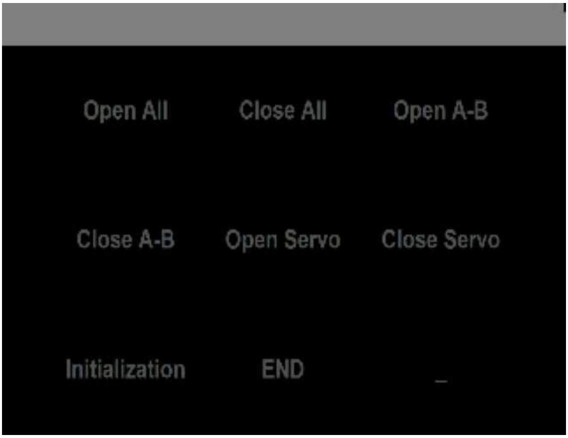


Figure 23 - Row/column paradigm introduced for the first time by Farwell and Donchin in 1988 [37].

For our experiment we have used a KTHand previously assembled and connected to an AVR32 controller. The AVR32 is a 32-bit RISC microprocessor architecture designed by Atmel.

The physical connection between the controller and the computer, where BCI2000 and MATLAB software elaborate and transmit the brain signals, is a serial port through which information transfers in or out one bit at a time with a speed rate of 115200 bit/s. The UDP communication protocol has been used for transferring data from BCI2000 and MATLAB. An algorithm programmed in MATLAB language manage both the UDP communication with BCI2000 and the serial connection with the controller.

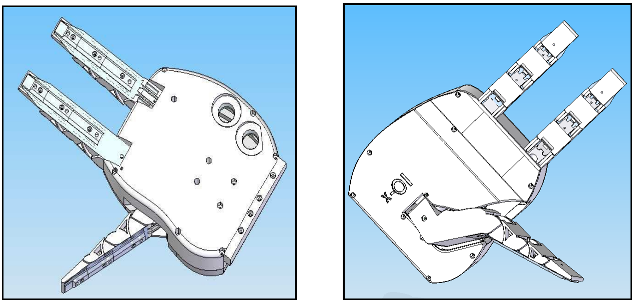


Figure 24 - The KTHand model.

Figure 25 and 26 show two different protocol for the SMR experiment. In the first case the user is asked to open or close the KTHand according to the command that was displayed on a screen. The interval presentation of these two visual stimuli was totally random, for example the first stimulus could appear after 1 sec and the second after also 5 sec. The user had to change the position of the KTHand immediately after the stimulus was displayed. In the second case the user was asked to mimic the same action of a person that randomly decides to close or open his hand. An explicative movie about our robotic hand application is available on internet at the following address: http://www.youtube.com/watch?v=AmfAynGhVaE.

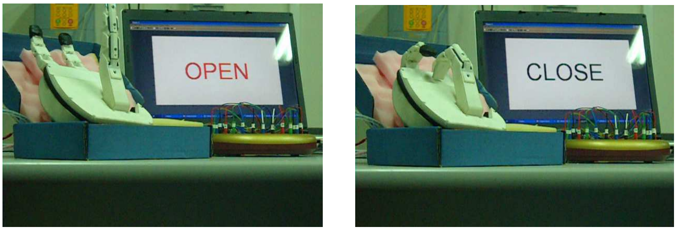
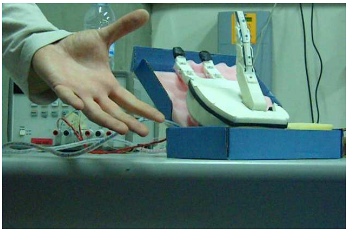


Figure 25 - In the first experiment the user have to close (he thinks to move the right hand) or open (he thinks to move the left hand) the KTHand modulating his sensory motor rhythms following the instruction displayed on a screen.



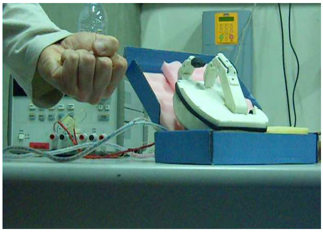


Figure 26 - In the second experiment the user have to close (he thinks to move the right hand) or open (he thinks to move the left hand) the KTHand modulating his sensory motor rhythms imitating the same gestures of a person that open and close his hand in a random way.

4.3 ALTERNATIVE FORM OF COMMUNICATION FOR PEOPLE WITH MOTOR DISABILITIES

Music composer

In this paragraph we present a novel interface for music composition. The following interface allows a user to create and modify short melodies in real time and provides aural and visual feedback to the user, thus affording them a controllable means to achieve creative expression.

Before to start the on line task the user has to perform a training session. During this step, the subject learns how to control the amplitude of his or her SMR by imagination or movement of the hands and of the feet, and specific features of EEG signals are determined because they differ from subject to subject. During the training session, the total variance *V* of the brain signals was calculated for all eight channels in the 0 to 70 Hz frequency range for determining the best channel location and the most suitable frequency band.

The music composer application has been tested exploiting the modules of the BCI2000 software [66], specifically the *CursorTask* module that is controlled by the output of the *SignalProcessing* module, that have been set thanks to the information extracted during the training session.

When the subject is ready for EEG acquisition, the notes are displayed on a screen as appear in Figure 27. Then, a cursor appears in the center of the blue squared and begins to move only when the user starts to modulate his sensory motor rhythms. The subject's task is to move the cursor vertically imaging to move the right (up) or the left (down) hand, and horizontally imaging to move both the hands (left) or the feet (right). The purpose of the user is to hit the desired target, that in our case is a note for composing a melody. Indeed, if the ball hit a target the corresponding note is placed on the pentagram and the related sound is emitted. At the end of the composition the entire melody is emitted.

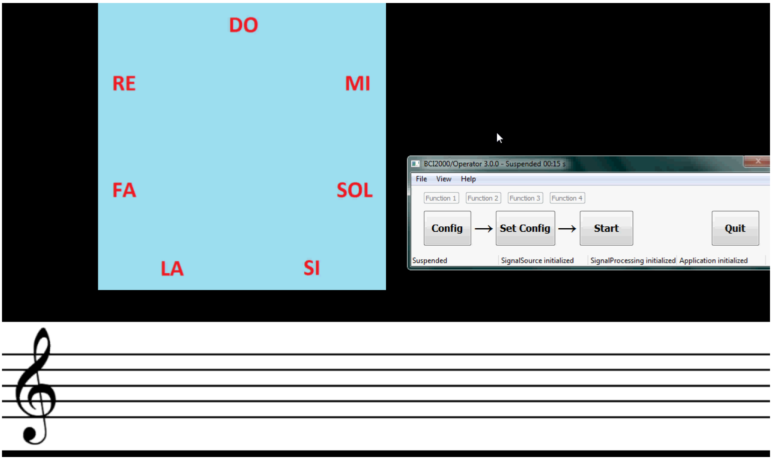


Figure 27 - Interface of Music composer BCI application based on modulation of sensory motor rhythms.

In order to create a richer composition environment, there are several areas for future modifications to this interface, for example a selection of different types of scales or different synthesized sounds could be insert. Additionally, implementing a “stop” button can allow the composer to take more time to plan the next note or to indicate when they are satisfied with what they have created.

Writing and painting robot

Other two SMR based BCI applications have been designed with the purpose to give to people with motor disabilities another way for communicating. The first one is the *writing robot* application that allows to a user to select letters of the alphabet, modulating his sensory motor rhythms, that will be sent to a robot equipped with a paintbrush (see Figure 29). The robot will reproduce on a sheet the letter that correspond to the target hit by the user on the screen. Feedback training has to be used to let users acquire control over sensorimotor rhythms because the changes in SMR occurring in untrained users are usually not strong enough to be detected by a classification algorithm. Thus, before starting to use the *writing robot* or the *painting robot* application the performance of training sessions is mandatory to determine the best channel location and the most suitable frequency band for a specific subject. The training allows to the user to learn how to control the amplitude of his or her SMR by imagination or movement of the limbs. During the training session, the computer screen is either blank, or displaying an arrow pointing left, right, up or down. The four different stimuli appear for several times in a random sequence. Depending on the direction of the arrow, the subject is instructed to imagine a movement of the left hand, of the right hand, of both the hands or of the feet. If the screen was blank the user is instructed to have a rest. The same task was performed several times in different days. The signals acquired during this step are analyzed and the total variance V are calculated for all the channels in the 0 to 70 Hz frequency range. The variance was calculated according to the equation (4). The results are visualized as in Figure 18. This measure provides a way to select the frequency band and locations where the EEG signals are more influenced by the task (left and right arm, both arms or feet imagery movement).

After that all the features have been set the subject can start to use the *writing* or *painting application*. The blue screen that appears when the task starts is shown in Figure 28. The same BCI2000 modules of the *music composer* application: the *SignalProcessing* and the *CursorTask* have been used for designing this application.

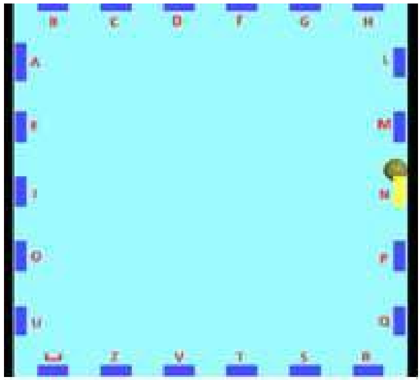


Figure 28 - Interface of Writing robot BCI application based on modulation of sensory motor rhythms.

The robots basic structure is the classic differential-drive, consisting of two actuated wheels and one smaller passive caster wheels whose function is to keep the robot statically balanced. The kinematic structure of the robots was created using the LEGO MINDSTORMS robotic kit due to its simplicity and reconfigurability [73].

Figure 30 illustrates all the sequences of the task. The blue screen with the letter of the alphabet and a cursor at the center is displayed and the user moves the cursor vertically imaging to move the right (up) or the left (down) hand, and horizontally imaging to move both the hands (left) or the feet (right). When a target has been hit the command that will be sent to the writing robot appear on the screen (for example if letter C has been chose ‘writing C’ will be displayed). The BCI2000 software communicates with the MATLAB software exploiting a UDP protocol. Then MATLAB sent to the robot, through a Bluetooth connection, the data elaborated by the BCI2000. When the robot receive the control command it starts to write the related letter on a sheet.

Figure 29 – Robot used for designing the *writing robot* and the *painting robot* applications. The paintbrush can be noticed at the center of the axis of the two wheels.

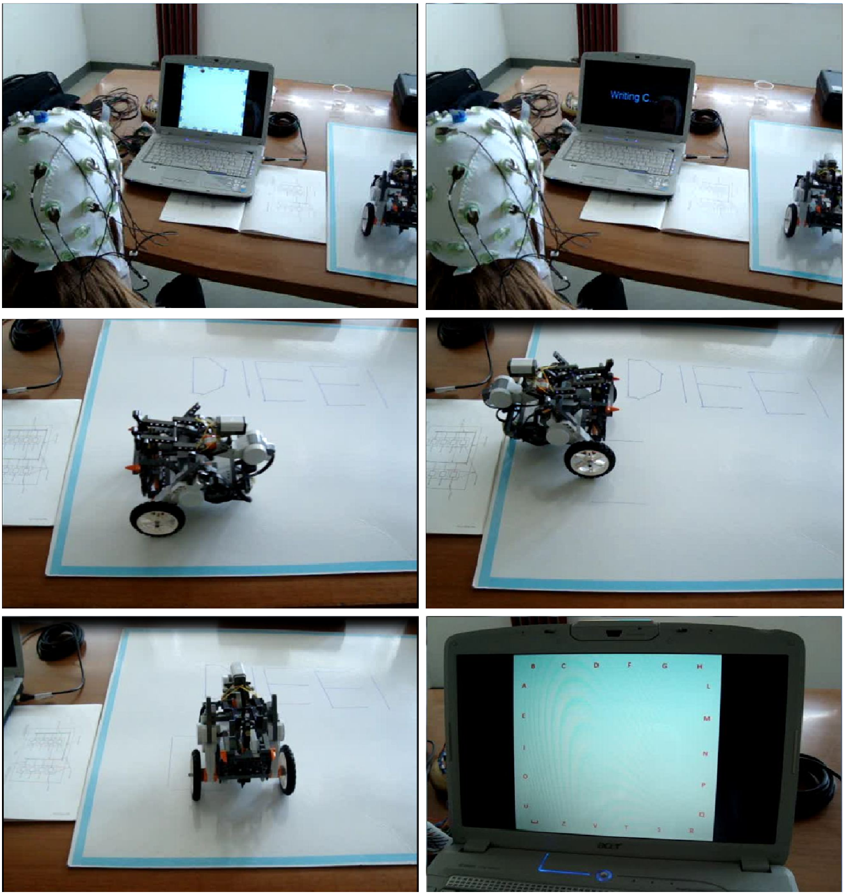


Figure 30 – Sequences of the task performed by a user with the writing robot BCI application. The user controls a cursor on a blue screen modulating his sensory motor rhythms. He chooses a letter of the alphabet. This information will be sent to a robot equipped with a paintbrush that will reproduce the same letter on a sheet.

The *painting robot* BCI application is similar to the last one, the difference are just the targets that the user can choose and that appear on the screen, shown in Figure 31.

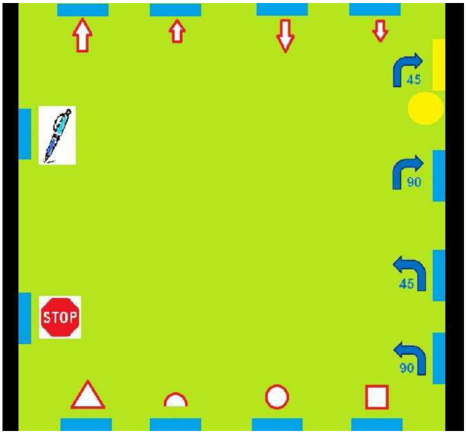


Figure 31 - Interface of *painting robot* BCI application based on modulation of sensory motor rhythms.

CHAPTER 5

CONCLUSION

In this manuscript three related aspects of research on BCI systems were discussed. These aspects were the evaluation of a nonlinear feature extraction algorithm for BCI, the analysis of the functional connectivity between the signals acquired in different brain regions when a user performs an operant conditioning paradigm with fMRI based BCI technology, and the development of BCIs applications for disabled subjects.

We have introduced a new EEG signals features extraction techniques based on nonlinear time series analysis. This signal processing approach was tested offline considering three sessions of imaginary motor tasks. The main objective is increasing the performance of BCI systems extracting a more robust feature. In order to reach this objective a fast algorithm that computes the largest Lyapunov exponent, the DivA [7], was used. This implementation results to be computationally less onerous than the conventional ones, since it is not based on the time-delay embedding concept and also no intermediate computational steps are needed to obtain the final result. For this reason the DivA is particularly suitable for real time analysis, thus for BCI applications. Our evaluations underline the capability and the potentiality of this method in respect to the classical approach. The idea for future works is to integrate the nonlinear algorithm investigated in this thesis in a BCI system, thus using it on line. The design of a BCI based on our nonlinear feature extraction method could improve the performance of the systems that use sensory motor rhythms as neurophysiologic signals.

The analysis of the functional connectivity between brain regions involved in the perception of pain is the second topic that were dealt with in this thesis. Thanks to the collaboration with the central institute of mental health, Heidelberg university in Mannheim, the dataset recorded with an fMRI based BCI technology have been analysed. The results reveal the possibility for a person to modulate the brain waves, in particular the neurophysiologic signals related to the perception of pain. Control over the pain modulatory system is an important target because it could enable a unique mechanism for clinical control over pain. Here, we found that using real-time functional MRI based BCI to guide training, subjects were able to learn to control activation both in anterior cingulated cortex and in the posterior insula. The BCI techniques could have an important role for treating disease, for example for the chronic pain treatment. An aspect that can be investigated in future work is the involvement of the medial cingulate cortex in the pain perception. Indeed when the subject deliberately induced increases or decreases in ACC or pIns fMRI activation, there was a corresponding change in the connection between the MCC and the other ROIs. In particular a more strong connection between MCC and pInsR can be noticed. In future works could be interesting to analyze the role of MCC in the perception of pain.

Finally, we proposed the designs of different EEG based BCI applications. We aim to provide a significant quality of life improvement to users with severe disabilities. All the applications designed have been tested for able-bodied users, the future idea is to test the applicability of such tools also for the locked-in patients.

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