POLITECNICO DI TORINO

MASTER 's Degree in BIOMEDICAL ENGINEERING

MASTER 's Degree Thesis

Machine Learning algorithms to classify voluntary and involuntary movements from EEG in a BCI for post-coma non-responsive patients

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Abstract

This work is part of a larger project that aims to investigate the level of consciousness in non-responsive patients (Vegetative State or Minimal Conscious State). The ratio of misdiagnosis is indeed very high at the moment. We are developing a Brain Computer Interface able to support the diagnosis. Our BCI uses Readiness Potentials (RP), first identified by Kornuber[2] , which arise just before the start of a voluntary movement. Therefore, the presence of an RP is a marker of presence of consciousness[4]. Within this project, the aim of this thesis was to create a robust machine learning algorithm that can predict whether a movement is voluntary or not.

We firstly investigated the characteristics of RP useful for this scope (feature extraction), then we selected the most informative ones (feature selection). Finally, we compared different classifiers model. More in detail, after the EEG pre-processing (i.e. the noise reduction and the correction of artifacts), a feature extraction has been performed in order to find the best RP's attributes for classification; this first part was the most critical one because the extraction of feature influence the performance of the classifiers. The section of feature selection was aimed at detecting which attributes were most informative, thus discarding the redundant or irrelevant ones, that could lead to misclassifications. The selected features were finally used to train and validate three different classifiers, one based on the K-Nearest Neighbour (K-NN), one Decision Tree (DT) and the other using Support Vector Machines (SVM). Significant results were obtained from the binary classification, and in particular: 73.3% specificity and 63.3% sensitivity for linear SVM, 73.3% specificity and 80% sensitivity for cubic SVM, 93.3% specificity and 73.3% sensitivity for K-NN and finally 73.3% specificity and 100% sensitivity for DT.

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Acronyms

AP

Action Potential

AUVP

Alert,Verbal, Pain, Unresponsive

BCI

Brain Computer Interface

BP

Bereitschaftpotential

DoC

Disorder of Consciousness

DT

Decision Tree

EMG

Electroencephalogram

EMG

Electromyogram

ERP

Event-Related Potential

GCS

Glasgow Coma Scale

GUI

Graphical User Interface

K-NN

K Nearest Neighbour

LOOCV

Leave-One-Out Cross-Validation

MSV

Minimally Consciousness State

PCA

Principal Component Analysis

PSP

Post-Synaptic Potential

RP

Readiness Potential

SMA

Supplemental Motor Area

SVM

Support Vector Machine

VS

Vegetative State

WHIM

Wessex Head Injury Matrix

Chapter 1

Consciousness

1.1 What is consciousness?

The definition of consciousness has been source of debates over the centuries, so long as academic's opinions differ about what exactly needs to be studied and explained as consciousness. Recently, consciousness has also become a significant topic of interdisciplinary research in cognitive science[19], including fields such as psychology, linguistics, anthropology, neuropsychology and neuroscience. To the purpose of this work consciousness definition offered by neurology and neuroscience seems to be the most suitable and most appropriate to start with. In neurology terms, the common conception of consciousness involves[6]:

- **awareness** of the surrounding environment.
- **wakefulness** characterized by a vigilante state.

These two concepts are the basis for the definition of a state of consciousness, but is it possible to measure how conscious a subject is?
The state of consciousness is difficult to evaluate because it is correlated to subjective parameters and is hardly measurable by instrumental investigations. If the subject is in a vigilante state and aware it's easy to say that he/she is aware, but when one or both components are lacking or malfunction, this is referred to as altered states of consciousness. In these cases, especially since the individuals concerned are unable to communicate with the outside world, it is difficult to quantify the

state of consciousness; one therefore speaks of disorders of consciousness.

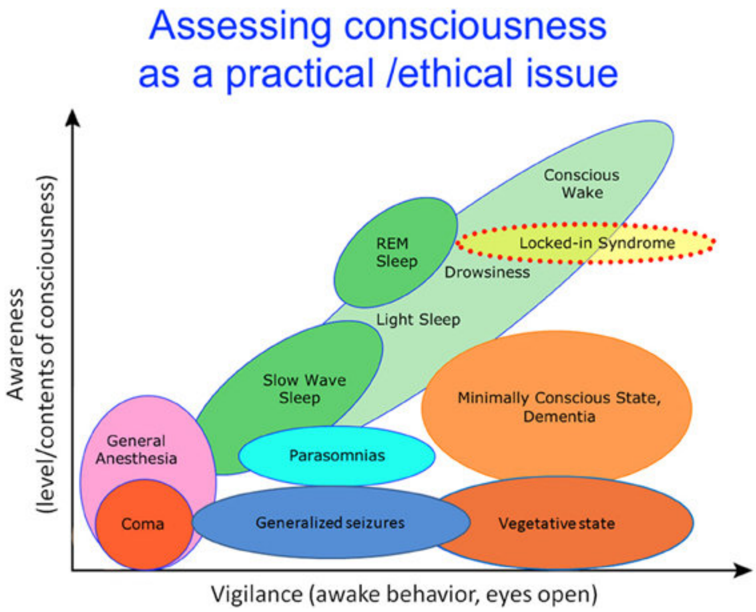


Figure 1.1: Awareness VS Wakefulness graphic

1.2 Disorders of consciousness

Disorders of consciousness (DOCs) are clinical conditions in which alteration or loss of consciousness[15] occurs. The deficit of awareness has different degrees of severity, in some cases the loss of consciousness is confined to certain areas of the brain, for instance in the case of **neglect**, where the subject experiences a deficit in attention, or **prosopagnosia** for the visual perception area; or when the alteration is temporary like in the **anosognosia**, the subject is unconscious of a part of the body, a condition that most often occurs post-stroke. Condition of greater severity are those affected by **coma** or **vegetative state**, where, in addition to a state of non-supervision, individuals are unable to communicate with the outside world.
Since a classification of the state of consciousness is difficult to make, rating scales have been proposed, as an help in diagnosis:

1.2.1 Glasgow coma state

The GCS assesses a person based on his/her ability to perform eye movements, to

speak, and to move the body. These three behaviour establish the three elements of the scale: eye, speech, and motion . A person's GCS score can range from 3 (completely unresponsive) to 15 (fully responsive). This score is used to guide immediate medical care after a brain injury (such as a car accident) and also to monitor hospitalized patients and track their level of consciousness.
Lower GCS scores are correlated with higher risk of death. However, the GCS score alone should not be used on its own to predict the outcome for an individual person with brain injury.

1.2.2 AVUP: Alert - Verbal - Pain - Unresponsive

It is a simplification of the Glasgow Coma Scale, which assesses a patient response through three measures: eyes, voice and motor skills. The AVPU scale should be assessed using these three identifiable traits, looking for the best response of each. AVPU is an acronym for *Alert, Verbal, Pain, Unresponsive.* Each of these letters identifies a level of consciousness based on the type of stimulus required to evoke a response from the patient.

- **Alert:**The patient is fully awake (although not necessarily oriented). This patient will have spontaneously open eyes, will respond to voice (although may be confused) and will have bodily motor function.
- **Verbal:** The patient shows some kind of response to external talk in any of the three components of eyes, voice or motor (patient's eyes open on being asked "Are you OK?"). The response could be as little as a grunt, moan, or slight move of a limb when prompted by the voice of the rescuer.
- **Pain:** The patient makes a response on any of the three components upon the application of pain stimulus, such as a central pain stimulus like a sternal rub or a peripheral stimulus such as squeezing the fingers. A patient with some level of consciousness (a fully conscious patient would not require a pain stimulus) may respond by using his/her voice, moving the eyes, or moving part of the body (including abnormal posturing).
- **Unresponsive:** Sometimes seen named 'unconscious', this outcome is recorded if the patient does not show any eye, voice or motor response to voice or pain.

For instance, following a car accident the AVUP is the first assessment the rescuer makes, the rating goes from least serious (A) to most serious (U). The AVUP scale is not suitable for long-term neurological observation of a patient; in this situation, the Glasgow Coma Scale is more appropriate.

1.2.3 WHIM: Wessex Head Injury Matrix

The *Wessex Head Injury Matrix* (WHIM; Shiel et al., 2000)[7] is a behavioural observational assessment tool commonly used for the assessment of patients in emerging from a coma and patients in the DOC. The scale is a 62-item observational matrix that collects data by observation as well as the person's reaction to specific stimuli with regard to his or her arousal level and concentration, visual consciousness, communication, cognition, and social behaviours by observing those behaviours that occur spontaneously or in response to stimulation.
What happens at the neuronal level?

1.3 The human brain and consciousness

In order to find the connection between brain activity and consciousness, it is important to understand how the human brain works. Consciousness is, from clinical definition, divided into two major components: awareness and wakefulness. The area of the brain responsible for wakefulness consists of brain-stem neuronal populations, previously called the reticular activating system, that directly project to both thalamic and cortical neurons. Instead, the awareness involves the activity of the areas of the cerebral cortex and its reciprocal sub-cortical connections. However, these two states may be related, as awareness requires wakefulness; despite, like it can happen in cases of severe trauma, if the subject is in a waking state, it does not mean that he is also aware of the external environment or what is going on around him.
Conscious knowledge is the cooperation of multiple areas of the brain. The activity of the brain results from electrical impulses generated by nerve cells (neurons), which process and store information. The impulses pass along the nerve fibres within the brain.

The brain stem connects the cerebrum with the spinal cords; the connection is called reticular activating system, which plays an important role in the regulation of basic functions, and it controls the levels of consciousness and alertness. This part of the brain also has the significant function of regulating certain critical body function: if the entire brain stem becomes severely damaged, consciousness is lost, and these automatic body functions cease (terminate) and brain death occurs. However, if the brain stem remains intact, the body may remain alive, even when severe damage to the cerebrum makes awareness, thought, and movement impossible.

1.3.1 Anatomy of the brain

The human brain is a very complex structure; it controls thoughts, memories, language, movements and the functionality of all organs of the body. The brain is divided into two hemispheres, left and right, each one also split into four lobes:

- **Frontal lobe:** the anterior part, is associated to voluntary movements, control of intellectual process (speech, though, concentration, judgments and planning), controlling and coordinating facial expressions and gestures with mood and feelings;

- **Parietal lobe:** in charge of the elaboration of stimuli, in particular for pain, tact and temperature, and language processing;

- **Temporal lobe:** responsible of generating memory and emotions, processing immediate events into recent and long-term memory, including sound and images;

- **Occipital lobe:** the rear part, this is where the termination of the optic nerve is located; it is related to processing and interpreting vision and also integrate visual perception with spatial information.

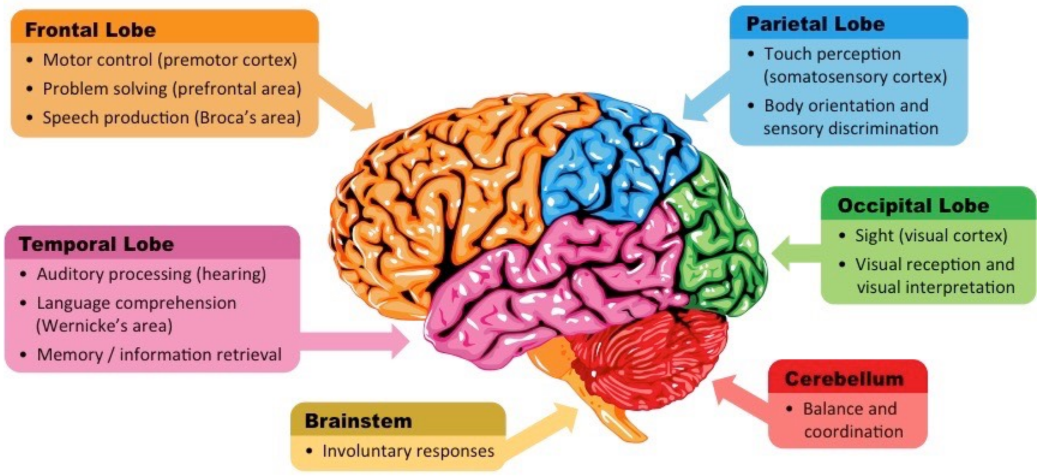


Figure 1.2: Different parts of the brain with their functions .

The information is directed into the various lobes of the brain by neurons, which may be classified into three different types according to their functionality:

- **Afferent** or **sensory neurons:** to convey information from tissues and organs into the central nervous system;
- **Efferent** or **motor neurons:** to transmit signals from the central nervous system to the effector cells;
- **Inter-neurons:** to connect neurons within specific regions of the central nervous system.

How is the information is propagated?
The neurons receive and send information through chemical or electrical signals, which are two different kinds:

- **Action potential (AP)** are the fundamental units (spikes) through which neurons interact with each other. They are short electrical signals that propagate along the axons. They have an amplitude too small to be measured by electrodes placed on the scalp;
- **Post-synaptic** are formed when the neurotransmitter binds to the receptor on the membrane of the post-synaptic cell. They can be excitatory if they

increase the probability that a post-synaptic neuron will produce an action potential, or inhibitory if they decrease this probability.

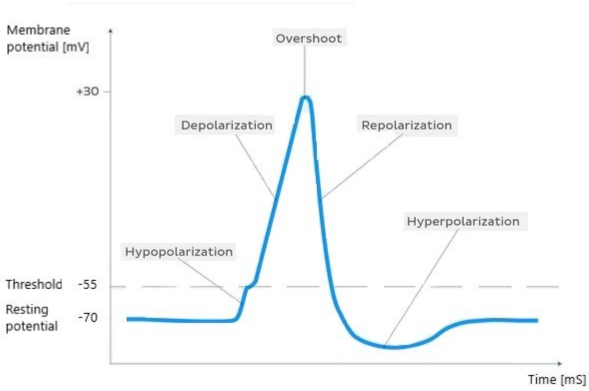


Figure 1.3: Action Potential curve: the stimulus from the pre-synaptic neuron depolarises the target neuron. Sodium channels open and sodium enters the cell. This results in depolarisation. At the peak, the potassium channels open and the ion exits out of the cell.

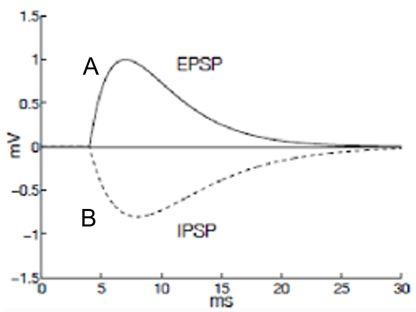


Figure 1.4: Post-Synaptic Potential: A)positive ions (Na+) enter the neuron, causing membrane depolarisation; B) inhibitory negative ions (Cl-) enter the neuron, causing hyperpolarisation of the membrane hyperpolarisation.

1.3.2 Brain areas for voluntary action

Voluntary action is viewed as a set of processes connected to specific brain areas, that therefore determine a sort of decision making[13]. In addition to voluntary actions, reflexes actions can also be distinguished and their difference, in how the movements originate, provides neuroscientific suggestions. Voluntary actions involve the cerebral cortex, while reflexes are not cortical movements but purely spinal. Moreover, voluntary actions and are two distinct subjective experiences: the first experience concerns the planning of an act and the second one concerns the experience of agency, which is when one action is influenced by a particular external event.

The human brain has several and distinct pathways for voluntary actions. The most important component is the primary motor cortex (M1) because it is the motor and the final common track to execute commands by transmitting them to the spinal cord and muscles. Motor areas are located in the rear side of the frontal lobe, known as the granular frontal cortex.

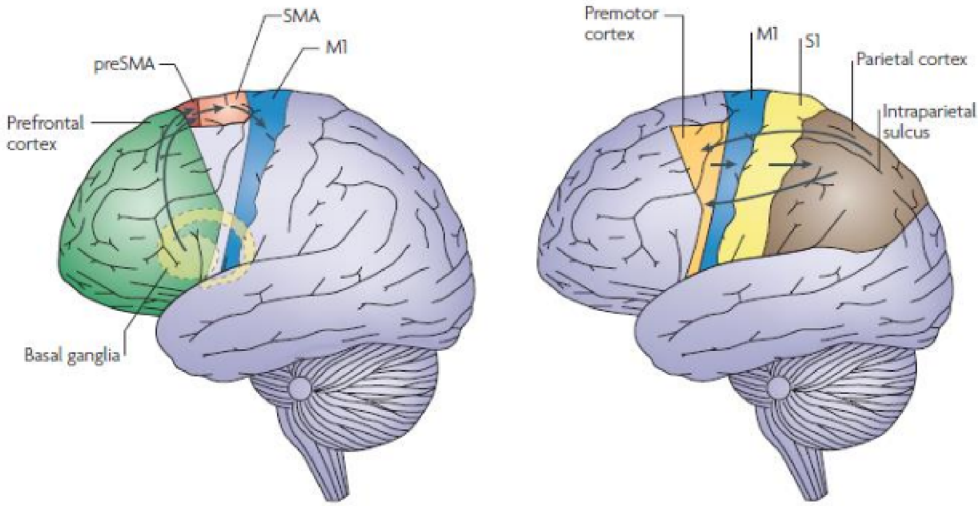
Before reaching M1, one input arrives at the pre-supplementary motor area (pre-SMA), which in turn receives inputs from the basal ganglia and the pre-frontal cortex. The pre-frontal areas represent the neuronal substrate, which would be at the basis of the development of the intentions, that precede and orient actions.

Several human-neuroimaging investigations have demonstrated that the pre-SMA has more vigorous activation for self-paced actions than for triggered stimuli. The pre-SMA is a part of the frontal cognitive network that involves pre-motor, the cingulate, and frontopolar cortices.

In the pre-SMA, a negative and prolonged slope occurs before the volitional movement. It can be said that the RP begins with a cascade of neuronal activity that spreads from the pre-SMA to the SMA until M1, which causes the movement. Concerning SMA, M1 represents a widely complex set of movements.

Conversely, a second cortical circuit converges on M1 and has a fundamental role for the immediate sensory guidance of actions. Information from early sensory cortices is sent to intermediate representations of the parietal lobe until the lateral pre-motor cortex, which projects in turn to M1. In the posterior parietal areas, classified as an associative area, neuronal activity, connected to motor acts, is observed; this means that the posterior parietal cortex has to be considered as a part of the cortical motor system. From an anatomical point of view, the parietal-frontal connections reveal a high level of specificity, and this is translated into the fact that each of these circuits appears involved in one particular sensory-motor transformation, as a description of a stimulus realized in sensory terms into one in motor terms.

The frontal and the posterior parietal cortices are strongly connected and form circuits to work in parallel and integrate sensory and motor information to certain effectors. The posterior motor areas receive cortical afferents from the parietal lobe, while the anterior motor areas, from the pre-frontal cortex and the cingulate.
Pre-frontal and cingulate regions are important to cognitive control processes and are responsible for intentions, planning in the long term, and the choice of when to act. These regions are interconnected with medial frontal regions that are the primary source of pre-movement activity.



How is it possible to study the brain activity mentioned above?

Chapter 2

EEG signals and Readiness Potential

2.1 Introduction

In the previous chapter, the definition of consciousness was addressed, which made it possible through the neuropsychological approach to point out the differences between the greatest global Disorders of Consciousness and their symptoms.
For establishing if a patient is clinically in Coma, Vegetative State or Minimal Conscious State, clinicians have to make an appropriate diagnosis through behavioural assessment methods, that are based exclusively on the behavioural observation of the patient. Behavioural responses are essential to provide useful data to describe the patient's clinical situation but, often, these are sporadic or non-existent. However, it has been demonstrated from several studies that diagnostic errors of VS and MCS are very frequent. Therefore, differentiating the Vegetative State from Minimally Consciousness State is often one of the most difficult issues facing clinical staff involved in the care of severely brain-injured patients.
To avoid misdiagnoses and to improve clinical assessment, behavioural observations must be integrated with neuroimaging and electrophysiological techniques to formulate a more complete and correct diagnostic picture. Particularly to explore cognitive function in unresponsive patients through a reproducible motor command, that is a sign of awareness, an ERP component linked to volitional intention

movement is Readiness Potential, on which the study of this thesis is based, to better understand its contribution during voluntary, semi-voluntary and involuntary movements acquired by electromyography (EMG), according to an experimental protocol. In effect, there have been findings, in which it is suggested EMG as a means for the awareness assessment objective in pathologies of consciousness, through recording muscle activity below the behavioural threshold, when patients make a voluntary movement to command.

2.2 The Electroencephalogram (EEG)

One of the most essential techniques to study the brain activity is the Electroencephalogram (EEG), invented by Hans Berger in 1929. What EEG records is mostly the PSPs of cortical neurons directed perpendicularly to the scalp, while a single neuron's electrical activity is too small to be detected. What we record, indeed, is the synchronous activity of thousands of neurons orientated in a similar way. Since pyramidal neurons of the cortex are particularly similar in orientation, near to the scalp and synchronous, they are thought to produce the majority of EEG signal[25].

Since the signals recorded are usually between only 10-100 μV, the amplitudes are very near to the electrical noise generated by the device. Moreover, most of the recordings suffer from some artifacts, which interfere with the useful signal, such as the eye and muscle movement or an electrode temporary detachment. For this reason, attention must be paid not only during the recording, to avoid any interference with other instruments, but also in filtering, artifact-removing and deleting any outcome that is corrupted.

The EEG can identify a spontaneous activity of the brain, which is always present. The frequency spectrum is characterized by bands, called rhythms, such as delta rhythm ($<$ 4 Hz), found during dreamless sleep, theta rhythm (4-7 Hz), found in sleep, meditation and hypnotic state, alpha (8-15 Hz), found in a very relaxed state of wake or in the moments immediately before falling asleep, Beta (16-30 Hz), in states of normal waking consciousness[16].

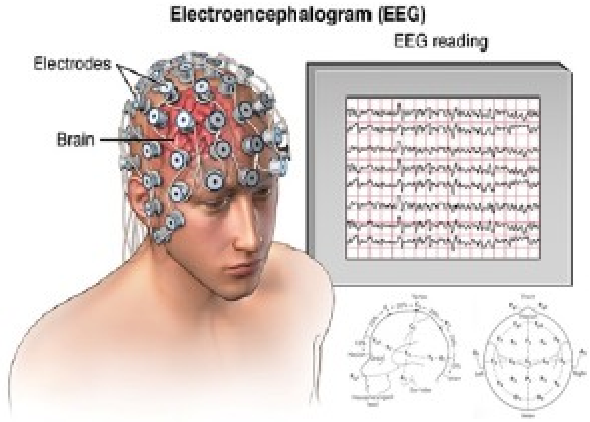


Figure 2.1: Example of EEG recordings

On the EEG trace, it is also possible to observe particular waves, called Event-related Potentials (ERPs), due to the administration of sensory stimuli or the performance of the motor or cognitive task.

2.3 Event-Realted Potential

The EEG can identify a spontaneous activity of the brain, which is always present. The frequency spectrum is characterized by bands, called rhythms, such as delta rhythm (< 4 Hz), found during dreamless sleep, theta rhythm (4-7 Hz), found in sleep, meditation and hypnotic state, alpha (8-15 Hz), found in a very relaxed state of wake or in the moments immediately before falling asleep, Beta (16-30 Hz), in states of normal waking consciousness. On the EEG trace, it is also possible to observe particular waves, called Event-related Potentials (ERPs), due to the administration of sensory stimuli or the performance of the motor or cognitive task. In addition to the clinical use, there is an increased interest in employing EEG/ERP paradigms to understand the brain function and develop brain control interfaces (BCI).

The ERPs signals due to an external input are, in most cases, related to an imagined or intentional movement[20]. Furthermore, the preparation of the movement produces a recognizable wave on the track before the movement performance[10]. In an experiment, if the subjects are instructed to make a series of occasional responses, with no eliciting stimulus, the response are preceded by a slow negative shift at frontal and central electrode sites that begins up to 1 second before the actual response. This is called the Bereitschaftspotental (BP) or more commonly known as Readiness Potential (RP)[8].

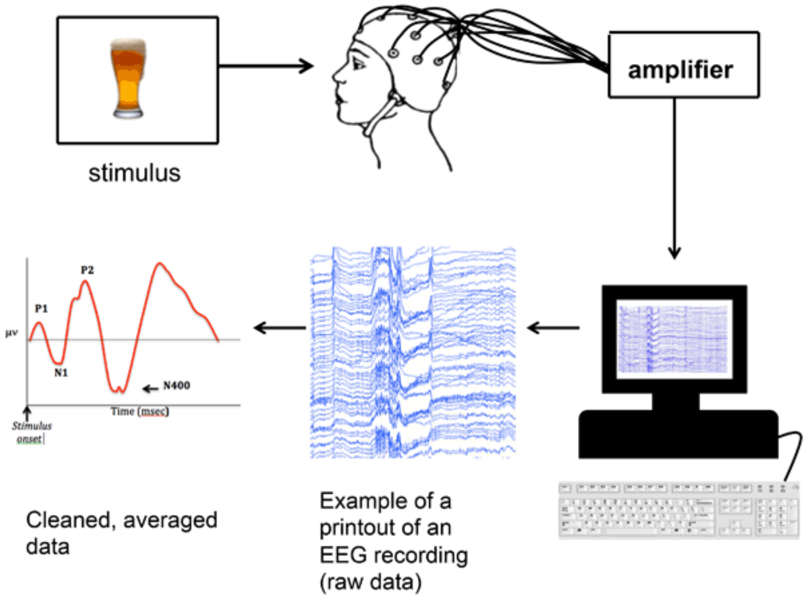


Figure 2.2: Example of ERP acquisition triggered by a visual stimulus

2.3.1 Neurophysiological mechanisms of Event-related potentials

ERPs are small time-locked voltages that arise corresponding to sensory, cognitive, or motor events. It is not possible to observe an ERP waveform in single trials because of how small the potential is respect to all the remaining EEG, and it is necessary to increase the SNR through averaging.
While for EEG is not possible to study the signal morphology, what we are interested to in ERP studies is the waveform and its parameters, and the factors influencing the amplitudes and latencies.
The ERPs reflect the coordinate PSPs activity of many thousands of neurons in response to internal or external stimuli; they are directly related to neuro-transmission

and can be used as bio-markers because of their sensitivity for individual differences.

2.3.2 Readiness Potential

The RP was independently discovered by Kornhuber and Deecke (1964). The scalp topography of the readiness potential depends on which effectors will be used to stimulate the response[8], with differences between the left and right sides of the body; it is important to highlight that brain activation is contralateral: if the movement is performed with the right side of the body then the left side of the brain will be activated and vice versa.
The lateralized portion of the RP named lateralized readiness potential has been widely used in cognitive studies. The LRP is particularly useful because it can be easily isolated from other ERP components. In the chapter 4 will be highlighted some characteristics useful to classify the RP signal[3].
The RP signal must be not confused with the contingent negative variation , a different event-related potential, cue-based, that is a negative variation between warning and imperative stimulus. Instead, the RP is self-placed, and it is a negative variation[1] of voluntary action.

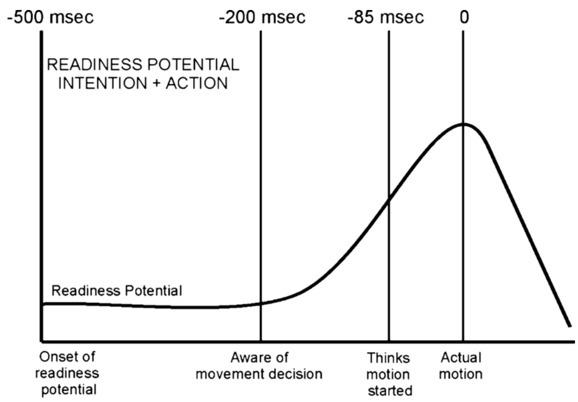


Figure 2.3: Example of *Readiness Potential* curve.

Early RP

he first component of the RP is the early RP, or BP1. This is an initial slow rising phase that lasts from about 1500 ms to about 400 ms before movement, but because of the high variability of the subject these values can be very different in different conditions. The early RP is topographically characterized by a vertex maximum and the main areas contributing to the early BP are the pre-motor cortex and the supplementary motor area (SMA), both bilaterally. This component is influenced by cognitive functions such as level of intention, preparatory state and movement selection in both amplitude and onset. One hypothesis is that the early RP reflects in part nonspecific preparation processes for the following movement.

Late RP

The second component of the RP is the late RP, or BP2, or Negative slope (NS'). This is distinguished from the other component from the abrupt increase in the gradient of the signal recorded by the central electrode corresponding to the movement, happening around 400 ms before movement onset. The negativity begins to shift to the central region contralateral to the hand that is moving, and while the early BP was generated in the premotor cortex and in the SMA, in the late RP the contribution of the primary motor cortex (M1) becomes prominent.
The late RP is maximal over the contra-lateral central area for hand movements (corresponding to electrodes C1 and C2 following the 10-20 standard) but for foot movements the maximum is found in the midline (Cz electrode). This difference is probably due to the different cortical locations of the portion controlling the hand and the portion controlling the foot in the primary motor cortex and is evidence of the involvement of M1 in the generation of this component. The late BP is influenced by features of the movement itself such as precision, discreteness and complexity.

Lateralized RP

In 1988 two groups introduced in literature the Lateralized Readiness Potential (LRP)[11], one in Groningen and one in Illinois. As already discussed, while the first part of the RP is equally distributed on right and left hemisphere, and early RP is therefore measured at the midline, the later part of the potential becomes lateralized, with larger amplitudes found in electrodes contra-lateral to the movement. A simple method for obtaining the LRP is subtracting the ipsilateral electrode signal from the contra-lateral one. In case of right-hand movements, the LRP is

obtained subtracting the ERP elicited in electrode C3 (contra-lateral) to the one elicited in electrode C4 (ipsilateral).
The LRP should be interpreted as a measure of the difference between the contralateral RP with respect to the ipsilateral: negative LRP values mean that for those time-points the contra-lateral side has a more negative values, and since the RP is a negative potential more negative values are larger signals. One of the studies that first assess the existence of the LRP also demonstrates the relation between the LRP and the onset of a peripheral motor response: EMG activity begins when the signal reaches a fixed threshold value, regardless of response accuracy or latency.
The LRP reaches the maximum amplitudes for hand movements, and due to the shape of the primary motor cortex for foot movements the polarity of the signal is reversed: the side where the highest voltage value is reached is the ipsilateral one to the movement instead of the contra-lateral.

2.3.3 Libet experiment

In the early 1980s, the neurologist Benjamin Libet performed landmark experiments aimed at investigating the role of consciousness in the generation of a motor action (Libet et al., 1983)[4]. Libet et al. (1983) measured the time when subjects became consciously aware of the decision to move. The experiment consisted of using a clock with a rapidly rotating dot: the subjects were asked to note the position of the moving dot when they were aware of the conscious decision to move a finger. Scalp EEG and finger EMG were used simultaneously to monitor brain activity and flex movement during the experiment. Libet et al. (1983) found a premovement build-up of electrical potential called readiness potential (RP) starting ∼550 ms before the movement. Unexpectedly, the conscious awareness of the decision or "the urge to move" emerged only 200 ms before movement, leaving therefore a time lag of ∼350 ms between the initial rising of the RP and the conscious awareness of the decision to flex. Libet et al. interpreted the early rise in the RP as a reflexion of neuronal computation that unconsciously prepare for the voluntary action.
Thus, according to Libet et al., our brain unconsciously plans our behaviour but allows for a conscious "veto" to alter the outcome of our volition. The findings of Libet et al. (1983) have had an unrivalled influence on the prevailing view that both our conscious "will" and subsequent actions are caused by prior neural activity.

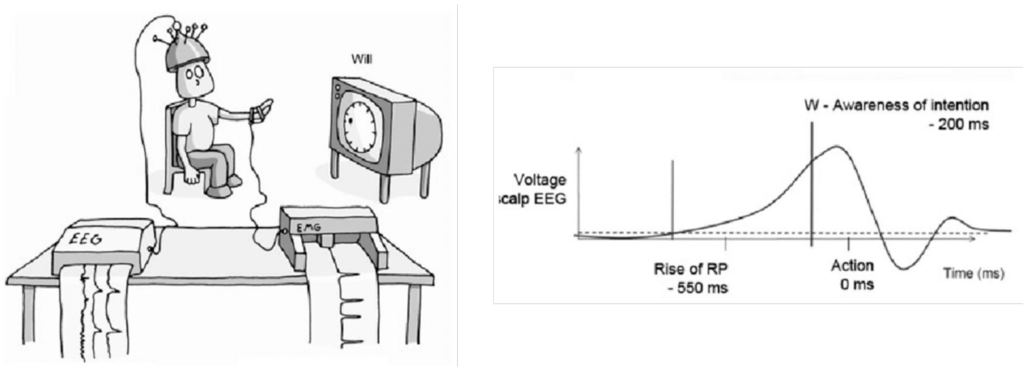


Figure 2.4: Caption

Therefore, since the presence of RP determinate the voluntary intention to move, if this signal is not present it should mean that there is no voluntary action. Being able to distinguish between voluntary/involuntary movements can be a possible method of revealing the presence of consciousness. This thesis work is concerned with identifying the features that best characterise the RP and finding an appropriate classification model.

Chapter 3

Recordings and categorisation of data

During this thesis work, an experimental phase was performed at "Centro Puzzle" in Turin. The EEG recordings have been acquired on healthy volunteers, both females and males, aged between 23-26, by using Galileo NT and its software. These EEG recordings were acquired by using an EEG cap with 7 or 34 passive Ag/AgCl electrodes. The EEG datasets were recorded with a sampling frequency of 512 Hz. Inspired by the movement that Libet made in his experiment, it was decided to have the subject perform the movement of a finger by recording an EMG signal. For this study, only signals from healthy subjects were analysed.

3.1 Protocols

3.1.1 Protocol 2012-2015

The experimenter starts the timer displayed on the computer at 5 seconds, the subject makes a flexion of the index finger of the right hand once every 10 seconds for 6 minutes (total 40 epochs). The start of the finger movement was monitored through the placement of two adhesive electrodes on the front and the back of the second phalanx of the index finger.
In addition to this standard task, alternative tests described below were performed:

- *Using the mouse*: instead of flexing the index finger, the movement of clicking the mouse button is used;

- *Use of both hands*: in order to remove the effect of the stereotyped movement, the subject uses both hands, and it is the experimenter who indicates which one;

- *Short trials*: the experiment is carried out in the same way as the standard one, but with a shorter trial duration (5 seconds). The aim is to validate the hypothesis of a lack of free will: the subject becomes aware of the action to be performed after the brain has been prepared for that action (Libet experiment);

- *Bimanual*: the experiment is performed with both hands simultaneously. This type of task stems from the need to investigate the cognitive condition of patients with anosognosia due to hemiplegia, a transitory condition that, in some cases, may afflict subjects in which the stroke has affected the right hemisphere of the brain, damaging the motor area. In these subjects, there is paralysis of the left side of the body, but the patient himself is not conscious of this, he openly claims that he has no problem and that he can move both the paralysed arm and leg correctly.

3.1.2 Protocol 2015-2018

In the experiment, are the subject is asked to perform a simple movement, observing a clock projected onto the PC screen: starting from second 5, the movement is repeated every 10 seconds, for 6 minutes and 40 seconds, for a total of 40 epochs. The movements required include: flexion of the index finger, the voluntary movement of the foot or leg, coordinated movement of the hand and leg and the patellar knee reflex. Some tasks are performed with the subject blindfolded: in this case, the operator observes the watch and gives the subject the indication when to perform the movement, in order to avoid a possible influence of the external environment on the subject.

3.1.3 Protocol 2018

The healthy volunteers had to perform three tasks in every experimental session:

- *Voluntary task:* the subject was instructed to bend the index finger. The firm movement had to be made during a time window of about 10 s-13 s, started by an acoustic signal. This experiment is intended to choose the timing of the movement and not to feel the urge to move. This movement is “self-paced”;
- *Semivolontario task:* also a flexion of the index finger was performed, but this time the subject has to move in correspondence with an acoustic signal, as soon as it is heard. Unlike the voluntary task, this experiment is “cue-based” because of the external trigger.
- *Involuntary task:* the patellar reflex is elicited in correspondence of the tendon with a reflex hammer. For this task, an acoustic signal is only heard by the experimenter wearing headphones, so that the subject does not expect the moment when the stimulus occurs. Starting from the first movement to the last, the degree of will decreases and the control of the voluntary muscles is greatly reduced.

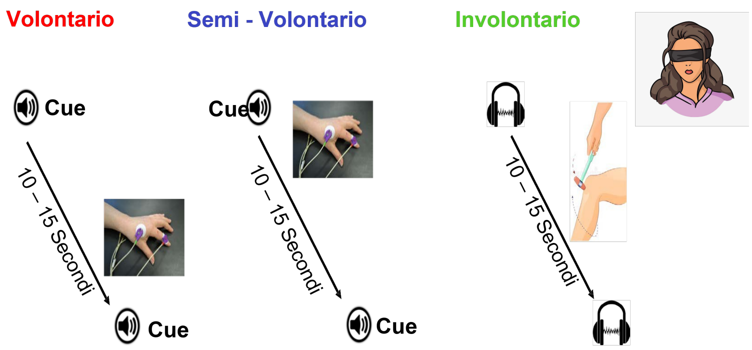


Figure 3.1: Schema relativo ai tre diversi task da compiere.

Every session is composed of 40 trials for each task and the acoustic signal is randomized to avoid the adaptation of the brain. The acoustic signal is emitted by a device LabJack and is converted into a voltage signal through LabJack’s DAQ to synchronize it with the EEG tracks. To organize the experiment, the software

OpenSesame was used, which allowed the experimenter, through a GUI, to choose the task and the respective number of repetitions that the subject will have to perform.

3.2 Experimental Setup

Figure 3.2: Data collection station.

- Data acquisition device: *Galileo Suite*, EB Neuro with amplifiers BE (Brain Explorer);
- The device of processing and display the EEG traces PC with Galileo software;
- The device with the stimulation system: PC with OpenSesame for the acoustic signal and the use of *LabJack*;
- Synchronization system: Labjack and photocoupler circuit;
- Recording tools: EEG cap, adhesive electrodes (4 for EOG signal and 2 for EMG signal), the ground electrode for EMG (for the wrist: voluntary and semi-voluntary tasks and the ankle: involuntary task), 2 earlobes reference electrodes for EEG;

- Additional accessories: TEN20 (conductive paste), NUPREP (abrasive paste), conductive EEG gel, a syringe with a blunt needle.

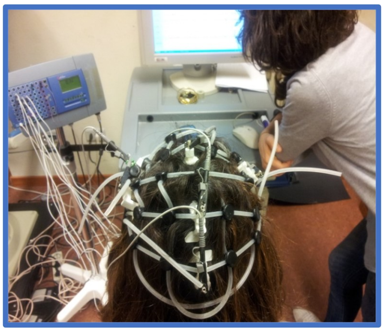


Figure 3.3: EEG Headset.

Figure 3.4: EMG electrodes.

3.2.1 The preparation stage

The preparation stage is the longest but also the most important setp, as it allows to obtain a legible EEG trace. During the experiment, two computers are used: a computer, in which OpenSesame software is loaded, is aimed at starting the task and emitting the acoustic signal; the other one, hosting Galileo software, is used to visualize, process, but also export subsequently, the signals acquired from the EEG head. The volunteer is seated on a raised chair to prevent the feet from touching the floor, to simply achieve the involuntary task, that is the patellar reflex. Furthermore, the subject is seated behind the computer, which contains Galileo software, while the second computer is placed on the table turning left from the position in which he is sitting, so as not to be influenced in any way during the experiment. Immediately thereafter, the preparation for signal acquisition begins. First of all, the electrodes for EOG and EMG recordings are placed using the TAN20 paste and then the earlobes and the wrist (or the ankle for 41 the involuntary

task) electrodes are mounted respectively, always using the TEN20 conductive paste. Once these electrodes are in place, the EEG cap is set on the head, trying to position the Cz electrode in the middle, between Nasion and Inion and also between the two earlobes reference electrodes. After placing the cap, the skin is cleaned, using the Nuprep abrasive paste, to remove sebum and dead scalp cells. Then, the inside of the cap electrodes is filled with the conductive EEG gel, through a syringe with a blunt needle.
The conductive EEG gel is used for two reasons:

- to improve signal conduction, lowering the electrode impendence to obtain a good electrode-skin contact;
- to improve adhesion with the skin, avoiding any problem of detachment caused by movement.

Before acquiring the EEG signal, the experimenter has to check that the electrodes' impendence does not exceed a certain threshold value, equal to 10 kΩ. At the end of the trial, the materials are cleaned, because dry gel residues on the electrodes can be a source of noise, using alcohol for earlobes and wrist (or ankle) electrodes and only water for the EEG cap.

3.3 Datasets organization

The data for the two protocols and the different tasks were classified and named according to the information on the subject, the type and method of acquisition of the biological signals and the specifications of the tools used. In the rating adopted, both the EMG signal and the Labjack signal were rated on a scale from 0 to 3, where 0 indicates that the signal has a poor quality while 3 indicates a signal of good quality. The considerations on the quality of the EMG signal are based on the variability of the signal itself and the amount of noise. The datasets have a name consisting of a string of 45 characters. More in detail, there are:

- 8 characters showing the name of the anonymised subject, read in the first letter of the first name, the first letter of the surname, the last digit of the year of registration, the last two digits of the year of birth, the month of registration and the character 0/1 if the subject is male/female (in case of homonymy, the last character is set to 2);

- 5 characters to decipher the EEG electrode montage: 32C18 is the acronym for the montage with the 34-electrode headset ('32 Channel 2018'), while OBE12 is the one with the bridge electrodes ('Over Bridge Electrodes 2012');
- 4 characters indicating the protocol used for the controls: A18C for the 2018 protocol ("After 2018 Controls"), B18C for the 2015-2018 protocol ("Before 2018 Controls") and VOPC refers to the 2012-2015 protocol data ("Very Old Protocol Controls");
- characters to describe the condition of the subject: the acronym FOL refers to blindfolded subjects and UNF to non-blindfolded subjects;
- 5 characters to identify the type of task performed: voluntary, semi-voluntary or involuntary, indicated by VOL18, SEM18 or INV18 respectively;
- 4 characters for the task: RFOF for right forefinger, LFOF for left forefinger, BFOF for bimanual forefinger, RMOU for right mouse, RLEG for right leg, LLEG for left leg, RFOO for right foot, LFOO for left foot, RHLE for right hand and leg, LHLE per left hand & leg;
- 4 characters to indicate the channel used for EMG: EMG1 for channel 1, EMG2 for channel 2, EMGX for the channel without any number;
- 4 characters to discriminate EMG and Labjack signal quality, thus: E + 0/1/2/3 for EMG and L+ 0/1/2/3 for Labjack (in protocols prior to the 2018 protocol, the last two characters correspond to L0, as the Labjack is not present).

3.4 Software

The software used for processing and analysing the post-acquisition data was MATLAB 2021b. In particular, a plug-in was implemented for the EEGLAB tool named MRCPLAB.

3.4.1 EEGLAB & MRCPLAB

EEGLAB is an interactive MATLAB toolbox, created by the Swartz Centre for Computational Neuroscience (SCCN). EEGLAB is used to process signals from electro-encephalography, magneto- encephalography and other electro-physiological signals[29].

A graphical user interface (GUI) allows the user to choose between different operations to be performed both in the time domain and in the frequency domain, such as applying filters, rejecting artefacts, averaging, event statistics and visualise data.

EEGLAB also allows the visualisation of brain dynamics related to events and to store and manipulate EEG data through functions already implemented. In addition, functions can be written to carry out real-time analysis and automatic analysis.

To process the EEG data acquired by the software, a plug-in was developed for EEGLAB, called MRCPLAB, which manages the integration of all the algorithms implemented with EEGLAB and also adds very useful functions for analysing the signal automatically.

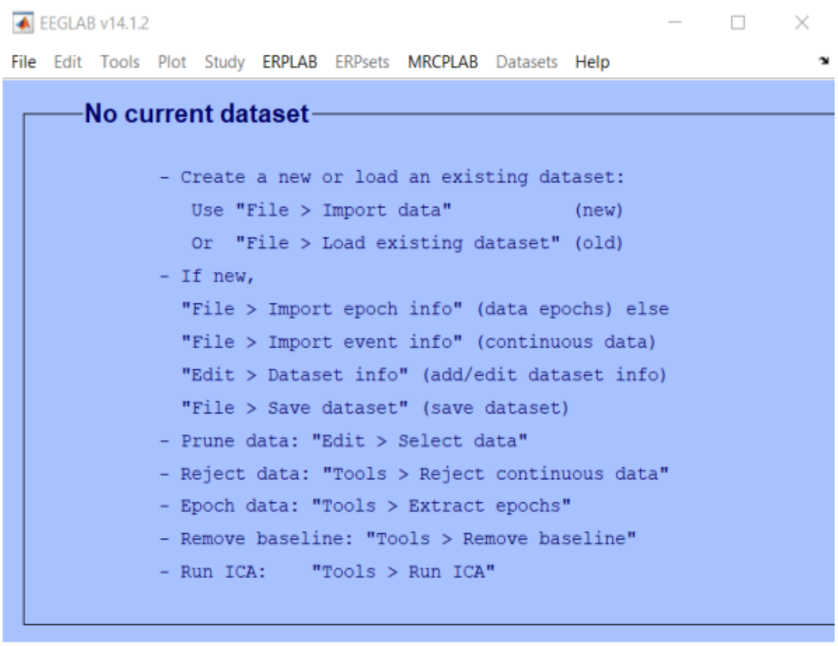


Figure 3.5: EEGLAB GUI with MRCPLAB plug-in

Chapter 4

Method and Project Development

4.1 State of the art

The first studies proposed on this matter were the Libet experiments mentioned above. Through the years many scientists approached this problem, especially focusing on the changes that occurr in the BP in several movement disorders, notably Parkinson's disease, in which the pattern is consistent with a failure of pre-SMA activation. The presence (or absence) of a clear preceding negativity can also have diagnostic importance for certain movement disorders. Several techniques of features extraction for RP characterization were implemented and various types of classifiers, mostly support vector machine, were utilized for classification, for example, imaginary and real voluntary movements; or if the RP were recorded from a patient or a healthy subject.
In this thesis a new approach was investigated: to characterise and classify whether a movement is voluntary or involuntary, in first for healthy subjects, and then for patients with hemiplegia or coma state.

4.2 Introduction

In this project the problem of RP signal classification was investigated, that basically consists in four work stage; the first, after the pre-processing part, during which the signals form the EEG were filtered, artifacts corrected and jitter compensated (three method were proposed in the plug-in), was targeted at selecting the 'good' signals among the different subjects. The second was consisting of the feature extraction part, that refers to the procedure of transforming raw data into numerical features that can be processed while preserving the information in the original data set. The third, the feature selection stage, was about choosing among the different attributes which most contribute most to the prediction variable or any specific output of interest. The fourth, and last, was regarding the classification process; some different types of classification were proposed and after an analysis of performance one classifier was selected.

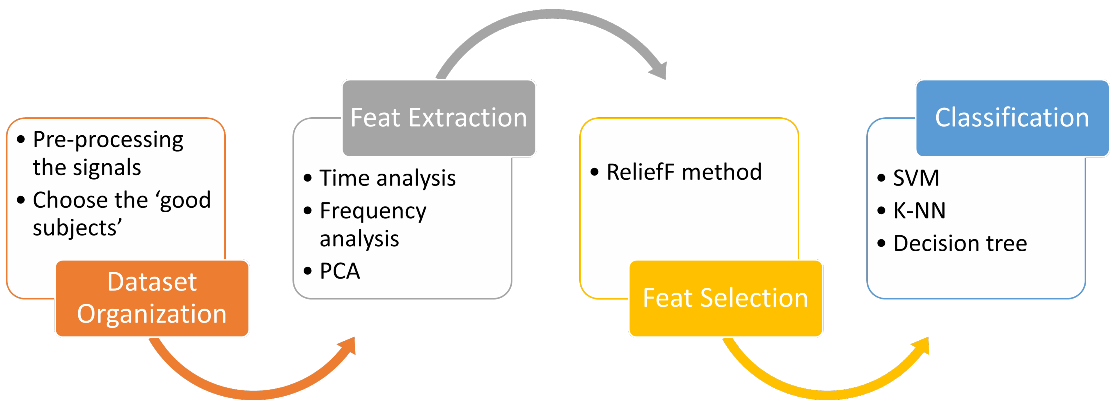


Figure 4.1: Work-Flow of the project.

4.3 Datasets review

For this work EEG signals from both 2015 and 2018 protocols were considered, trying to select subjects who performed different tasks in a balanced way.

4.3.1 Pre-processing

At the beginning, after the recording and anonymisation of data, the MRCPLAB plugin on Matlab were open. The operations to do in order to load, examinate and process the data are explained below.
First, loading the data: from the entry "import/save data" it was possible to import the data for the first time form ".asc" file and the data were automatically filtered and saved into a ".set" format. Afterwards, the opening of the data was possible form the ".set" file.
After that, many actions to clean the signal could be performed:

- Seek noisy channels, to detect particularly noisy channels.
- Select or reject data, to select or delete portions of data; by selecting or deleting time ranges, epochs or entire channels.
- Artifact correction
- Interpolate electrodes
- Spatial filtering

The choices of pre-processing options were up to the operator.
Then, the signal had to be divided into epochs through the command "Epoch operation" and the epoch should be realigned with "jitter compensation" command; thereafter, an average is made and the channels of interest **Fcz**, **Fc3**, **Fc4**, **Cz**, **Pz**, **C3** and **C4** were extracted.

4.3.2 Selection of datasets

A manual selection of the subjects who do not have good EEG tracings and who could mislead their classification was performed. In order to be as objective as possible, some characteristics were selected to determine whether or not a set had to be deleted:

- **Bad EMG signals**; if the set had E1 or E0, which means that the quality of EMG is bad, was not considered.

- The **number of epochs**; if the set had less than 10 epochs the experiment may be invalid, since the EEG recordings were not made by experts, they could be incorrect.
- **Signal to noise ratio (SNR)**; it had to be positive when the RP signal is present and negative in the other cases.

Following the evaluation of these attributes, we were able to select the set of data in order to proceed to classification. In total, 15 subjects from involuntary, and 15 subjects from voluntary task groups were taken, in order to have available a balanced dataset.

4.4 Feature Extraction

What is a *feature*?
Features, or attributes, were defined as any extractable measurements, evaluation, judgment, in other words data[12]. Several categories can be distinguished:

- **Binary**: they assume values 0 or 1.
- **Categorical** data: they assume a predefined set of values that can be ranked or not.
- **Integer** or **Numerical** data.

The aim of the extraction of these characteristics is to identify the most significant ones to summarise our problem. This can be done by relying on the judgement of an expert operator or, as in our case, by referring to existing studies on component characterisation and classification of the RP signal. Feature extraction is the most crucial part of biomedical signal classification because the classification performance might be degraded if the features were not properly selected.

4.5 RP feature

All the features were picked out from the windowed signal 1 second before and 1.5 seconds after 0, both time and frequency domain were investigated:

- *Time domain:*
  - **Peak amplitude** (**Amp**): -5uV to -20 uV. The negative peak represents the potential of neurons activated when there is an intention to move. When the movement is only imagined the amplitude is less negative. It was evaluated in the motor area (C line).
  - **Negative Slope** : it occurs before the movement onset and for this reason is evaluated in the pre-motor area (Fc line).
  - **Onset** of RP: that is the number of seconds elapsed before reaching the peak. considering the start of the slope as 0. As in the previous cases it must be considered the pre-motor zone (Fc line).
  - Also, more general features were extracted like **variance**, **mean value**, **skewness** and **kurtosis** in the motor area (C line).
  - **Principal component analysis (PCA)** on the signal (C line)
  - **Signal to noise ratio** evaluation: which is positive when the signal exceeds the noise. Variance and mean were calculated in the motor area (C line).
- *Frequency domain*
  - Since the signal has slow fluctuation in a range between 3 and 5 Hz, due to neuronal synchronicity, the distribution of average **signal power** in the band of interest was calculated.
  - **Principal component analysis (PCA)** on the power spectral density (PSD).
    All the analysis were done on the C line.

In this study, a *Principal Component Analysis* was performed on both the signal and the PSD.

4.5.1 Principal Component Analysis

PCA was used to extract a new dataset where every pattern was a linear combination of the original ones. The new patterns were orthogonal (un-correlated) and were

the principal components. In other words, PCA can reduce the dimension of the dataset[21], providing computational benefits, so as to represent the dataset by a linear combination of less than: the number of samples for the signal or, for the PSD, the squared magnitude units of the time series data per unit frequency. Then, only the components with higher variance were considered.
Thus, a feature vector was created, and the set of original data was reduced into relevant ones. But all the features have the same influence on the classification? and are all those found useful for classification, or can they lead to misclassification?

4.6 Feature selection

The central premise when using a feature selection technique was that the data contains some features that were either redundant or irrelevant and can thus be removed without incurring much loss of information. The concepts of “redundant” and “irrelevant” were two distinct notions, since one relevant feature may be redundant in the presence of another relevant feature with which it is strongly correlated, while irrelevant means that it carries no information[14].
Feature Selection is the process in which it is possible to select automatically or manually those features which contribute most to the prediction variable or output of interest[26]. The benefits obtained not only lead to a better interpretation of the problem (in our case a better classification), but also help the computational costs and time spent. The major advantages are:

- Reduces overfitting: less redundant data means less opportunity to make decisions based on noise.
- Improves accuracy: less misleading data means modelling accuracy improvement.
- Reduces training time: fewer data points reduce algorithm complexity and algorithms train faster.

Three main types of feature selection can be considered: filter techniques, wrapped method and embedded techniques.

- *Filter techniques*: the relevance of features was considered only looking at intrinsic properties of the data and selection was a pre-processing before the classification model. The relevance of features was calculated, and the less relevant features were ignored. This kind of selection is fast, easy and it is not dependent on the classifier.
- *Wrapped methods*: these methods integrate feature selection and the classification model. A subset of feature is used to perform the classification and is evaluated in terms of classification performance. Thus, the subset will be specific for the classification model. This interaction between subset

and classifier is an advantage, but there is the risk of overfitting, and the computational cost can be high, depending on the classification model.

- *Embedded techniques*: the selection was embedded in the classifier construction. Like wrapped methods, embedded techniques performed an interaction between features and classifier, but their computational cost is cheaper.

For this study filtering techniques were applied, and EEG features may be classified by means of linear algorithms, thus allowing the evaluation of the relative weight of each individual feature. Common sequential methods that use dimensionality reduction, such as principal components analysis (PCA), do not guarantee good classification since the best discriminating component may not be among the largest principal components. In this work a filtered method is proposed; a proxy measure was utilized to score a feature subset.

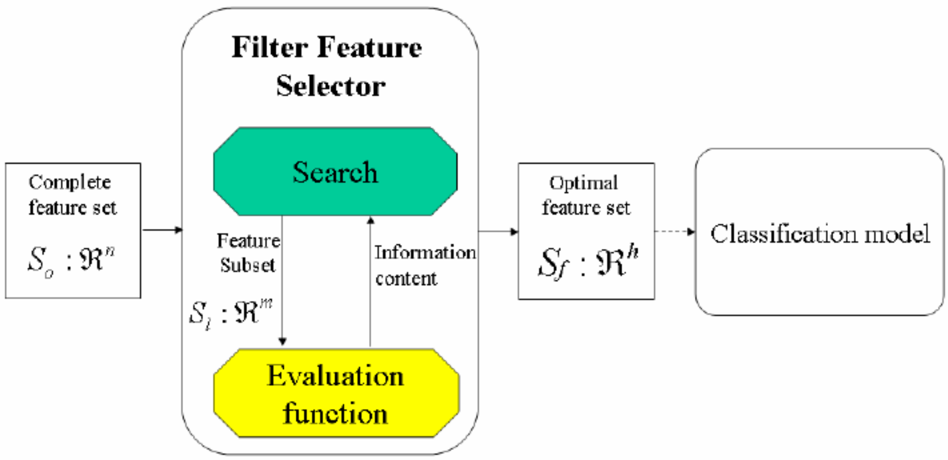


Figure 4.2: An example of general feature selection with filtered method.

4.6.1 FS: ReliefF method

Relief

Proposed for the first time by Kira and Rendell in 1992, as an individual evaluation filtering feature selection method, Relief[5] calculates a proxy statistic for each feature that can be used to estimate feature 'quality' or 'relevance' to the target concept. The original Relief algorithm was limited to binary classification problems

and had no mechanism to handle the missing data.
The original algorithm is proposed below:

Require: for each training instance a vector of feature values and the class value
$n \leftarrow$ number of training instances
$a \leftarrow$ number of features (i.e. attributes)
Parameter: $m \leftarrow$ number of random training instances out of n used to update W

initialize all feature weights $W[A] := 0.0$
for i:=1 **to** m **do**
  randomly select a 'target' instance R_i
  find a nearest hit 'H' and nearest miss 'M' (instances)
  for A:= 1 **to** a **do**
    $W[A] := W[A] - diff(A, R_i, H)/m + diff(A, R_i, M)/m$
  end for
end for
return the vector W of feature scores that estimate the quality of features

Figure 4.3: Relief algorithm.

First a vector of zeros of length equal to the number of features is created, than the algorithm cycles through m random training instance (R_i), selected without replacement, where m is a user-defined parameter. Each cycle, R_i is the 'target' instance and the feature score vector W is updated based on feature value differences observed between the target and neighbouring instances. Therefore, each cycle, the distance between the 'target' instance and all other instances is calculated. Relief identifies two nearest neighbour instances of the target; one with the same class, called the nearest hit (H) and the other with the opposite class, called the nearest miss (M). The last step of the cycle updates the weight of a feature A in W if the feature value differs between the target instance R_i and either the nearest hit H or the nearest miss M. Features that have a different value between R_i and M support the hypothesis that they are informative of outcome, so the quality estimation W[A] is increased.
Conversely, features with differences between R_i and H provide evidence to the contrary, so the quality estimation W[A] is decreased. The diff function calculates

the difference in value of feature A between two instances I1 and I2, where I R 1 = i and I2 is either H or M, when performing weight updates for continuous feature, diff is defined as:

$$diff(A, I_1, I_2) = \frac{|value(A, I_1) - value(A, I_2)|}{max(A) - min(A)}$$

The maximum and minimum values of A are determined over the entire set of instances. The diff function is also used to calculate the distance between instances when finding nearest neighbours. The total distance is simply the sum of diff distances over all attributes, for example Manhattan distance. The original Relief algorithm used Euclidean distance instead of Manhattan distance. However, experiments indicated no significant difference between the results. Thus the simplified description of the Relief algorithm has become standard for this reason. In our case, a Euclidean metric measure was applied. At the end all the value inside the vector will be between -1 (that denotes the worst feature) and 1 (that indicates the best feature).

Originally the description of Relief algorithm specified an automated method, a *relevance threshold* τ was defined such that any feature with a relevance weight W[A]>τ would be selected. Kira and Rendell demonstrated that "statistically, the relevance level of a relevant feature is expected to be larger than zero and that of an irrelevant one is expected to be zero (or negative)". Therefore, generally the threshold should be selected such that $0<\tau<1$.

In practice, rather than choosing a value of τ, it is often more practical to choose some number of features to be selected a priori based on the functional, computational, or run time limitations of the downstream modelling algorithms that will be applied. Ultimately the goal is to provide the best chance that all relevant features are included in the selected set for modelling, but at the same time, remove as many of the irrelevant features as possible to facilitate modelling, reduce overfitting, and make the task of induction tractable. In order to be as generic as possible, all the weights greater than 0 were considered.

Strengths and limitations

Regarding strengths, Relief has been presented as being both **non-myopic**, as it estimates the quality of a given feature in the context of other features, and **non-parametric**, as it makes no assumptions regarding the population distribution or sample size. The efficiency of the algorithm has been attributed to the fact that it doesn't explicitly explore feature subsets and because it does not bother trying to identify an optimal minimum feature subset size. The major limitation of this algorithm being very sensitive to noise and unaffected by feature interactions. For these reasons different Relief algorithms were implemented through the years.

ReliefF

The original Relief algorithm is rarely applied in practice and has been supplemented by ReliefF[27]. The "F" in the name refers to the sixth variation of the algorithm proposed by Kononenko. Here we highlight four key differences between ReliefF and Relief.

1. ReliefF relies on a 'number of neighbours' user parameter k that specifies the use of k nearest hits and k nearest misses in the scoring update for each target instance (rather than a single hit and miss). This change increased weight estimate reliability. [ReliefA]

2. Three different strategies were proposed to handle the missing value. The best approach (ReliefD) sets the diff function equal to the class-conditional probability that two instances have different values for the given feature. This is implicitly an interpolation approach. [Relief(B-D)]

3. Two different strategies were proposed to handle multi-class endpoints. These strategies were proposed under the names ReliefE and ReliefF. ReliefF finds k nearest misses from each 'other' class and averages the weight update based on the prior probability of each class. Conceptually, this encourages the algorithm to estimate the ability of features to separate all pairs of classes regardless of which two classes are closest to one another. [Relief(E-F)]

4. Since it is expected that as the parameter m approaches the total number of instances n, the quality of the weight estimates becomes more reliable,

Kononenko proposed the simplifying assumption that m=n: every instance in the dataset gets to be the target instance one time.

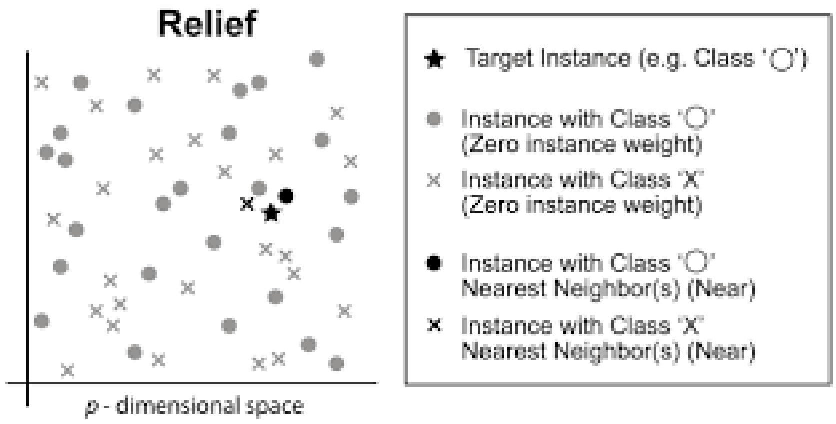


Figure 4.4: RealiefF

The steps of ReliefF function implemented in Matlab were:

1. Set all predictor weights Wi to 0.

2. Select randomly the Xr observation

3. Find the k-nearest observation to Xr, with k equal to 10, for each class (Xq)

4. Calculate the weight for each feature Fi, the value will be between -1(worst) and 1 (best).
   For continuous data, the formulas for updating the weights were as follows:

   - Same class:
   $$W_i{}^i = W_i^{i-1} - \frac{\Delta(x_r, x_q)}{m} \cdot d_{rq}$$

   - Different class:
   $$W_i{}^i = W_i^{i-1} + \frac{p_{yq}}{1 - p_{yr}} \cdot \frac{\Delta(x_r, x_q)}{m} \cdot d_{rq}$$

   In this case *Manhattan* distance where used:
   $$\Delta(x_r, x_q) = \frac{|x_{rj} - x_{qj}|}{max(F_j) - min(F_j)}$$

4.7 Classification

The last part of this work was the classification of the voluntariness or involuntariness of a movement; therefore, it was a binary classification.
The term classification, in statistics, includes all those algorithms that divide or categorise data into groups or types using attribute (features). The classifier applied those features as an information to decide in which class to assign the data. Different classifiers could be used, and there was the possibility to divide them into those with supervised or unsupervised learning. In supervised learning, the classification of part of data was known a priori and could be used to train the classifier (training set). The result of the training part was about the selection of free parameters that allowed the classifier to fit the training dataset.
At first, a classifier well-known in literature, the Support Vector Machine (SVM) was used[23, 18]. After, two other classifiers were implemented: K-NN, which follows the model used for feature selection, and the decision tree (DT). For each machine learning algorithms, the leave-one-out cross-validation procedure was used to estimate the performance.

4.7.1 Support Vector Machine

SVM, developed by Vapnik and Co. in 1963-1992, was one of the most robust predictor models based on statistical learning frameworks. The algorithm could be applied for both regression or classification in order to solve linear and non-linear problems[17].
The idea of SVM was simple[9]: the algorithm creates a line or a hyperplane which separates the data into classes. SVM works by mapping data to a high-dimensional feature space so that data points can be categorized, even when the data were not otherwise linearly separable. A separator between the categories was found, named decision boundary. For example, whether the data could be separated by a line: anything that falls into one side will be classified as one class, and anything that falls into the other as another class (binary classification).The idea behind the binary SVM was to split the dataset in two hyperspaces of features, separated by an hyperplane. Of course, more than one hyperplane can exist allowing the wanted split between classes.

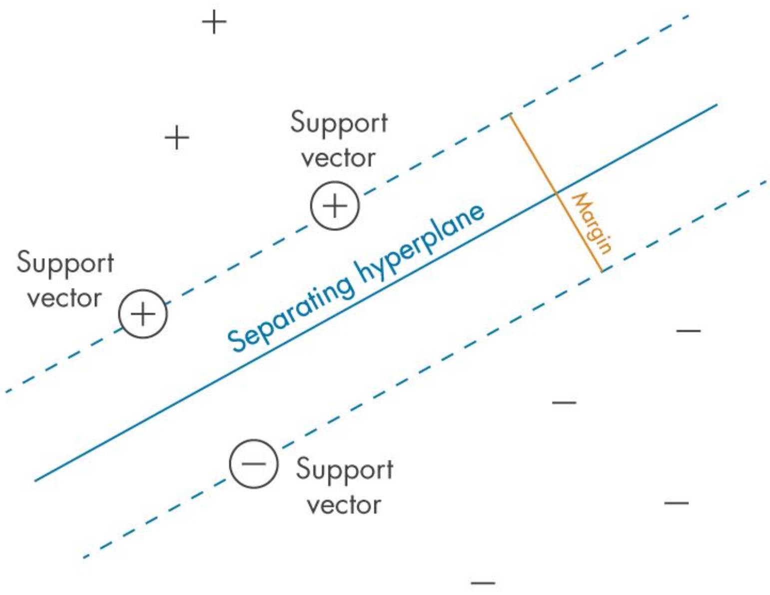


Figure 4.5: Example of hyperplane, margin and support vectors for a SVM.

The SVM algorithm tried to find the solution which maximizes the margins from both tags. In other words: the hyperplane (remember it's a line in this case) whose distance to the nearest element of each tag is the largest. The data points nearest to the hyperplane were named *support vectors*, the points of a data set that, if removed, would alter the position of the dividing hyperplane. Because of this, they could be considered the critical elements of a data set. Following this, characteristics of new data can be used to predict the group to which a new record should belong. What about no-linear data?
Other dimensions could be added, or different types of kernels applied like, for example, Gaussian, Radial Basis Function (RBF), sigmoid or others. However, the approach to the problem remains identical, to seek the best separation between classes that could be more than two.
For this paper, both SVM with linear kernel and cubic polynomial kernel were applied.

4.7.2 K-NN

The k nearest neighbour algorithm developed by Fix and Hodges in 1951, and later updated by Cover, was applied for classification and regression problem. Limiting ourselves, as in our case, to a classification problem, the input consisted of the k closest training examples in a data set. While the output was a class membership. An object was classified by a plurality vote of its neighbours, with the object being assigned to the class most common among its k nearest neighbours[22]. The steps of the algorithm were as follows[24]:

1. Select the number of the K nearest neighbour.
2. Calculate the distance of K number of neighbour, that could be Euclidean, Cityblock, Chebychev, etc.
3. Take the K nearest neighbour as per calculated distance.
4. Among these K neighbours, count the number of the data points in each category.
5. Assign the new data points to that category for which the number of the neighbour is maximum.

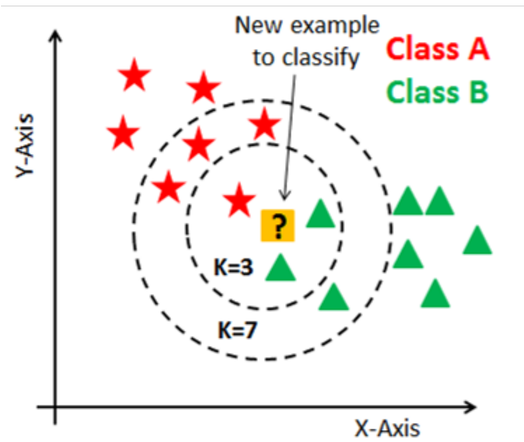


Figure 4.6: Example of K-NN.

4.7.3 Decision Tree

The decision tree predicting model could be applied both for classification and regression problem (supervised learning)[28]. The algorithm on which this is based is very intuitive and simple to intemperate. This characteristic is fundamental in some specific areas in which a major simplicity of understanding is preferable to greater accuracy of the model.
The decision tree algorithm was articulated as follows; the input data were continuously separated on the basis of previously known criteria. The information integration of the separation criteria was explained above; first it was important to define some key concepts:

- **Root Node**: the base of the decision tree.
- **Nodes**: represent a condition on which the separation of data is based.
- **Splitting**: the process of dividing a node into multiple sub-nodes.
- **Leaf node**: when a sub-node does not further split into additional sub-nodes; represents possible outcomes.
- **Pruning**: the process of removing sub-nodes of a decision tree.
- **Branches**: intermediate or final step, the places where the data end up once separated. If the separation was not possible anymore, so it come to an end, the branch was called leaf.

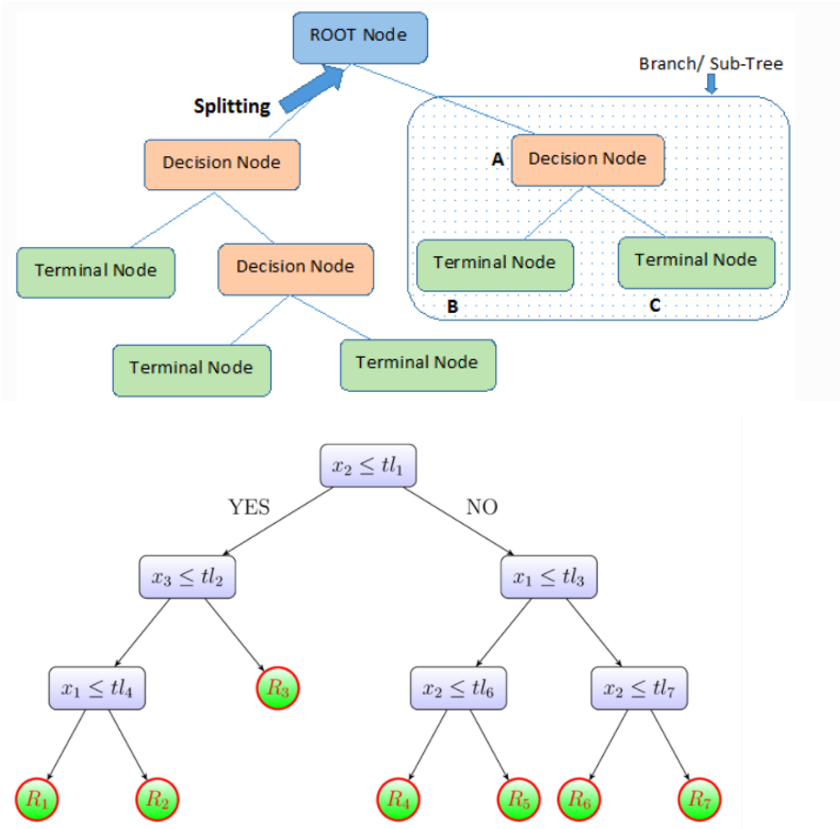


Figure 4.7: Examples of generic Decision tree

A fundamental point of the Decision Tree was to select the *Root Node* and the other *Nodes* that allow the tree to branch. The target was to find the values of the variable for which the best split could be achieved. The choice of the best could be made through various metrics, depending on whether the dealing was a classification or regression case. For example, for classification cases it was feasible to use *Entropy* or *Information Gain* or the *Gini index*, calculated as follows:

- Entropy:

$$Entropy = -\sum_{i=1}^{N} p_i(x) \log_2 p_i(x) \tag{4.1}$$

- Gini index:

$$Gini = 1 - \sum_{i=1}^{N} p_i^2 \tag{4.2}$$

N: number of classes.

p_i :proportion of the samples that belongs to class N for a particular node.

- Information Gain:

$$InformationGain(i) = Entropy(before) - \sum_{i=1}^{N} Entropy(i, after) \tag{4.3}$$

N: number of subsets generated by the split; for binary case, equal to the number of classes.
"before" was the dataset before the split.
"after" is the subset i after the split.

In general, however, the objective was to divide the initial population by the value of a variable to create two groups that were as internally homogeneous as possible and as in-homogeneous as possible.
It is important to note that in this case the attributes can also be categorical, whereas in previous cases it was necessary to discretize the features.

4.7.4 Performance of Machine Learning Algorithms

After selecting a classification model type and setting the parameters, it was important to evaluate predictions for classification problems.

Leave-One-Out Cross-Validation (LOOCV)

One possible technique, which corresponds to the one used in this thesis, was cross-validation using the leave-one-out method. This was a special method where the number of folds equals the number of instances in the data set. Thus, the learning algorithm was applied once for each instance, using all other instances as a training set and using the selected instance as a single-item test set. This process was closely related to the statistical method of jack-knife estimation. The Leave-one-out cross-validation uses the following approach to evaluate a model:

1. Split a dataset into a training set and a testing set, using all but one observation as part of the training set. Note that only one observation was left out form the trainset.

2. Build the model using data only originating from the training set.
3. Use the model to predict the response value of the one observation left out of the model.
4. Repeat the process n times, where n was the number of observations (subject in our case), leaving out a different observation from the training set each time.
5. Create the confusion matrix that allows visualization of the performance of an algorithm.

Chapter 5

Results

5.1 Introduction

In this chapter the criticalities and results collected on the selection of the datasets, feature extraction & selection and classification are presented.

5.2 Datasets selection

For the choice of datasets to be used, as it was explained in chapter 4, an attempt was made to be as generic and objective as possible. Here below some figures that help to better explain how the choice was made, consisting in the signal representations after pre-processing and the signal to noise ratio (SNR), for both voluntary and involuntary tasks. Three types of sets were selected: one acceptable, one unacceptable and one borderline.

The case of Involuntary task

a) Good Dataset

Acceptable case: as it was possible to see the signal was approximately flat, there was a trend towards a positive signal, but it is not significant of an RP signal. For the SNR, that was always negative, it means that there was a preponderance of noise compared to the signal. This situation was optimal and an indication that there was no signal, as it should happen in the case of involuntary movement and more specifically of a reflex. In this case the subjects were from the protocol 2015 and blindfolded.

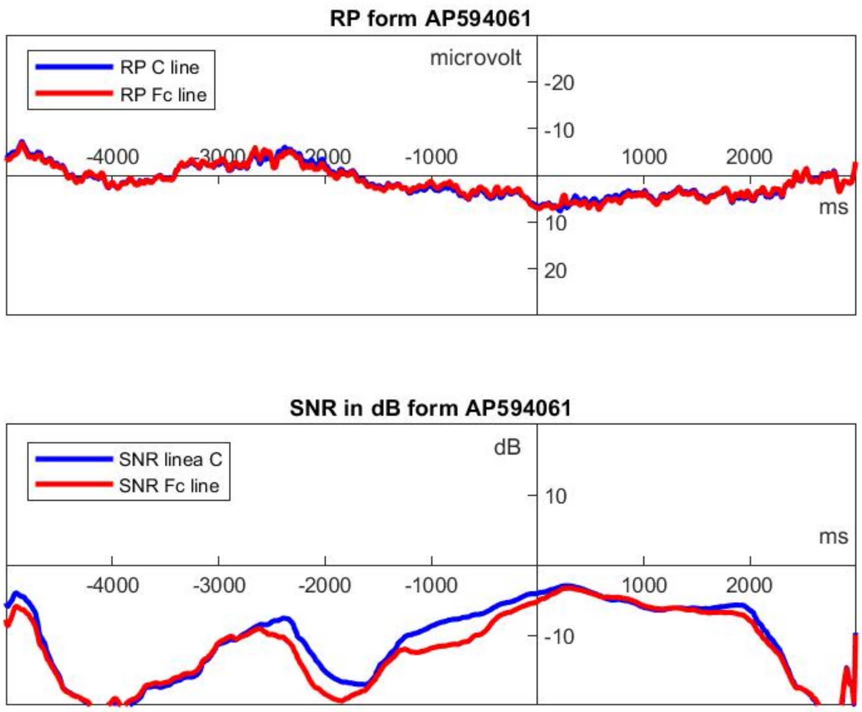


Figure 5.1: Acceptable set

b) Bad Dataset

Unacceptable case: the signal in this case was similar to an RP, one can observe a trend towards negativity and then a return towards zero. The SNR in this case was positive in the window where there should be an RP signal, 200 ms before the EMG onset, which was why the subject cannot be considered for the study. The subject was from the protocol 2015 and unblindfolded.

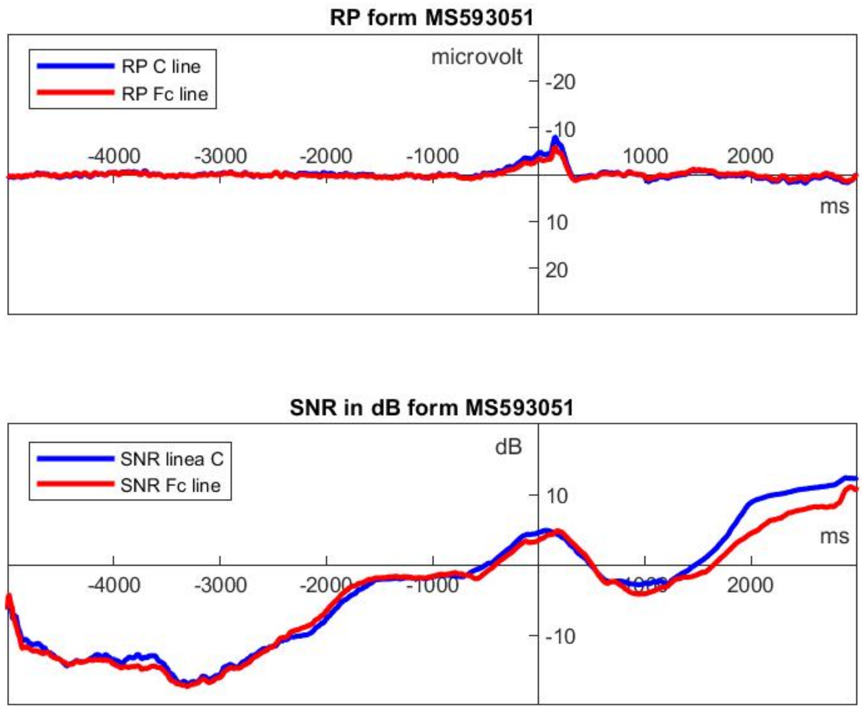


Figure 5.2: Unacceptable set

c) Borderline Dataset

Borderline case: the signal of this subject had a negative slope, but as it can also be seen from the graph, the slope is not as steep. The decision to keep this signal was based mainly on the SNR which, in the window of interest, was negative and therefore there was a preponderance of noise in relation to the signal. The signal of the subject was from protocol 2018.

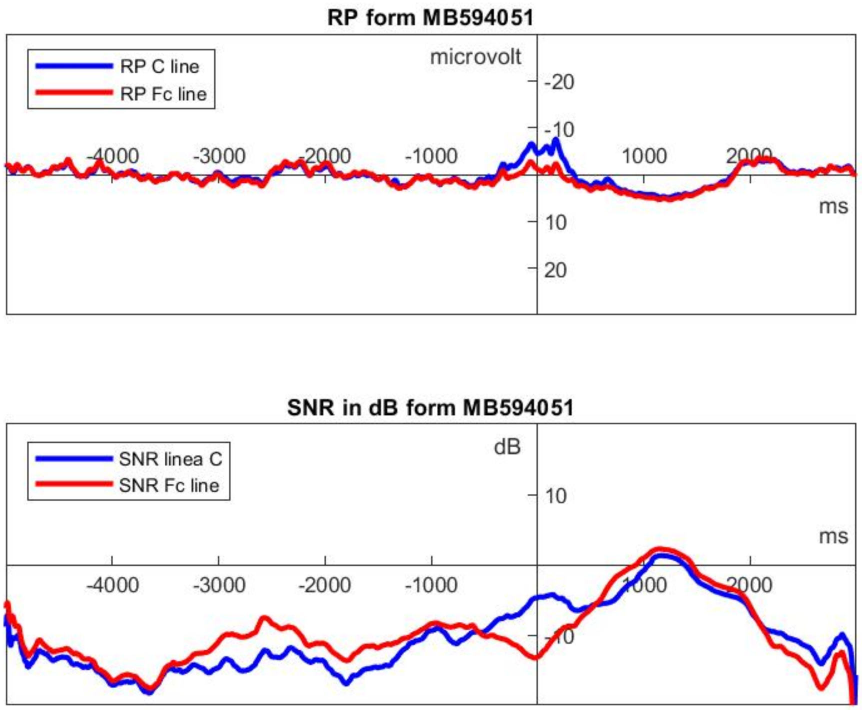


Figure 5.3: Borderline set

The case of Voluntary task

a) Good Dataset

Acceptable case: in this case the RP signal is clearly visible; the negative slope was pronounced, and the signal reached a peak around the -19 uV, fully in the range of an RP signal. SNR was positive in the window, thus giving an indication of a signal exceeding the background noise. Subject blindfolded from protocol 2015.

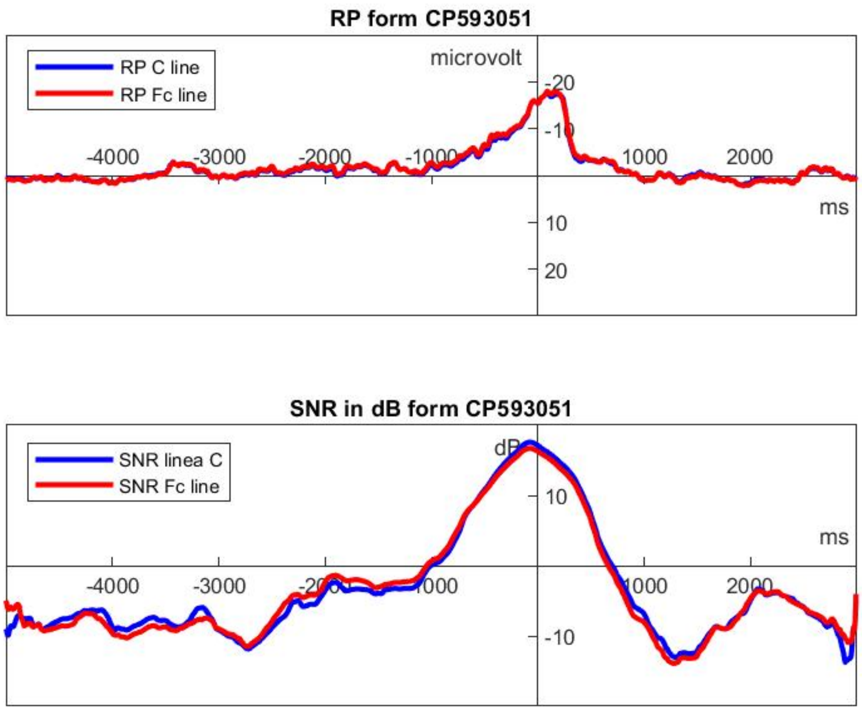
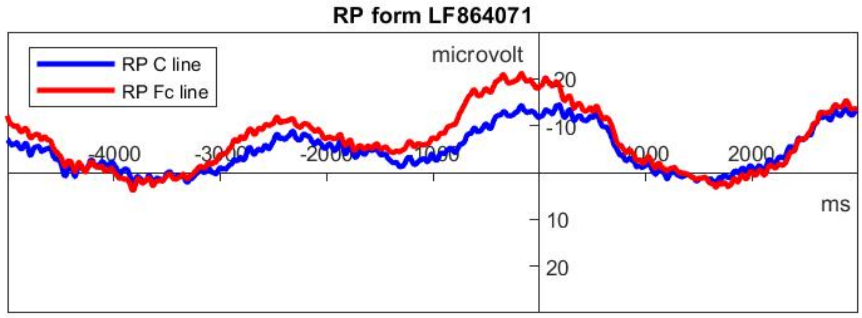


Figure 5.4: Acceptable set

b) Bad Dataset

Unacceptable case: in spite of the fact that there was a trend towards negativity, the signal is very spanned and not RP-like; furthermore, the SNR was almost negative in the time zone of interest, especially on C line, so this signal must be discarded. Subject from protocol 2018.



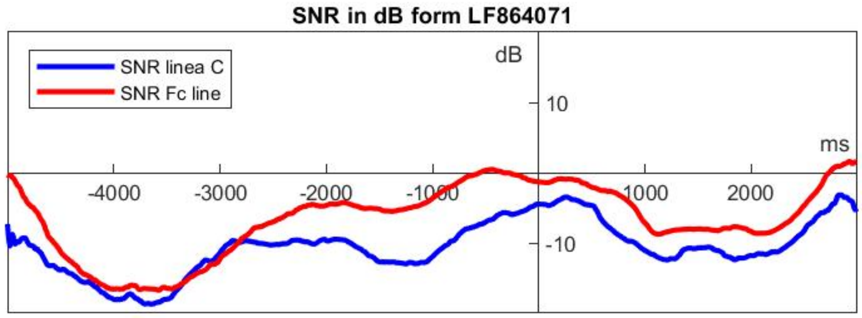


Figure 5.5: Unacceptable set

c) Borderline Dataset

Borderline case: the signal was similar to an RP but the slope was not very evident and the peak was not very high, around -5uV. The signal to noise ratio was positive in the time range; although, as in the signal in figure 5.4, the values were not high, thus suggesting not to discard this signal for the project because it may happen sometimes that the signal could not reach sufficiently high values. Subject blindfolded from protocol 2015.

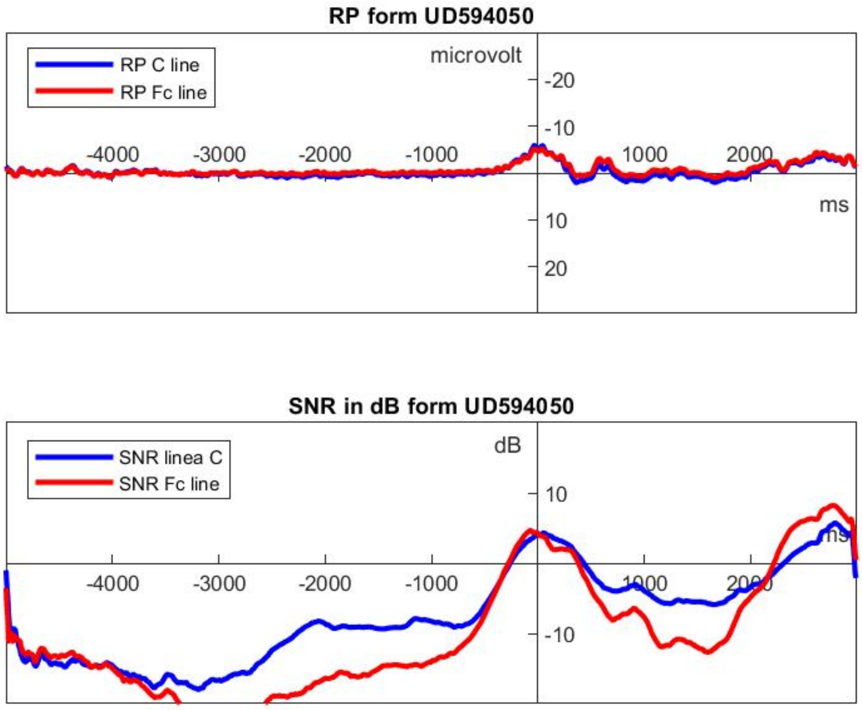


Figure 5.6: Borderline set

5.3 Feature extraction & selection

At this stage, the most crucial of the entire project, a key choice had to be made as to which features could be considered. Since the literature was a little sparse on this point, efforts were made to be as specific as possible in searching for the features that differentiate the RP signal from other ERPs .
Here is an example of feature extracted from one subject:

Feature	Voluntary dataset	Involuntary dataset
Peak Amplitude	-12.23	10.93
Slope	-0.0104	0.0005
Variance	14.33	61.09
Mean value	-1.61	5.87
SNR variance	3.78	7.81
Area	-11095	34631
Kurtosis	-1.620	-0.941
Skewness	-0.120	0.080
Power on delta-theta band	5.26	2.17
PCA1(PSD)	0.025	0.294
PCA1(Signal)	-0.172	0.267
PCA2(Signal)	0.094	0.435
PCA3(Signal)	0.128	-0.370
PCA4(Signal)	0.187	0.008

Table 5.1: Table of all the extracted features: from voluntary dataset CP593041 figure 5.4 and involuntary dataset AP594061 figure 5.1.

Through the feature selection algorithm ReliefF based on K-NN method with k equal to 7, only the most informative features were selected. The total dataset was reduced to 5 features: the peak, the slope, the skewness and the second and the fourth component extracted with PCA from the signal.

Feature	Voluntary dataset	Involuntary dataset
Peak Amplitude	-12.23	10.93
Slope	-0.0104	0.0005
Skewness	-0.120	0.080
PCA2(Signal)	0.094	0.435
PCA4(Signal)	0.187	0.008

Table 5.2: Table of the selected features: from voluntary dataset CP593041 figure 5.4 and involuntary dataset AP594061 figure 5.1.

5.4 Classification

As reported in chapter 4, three different types of models were utilized for this thesis, in particular: two different approaches for SVM, one K-NN model and one decision tree. Each of the four implementations was confronted by the accuracy value described in the tables 5.3 & 5.4.

5.4.1 SVM

For this project two types of binary SVM were implemented for the classification. Both the performance of the classifications were calculated with LOOCV, and a confusion matrix was created to display the (multivariate) frequency distribution of the classification output variables.

Linear SVM

The first one was a linear SVM; the performance of the classification has been reported in the confusion matrix in figure below.

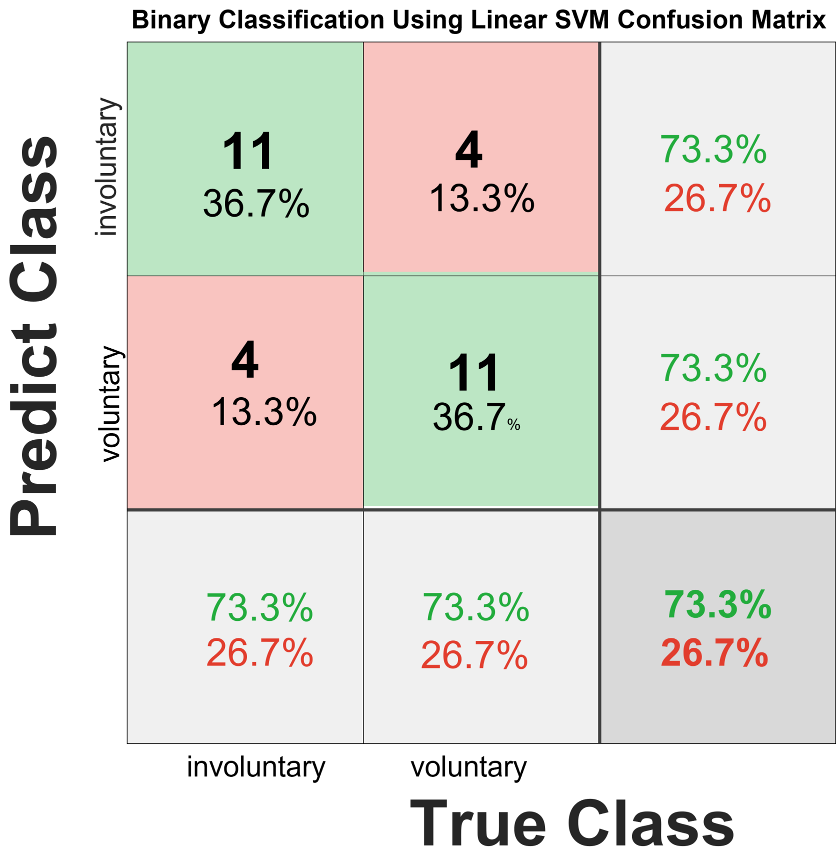


Figure 5.7: Confusion Matrix for Cubic SVM Model.

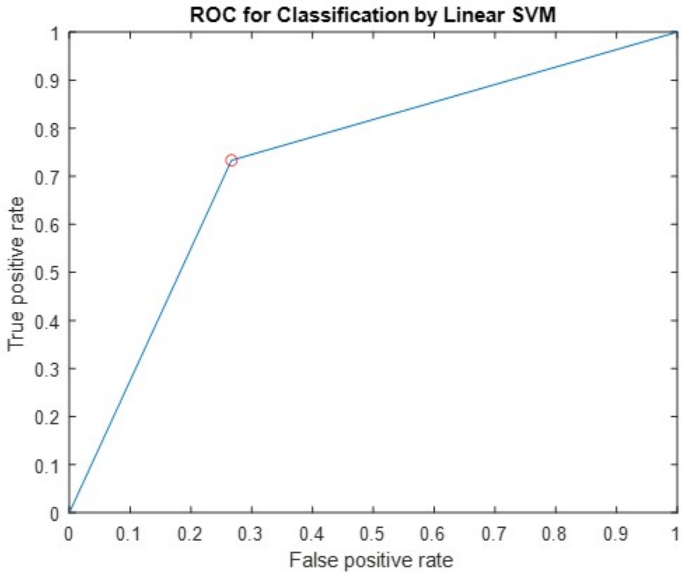


Figure 5.8: ROC curve for Linear SVM Model.

Cubic SVM

The second SVM realized was one with a polynomial kernel; different degrees of the polynomial were tried and, at the end, it was decided to opt for a cubic SVM.

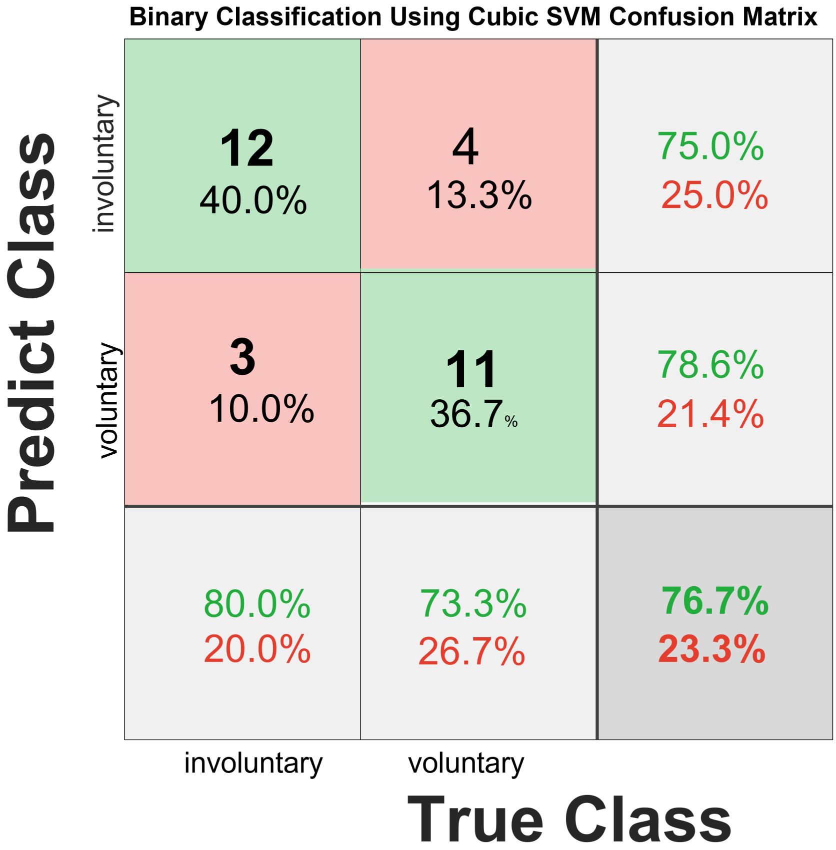


Figure 5.9: Confusion Matrix for Cubic SVM Model.

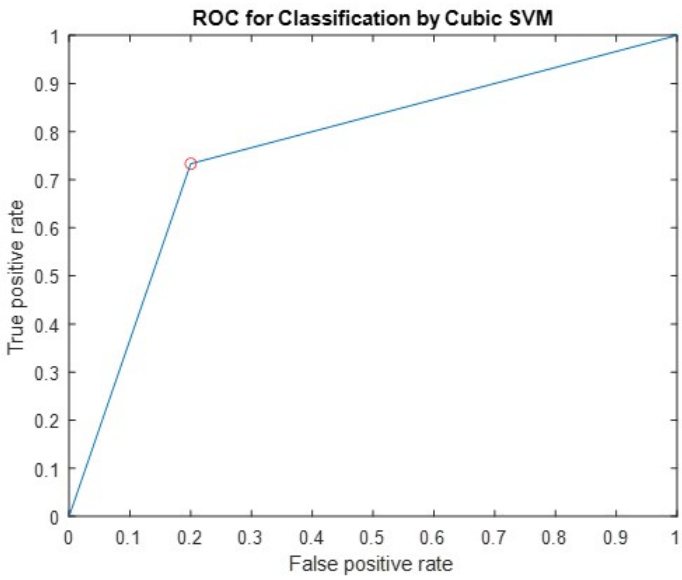


Figure 5.10: ROC curve for Cubic SVM Model.

5.4.2 K-NN

For K-NN several neighbouring k-values have been tested, and at the end the optimal k-value was 7. Instead, a standardised Euclidean metric was used to assess the distance between neighbours. The performance of the classification was calculated with LOOCV, and a confusion matrix was created to displays the (multivariate) frequency distribution of the classification output variables.

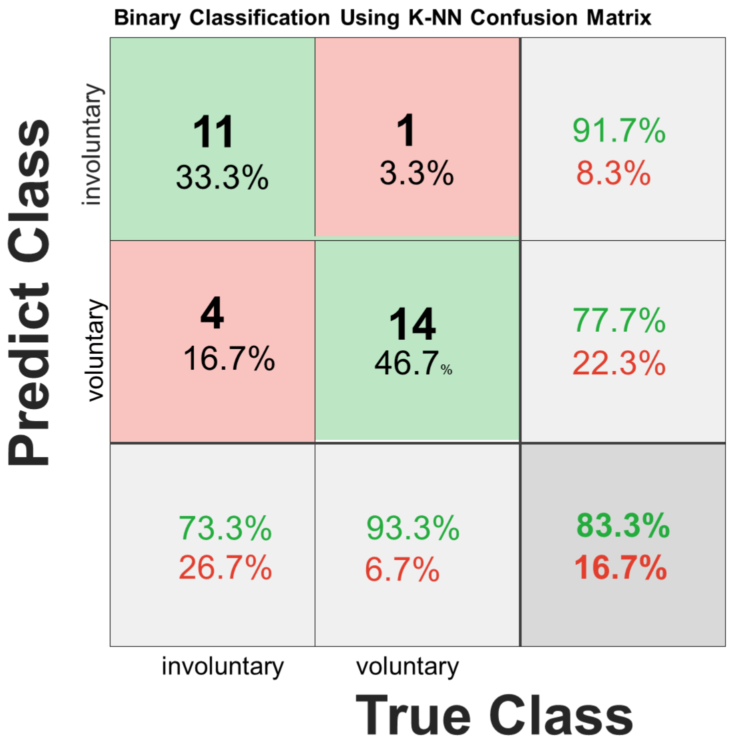


Figure 5.11: Confusion Matrix for K-NN Model.

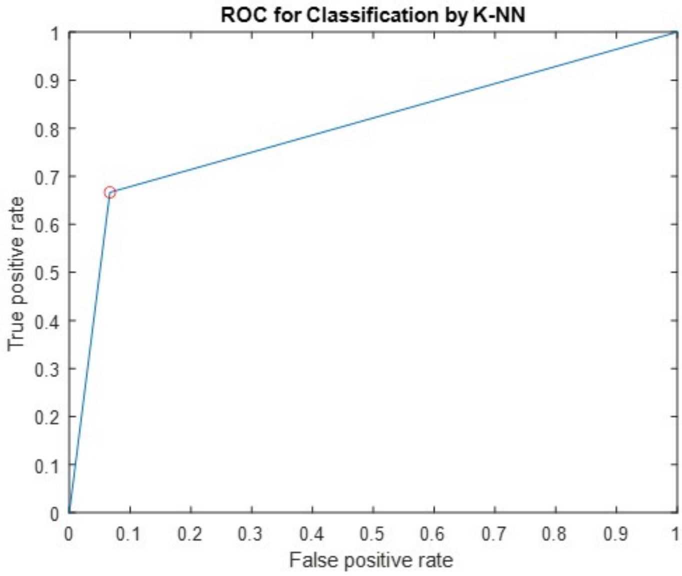


Figure 5.12: ROC curve for KNN Model.

5.4.3 Decision Tree

For DT, Gini index was applied in order to evaluate which feature best split the data, at the end two nodes were found: the Root Nodes was the peak amplitude (x1) and the other node was the second component of the PCA done on the signal (x4), illustrated in figure 5.13:

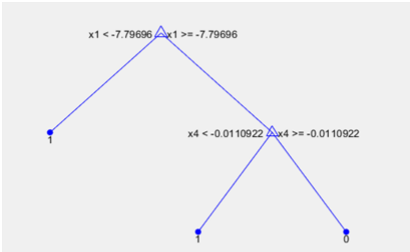


Figure 5.13: Decsion Tree implemented in Matlab with the fitctree function whit the *Root Node* as x1 and the second *Leaf Node* as x4.

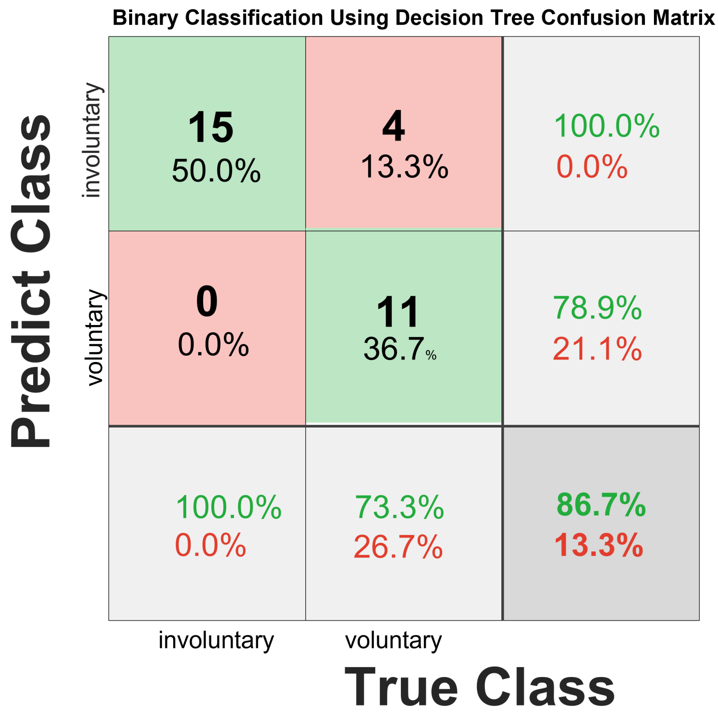


Figure 5.14: Confusion Matrix for Decision Tree Model.

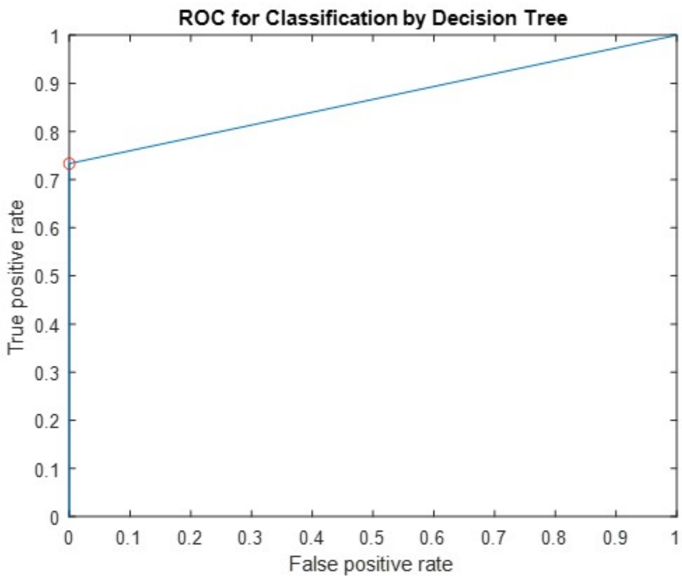


Figure 5.15: ROC curve for Decision Tree Model.

5.4.4 Tabeles of Performances

W/ Feature Selection, 5 Features

	Linear SVM	Cubic SVM	K-NN	Decision Tree
Accuracy	73,3%	76,7%	83,3%	86,7%
K Statistics	46,7%	53,3%	66,7%	73,3%
Specificity	73,3%	78,6%	77,8%	100,0%
Sensitivity	73,3%	75,0%	91,7%	78,9%
AIC	26,73	18,72	-1,47	-14,86

Table 5.3: Table of classification performances with the algorithm for feature selection, in this case the features were 5.

W/O Feature Selection, 14 Features

	Linear SVM	Cubic SVM	K-NN	Decision Tree
Accuracy	73,3%	63,3%	76,7%	86,7%
K Statistics	46,7%	26,7%	53,3%	73,3%
Specificity	81,8%	60,0%	75,0%	100,0%
Sensitivity	68,4%	70,0%	78,6%	78,9%
AIC	26,73	45,84	18,72	-14,86

Table 5.4: Table of classification performances without the algorithm for feature selection, in this case the features were 14.

Chapter 6

Conclusions

During this work it was shown how a Brain Computer Interface in support of the diagnosis of consciousness disorders can be very useful. In particular, a machine learning model added to a BCI allowed to achieve an objectivity much higher than simply using rating scales operator dependent. To date, as mentioned in chapter 1, scales are used to evaluate the degree of conscience of a subject; obviously they are subjective and operator-dependent, that is mainly affected by his/her skill or state of concentration.To eliminate this dependence, it was decided to implement a support BCI which, after cleaning the EEG signal, classifies whether the signal found corresponds to a voluntary or involuntary movement. In particular, in this thesis a machine learning algorithm has been developed for the classification on the presence or absence of voluntariness in the movement.
It is important to notice that the selection of good datasets greatly influences the performance of the classifiers; since an attempt was made to take subjects from the various tasks in a balanced manner, it was noted that for involuntary tasks, i.e., when the movement was dictated by a reflex, a preponderance of acceptable datasets was when the subject was blindfolded. Instead, for voluntary movement, it was observed that if the task consisted in moving two parts of the body (i.e., hand and leg), in some subjects the occurrence of two peaks, resulting from moving two distinct body part, was notable.
Afterwards, feature extraction and selection were performed. Since according to the state-of the art in literature the RP were best detected in the pre-motor and

motor area of the scalp, it was decided that the feature could be extracted in the C line (motor area) and Fc line (pre-motor area), so as to obscure any ERPs arising from other external stimuli (i.e., auditory). Subsequently, the selection of the most informative feature was performed mainly to reduce the computational cost and delete the irrelevant and redundant ones. As it can be seen in table 5.3 and 5.4 the performances of the classifiers were strictly correlated with the feature selection. In particular, for linear SVM with the feature selection algorithm, despite of the same performance, a lower computational cost was observed. In cubic SVM the performance of the classifier with selection showed an improvement, that happened also for K-NN model. On the other hand, with the DT it was possible to see that both the root node and the leaf node coincide (peak amplitude for the root node and the second component of the PCA on the signal for the leaf node), but in this case, too, FS algorithm based on K-NN, implied a lower computational effort.

6.1 Issues and limitations

Before concluding this thesis and articulate some ideas for the future, however, it is important to examine the main problems encountered while developing the project and the limitations of the described approach. Some issues about the datasets were mentioned in chapter 4. In particular, for the Protocol 2018, the available measurements were mostly badly taken or corrupted by noise. These types of problems could be related to poor-quality recordings of the EEG signal (i.e. misplaced electrodes, movements of the subject during the experiment, etc.). This problem was most noticeable in subjects with semi-voluntary tasks, due to which the corresponding datasets were not used in this work. Since only the control group was used in this work, in order to have good results for the patient, it should be fundamental to have high quality recordings .

The issues for the classification are strictly correlated to the EEG recordings; in the preliminary study it was possible to evaluate only a binary classification, because the signal from the semi-voluntary task had poor quality.

Finally, a limitation of this approach is the possible, and not detectable, involuntary reflex of the patient, as his/her will to move is a sign of consciousness, but we cannot say that the absence of this will is a sign of unconsciousness. In addition, the signals from the patient were less marked (i.e., the peak amplitude usually is lower because the movement is imagined) and more difficult to analyse.

6.2 Idea for the future

In accordance with the problems encountered during the development of the project, the first step is to enlarge the dataset with real good measurements. By testing a larger dataset, the study of the classification algorithms may become more accurate. Once the dataset is enlarged, particular attention should be given to the Protocol 2018 and in particular, in the second experiment, the semi-voluntary actions, in order to be able to implement a non-binary classification.
Also linked to possible improvements of the machine learning algorithm, as it can be seen in table 5.3, the performance of K-NN and DT model are rated good. A future implementation of a new model, maybe a second Decision Tree, that takes in input the output of the K-NN and DT, could even lead to a better classification model. Moreover, it could be possible to add more classes; for example, to investigate the Lateralized Readiness Potential so as to evaluate if the right or the left part was moved (or it was an imagined movement). It is important to notice that the brain activation is contra-lateral: if the subject moves, for example, the right hand, the left hemisphere of the brain would be activated and vice-versa.
Finally, the approach could be tested on brain-injured patients: this would be the final and most important phase of the project, but also the most critical. As we already said, the EEG measurement phase was already a demanding step in the healthy subjects. Most of them had to be discarded due to the high electrode impedance, and this noise only get worse in patients. Moreover, contrary to what happens in healthy subjects, patients are not able to repeat the trials as many times as needed, and for this reason the ERP components might become very difficult to be interpreted. In the end, however, with some strong pre-processing of the EEG signals, we could be able to demonstrate if this approach works. We could thus prove to have found a new method to identify signs of consciousness by using a mathematical measure of easy and fast calculation.

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