Critical review and future perspectives of non-invasive brain-machine interfaces

Final Report

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Available on the ACT website
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Ariadna ID: 05/6402
Study Duration: 2 months
Contract Number: 19707/06/NL/HE

Table of Contents

Executive Summary

This document provides a critical review and future perspectives of brain-machine interfaces (BMI). A BMI provides users with the possibility of sending commands to a machine without using their muscles. Chapter 1 introduces BMIs, first as a particular case of hybrid bionics systems (HBS), and then as communication devices for locked-in patients, which is historically and currently their main application field. In the context of HBSs, BMIs can be used as an *augmentation device*, i.e. as a device that allows additional communication channels to able-bodied people. This is the context in which we envisage BMIs to be useful for space applications.

Chapter 2 provides an overview of the anatomy and physiology of the human brain. It is not intended to be an exhaustive description, but rather targeted at introducing the concepts necessary for the understaning of the remaining of the document. It describes the brain from a functional perspective, and cerebral rhythms, i.e. rhytmical cortical brain activity measured by means of electroencephalography (EEG), classified into several frequency bands.

Chapter 3 provides an overview of BMIs, independently from their underlying functioning principle. According to their peculiar features, BMIs can be classified into: dependent vs. independent, invasive vs. non-invasive, spotaneous vs. evoked vs. event-related, and synchronous vs. asynchronous. Chapter 3 also describes the common features of BMIs, explaining how the functioning of BMIs is related to the user's ability, the translation algorithms used for transforming the extracted relevant features of brain signals into commands directed to the machine, output and feedback methods of brain-machine communication. It also describes the issues, both positive and negative, related to learning effects and neural plasticity.

Chapters from 4 to 8 describe the main non-invasive technologies on which BMIs can be based. Chapter 4 deals with EEG, so far the most deeply explored technology for BMIs, because of its advantages of being non-invasive and having a good time resolution. Chapter 5 describes position emission tomography (PET), a functional imaging technique only theoretically suitable for BMIs, since it requires the use of beta-decaying radionuclides. It also provides poor spatial and temporal resolution. Better spatial resolution is possible by means of functional magnetic resonance imaging (fMRI), described in Chapter 6, a radiofrequency-based technique that is very powerful for brain-mapping and activation studies. PET and fMRI both require bulky and expensive scanners. Chapter 7 describes near-infrared spectroscopy (NIRS), a technique which, similarly to PET and fMRI, is capable of measuring blood oxygenation level-dependant (BOLD) effects. From this point of view, PET, fMRI and NIRS share the factor that they do not measure brain activity directly: rather, they measure the metabolic effects that derive from brain activity. On the other hand, magnetoencephalography (MEG), as also EEG, is able to detect the electro-magnetic effects of neuronal activity. MEG is described in Chapter 8. MEG is characterized by high temporal resolution, at the millisecond level. Spatial resolution is high for brain cortex and decreases for deep brain structures. MEG requires very expensive and bulky scanners based on superconducting quantum interference devices (SQUID). The magnetic signals measured are in the range of 10^{-13}T, therefore shielding from external magnetic fields, including the Earth's magnetic field, is necessary. In addition, a great source of noise is in the human body itself: the biomagnetic signals produced by eye movement, eye blinks, heartbeat, breathing, and all other muscular actions interfere with the measurements. Therefore, apart from the cost and bulkiness problems, MEG cannot be used as an augmenting interface.

Chapter 9 deals with mechanically invasive technologies, i.e. intracortical electrodes and electrode arrays. Direct neuronal recordings currently offer the best performance among all other technologies of BMI, since they are able to record brain signals directly at the source of the activity itself. However, this technology is inherently risky and many ethical and practial issues are associated to their use, especially in healthy patients. Intracortical recordings have been carried out in animal experiments and in some patients that underwent neurosurgery. Long-term effects of implants are still unknown.

For each chapter from 4 to 9, we describe the theory of the concepy, methodologies for BMIs, the device hardware, current applications, foreseen improvements, an outline on the suitability for space applications, with pros and cons, and the list of worldwide researching groups that employ the described technology for BMIs research.

Chapter 10 illustrates the advantages of multi-modal techniques, which have great potential in neurophysiological studies and are useful for integrated brain mapping and activation studies. The additional information gained in multi-modal studies can be exploited for designing more powerful BMIs.

Chapter 11 discusses the current possibilities and perspectives of BMIs for space applications. First, the potential advantages derived from the use of BMIs are described, both for general applications and space-specific applications, followed by the description of environment effects on the functioning of BMIs. Subsequently, we analyze the readiness of the technologies that are needed both for BMIs and for the applications. Rather than suggesting out-of-the-box solutions, we derive the definition of possible demonstrators by merging the needs of space applications to the current performance of BMIs. We first define scenarios and contexts for the use of BMIs in rehabilitation applications, the only field where the use of BMIs has been truly investigated so far. Subsequently we define the scenario of domotic applications and environmental control, a context where BMIs, given their characteristics, have good perspectives to be applied. Finally, we define possible scenarios for the use of BMIs for space applications. To summarize, we plot the requirements, in terms of *throughput* and *latency*, of the all applications listed in the previous scenarios. Subsequently, we list the main types of available human/machine interfaces, both standard human-computer interfaces and BMIs, and characterize them also in terms of throughput and latency. This characterization allows us to merge the performance of the interfaces with the needs of applications and to derive currently feasible space applications for BMIs. In the following, we identify and describe three of these applications that we have chosen as demonstrators for both extra-vehicular activities (EVA) and intra-vehicular activities (IVA), namely: 1) BMI-driven rover (EVA); 2) BMI-based hands-free control of steerable cameras and dynamic maps (IVA or EVA); 3) BMI for spaceship environmental control.

In the following of Chapter 11, we provide further details about the implementation of the “BMI-based hands-free control of steerable cameras and dynamic maps” because this system has a great potential for being an augmenting BMI. In the remaining parts of the chapter, we point out possible showstoppers, challenges and practical problems associated to the BMI use for space applications and try to outline the prospective applications of BMIs: we define real-world scenarios for BMI usage, future scenarios for space applications which drive human capabilities beyond currently possibilities in teleoperation, prosthetics and orthotics. We conclude the long chapter with some futurology statements about the evolution of interfaces, robotics and space applications and the list of worldwide researching groups on BMIs for space applications.

Eventually, Chapter 12 tries to define hardware and software roadmaps to illustrate the future of BMIs. We try to point out open issues and current and future research activities to be carried out on BMI hardware, software and complete systems. We discuss the issues of independence from neuromuscular output channels, dependence on the physiological brain activity, the problem of feedback, invasive BMIs, extracerebral biological artefacts, relevant signal components, signal analysis for the extraction of components, and transduction algorithms, operative protocols, smarter control of devices and novel applications. We conclude this study report with the expected benefits that can result from the use of BMIs for different categories of users, in the near and far future. Apart from the technical discussions on which technology bears the greatest potential to be applied to BMIs, a lot of effort has to be devoted to research on BMIs to transform these potentials into reality.

1. Introduction

“One of the most important and distinguishing aspects of humans is the ability to communicate. Communication between people is richer and more complex and than any other form of communication, and plays a vital role in any relationship. Similarly, as artificial devices become more complicated and play a rapidly waxing role in everyday life, communicating effectively with them becomes increasingly important.

It is impossible to directly convey thoughts, emotions, or concepts between people. Instead, these must be translated into verbal or written statements, gesticulations, facial gestures, drawings, or other recognizable expressions. Though not typically regarded as such, much of human anatomy is designed to act as a natural interface, allowing people to convey ideas from one brain to another. Verbal and written messages are typically sent using the mouth and throat or the hands and are received by the ears or eyes, all of which are mediated by extensive processing mechanisms in the brain.

While communication between humans has been extensively developed and studied, communication between people and devices – especially sophisticated electronic systems – is relatively embryonic. Only 60 years ago, state of the art computing systems like ENIAC or UNIVAC required punch cards for communication. An efficient interface is no less important that the device itself; imagine trying to use a modern computer with punch cards. Modern means of interfacing with a computer such as a keyboard and mouse are vastly superior, but remain non-intuitive and are being continually developed.

The use of sophisticated computer tools such as real-time graphics, multimedia, and ubiquitous computing, combined with future developments in 3-D representation, are creating a complex computational environment in which information overload is common. In such an environment, the usual modes of communicating with a computer, such as keyboard and mouse, are very slow and inefficient. The trend to solving this problem has involved the development of automated task managers, better visualization tools, and the development of more intuitive interfaces that recognize innate human skills, such as handwriting, gesture, and speech.” (Allison, 2003)

For decades scientists have dreamed about, pondered, and speculated on the possibility of a direct interface between a brain and a machine, but only in the late 1990s did scientists start learning enough about the brain and signal processing to demonstrate the feasibility of the approach and offer the hope that this vision could become reality. This report reviews the current states of the arts and tries to define the future perspective of brain/machine communication.

1.1 Hybrid bionic systems

From a control system viewpoint, we can schematically represent the information processing that happens in everyday life, as we interact with the outside world, as depicted in Figure 1.1. Our intention to interact with an object (e.g. grasp it), which resides in some cognitive network inside our brain, is translated into motor commands in the motor cortex and then sent to our limbs through the efferent pathways. The results of our action is then gathered by our sensing system (eyes, touch, etc.), translated to sensory signals and sent back to the central nervous systems through the afferent pathways.

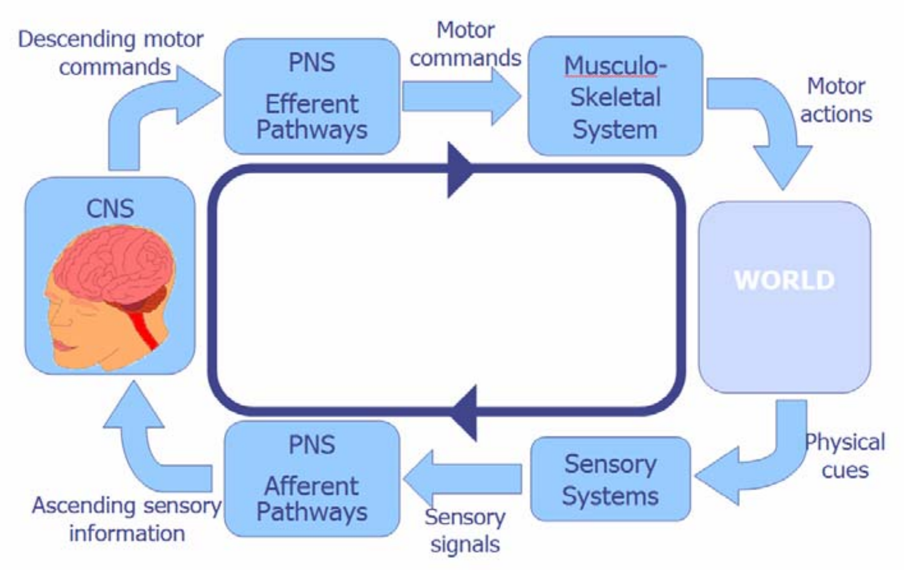

Figure 1.1: Schematization of the human sensori-motor processing loop.

This representation is simplistic, since feedback is believed to behave at various levels, through several loops that operate at different frequencies, but it is useful in this chapter for introducing the concept of Hybrid Bionics System (HBS) and of Brain/Machine Interfaces (BMI).

Similarly, modern robotics has evolved since the advent of mechatronics. The term mechatronics was coined in 1969 and the discipline is centred on mechanics, electronics and computing which, combined, make possible the generation of simpler, more economical, reliable and versatile systems. Wikipedia defines mechatronics as “is the synergistic combination of mechanical engineering ("mecha" for mechanisms), electronic engineering ("tronics" for electronics), and software engineering (see Figure 1.2). The purpose of this interdisciplinary engineering field is the study of automata from an engineering perspective and serves the purposes of controlling advanced hybrid systems.” Mechatronics may alternatively be referred to as "electromechanical systems" or less often as "control and automation engineering".

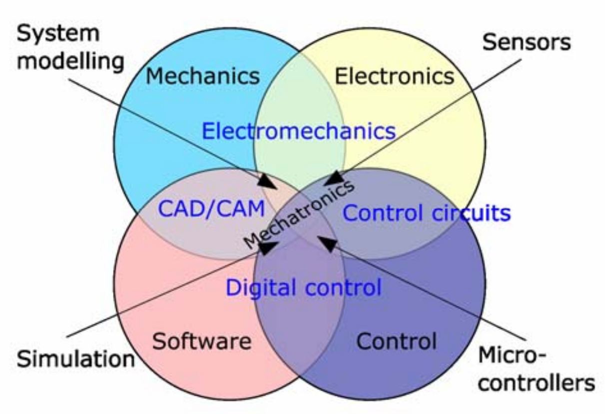

Figure 1.2: A typical mechatronics diagram, Mechatronics is the synergistic combination of several engineering disciplines.

In the mechatronics description, the control loop that describes the interaction of the robot system with the outside world mirrors the one used above for the humans. In particular, humanoid robots try to replicate and mimic as closely as possible the structure of the human perceptual-motor and control system (see Figure 1.3).

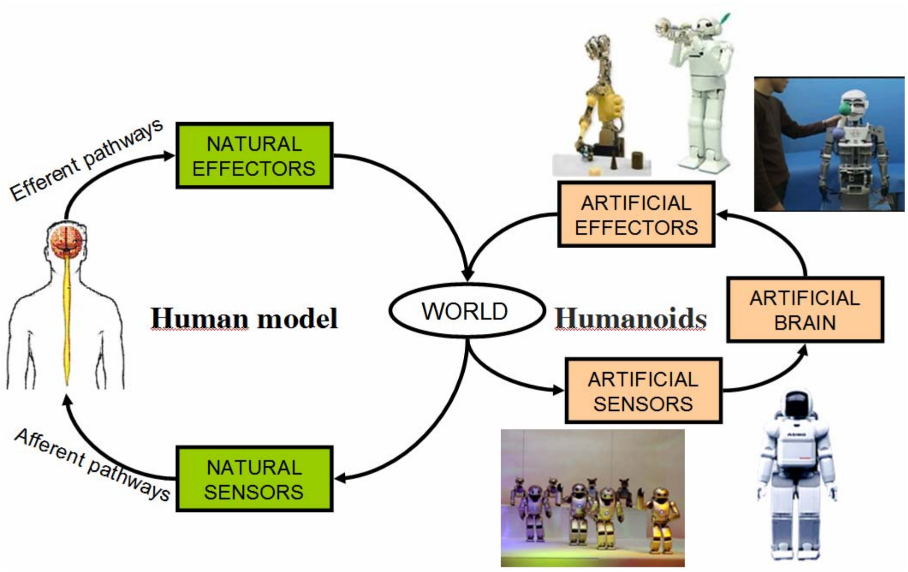

Figure 1.3: The human and humanoid control models are ideally identical (Photos: www.takanishi.mech.waseda.ac.jp, asimo.honda.com, Toyota Inc.).

Referring to the present development of the discipline, Hybrid Bionic Systems (HBSs) can be generically defined as systems that contain both technical (artificial) and biological components. They can include:

- artificial systems with biological elements or subsystems. In such a case, the biological system is a complementary or supplementary element to the technical system;
- biological systems with artificial elements or subsystems. The artificial subsystem, e.g. a robotic artefact, is a complementary or supplementary element to the biological system.

In recent years, many scientific and technological efforts have been devoted to create HBSs that link, via neural interfaces, the human nervous system with electronic and/or robotic artefacts. In general, this research has been carried out with various aims: on the one hand, to develop systems for restoring motor and sensory functionalities in injured and disabled people; on the other hand, for exploring the possibility of augmenting sensory-motor capabilities of humans in general, not only of disabled people.

The connection scheme of HBSs is illustrated by the red arrows in Figure 1.4. The Integrated Project "NEUROBOTICS: the Fusion of Neuroscience and Robotics", funded by the European Commission in the IST FET Programme and coordinated by Scuola Superiore Sant'Anna, investigates Hybrid Bionic Systems and the ways how robotic parts can be connected to a human body (http://www.neurobotics.info) (Navarro et. al, 2005).

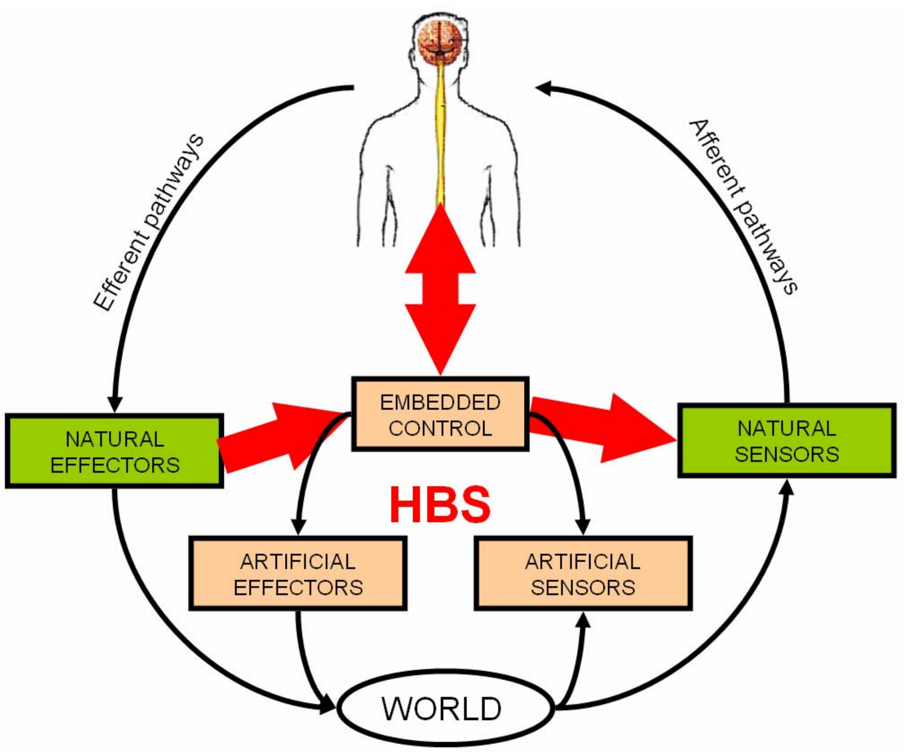

Figure 1.4: Connection scheme of a HBS. The external loop through the green blocks are the natural sensorimotor loop. The inner loop through the orange blocks are the artificial control loop. The connections drawn with red arrows are those that characterize a HBS.

As regards restoring motor capabilities, several technologies have been devised to exploit the residual nervous and/or muscular activities of the (paralyzed or amputated) limbs (Craelius 2002). According to (Gasson et al., 2002), such technologies can be basically classified into:

- technologies for the control of prosthetic limbs (Prochazka et al. 1997; Lauer et al., 2000; Craelius, 2002; Popovič 2003). New materials, microfabrication technologies, advanced robotics mechanisms, computational algorithms and regenerative electrodes have been explored (Ramachandran et al., 1993; Bogdan et al., 1994; Montelius et al., 1996; Prochazka et al., 1997; Abboudi et al., 1999; Dario et al., 1998; Ceballos et al., 2002);
- the control of external electrically powered systems. For instance, a system allowing to control an electrically powered wheelchair without using the hands has been developed (Felzer et al., 2002), that relies upon electromyogram (EMG) as input signal.

Restoration of lost sensory-motor functions has been pursued through neuroprostheses for subjects with neurological disorders, such as those caused by spinal cord injury (SCI) or stroke/head injury (Stein et al. 1992; Popovic and Sinkjaer 2000; Lauer 2000), or by robotic devices like the RoboWalker, an active exoskeleton which can augment or replace muscular functions of the lower limbs, for example to assist motor-impaired individuals (http://www.yobotics.com/).

As for sensory functionalities, important results have been achieved in restoring hearing and sight capabilities. Some improvements in auditory performance of people with hearing loss can be obtained with cochlear implants (Simmons et al., 1965; Blume 1999; Loizou 1999; Spelman 1999; Marsot-Dupuch et al., 2001). Retinal implants can be realized in the attempt to regain lost visual functionality. Neuroprosthetic solutions can be classified as *cortical* (Normann et al., 1999; Dobelle 2000; Normann et al., 2001), *retinal* (Eckmiller 1997; Peyman et al., 1998; Walter 1998; Rizzo et al., 1999; Zrenner et al., 1999; Walter et al., 1999; Chow et al., 2001; Humayun et al., 2001; Meyer 2002), and *optic nerve based* (Veraart et al., 1998). A thorough review of the state of the art in the fields of epiretinal, subretinal and optic nerve implants can be found in (Margalit et al., 2002). An interesting approach is the design of an ocular prosthesis with an autonomous ocular motor system that permits the artificial eye to move more naturally (Gu, 2000).

As for augmenting capabilities of able-bodied persons, it is worth to mention the US Defence Advanced Project Agency (DARPA) initiative that is currently trying to develop exoskeletons for human performance augmentation (EHPA), although focussed on military application. In particular, four EHPA projects work on the development of small actuators, lightweight structures, and control technology to be integrated in devices 'wearable' by a human and able to augment his/her physical capabilities (http://www.darpa.mil/dso/thrust/matdev/ehpa.htm).

Neural interfaces connect the nervous system with artefacts. The connection scheme is illustrated in Figure 1.5. The control of artificial systems by means of direct interfaces to the nervous system, either in animals or in humans, has been recently investigated by a few groups, especially in the US (Chapin et al., 1999, Levine et al., 2000, Donoghue, 2002, Tatlor et al., 2002, Nicolelis 2003). Multielectrode recordings allowed researchers to simultaneously monitoring the extracellular activity of over a hundred single neurons in both anaesthetized and awake animals, and to predict the outcomes of the animal's behaviour during learning of a motor task (Nicolelis 2001, Nicolelis et al., 2002). This has led to the possibility of investigating how information is processed and encoded in living cultured neuronal networks of animals by interfacing them to a computer-generated animal, the Neurally-Controlled Animat, living in a virtual world (Demarse et al., 2001). Researchers at the University of Illinois and at the University of Genoa have jointly fabricated simple hybrid creatures with a mechanical body controlled by the brain of a lamprey (Graham-Rowe 2000; Reger et al., 2000). The robot is the Kephera, and the lamprey brainstem with part of its spinal cord was extracted and maintained in an oxygenated and refrigerated salt solution. Chapin and colleagues (Chapin et al., 1999) demonstrated that simultaneous recordings from ensembles of cortical and thalamic neurons can be decoded in real time to allow a rat to control mono-dimensional motion of a robotic arm. Large pyramidal neurons in motor cortex (red triangles) send axons to spinal cord, ending on interneurons and motoneurons. Microelectrodes could record neural activity, which is transformed by an artificial neural network into signals required to operate a robotic arm (Fetz 1999). A similar experiment has been carried out on primates. Wessberg and collegues (Wessberg et al., 2000) recorded the simultaneous activity of large populations of neurons, distributed in the premotor, primary motor and posterior parietal cortical areas, as non-human primates performed two distinct motor tasks. Cortically derived signals have been successfully used for real-time three-dimensional control of robotic arms. These results suggest that long-term control of complex prosthetic robot arm movements can be achieved by simple real-time transformations of neuronal population signals derived from multiple cortical areas in primates.

Among the few experiments carried out so far on human subjects, a remarkable example is described in (Kennedy et al., 2000), where humans with brain-implanted chip have learned to drive a cursor on a computer monitor. This system requires implantation of a Neurotrophic Electrode (that uses trophic factors to encourage growth of neural tissue into the hollow electrode tip) into the outer layers of the human neocortex. The recorded signals are transmitted to a nearby receiver and processed in front of the patient. Another recent experiment consisted in implanting a 100 microelectrodes array onto the median nerve of a human subject. A number of experiments have been carried out using the signals detected by the array. The subject was able to control an electric wheelchair and an intelligent artificial hand. In addition to being able to measure the nerve signals, the implant was also able to create artificial sensation by stimulating individual electrodes within the array (Gasson et al., 2002; Warwick et al., 2003). In Europe, the FET-CYBERHAND project (http://www.cyberhand.org), funded by the Fifth Framework Programme of the European Communities and coordinated by Scuola Superiore Sant'Anna, has the goal to produce the fundamental knowledge on neural regeneration and sensory motor control of the hand in humans, and the technological means, with the ultimate aim to develop a new cybernetic prosthesis, directly controlled via bi-directional peripheral neural interfaces (Dario et al., 2002; Carrozza et al., 2003).

A less invasive way to connect the CNS to artefacts or computers is the use of Brain/Machine Interfaces (BMI), often also called Brain/Computer Interfaces (BCI).

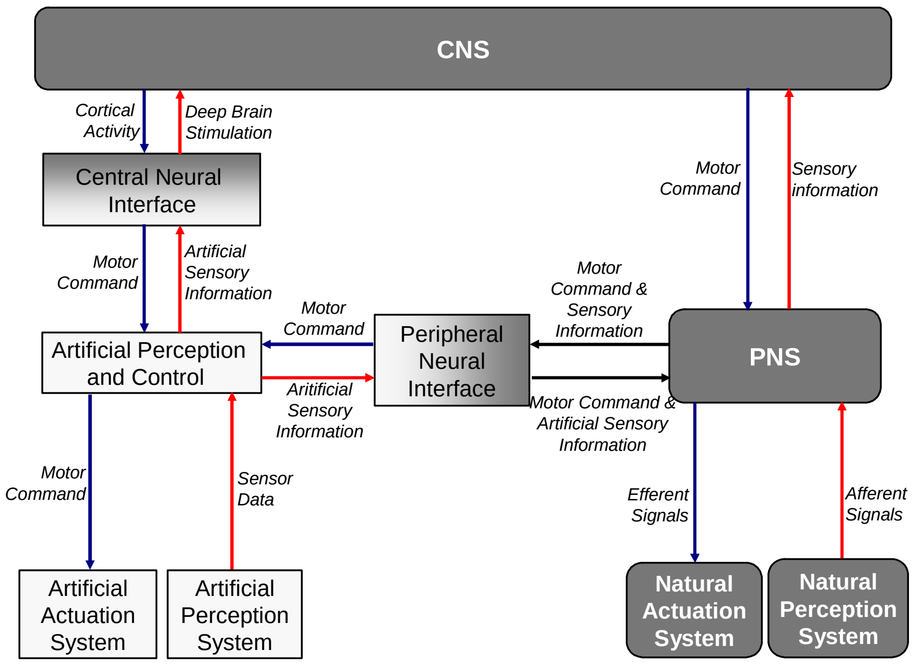

Figure 1.5: A scheme of an HBS: The CNS and the PNS are the human ones. Actuation and perception systems can be both natural and artificial. Artificial ones have a module for control and perception. Neural interfaces convey artificial afferent signals as well as efferent signals to the artefact, either at the peripheral or the central level.

1.2 Brain machine interfaces

Through mechanisms only partially known, the neuronal firing of neuronal aggregates within a distributed cortico-subcortical network is translated in skilled movements of an extremely rich repertoire. There are several pathological and disease conditions able to disrupt, destroy and interrupt the network and pathways from brain to muscles, a system which connects the human body with the external environment and regulates the adaptations of the former to modulations of the latter, governs the execution of behavioural tasks and maintain homeostatic conditions. Just to mention few of them, we might remind Amyotrophic Lateral Sclerosis (ALS) in its final stages, cerebrovascular accidents (stroke), brain and spinal cord traumas, severe muscular dystrophies, Parkinson's Disease (PD), severe forms of Multiple Sclerosis (MS); all conditions which in their most severe expressions can damage and completely interrupt the neural tracts which control voluntary movements. Such conditions affect about two millions of subjects in U.S.

(Ficke, 1991; Murray and Lopez, 1996; Carter, 1997), with a devastating impact on their quality of life as well as on that of their caregivers and with high costs for health and social assistance. For instance in quadriplegic patients even the simplest act of breathing, speaking, drinking, feeding cannot be executed without human or mechanical assistance. Generally speaking, such extreme disease conditions leave unaffected a minimal amount of neuromuscular connections which allow patients to communicate, but there are cases in which there is the total loss of any control on voluntary musculature (including respiratory and oculomotor control) a situation which is defined "locked in". Modern medical technologies guarantee longer survivals, but insufficient attention has been devote – so far – to quality of life. Provided the fact that there are not yet available efficacious treatments we remain with three possible solutions in order to help patients and their caregivers:

1) To increase the residual abilities by utilizing the few muscles still under voluntary control in order to vicariate the functions previously carried out by the lost muscles. In example patients completely paralysed due a brainstem lesion can utilize eye movements to answer questions, provide simple commands or even run word-processing programs; severely dysartric patients can use hand movements to produce artificial language (e.g. Damper e al., 1987; LaCourse and Hladik, 1990; Chen e al., 1999; Kubota e al., 2000).

2) To bypass the site of lesional interruption of the neuromuscular connections. For instance in patients with complete spinal cord sections, the electromyographic (EMG) activity of muscles above the lesions can control -through an appropriate electronic device- the paralyzed muscles with partial restitution of the lost movements (Hoffer e al., 1996; Kilgore e al., 1997; Ferguson e al., 1999).

3) To create a completely new connection as a substitute of muscular apparatus, i.e. a computer able to identify, translate and execute messages and requirements from brain: a Brain/Machine Interface (BMI) (Figure 1.6).

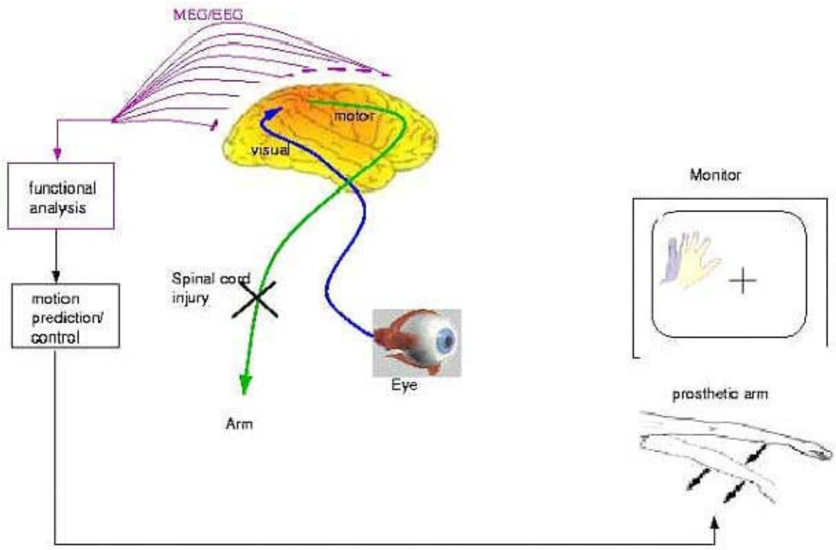

Figure 1.6: A BMI system is providing a completely new connection as a replacement of the one interrupted due to spinal cord injury. (Source: WWW).

We started this section with the desciption of neurological diseases because this was the motivating factor for research of BMIs and is today the main application field for developments and experiments with those interfaces.

A BMI provides users with the possibility of sending commands to a machine without using their muscles. ABMI system, therefore, should be able to extract the relevant information from the brain and translate it in an active command. But which are the activities, the brain signals best to use for such an aim? There is a huge variety of methods which have been employed in order to monitor brain activity which might support a BMI (see Table 1.1). They include: electroencephalographic signals (EEG), magnetoencephalographic signals (MEG), positron emission tomography (PET), functional magnetic resonance imaging (fMRI), near-infrared spectroscopy (NIRS) and invasive methods of EEG recording. MEG, PET and fMRI still require bulky recording apparata which cannot be foreseen to be reduced in size for use in spaceships. They are also extremely expensive and – with the exception of MEG – they also provide a poor time discrimination that does not allow sufficient information transfer rate for most applications. It is therefore conceivable that EEG and related methods currently have most appropriate costs/benefits characteristics for use as a BMI.

Modality	Spatial resolution (mm)	Temporal resolution (s)	Energy	Information
MRI	.5 x .5 x 1	10	RF	p^+ density in H_2O
fMRI	2 x 2 x 3	10	RF	Fe in Hb
SPECT	5 x 5 x 10	100	Tc 99 $\rightarrow \gamma$	Metabolic
PET	5 x 5 x 10	100	$e^+ + e^- \rightarrow 2\gamma$	Metabolic
CT	.1 x .1 x 1	2	X-ray	Density
EEG	8-10	0.001	Electric current	Brain activity
MEG	2-4	0.001	Magnetic dipole	Brain activity
NIRS	1 x 1 x 5	0.005	~750nm γ	Blood flow

Table 1.1: Comparative analysis amongst different techniques of functional and anatomical brain imaging.

1.3 Objectives

BMIs are the focus of this document. Aim of this report is to describe the current state of the art of Brain/Machine Interfaces. We just illustrated the main application field for BMIs, i.e. communication devices for neurologically disabled locked-in patients. In the following chapters, after a brief description of the brain anatomy and physiology (Chapter 2), aimed at the understanding of the functioning of BMIs, we will describe the main technologies that allow to use BMIs as communication devices (Chapters 3-8). Chapter 9 briefly outlines invasive interfaces, which currently have the greatest potential – but also risk – among technologies for BMIs. Chapter 10 illustrates the potential of multi-modal imaging.

As will emerge from the following chapters, at the current state of technology, BMIs are essentially devices that allow to send information from the brain to the machine (which are called *output* devices by neuroscientists, which consider the human as main actor of the communication, and *input* devices by roboticists, which consider the machine as the main actor of the communication, see Figure 1.7). Apart from this naming problem, the main limitation of current BCIs is worth to be told in advance and is clearly illustrated in Figure 1.8: current BMIs are *uni-directional interfaces*. It is possible, by means of several technologies, to extract information from the human brain to drive a machine; on the other hand, it is much more difficult – and dangerous – to send information back from the machine to the human CNS. Instead, natural afferent pathways are used for communication feedback. The reason for this will be clear in the following chapters.

Finally, Chapter 11 discusses the current possibilities and perspectives of BMIs for space applications and Chapter 12 tries to define hardware and software roadmaps to illustrate the future of BMIs.

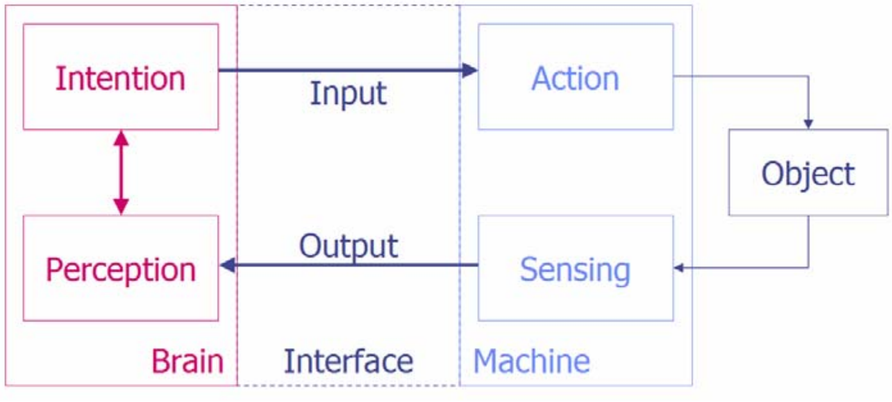

Figure 1.7: Input and output of a BMI from the robotics engineering viewpoint.

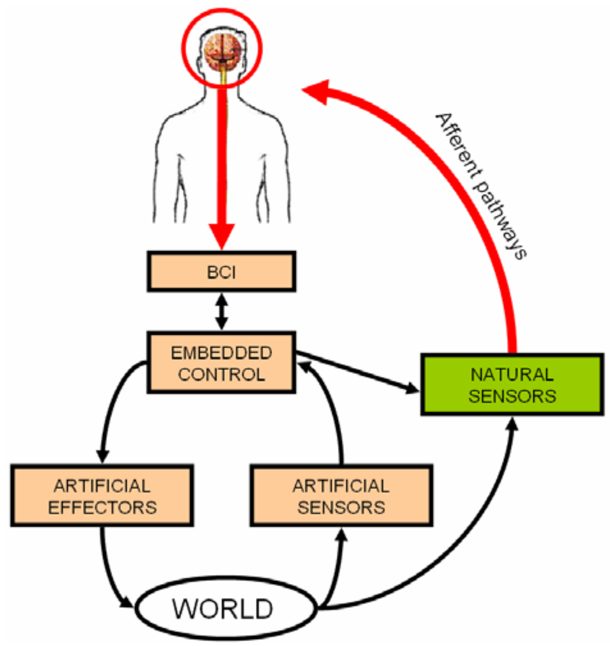

Figure 1.8: The connection scheme of a typical HBS driven by a BMI..

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2. Brain anatomy and physiology

2.1 Introduction

The human brain is a complex organ that allows us to think, move, feel, see, hear, taste, and smell. It controls our body, receives, analyzes and stores information (our memories). The brain produces electrical signals, which, together with chemical reactions, let the parts of the body communicate. Nerves send these signals throughout the body. Brain cells include neurons and glial cells. The brain is part of the *central nervous system* (CNS), which consists of large brain, little brain (or cerebellum), brainstem and spinal cord (Saladin, 2001; Burt, 1993; Figure 2.1)

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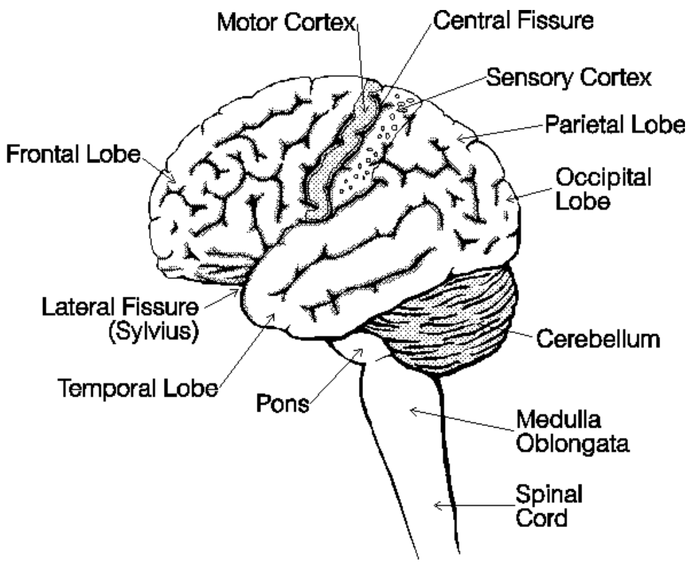

Figure 2.1: The anatomy of Central Nervous System. (Source: WWW).

The brain is connected to the spinal cord, which runs from the neck to the hip area. The spinal cord carries nerve messages between the brain and the body. The nerves that connect the CNS to the rest of the body are called the *peripheral nervous system*. Finally, the *autonomic nervous system* controls our life support systems that we don't consciously control, like breathing, digesting food, blood circulation, etc.

The brain is found inside the bony covering called the cranium. The cranium protects the brain from injury. Together, the cranium and bones that protect our face are called the *skull*. *Meninges* are three layers of tissue that cover and protect the brain and spinal cord. From the outermost layer inward they are: the *dura mater*, *arachnoid* and *pia mater*. In the brain, the *dura mater* is made up of two layers of whitish, inelastic (not stretchy) film or membrane.

The outer layer is called the periosteum. An inner layer, the dura, lines the inside of the entire skull and creates little folds or compartments in which parts of the brain are neatly protected and secured. There are two special folds of the dura in the brain, the *falx* and the *tentorium*. The falx separates the right and left half of the brain and the tentorium separates the upper and lower parts of the brain. The second layer of the meninges is the *arachnoid*. This membrane is thin and delicate and covers the entire brain. There is a space between the dura and the arachnoid membranes that is called the subdural space. The arachnoid is made up of delicate, elastic tissue and blood vessels of different sizes. The layer of meninges closest to the surface of the brain is called the *pia mater*. The pia mater has many blood vessels that reach deep into the surface of the brain. The pia, which covers the entire surface of the brain, follows the folds of the brain. The major arteries supplying the brain provide the pia with its blood vessels. The space that separates the arachnoid and the pia is called the *subarachnoid space*. It is here where the *cerebrospinal fluid* is found. Cerebrospinal fluid, also known as CSF, surrounds the brain and the spinal cord. It is a clear, watery substance that helps to cushion the brain and spinal cord from injury. This fluid circulates through channels around the spinal cord and brain, constantly being absorbed and replenished. It is within hollow channels in the brain, called *ventricles* (Figure 2.2), where the fluid is produced. A specialized structure within each ventricle, called the *choroid plexus*, is responsible for the majority of CSF production. The brain normally maintains a balance between the amount of cerebrospinal fluid that is absorbed and the amount that is produced. Often, disruptions in the system can occur.

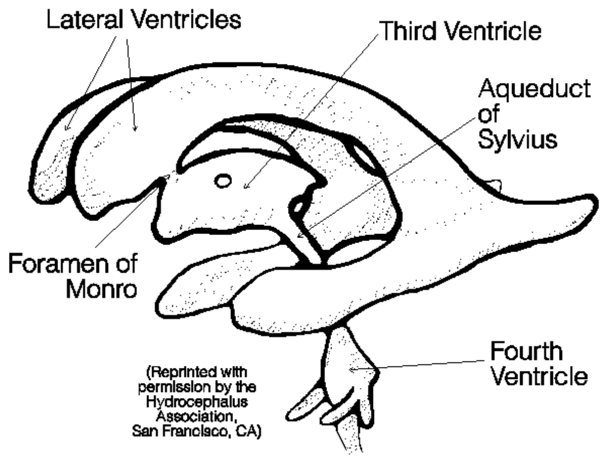

Figure 2.2: Anatomy of ventricles. (Source: WWW).

2.2 Functional perspective

From a functional perspective, the brain is divided into three parts:

- *Large brain, forebrain, or cerebrum*: controls higher mental function such as languages and abstract reasoning and consists of diencephalon and telencephalon;
- *Brainstem*: where neurological functions necessary for survival (breathing, digestion, heart rate, blood pressure) and for arousal (being awake and alert) are located, and visual and auditional functions happen. The brainstem consists of Midbrain, Pons and Medulla Oblongata.
- *Cerebellum or little brain*: handles the motor control and movement.

2.2.1.1 Cerebrum

The Cerebrum or forebrain is divided into two subdivisions: the *telencephalon* and the *diencephalon* (Saladin, 2001; Burt, 1993). The primary structures of the *telencephalon* include the cerebral cortex, basal ganglia, and the limbic system. The cerebral cortex of left hemisphere controls higher mental function such as languages, verbal intelligence and memories, information processing, analytic reasoning, and perception of details. The right hemisphere is associated with 'unconscious' awareness, perception and comprehension of body language and social cues, creativity and insight, intuitive reasoning, visual-spatial processing, and holistic comprehension. The basal ganglia have an important role in motor control. Moreover, the limbic system is involved with emotion, motivation, multifaceted behaviour, and memory storage and recall.

The *diencephalon* includes the thalamus and the hypothalamus. The thalamus is the relay station for incoming sensory signals and outgoing motor signals passing to and from the cerebral cortex. The hypothalamus is comprised of distinct areas and nuclei which control vital survival behaviours and activities; such as: eating, drinking, temperature regulation, sleep, emotional behaviour, and sexual activity.

2.2.1.2 Brainstem

Brainstem is the lower extension of the brain where it connects to the spinal cord (Saladin, 2001; Burt, 1993; Figure 1). Neurological functions located in the brainstem include those necessary for survival (breathing, digestion, heart rate, blood pressure) and for arousal (being awake and alert). Most of the cranial nerves come from the brainstem. The brainstem is the pathway for all fibre tracts passing up and down from peripheral nerves and spinal cord to the highest parts of the brain.

Midbrain - The midbrain serves as the nerve pathway of the cerebral hemispheres and contains auditory and visual reflex centres. The midbrain is an important centre for ocular motion.

Pons - The pons is a bridge-like structure which links different parts of the brain and serves as a relay station from the medulla to the higher cortical structures of the brain. It contains the respiratory centre. The pons is involved with coordinating the eye and facial movements, facial sensation, hearing and balance.

Medulla Oblongata - The medulla oblongata functions primarily as a relay station for the crossing of motor tracts between the spinal cord and the brain. It also contains the respiratory, vasomotor and cardiac centres, as well as many mechanisms for controlling reflex activities such as coughing, gagging, swallowing and vomiting. These functions are important to our survival.

The *reticular activating system* is found in the midbrain, pons, medulla and part of the thalamus. It controls our level of wakefulness, the attention we pay to what happens in the world that surrounds us and our pattern of sleep.

2.2.1.3 Cerebellum or little brain.

The *cerebellum* is located at the back of the brain beneath the occipital lobes (Figure 1). It is separated from the cerebrum by the *tentorium* (fold of dura). The cerebellum's primary function involves control of bodily movements. It serves as a reflex centre for the coordination and precise maintenance of equilibrium. Voluntary and involuntary bodily movements are controlled by the cerebellum. Visual, auditory, vestibular, and somatosensory information is received by the cerebellum, as is information on the movements of individual muscles. Processing of this information results in the cerebellum's ability to guide bodily movements in a smooth and coordinated fashion.

2.2.2 The cerebrum

Cerebral Cortex: Likened to the bark on a tree, the cerebral cortex surrounds the cerebral hemispheres. The cerebral cortex is the folded, convoluted tissue commonly imagined when an image/thought of the brain is recalled from memory. The folded, crumpled structure contains an enormous amount of small and large grooves (sulci and fissures) and bulges (gyri). This type of structure is beneficial for it greatly increases the overall surface are of the cortex. The cerebral cortex is commonly referred to as *grey matter*. This is based upon the appearance of the cortex which, due to the predominance of cells appears greyish brown. The neurons of the cerebral cortex are connected to other neurons within the brain via millions of axons located beneath the cortex. This area is white in colour due to the concentration of myelin; it is often called *white matter*. The brain is made up of two types of cells: neurons and neuroglia. The neuron is responsible for sending and receiving nerve impulses or signals. Neuroglia provide neurons with nourishment, protection and structural support. Astroglia or astrocytes, oligodendroglia and ependymal cells are the types of glial cells commonly found in the brain.

Cerebral hemispheres. One of the most apparent visible features of the brain is the division between the left and right hemispheres of the cerebral cortex. Through evolutionary advances the functions of each hemisphere have evolved. Mental and emotional differences between men and women are speculated to result from different modes of functioning between the two hemispheres. In most cases the left hemisphere is deemed the dominant half of the brain. This is due to its superior language abilities as well as its analytic, sequential. In general terms it is well understood that the left hemisphere controls linguistic consciousness, the right half of the body, talking, reading, writing, spelling, speech communication, verbal intelligence and memories, and information processing in the areas of math, typing, grammar, logic, analytic reasoning, and perception of details. The right hemisphere is associated with 'unconscious' awareness (in the sense it is not linguistically based), perception of faces and patterns, comprehension of body language and social cues, creativity and insight, intuitive reasoning, visual-spatial processing, and holistic comprehension. Communication between the two hemispheres takes place through the *corpus callosum*. The surface of the cerebral hemispheres is divided into four lobes corresponding to the names of the skull plates that protect them: the *frontal lobe*, *parietal lobe*, *temporal lobe*, and the *occipital lobe* (Figure 4). In addition to these four lobes, a fifth lobe exists called the *insula*. This lobe is internal and is not visible from the surface of the brain. The *corpus callosum* is the primary connection between the left and right hemispheres of the cerebral cortex. Connection between the two halves takes place through axons that unite geographically similar regions of the two cerebral cortices.

Somatomotor and somatosensory cortex. The *main motor cortical area* is located on the anterior wall of the central sulcus and the adjacent portion of the precentral gyrus. This area corresponds to area 4 of Brodmann. It is rich in pyramidal neurons, which provide the anatomical substrates for the motor output function of area 4. Electrical stimuli over area 4 produce activation of contralateral muscles; the face, mouth, and hand muscles occupy about two thirds of the primary motor area (Penfield and Rasmussen 1952). The size of cortical representation of muscles is less a function of the muscle mass than of precision of the muscle movements (Figure 2.3). Other motor areas, "*premotor" cortex* (lateral area 6) and "*supplementary" motor area* (area 6 on the medial wall) can be mapped roughly around the primary motor cortex. The primary motor cortex contributes more fibres to the corticospinal tract than any other region. Numerous observations support contributions from several other areas, including the frontal and parietal cortices. Ipsilateral projections are far less numerous than contralateral, estimated between 1.8-5.9% of corticospinal connections. Fibres of the corticospinal tract and corticobulbar tract originate from the sensorimotor cortex around the central sulcus. The human pyramidal tract contains over 1 million fibres. Most fibres are myelinated and have a small diameter (1-4 mm); only a small portion (3-5%) are large-diameter fibres (10-22 mm) that originate in Betz cells from area 4. In humans, only 5% of the fibres of the corticospinal tract originate from Betz cells in area 4. The concept of pyramidal pathways with fibres originating only from Betz cells in the primary motor cortex has been invalidated. A large part of the corticospinal neurons have non-motor

function, especially those originating in sensory or associative areas.
There are thought to be nine cortical areas with primarily somatosensory function: the *primary somatosensory cortex* (S1 – comprising areas 3a, 3b, 1 and 2, the *second somatosensory area* (S2) located along the superior bank of the lateral sulcus (Maeda et al. 1999), the granular insula and retroinsular cortex (Schneider et al. 1993), and in the posterior parietal cortex areas 5 and 7b. Like the primary motor cortex, S1 is organised somatotopically (Penfield and Rasmussen 1952; Maldjian et al. 1999; Figure 3). There is also some evidence for rough somatotopy along the secondary somatosensory cortex (Maeda et al. 1999). While S1 is typically only activated contralaterally by unilateral touch (Maldjian et al. 1999), it is common to see bilateral activation of S2 and the insula (Schneider et al. 1993). There has been controversy concerning the extent to which touch information is processed serially from S1 to S2. Although initially it was thought that only S1 received thalamic input, it has now been demonstrated that the ventroposterior nucleus of the thalamus (VP) sends direct reciprocal projections to both S1 and S2 (Jones 1986). This therefore led to the belief that somatosensory information was processed in parallel. There are several studies lending further support to the idea of parallel processing of somatosensory information. Other data are consistent with a serial processing scheme with information passed mainly from VP via S1 to S2. Evidence from humans also supports the serial processing model. Using MEG, Mima et al (Mima et al. 1998) found that the earliest responses to electrical stimulation of the median nerve occurred at 20ms and were maximal over the hand area of contralateral S1. Later responses, at 100-200ms, were found over bilateral temporal-parietal areas, thought to correspond to S2. The evolutionary stage at which the switch from parallel to serial processing occurs is debatable.

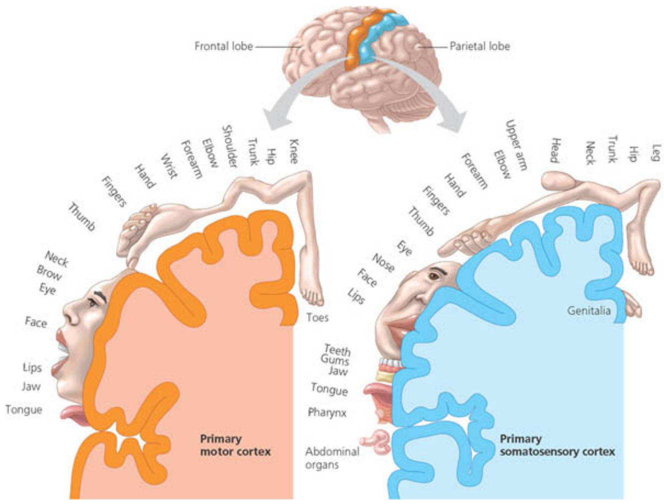

Figure 2.3: Cortical representation of muscles (primary motor cortex) and sensory areas (primary somatosensory cortex) of body is represented in the figure. (Source: WWW).

In conclusion, in higher primates, and arguably in humans, processing of touch information occurs largely in series, with information passing from the thalamus to S1 and from S1 to S2. The fact that the anatomical evidence points towards a serial processing model has implications for studies of attention and plasticity in the somatosensory system. In a serial, hierarchical processing model there is typically controversy over the degree to which early areas can be modulated by factors such as attention.

Lobes of the cortex. In the *Frontal lobes* the primary motor cortex or precentral gyrus are found. The prefrontal cortex plays an important part in our memory, intelligence, concentration, temper and personality. It helps us set goals, make plans and judge our priorities. The *premotor cortex* is a region found beside the primary motor cortex. It guides our eye and head movements and sense of orientation. *Broca's area*, important in language production, is found in the frontal lobe, usually on the left side. The *Occipital lobes* contain regions that contribute to our visual field or how our eyes see the world around us. They help us see light and objects and allow us to recognize and identify them. This region is called the *visual cortex*. The occipital lobe on the right interprets visual signals from your left visual space, while the left occipital lobe does the same for your right visual space. Damage to one occipital lobe may result in loss of vision in the opposite visual field. In the *Temporal lobes* we can find the *primary auditory cortex* that helps us hear sounds and gives sounds their meaning, e.g. the bark of a dog. The temporal lobes are the primary region responsible for memory. It contains *Wernicke's area* (language and speech functions.). The *parietal lobes* interpret, simultaneously, sensory signals received from other areas of the brain such as our vision, hearing, motor, sensory and memory. Together, memory and the new information that is received give meaning to objects. A furry object touching your skin, that purrs and appears to be your cat, will have a different meaning than a furry object that barks and you see to be a dog.

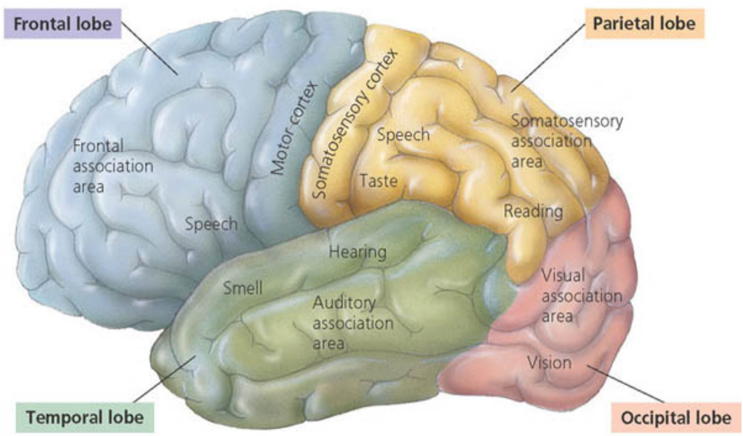

Figure 2.4: Localization and function of different areas belonging to the cerebral lobes. (Source: WWW).

Basal Ganglia. The term "basal ganglia" (Figure 2.5) refers to a loosely grouped collection of large subcortical nuclear (grey) masses derived from the telencephalon and located deep within each cerebral hemisphere. The nuclear components include the *claustrum*, *amygdaloid nuclear complex*, *nucleus accumbens,* and the *corpus striatum*. The term is now used to refer more specifically to the corpus striatum and two additionally related nuclei, the *subthalamic nucleus* and the *substantia nigra;* derivatives of the diencephalon and mesencephalon, respectively. Although not part of the telencephalic basal ganglia these nuclei are reciprocally connected with and functionally related to the corpus striatum. We know from our understanding of their organization, connections, and deficits that ensue from their pathology that the corpus striatum and related nuclei play an important role in motor control. Interestingly, the component nuclei themselves have no direct projections to spinal cord levels. They influence motor activity by interacting with areas of the cerebral cortex that give rise to descending motor pathways through a number of feedback loops. The corpus striatum, related nuclei, and connections are sometimes described as forming the "*extrapyramidal motor system*." Their functions involve: monitoring the progress of movement, transfer and modification of information from the neocortex to motor areas (particularly premotor and supplementary motor areas), automatic execution (remembering instructions for initiation, control and cessation) of learned motor activity, modulation of limbic activity and cognition involving prefrontal association cortex.

Limbic System. The limbic system is a collection of brain structures involved with emotion, motivation, multifaceted behavior, and memory storage and recall. The *hippocampus* and the *amygdala*, along with portions of the hypothalamus, thalamus, caudate nuclei, and septum function together to form the limbic system.

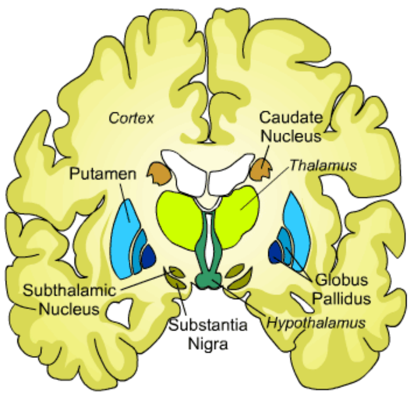

Figure 2. 5: Basal Ganglia. (Source: WWW).

Thalamus. The thalamus (Figure 2.5) is the relay station for incoming sensory signals and outgoing motor signals passing to and from the cerebral cortex. With the exception of the olfactory sense, all sensory input to the brain connected to nerve cell clusters (nuclei) of the thalamus.

Hypothalamus. The hypothalamus (Figure 2.5) is comprised of distinct areas and nuclei which control vital survival behaviours and activities; such as: eating, drinking, temperature regulation, sleep, emotional behaviour, and sexual activity. It is located just beneath the thalamus and lies at the base of the brain. The autonomic nervous system and endocrine system are controlled by the hypothalamus.

2.2.3 The neuron

A *neuron* (Figure 2.6) is a cell specialized to conduct electrochemical impulses called nerve impulses or action potentials. All neurons outside the central nervous system (and many within it) conduct impulses along hair-like cytoplasm extensions, the nerve fibres or *axons*. The axons connecting your spinal cord to the foot can be as much as 1 m long (although only a few micrometers in diameter). Axons grow out of the cell body, which houses the nucleus as well as other organelles such as the endoplasmic reticulum. The length of some axons is so great that it is difficult to see how the cell body can control them. Nevertheless, there is a steady transport of cell components (e.g., vesicles, mitochondria) from the cell body along the entire length of the axon. This flow is driven by moving along the many microtubules in the cytoplasm within the axon. In many neurons, nerve impulses are generated in short branched fibres called *dendrites* and also in the cell body. The impulses are then conducted along the axon, which usually branches several times close to its end. Many axons are covered with a glistening fatty sheath, the *myelin sheath*.

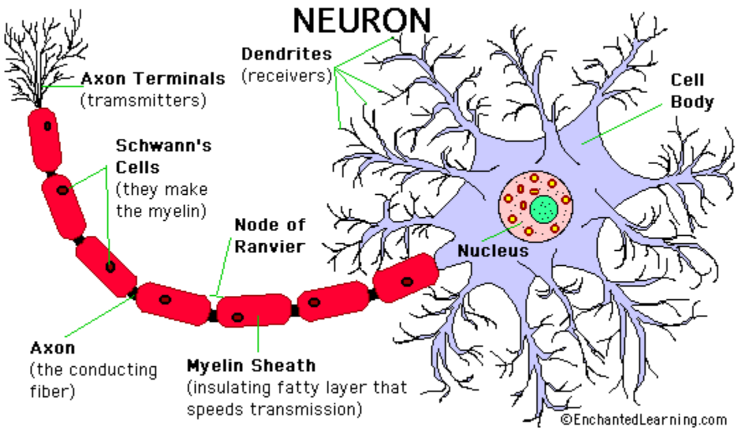

Figure 2.6: The structure of Neuron. (Source: WWW).

It is the greatly-expanded plasma membrane of an accessory cell, the *Schwann cell*. Schwann cells are spaced at regular intervals along the axon. Their plasma membrane is wrapped around and around the axon forming the myelin sheath. Where the sheath of one Schwann cell meets that of the next, the axon is unprotected. This region, the *node of Ranvier*, plays an important part in the propagation of the nerve impulse.

There are three major classes of neurons:

1. *Sensory neurons*: they run from the various types of stimulus receptors (e.g. touch, odour, taste, sound, vision) to the central nervous system (CNS), the brain and spinal cord; the cell bodies of the sensory neurons leading to the spinal cord are located in clusters, called ganglia, next to the spinal cord. The axons usually terminate at interneurons
2. *Interneurons*: these are found exclusively within the spinal cord and brain; they are stimulated by signals reaching them from sensory neurons, other interneurons or both. Interneurons are also called association neurons, and it is estimated that the human brain contains 100 billion (1011) interneurons averaging 1000 synapses on each; that is, some 1014 connections. The term interneuron hides a great diversity of structural and functional types of cells. In fact, it is not yet possible to say how many different kinds of interneurons are present in the human brain. Certainly hundreds; perhaps many more.
3. *Motor neurons*: these transmit impulses from the central nervous system to the muscles and glands that carry out the response. Most motor neurons are stimulated by interneurons, although some are stimulated directly by sensory neurons.

Synapses. Information from one neuron flows to another neuron across a synapse. The synapse is a small gap separating neurons. The synapse consists of: 1) *presynaptic ending* that contains neurotransmitters, mitochondria and other cell organelles; 2) *postsynaptic ending* that contains receptor sites for neurotransmitters and 3*) synaptic cleft* or space between the presynaptic and postsynaptic endings (Figure 2.8). It is about 20nm wide. An electrical signal (or action potential)cannot cross the synaptic cleft between neurones. Instead the nerve impulse is carried by chemicals called neurotransmitters. These chemicals are made by the cell that is sending the impulse (the pre-synaptic neurone) and stored in synaptic vesicles at the end of the axon. The cell that is receiving the nerve impulse (the post-synaptic neurone) has chemical-gated ion channels in its membrane, called neuro-receptors. These have specific binding sites for the neurotransmitters.

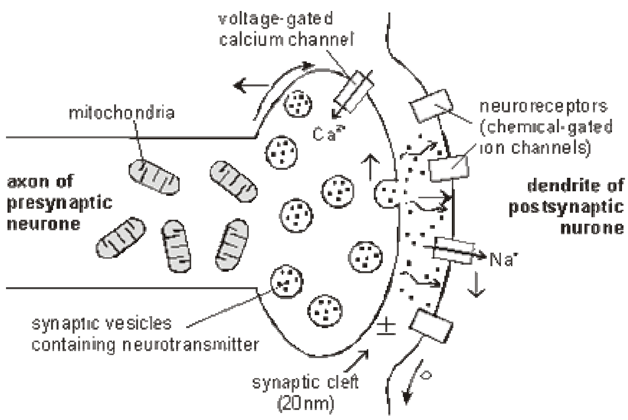

Figure 2. 7: The Synapse. (Source: WWW).

1. At the end of the pre-synaptic neurone there are voltage-gated calcium channels. When an action potential reaches the synapse these channels open, causing calcium ions to flow into the cell.
2. These calcium ions cause the synaptic vesicles to fuse with the cell membrane, releasing their contents (the neurotransmitter chemicals) by exocytosis.
3. The neurotransmitters diffuse across the synaptic cleft.
4. The neurotransmitter binds to the neuro-receptors in the post-synaptic membrane, causing the channels to open. In the example shown these are sodium channels, so sodium ions flow in.
5. This causes a depolarisation of the post-synaptic cell membrane, which may initiate an action potential, if the threshold is reached.

6. The neurotransmitter is broken down by a specific enzyme in the synaptic cleft; for example the enzyme acetylcholinesterase breaks down the neurotransmitter acetylcholine. The breakdown products are absorbed by the pre-synaptic neurone by endocytosis and used to re-synthesise more neurotransmitter, using energy from the mitochondria. This stops the synapse being permanently on.

The human nervous system uses a number of different neurotransmitter and neuroreceptors, and they don't all work in the same way. We can group synapses into 5 types:

1. *Excitatory Ion Channel Synapses*: these synapses have neuroreceptors that are sodium channels. When the channels open, positive ions flow in, causing a local depolarisation and making an action potential more likely (*excitatory postsynaptic potential* - EPSP) . This was the kind of synapse described above. Typical neurotransmitters are acetylcholine, glutamate or aspartate.
2. *Inhibitory Ion Channel Synapses*: these synapses have neuroreceptors that are chloride channels. When the channels open, negative ions flow in causing a local hyperpolarisation (inhibitory postsynaptic potential – IPSP) and making an action potential less likely . So with these synapses an impulse in one neurone can inhibit an impulse in the next. Typical neurotransmitters are glycine or GABA.
3. *Non Channel Synapses*: these synapses have neuro-receptors that are not channels at all, but instead are membrane-bound enzymes. When activated by the neurotransmitter, they catalyse the production of a "messenger chemical" inside the cell, which in turn can affect many aspects of the cell's metabolism. In particular they can alter the number and sensitivity of the ion channel receptors in the same cell. These synapses are involved in slow and long-lasting responses like learning and memory. Typical neurotransmitters are adrenaline, noradrenaline (NB adrenaline is called epinephrine in America), dopamine, serotonin, endorphin, angiotensin, and acetylcholine.
4. *Neuromuscular Junctions*: these are the synapses formed between motor neurones and muscle cells. They always use the neurotransmitter

acetylcholine, and are always excitatory. We shall look at these when we do muscles. Motor neurones also form specialised synapses with secretory cells.
5. *Electrical Synapses (Gap junctions)*: in these synapses the membranes of the two cells actually touch, and they share proteins. This allows the action potential to pass directly from one membrane to the next. They are very fast.

2.2.4 Action potential

In response to the appropriate stimulus, the cell membrane of a nerve cell goes through a sequence of depolarization from its rest state followed by repolarization to that rest state (for review E. Kandel et al, 2000). *Rest potential* of neuron is due to membrane permeability characteristics and different ionic currents and pumps, in particular *ATP-dependant* Na^+/K^+ *pump,* that transports sodium ions from intracellular to the extracellular compartment and potassium ions in the opposite direction with a ratio of 3/3; thus, the intracellular compartment is more negative than the extracellular compartment. In the sequence, during *action potential* the cell membrane reverses its normal polarity for a brief period before re-establishing the rest potential. The recovery time to rest potential was more like 100 msec. The action potential sequence is essential for neural communication. The simplest action in response to thought requires many such action potentials for its communication and performance. For modelling the action potential for a human nerve cell, a nominal *rest potential* of -70 mV will be used. The process involves several steps (figure 8) :

1. A stimulus is received by the dendrites of a nerve cell. This causes the Na+ channels to open. If the opening is sufficient to drive the interior potential from -70 mV up to -55 mV (Figure 2.8,- *point 1*-), the process continues.
2. Having reached the action threshold, more Na+ channels (sometimes called voltage-gated channels) open. The Na^+ influx drives the interior of the cell membrane up to about +30 mV. The process to this point is called *depolarization* (Figure 2.8,- *point 2* -).
3. The Na^+ channels close and the K^+ channels open. Since the K^+ channels are much slower to open, the depolarization has time to be completed. Having both Na^+ and K^+ channels open at the same time would drive the system toward neutrality and prevent the creation of the action potential (Figure 8,- *point 3* -).
4. With the K^+ channels open, the membrane begins to repolarize back toward its rest potential (Figure 8,- *point 4* -).

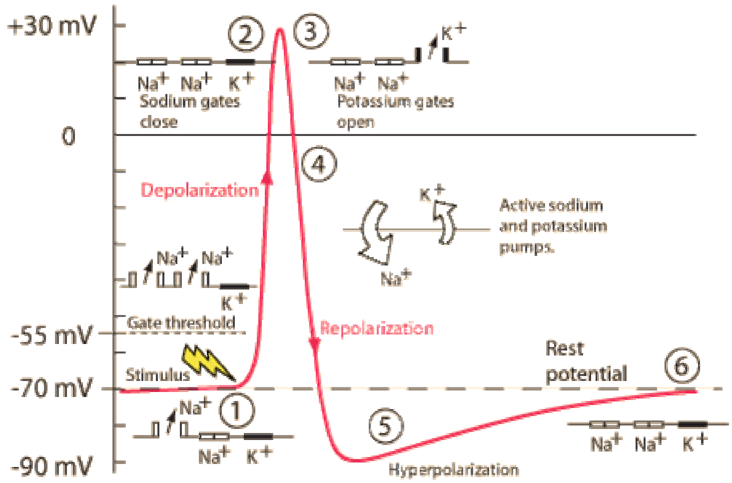

Figure 2.8: Different steps of action potential generation are represented. (Source: WWW).

5. The repolarization typically overshoots the rest potential to about -90 mV. This is called *hyperpolarization* and would seem to be counterproductive, but it is actually important in the transmission of information. Hyperpolarization prevents the neuron from receiving another stimulus during this time, or at least raises the threshold for any new stimulus. Part of the importance of hyperpolarization is in preventing any stimulus already sent up an axon from triggering another action potential in the opposite direction. In other words, hyperpolarization assures that the signal is proceeding in one direction (Figure 8,- *point* 5-).
6. After hyperpolarization, the Na^+/K^+ pumps eventually bring the membrane back to its resting state of -70 mV (Figure 2.8,- *point 6* -).

A nerve cell is like a receiver, transmitter and transmission line with the task of passing a signal along from its dendrites to the axon terminal bundle. The stimulus triggers an action potential in the cell membrane of the nerve cell, and that action potential provides the stimulus for a neighbouring segment of the cell membrane. When the propagating action potential reaches the axon, it proceeds down that "transmission line" by successive excitation of segments of the axon membrane. Just the successive stimulation of action potentials would result in slow signal transmission down the axon. The propagation speed is considerably increased by the action of the myelin sheath (Figure 2.9).

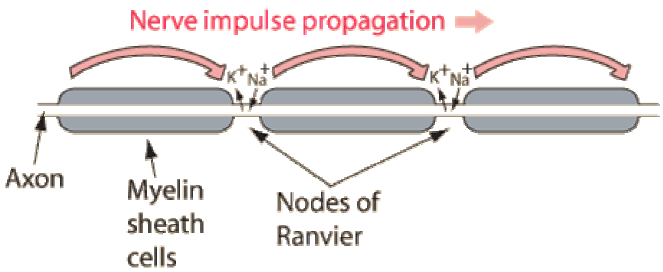

Figure 2.9: Nerve impulse propagation along the axon (saltatory conduction). (Source: WWW).

The myelin sheath around the axon prevents the gates on that part of the axon from opening and exchanging their ions with the outside environment. There are gaps between the myelin sheath cells known as the *Nodes of Ranvier*. At those uncovered areas of the axon membrane, the ion exchange necessary for the production of an action potential can take place. The action potential at one node is sufficient to excite a response at the next node, so the nerve signal can propagate faster by these discrete jumps than by the continuous propagation of depolarization/repolarization along the membrane. This enhanced signal transmission is called *saltatory conduction*. The axon is made up of connected segments of length about 2 mm and diameter typically 20 mm. Axon diameters may vary from 0.1 mm to 20 mm and may be up to a meter long. The myelin sheaths are about 1mm in length. The action potential travels along the axon at speeds from 1 to 100 m/s.

2.3 Frequency bands

Since many years researchers have studied and measured cerebral activity by means of different techniques, in particular *ElectroEncephaloGram* (EEG). The EEG is generated by cortical nerve cell inhibitory and excitatory postsynaptic potentials of neurons in the underlying cortex, mainly pyramidal cells. Rhythmical cortical EEG activity arises from an interaction between the thalamus and cortex. Many thalamic, thalamocortical and cortical neurons have intrinsic oscillatory firing properties that allow them to participate in cellular networks that generate rhythmic EEG activity. On the basis of frequency, we can identify several cerebral rhythms (Figure 2.10): delta [0,5-3,5 Hz], theta [4-7,5 Hz], alpha [8-12,5 Hz], beta [13-30 Hz], gamma [>30 Hz].

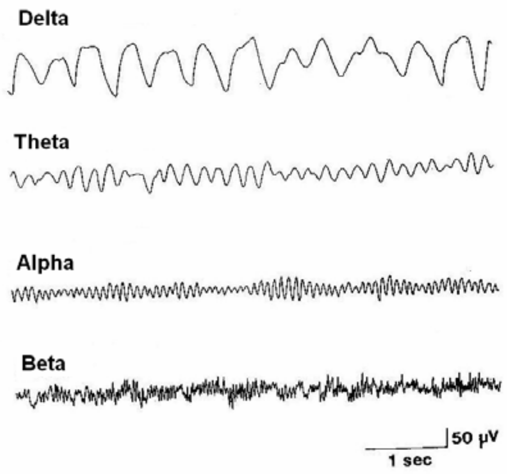

Figure 2.10: Principal components of cerebral EEG activity. (Source: WWW).

2.3.1 Alpha rhythm

This is a rhythm at 8-13 Hz occurring during wakefulness over the posterior regions of the head, generally with higher voltage over occipital areas. It has a waxing and waning morphology, rhythmic and regular. Best seen with (the patients) eyes closed and under physical relaxation and relative mental inactivity. Alfa-rhythm is blocked or attenuated by attention, especially visual and mental effort. Occasionally the alpha-rhythm is of very low amplitude or even not identifiable. Failure of the alpha-rhythm to attenuate on one side with either eye opening or mental alerting indicates an abnormality on the side that fails to attenuate.

2.3.2 Mu rhythm

The 'μ' stands for motor and it is strongly related to movement functions of the motor cortex. Most commonly detected at frequencies between 9-11 Hz and values of 8 Hz or below may indicate brain abnormality. This rhythm has an archlike shape; it is most often asymmetric and asynchronous between the 2 sides and it may be unilateral. Rhythm is blocked by movement, which may be active, passive or reflexive. The blocking effect is bilateral but more stronger in contralateral side i.e. if left hand is moved, the blocking is stronger in the right side. This blocking appears before actual movement of the muscles, therefore it seems to related to conceptual planning of the movement. The μ-rhythm is also blocked by light tactile i.e. touching the skin lightly, so some researchers consider the μ -rhythm to be the 'idling' state of the sensory cortex and its vicinity

2.3.3 Beta rhythm

Beta-rhythm band consists of all frequencies above 13 Hz, overall from 18 to 25 Hz, less commonly at 14-16 Hz. Spatially beta -rhythm can be found frontal and central regions. The central beta-rhythm is related to

Rolandic μ-rhythm and can be blocked by motor activity and tactile simulation (planning to move). Beta-rhythm is usually associated with increased arousal and activity. Two main types exist in adults: 1) the precentral type: predominantly over the anterior and central regions; related to the functions of the sensorimotor cortex and reacts to movement or touch, 2) the generalized beta activity: induced or enhanced by drugs; may attain amplitude over 25 microvolts.

2.3.4 Theta rhythm

The term theta was coined by Gray Walter in 1944 when it was believed that this rhythm was related to the function of the thalamus. Occurs as a normal rhythm during drowsiness. In young children between age 4 months and 8 years it has predominance over the fronto-central regions during drowsiness. In adolescents sinusoidal theta activity can occur over the anterior head regions during drowsiness. In adults theta components can occur diffusely or over the posterior head regions during drowsiness. Finally, single transient theta waveforms or mixed alpha-theta waves can be present over the temporal regions in older adults. Theta-rhythm is associated with marking the maturity of the mechanism linking the cortex, the thalamus and the hypothalamus. Also it is linked with feelings of disappointment and frustration. For some people the theta-rhythm is present when performing mental tasks e.g. problem solving or visualization.

2.3.5 Delta rhythm

This rhythm is detected when the subject is in deep sleep at later sleep periods. Delta-rhythm has a relatively high amplitude and low frequency, 3 Hz or less. Delta-rhythm decreases with age and can be a sign of brain abnormality if detected in the awake state.

2.3.6 Gamma rhythm

This oscillation, which is beyond 30 Hz, is involved in feature binding processes in the brain. It is also believed to be the triggering factor in perception and attention. Oscillatory activity in the gamma-band range (>30 Hz) has been proposed as a correlate of cortical network synchronization. In human electroencephalogram (EEG), enhanced gamma-band activity has been found in relation to processes ranging from visual gestalt perception to selective attention, learning and memory (Kaiser J and Lutzenberger W., 2005). Research in neuroscience indicates that oscillatory activity in the gamma band (25-50 Hz) can be correlated with both sensory acquisition and pre-motor planning, which are non-continuous functions in the time domain. From this perspective, gamma-band activity is viewed as serving a broad temporal binding function, where single-cell oscillators and the conduction time of the intervening pathways support large multicellular thalamo-cortical resonance that is closely linked with cognition and subjective experience (Ribary U, 2005).

2.4 References

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3. Overview of BMIs

3.1 General BMI elements

BMIs can be defined as any system that can monitor brain activity and, from it alone, translate a person's intentions into commands to any man-made device. This implies that even if a mental activity results in signals going to muscles, spinal cord, peripheral nerves, and/or the autonomic nervous system and its outputs, a BMI will not use any of these and will do the translation task based exclusively on the brain signals (see dependent vs. independent BMIs below).

But, which are the brain signal monitoring systems best suited for this challenging task? There is a variety of methods that have been employed to this end. They include, but are not limited to: electroencephalographic signals (EEG), magnetoencephalographic signals (MEG), positron emission tomography (PET), functional magnetic resonance imaging (fMRI), optical imaging (NIRS, near-infrared systems) and implanted methods of recording electrical activity, e.g., via electrocorticograms. Of the above, only EEG and MEG have the two properties that are essential for most realistic BMIs: non-invasiveness and portability. NIRS are portable as well, but they have an invasive component, in the strictest sense of the world: brain function is equated to the amount of infrared light reflected by brain tissue, the emitter and sensor being near each other on the scalp. Significant near-infrared light is absorbed by the brain tissue, the long term effects of which have not been investigated yet. PET requires the administration of radioactive substances to the human subject, and fMRI still requires very bulky and heavy equipment, both of which are therefore not suitable for BMI applications, though they are very powerful tools for studying brain function in laboratory settings.

Regardless of the sensor type, however, there are a number of elements that are common to all BMIs (Figure 3.1). First, the experimental protocol must be designed to suit the application and the environment in which the BMI will be used. This includes choice of mental task, stimulus parameters (e.g., visual scenery timing and constraints), an minimization of unwanted stimuli and distractions that may affect the properties of the signals to be monitored. Once a suitable protocol is designed, signals can be monitored and use. This can be done by means of the bioinstrumentation mentioned above, including the necessary amplifiers and analog filters to remove some of the unwanted interferences.

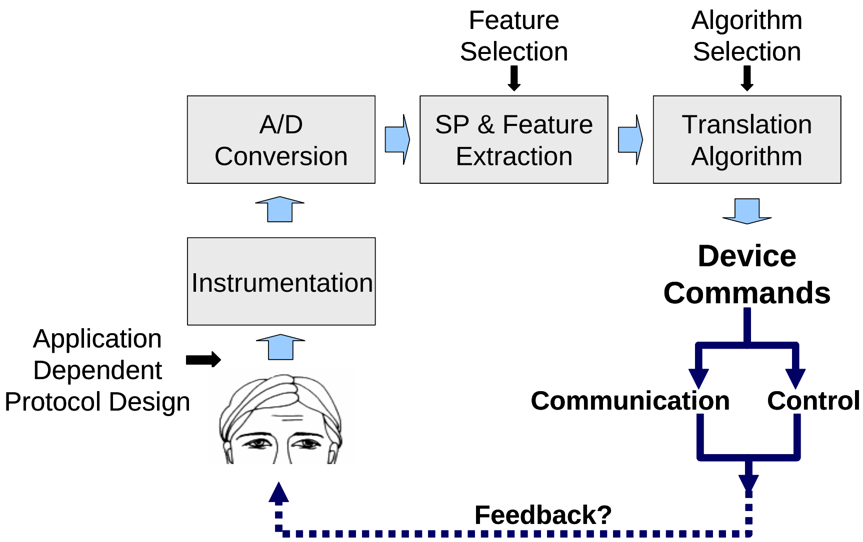

Figure 3.1: Main elements of a general BMI. (Source: WWW).

The signals acquired with the instrumentation are then converted to digital format, using the standard sampling rate of at least twice the expected highest relevant frequency component in the signal. The digitized signal can now be further filtered and used for extracting information that is relevant to the mental task under investigation. Before the signals are used, however, some unwanted artifacts need to be removed. These can be, for example, large amplitude oculomotor signals (very frequent in EEG readings) and cannot be removed by standard digital filters alone. Once any unwanted signal components are removed as much as possible, features (or specific parameters or wave shapes) can be extracted from, the data. Without exaggeration, thousands of different features have been used in BMIs, being divided into three general domains: a) time domain, b) frequency domain, and c) joint time-frequency domain (more on this on Chapter 4). The features are likely to be location specific as well. Few features within these domains will yield information that correlates well with a mental task class under any protocol conditions. Indiscriminate use of as many features as possible can thus make the subsequent translation task non-realizable on account of the large amount of irrelevant information. Thus, proper design of BMIs include a 'feature selection' study for the specific conditions of the envisioned application. Once this selection is done, the overall process only requires extraction of the pre-selected features from the real-time data. However, some adaptive systems can do some level of feature selection on-line as well.

Once the relevant features have been extracted, they can be fed into a translation algorithm (previously selected among many for the task). Translation algorithms (also wrongly called 'transduction' algorithms) can be as simple as 'if-then' rules or a previously determined linear discriminate. However, more often than not the complexity of the data requires the use of non-linear classifiers such as machine learning algorithms. The translation algorithm then yields commands to be used by various devices (the 'control' case) or to lead to explicit communication of thoughts (the 'communication' case).

For almost all studies to date, the response of the controlled device as a result of the BMI's processing is not explicitly fed back to the BMI user. Further, while we do know that the user adapts to the entire system and that the device's response plays a role in this process, subject adaptation mechanisms have only recently begun to be investigated with regard to BMIs.

Please note that, as stated above, the discussion in this chapter applies to BMIs based on any instrumentation type, regardless of whether the signals are electrophysiological, optical, magnetic, or otherwise. More will be said below concerning some of the elements shown in Figure 3.1.

3.2 BMI types

BMIs have been categorized in many ways in recent years. Most subdivisions fall under one of the following:

- Dependent vs. independent.
- Invasive vs. non-invasive.
- Spontaneous vs. evoked vs. event-related.
- Synchronous vs. asynchronous.

These have so far been studied in exclusive fashion (e.g., either spontaneous or event-related signals), but future BMIs may combine some or all of the above in one system. All types are discussed below.

3.2.1 Dependent vs. independent BMIs

BCI devices have been classified as Dependent and Independent (Wolpaw et al., 2000). A dependent BCI does not employ the usual ways of brain output to transport and dispatch the relevant message, but it requires some -even if little- surviving function of such a physiological channels in order to generate the relevant EEG activity. In other words, a dependent BMI requires the presence but does not use normal output pathway to produce the brain signals that feed the interfacing computer. For instance, let us consider a matrix of alphabet letters presented in a video display, which are sequentially illuminated; the human subject is trained to choose the letter he/she wants just via ocular fixation (foveolization). This act produces a Visual Evoked Potential (VEP) on the occipital scalp significantly larger than the responses provoked by the other flashing letters which are not fixated by the Patient (Sutter, 1992). Therefore, the relevant signal is coming from the EEG, but it is due to the sight focus direction.

An Independent BMI, on the other hand, is entirely free from the physiological output pathways of brain as the relevant signal is not generated by propagating signals along peripheral nerves, muscles, or other physiological outputs. A practical example can be found in the same character matrix discussed above. In this case, the subject selects a character just by paying attention to the letter he/she wants; he/she does not need to gaze directly at the letter of interest. This attention mechanism elicits an increase in a brain cognitive potential (known as the P300 wave) shortly (300ms) after the target letter flashes (Farwell and Donchin, 1988; Donchin et al., 2000; Sutton et al., 1965; Donchin, 1981; Fabiani et al., 1987; Polish, 1999). The usual brain outputs do not play an important role in independent BMIs, which provide a wider variety of brain 'outputs' and are therefore of great interest, particularly for subjects who are completely paralyzed.

3.2.2 Invasive vs. non-invasive

Aside from the clear distinction between -invasive - implanted electrodes (eg., subdural, epidural, or intracortical electrocorticogram, ECog,) and those –non invasive- that go on the skin surface (EEG), there is a wider issue concerning the term 'invasive'. In biomedical engineering, any technology that deposits any eternal elements on the sub-epidermal tissue (i.e., any tissue excluding hair and skin) is considered invasive. The deposited element could be a device of any material, a chemical, nuclear and subnuclear particles, or even electromagnetic energy. Thus, in the strictest sense of the world, technologies such as NIRS (which deposit near infrared light on the tissue), fMRI (which applies magnetic fields) and PET (which requires the administration of a radioactive substance) are all invasive as the very mechanisms by which they work requires that the observed tissue (and surrounding ones) be internally disturbed. In the case of NIRS, which may become popular devices in the future, the effects of the absorbed energy on the brain tissue have not been studied concerning long term and even short term but prolonged use (e.g., rare occasions, but with hour of use every time).

Thus, of the technologies described here, only EEG and MEG are truly non-invasive.

3.2.3 Spontaneous vs. evoked vs. event-related.

Evoked potentials (EPs) appear in the brain as a result of a particular stimulus, e.g., a flashing letter, whether the subject is interested in it or not. EPs are time locked to the stimulus. Other brain signals can be completely spontaneous, such as those related to movement intentions in the sensory motor cortex and are thus not a result of specific input. Finally, a third class of signals is dubbed 'event-related potentials' (ERP). These are related to evoked potentials but include brain responses that are not directly elicited by the stimulus; they can include cognitive signals, among other psychological manifestations (Rugg and Coles, 1995). In fact the term ERP is seen as a more accurate term for all but the most restricted simulation protocols. It is thus the preferred term instead of EP.

3.2.4 Synchronous vs. asynchronous

Following the description in the paragraph above, another pair of terms is widely used in the BMI literature. Asynchronous interfaces (Allison and Pineda, 2005) are those that use truly spontaneous signals for its operation (e.g., Graimann et al., 2004; Mason et al., 2004; Townsend et al., 2004; Kennedy et al., 2000; Yom-Tov and Inbar, 2003). Brain signals relevant to a subject's intention will thus be produced any time, with or without stimulus, thus making classification of the intention difficult as the computer will first need to find when an intention took place, the so called 'onset detection' problem). Synchronous interfaces, on the other hand, will use either evoked or event related potentials (e.g., Pfurtscheller et al., 2003; Gao et al., 2003; Farwell and Donchin, 1988; Sutter, 1992; Middendorf et al., 2000). Such BMIs look into features that are at known times after a particular clue, whether it is a flashing letter, or a command to imagine a hand movement. These are thus 'cue-linked' and therefore do not have to deal with the on-set detection problem.

While most work to date has used cue-linked (synchronous) interfaces, future BMIs will likely require more asynchronous features as these are more natural and do not require that the subject be paying full attention to a given stimulus.

3.3 BMIs and the user's ability

Successful use of BMIs as developed to date requires that the user maintain his/her ability to learn and retain new abilities in controlling not the usual neuromuscular channels but the EEG pattern that is recognized as relevant by the BCI. This does not imply a training period per se. For instance, the ability to generate an increased P300 wave in response to flashing of the chosen letter is independent from training. It only requires the subject to be able to identify the chosen letter as the 'target' of his/her attention and to ignore all the remaining letters. Of course, some degree of learning is needed even in this kind of operation. In fact, it has been noted that the production of the P300 signal progressively adapts as the subject becomes familiar with it (Rosenfield, 1990; Coles and Rugg, 1995). This ability of humans to self-control their EEG rhythms and transient waves has been reported for several decades (Wyrcka and Sterman, 1968; Dalton, 1969; Black et al., 1970; Nowles and Kamiya, 1970; Black, 1971, 1973; Travis and al., 1975; Kuhlman, 1978; Rockstroh and al., 1989; for a review see Niedermeyer 1999). More recently, experiments with primates have shown that the firing rate characteristics of individual neurons can be controlled by learned conditioning. This opened new avenues for controlling BMIs (Fetz and Finocchio, 1975; Wyler and Burchiel, 1978; Wyler et al., 1979, Schmidt, 1980; Dewan, 1967). In fact, this has led to work on the operant conditioning approach of many groups, notably Wolpaw's and Birbaumer's work (see below).

3.3.1 Operational protocol

Every BMI has its own operational protocol which defines the procedures for switching ‘on’ and ‘off’, the continuity or discontinuity of the communication, whether the relevant signal is generated consciously by the subject or in response to a stimulus triggered by the BMI (i.e., event-related), the exact sequence of interactions between the subject and the BMI, and the type of feedback provided to the subject. In real life the subject must be able to choose the message and must be able to carry out the switching ‘on’ and ‘off’ procedures. The great majority of BMIs to dater have not addressed these issues, but they are integral parts of any useful BMI for the future and should thus be considered in the general design of the system.

3.4 Translation algorithms

The relevant extracted features must be transformed into commands directed to the device which has to execute the subject’s intentions. This algorithm can be based on linear (e.g., classical statistics) or non-linear (e.g., neural networks) techniques. Examples of Artificial Intelligence methods used are Linear Discriminant Analysis, Artificial Neural Networks, Genetic Algorithms, Kernel-based learning methods (Support Vector Machines, Kernel Fisher Discriminant), Bayesian networks, Hidden Markov Models. Whatever the method, the algorithm transforms the independent variables (i.e. the relevant signal) into dependent ones (i.e. commands controlling the device).

In order to be really efficient, an algorithm should adapt to the human subject at least at three levels:

1) **Initial training of the algorithm**: This is important in the early stages of mutual adaptation. For instance, if the relevant feature is represented by the amplitude of the mu rhythm as it is generated in the sensorimotor cortex, the algorithm should adjust on the average amplitude of this particular rhythm. On the other hand, if the relevant signal is represented by the firing rate of an individual neuron, the algorithm should adjust on the range of firing which is characterizing this specific neuron. If the BMI is remains at this first level and is unable for subsequent adjustments, then it will remain efficacious only if the subject is able is able to maintain stable performances. Unfortunately, the EEG is typically variable due to chronobiological changes (time hours, blood glucose and salts levels, external environments characteristics, physical and mental fatigue, general health status, use of neuro and psychoactive drugs) as well as for non-biological factors (i.e. skin/electrode contact and impedance). Therefore at least a second level of adaptation is needed in order to have an efficacious BCI.
2) **Adaptation with periodic on-line adjustments:** this will reduce the influence of unpredictable variables. A good translation algorithm will self-adapt to variations of the important components of the relevant signal and will maintain a stable range of the output commands dispatched to the device. Such adaptations can happen

within periods as short as seconds or as long as years (e.g., in the possible case of long term, chronic users). However, despite their importance, the first two levels of adaptation just described are not yet sufficient to address the main problem towards suitable BMIs: appropriate interaction between the BMI and the brain.

3) **Mutual adaptation and reinforcement**: In the best scenario -that is the one of a fully adapted BMI- the brain will progressively modify the important components of the relevant signal pointing toward a progressive improvement of the BMI performance. If, for instance, the relevant feature is the mu rhythm amplitude, the relationship between this parameter and the subject's intention will improve with time. Thus, algorithm adaptation is needed for taking advantage of such an improvement so that the subject receives a reward (or similar), for example, by accelerating communication with the BCI device. On the basis of our example, the subject should move the cursor and select the appropriate letters more rapidly once he/she learned to implement the relationship between the relevant signal and the personal intention. Meanwhile, it is important not to make the task too difficult, since anxiety, frustration and fatigue can all affect subject's performances particularly during the training and learning stages (Dibartolo et al., 1997; Lang and Kotchoubey, 2000).

3.4.1 Pattern recognition vs operant conditioning approach

Birbaumer, in Germany, and Wolpaw, in the U.S., demonstrated that instead of using cognitive tasks, an operant conditioning approach could be used to train subjects to control a cursor. This approach was based on the idea that it is sufficient to provide an appropriated feed-back (i.e., seeing the moving cursor) to let the brain progressively learn which components of its signals are relevant in controlling the BCI device (Pfurtscheller et al., 1993). In Wolpaw et al. (1991) subjects adopted different strategies in order to move the cursor (i.e., to lift a weight to move cursor down and to relax to move cursor up) during the conditioning period. Thereafter, they did not use the weight lifting strategy any longer as the cursor control could be done just by imagining the task.

3.5 Output and feedback methods

3.5.1 Output

In most BMIs to date, the output is presented on a monitor that presents different possible choices, usually under the form of letters and icons (e.g., Farwell and Donchin, 1988; Wolpaw et al., 1991; Perelmouter et al., 1999; Pfurtscheller et al., 1999; Pfurtscheller et al., 2000a). Some BMIs provide an additional output showing the interaction with the subject in the instant preceding the selection, such as the cursor's movement toward the target (Wolpaw et al., 1991; Pfurtscheller et al., 2000a). In this case, the output, besides being the product of brain activity, also represents useful feedback that the subject's brain can utilize to improve on the communication speed and accuracy.

Recent studies have investigated the possibility of controlling neuroprostheses and/or orthoses via a BMI. In two studies, attempts were made to control either a real (via neuromuscular electrical stimulation) or artificial hand in subjects with complete section of the cervical spinal cord (Lauer et al., 2000; Pfurtscheller et al., 2000b), with some success. However, some researchers have pointed out that BMIs are not yet reliable of fast enough to be used with some neural prostheses. For example, BMIs are not yet useful for controlling walking induced by functional neuromuscular electrostimulation, FES (see e.g., Sinkjaer, et al. 2003).

3.5.2 Feedback

As mentioned above, most BMI studies use outputs on a computer monitor. The use of this visual information as feedback present problems for fast applications. Treisman and Kanwisher (1998) concluded that it takes at least 100ms after stimulus presentation for object recognition to occur and nearly another 100 ms for the information to be become conscious. This relatively long delay to process conscious information complicates the use of visual feedback as the only one for error correction in real-time in BMIs that require fast responses, e.g.,. in dynamic and complex situation like the one represented by a moving arm.

Subjects with complete deprivation of proprioceptive feedback (such as in some cases of peripheral neuropathy) can move their limbs using visual feedback (e.g., by looking at the limb), but their movements are typically sluggish, coarse, and require substantial mental concentration and attention (Gordon et al., 1995; Sainburg et al., 1993). Corrections are therefore delayed and often cause other mistakes, leading to movements that share some of the choreo-athetoid chracteristics found in human diseases such as Huntington Chorea. The simple dynamics (e.g., less degrees of freedom to control and less compliance) in a virtual or an artificial mechanical limb may lead to this scenario being less affected by such delays, but this hypothesis has yet to be tested.

An number of possible solutions may be tried in the future to reduce problem related to perceptual delays. Among them, the use of haptic feedback and electrotactile sensations. Another possibility is to employ direct electrical stimulation of the sensory brain areas or nearby afferent pathways. For instance, cochlear implants (Loeb, 1990) represent the best interface between the nervous system and an artificial system to date. This device has been implanted in more than 40,000 people worldwide. Unfortunately, attempts to directly stimulate more central brain areas such as the motor cortex have been less satisfactory, though this may be related to the absence of relevant information that usually present under normal physiological conditions, e.g., from peripheral receptors in the skin, joints, muscles, etc. (Rauschecker and Shannon, 2002). Direct stimulation of the central somatosensory system - including regions processing proprioception- would probably represent the most physiological approach to movement-related feedback (Immann et al., 2001). However in many clinical conditions, receptors and peripheral nerves are no longer functioning properly, thus complicating the picture. Further, the perceptual effects of direct electrical stimulation of the sensory cortex are not fully understood yet.

Experiments with monkeys (Romo et al., 2000) have demonstrated the possibility of distinguishing different frequencies of stimulation regardless their are secondary to mechanical stimulation of the fingertips and for direct cortical electrical stimulation, but their efficacy in absence of a real proprioception has never been demonstrated. However, although vision plays a secondary role in controlling movement on-line, it is pivotal for motor learning. Monkeys trained to control a cursor in a visual environment using implanted electrodes (Taylor et al., 2002, Figure 3.2 below) were able to utilize their visual system to adapt their cerebral control to the cursor's movement. The control algorithm had been implemented to adapt itself to changes of the firing characteristics of the recorded neurons. In all sessions such changes tended toward a stabilized pattern, thus suggesting that CNS was moving from a state of "direct control" to a state of "cerebral control".

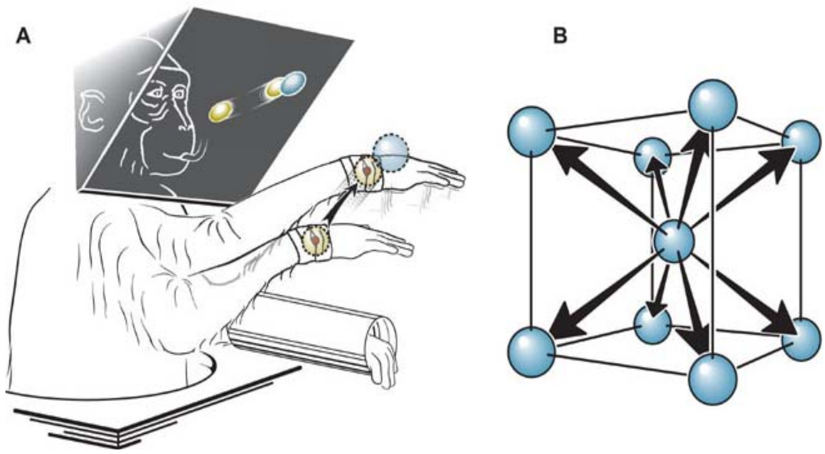

Figure 3.2: BMI using implanted electrodes in a monkey. Sensory-motor cortex signals were used by the BMI to determine the 3D final location of a virtual object. A) The setup and the monkey's movements; B) the virtual object's end points. The size of the balls is indicative of the error between the actual position of the monkey's hand and that of the estimated location based on the brain's signals. (Reproduced from Taylor et al., 2002).

3.6 Learning effects and neural plasticity

Throughout the repeated execution of any task, the brain undergoes plastic adaptation that may be relatively short lived or more persistent depending on the stimulation type and timing, amongst other factors, and on the overall interaction between human subject and machine. From a systems point of view, this plasticity is in essence a transfer function change on the human subject side that inevitably affects the overall behaviour of the BMI and requires adaptation on the machine side as well.

For most purposes, learning can be defined as response changes due to experience or information. In the nervous system, the main underlying mechanism for these changes are in the form of neural plasticity, i.e., relatively persistent changes (minutes to years) that may involve elements form the molecular to the systems level. Three of the most basic processes resulting from plasticity are:

- Habituation (response decreases as a result of frequent input)
- Sensitization (response to input increases)
- Associative Learning (inputs A and B together cause adaptation)
    - A special case: Long Term Potentiation (LTP) and Depression (LTD)

These are briefly described below.

3.6.1 Habituation

As the nervous system is exposed to prolonged or very strong stimuli (e.g., a very loud environment), it tends to reduce its response, thus ‘habituating’. All sensory inputs can and do lead to habituation, thought the time or onset of this phenomenon and the persistence of the habituated state depend on many variables. Most habituation states, however, last from just a few minutes to years.

In habituation, it has been established that sensory axons are not where the adaptation takes place (Kolb & Wishaw, 2005). In some cases, the sensor themselves habituate (e.g., the case of retinal phototreceptors), but in the most persistent cases, there is evidence that the change is at the junction (synapse) between the sensory neuron (or a neuron in the sensory pathway) and the neurons that are linked to the CNS’s response to the stimulus. For example, in the case of a simple, monsynaptic motor reflex (Figure 3.3), the change would be at the synapse between the sensory and the motor neurons. More specifically, the changes have been found to be in the presynaptic regions, whereby less neurotransmitter is released as a result of $Ca2+$ mediated effects triggered by the prolonged or very strong stimulus. Less $Ca2+$ enters the presynaptic release sites, thus causing less neurotransmitter vesicles to mobilize themselves from the anchor points to the active sites on the synaptic membrane. How a prolonged stimulus causes less $Ca2+$ to enter the presynaptic site is not yet known. It was thought that $Ca2+$ slowly depleted from the synaptic cleft (the space between the pre and the postsynaptic sites) due to a prolonged input, but this does not explain how the phenomenon persists, as $Ca2+$ concentrations in the cleft seem to return to normal fairly quickly. Instead, evidence points to the presynaptic $Ca2+$ channels becoming less responsive (Edmonds et al., 1990). The causes of this loss of responsiveness are not yet understood.

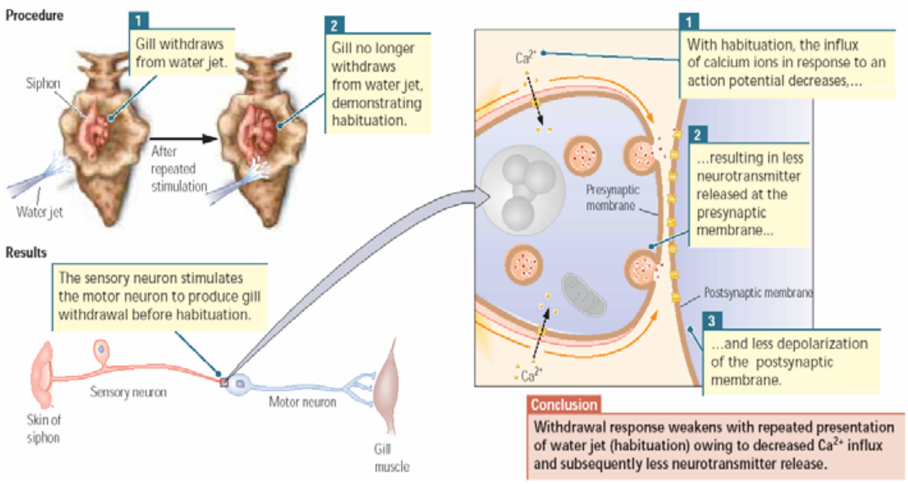

Figure 3.3: Example of habituation in the simple reflex in a snail (often used as a study model due to its simplicity). (Reproduced from Kolb Kolb & Wishaw, 2005).

3.6.2 Sensitization

The opposite of habituation, i.e., sensitization, also takes place in the CNS. The CNS's response to a stimulus can increase in some cases. More specifically, when a stimulus takes place at the same time as another input to the same neuron, the sensory cell can be caused to release more neurotransmitter than if only the stimulus was present (i.e., the extra input to the cells was not present). Studies on sensitization (e.g., Figure 3.4) have found that the required extra input (an interneuron) actually synapses with the sensory terminal, not with the postsynaptic cell that is linked to response pathways. This interneuron input modulates the amount of neurotransmitter to be released by the sensory cell and has been found to be linked with interneurons that release 5HT (serotonine). 5HT reduces the amount of K+ released by sensory cell, keeping the sensory terminal highly excited an thus causing more Ca2+ to enter the terminal. This in turn leads to more neurotransmitter being released by the sensory cell, thus increasing the response of the postsynaptic cells. The resulting increased response is thought to persist due to long lasting effects on the K+ channels (Edmonds et al., 1990), but the cause of this mechanism is not yet understood.

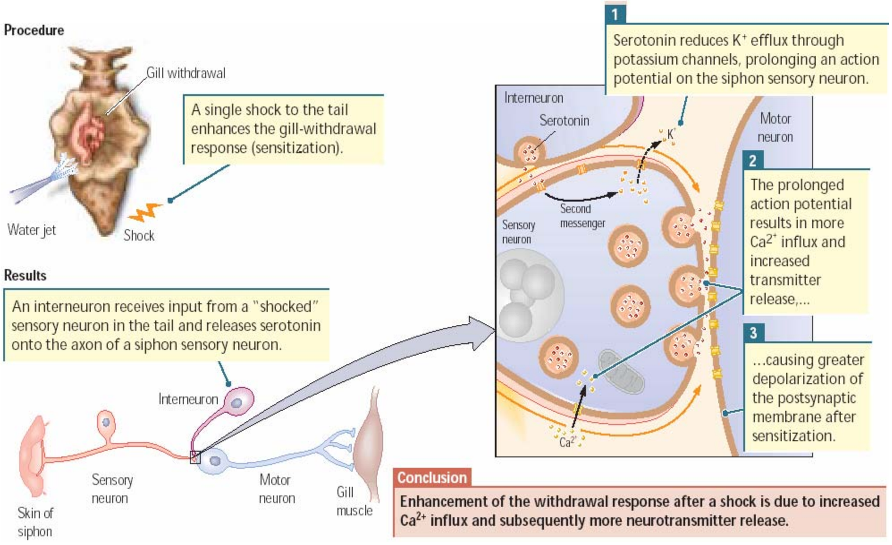

Figure 3.4: Example of sensitization in the simple reflex in a snail. (Reproduced from Kolb & Wishaw, 2005).

3.6.3 Associative learning

In associative learning, at least two inputs are needed onto a postsynaptic cell. In contrast to the sensitization case, the second input in this case does not synapse with the sensory cell. In fact, so long as the second (or third, etc.) input affects the excitation state of the postsynaptic (response) cell when the sensory input comes in, regardless of how far in space the sensory and the other inputs are, the synapse between the sensory and the response cell (not necessarily motor) will suffer persistent changes. If both the sensory and the response cell are excited at the same time, the connection between the two cells will be strengthened, i.e., the response to a stimulus will increase. Moreover, after this effect consolidates itself, stimulation of the second input will cause the same response as if both inputs were present, hence the 'associative' term. For example, if someone surveys a scene that has strong smells, along with the usual visual, auditory and tactile inputs, the combination of inputs will cause the person's retention of the scene, and the resulting navigation through it, to be stored by means of the associative mechanism described here. Later, presentation of a single one of the inputs (e.g., smell), can elicit recall of the entire scene and the person can thus recreate the navigation sequence without being back in the scene that was learned. This process has been to happen predominantly in the hippocampus (Figure 3.5), in the form of long term potentiation, but its effects are felt throughout the brain.

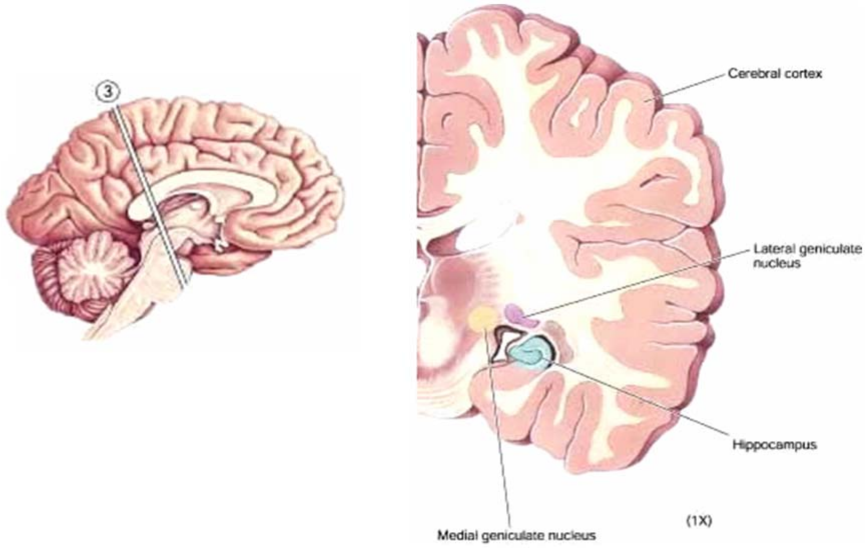

Figure 3.5: Established locus of long-term potentiation, an associative learning process. (Reproduced from Bear et al., 2001).

3.6.4 Other types of adaptation

There are a number of structural and functional adaptations in addition to and as a result of the above processes. For example, if sensitization and habituation persist, they can lead to the respective appearance and disappearance of synaptic branches between two cells (Figure 3.6).

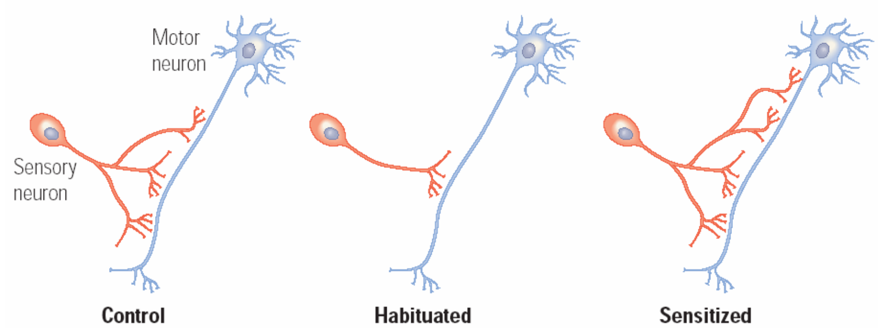

Figure 3.6: Structural effects of prolonged sensitization and habituation. Observe the changes in the number of synaptic branches between the two cells compared to the standard (control) case. (Reproduced from Kolb & Wishaw, 2005).

Several other plasticity processes cab be observed within the pre and postsynaptic cells as well, but these are beyond the scope of this report. However, the overall effects can lead to structural as well as functional rewiring. An example of the former can be seen in Figure 3.7. This rewiring, together with changes in shape and size of neuronal dendritic trees, can lead to the latter functional remapping. I.e., parts of the brain that were previously processing information related to one part of the body, or to a particular cognitive task, may now be linked with other areas/tasks In the study, two populations of monkeys were trained, one to retrieve food from a small well (left figure) and another one to retrieve food from a large well. The small well task requires more use of the fingers, while the large well task requires more use of wrist and forearm. The figures show how the two populations differ with regard to which areas of the brain control which part of the upper limbs.

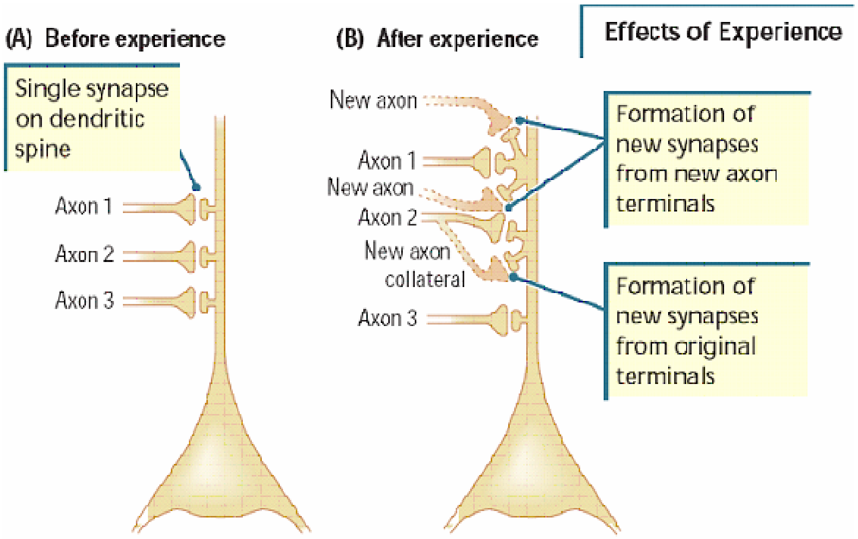

Figure 3.7: Local rewiring as a result of experience. (Reproduced from Kolb & Wishaw, 2005).

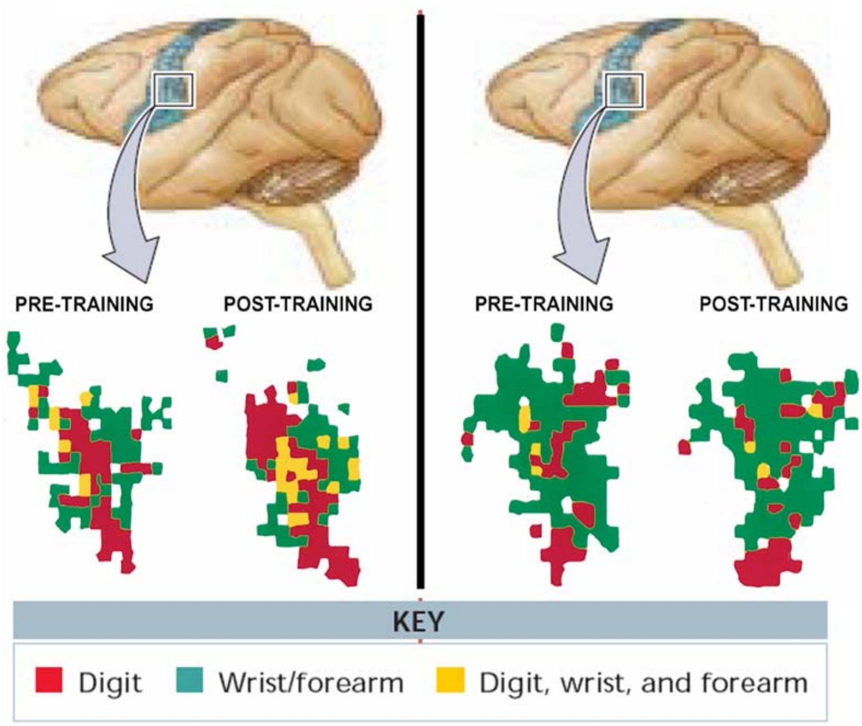

Figure 3.8: Remapping of sensorimotor cortex as a result of experience (adapted from Nudo et al., 1997). Left: monkeys trained to retrieve food from a small well. Right: monkeys trained to retrieve from a large well.

3.7 Significance of learning and plasticity for BMIs

The above structural and functional changes are crucial to the development of BMIs in that they introduce neural adaptive mechanisms that must be taken into account both ion the design of the algorithms for the BMI and in the design of the stimulus and tasks to be used.

Habituation and sensitization: these two phenomena will affect the strength with which the brain will respond to stimuli. While intelligent translation algorithms may be able to track some of these changes, there are situations in which habituation can be so strong as to lead the detected relevant brain waves to disappear. This could happen, for example, if a person uses a P300-based protocol for prolonged periods. It is possible that the P300 wave ill no longer be strong enough to be detected.

Associative learning: The combination of inputs (not necessarily of different modalities) can lead to both desired and unwanted associations. Care must be taken to minimize unwanted associations, or to minimize the changes due to them.

Functional remapping: This is one of the most difficult effects to track in a translation algorithm. In practice, we find the algorithm interpreting signals that are no longer associated with part of the body as compared with the time when the algorithm was designed. Further, it is so far impossible to predict the remapping. Algorithms and stimulus protocols will have to include routines for recalibrating themselves as a result of new functional maps. For example, In the case of BMIs using EEG, simple tasks might be done occasionally to examine dipole map changes and from that to adapt the translation algorithm.

The above factors have only recently been considered in connection with BMIs, but to date no BMI system has been designed to address these problems. Further, the variability of such effects between subjects, and even for a single subject, is expected to be large, thus further complication the BMI design task. On the other hand, these factors may be used to advantage as well. For example, an unwanted response that confuses the BMI my be reduced by including mechanisms to habituate the undesirable responses.

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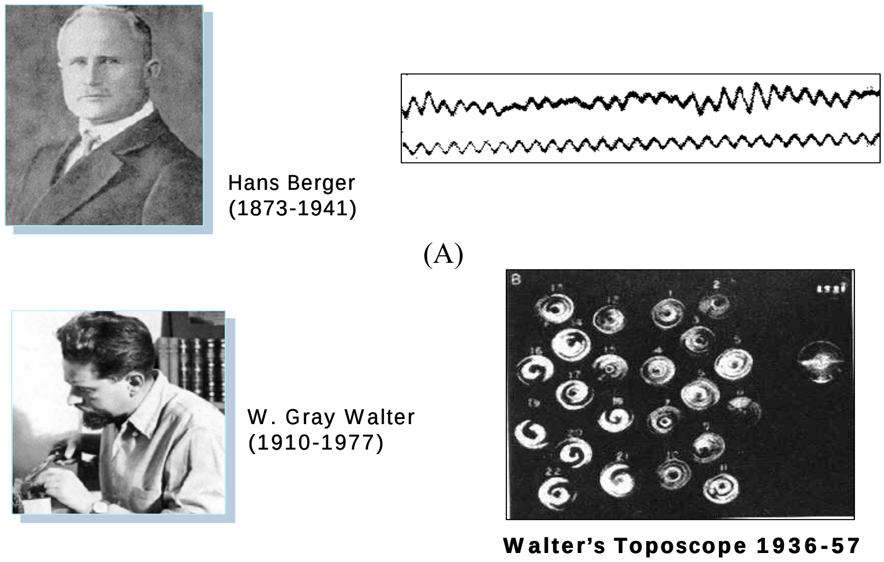
4. Electroencephalograpy (EEG)

Note: this chapter assumes the more accepted terminology in which EEG refers to the use of electrodes outside the skull only. Other techniques using intracortical, subdural, or other implanted electrodes are not covered here.

4.1 A bit of history

Electroencephalography (EEG) consists of brain electrical activity patterns as measured from the outside of the skull. The first observation of such patterns in animals was made by Richard Caton, in Liverpool, in 1875 (Cooper et al., 1969). Caton was studying brain activity in cats, monkeys and rabbits using cortical non-polarizable electrodes connected to a galvanometer when he observed that "feeble currents of varying direction pass through the multiplier [instrumentation] when two electrodes are placed on two points of the external surface". In 1876, Danilevskey observed a change in cortical potentials due to acoustic stimuli.

It was not until 1929 that similar studies were reported in humans. At that time, Hans Berger (Figure 4.1.A), in Germany, reported on a study using platinum wires pushed into the scalp, zinc-plated steel needles, and various other metals in an attempt to observe electroencephalographic activity in humans. Berger also gave electroencephalography its name. He is widely considered to be the inventor of EEG. Later, after 1930, when the galvanometer was replaced by valve amplifiers and a.c. coupling, better technology was available. One of the most important developments was the multi-channel EEG system developed by Grey Walter, which he called the EEG toposcope (Figure 4.1.B). This device allowed for studies of brain potentials and their temporal relationships. It is a very useful tool and inspired the multi-channel devices used today. Meanwhile, Edgard Adrian and others continued Berger's work. In the 50's, after the invention of the transistor, researchers returned to using d.c. instrumentation. Since then, most developments have been made on making the instrumentation less prone to noise and developing better electrodes (see EEG Hardware below).



(B)

Figure 4.1: Some of the pioneers in the development of EEG technology. A) Hans Berger and the first reported human EEG signals. B) Grey Walter and the EEG toposcope. (Modified from Sabbatini, 1997).

4.2 The physiological origin of EEG

EEG measures the electrical activity by detecting the electrical potential difference between a point on the scalp and a ground (more on this in the next section). More specifically, EEG mostly measures the potentials resulting from current flow during excitation of the dendrites of pyramidal neurons in the cerebral cortex. Other, deeper cells may contribute to the detected signal as well, but this is usually a small affect.

The amplitude of the potentials measured on the neural cells' membranes is in the order of several tens of mV. However, the tissues between the electrode and the monitored cells, and the distance between the neurons and the electrodes, cause the signal to be attenuated by many orders of magnitude. Thus, the activity of a few neural cells cannot be detected through EEG. Instead, EEG is a result of joint activity of thousands of underlying neurons activated together (so called synchronous activity). The amplitude of the EEG signal is proportional to the number of synchronously activated neurons and the size of the synchronous area. Even so, at best EEG amplitudes are usually in the order of 100 microvolts or less.

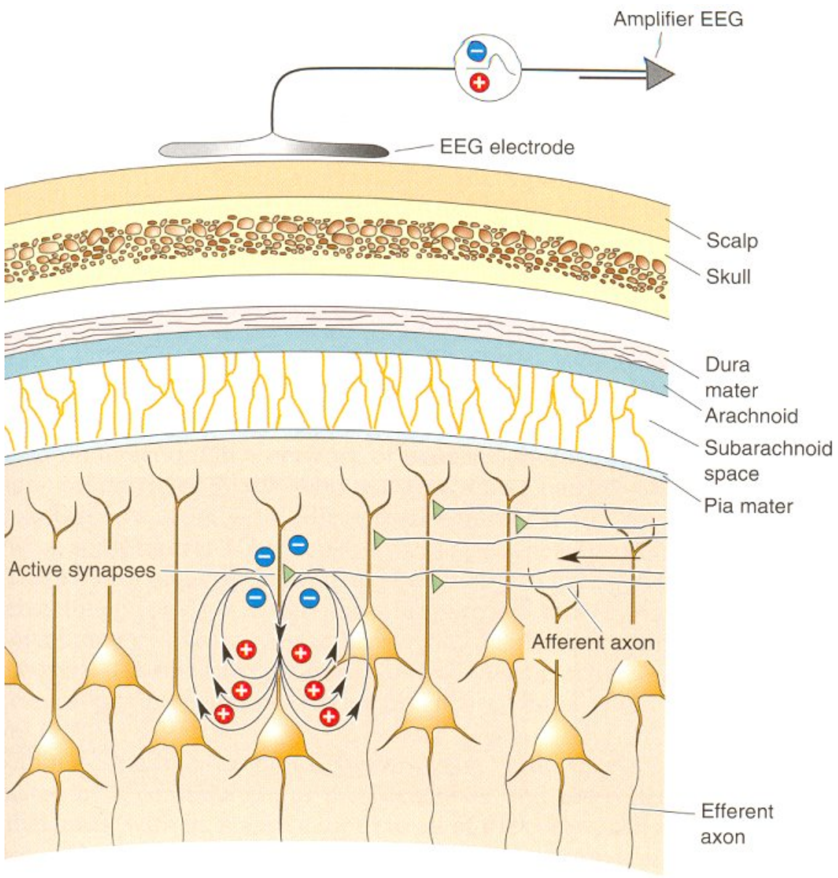


Figure 4.2: The generation of cortical potentials that are measured from the skull using EEG instrumentation. (Reproduced from Bear et al. 2001).

Tissue Effects on EEG

Aside from the **amplitude related effects** discussed above, the tissues shown above between an electrode and the monitored neurons (which also includes circulatory, fat, and other tissue), particularly the skull, have **Geometric effects**: cortical signals are spread through a large area on the skull, thus making localization of the source a very difficult task, in spite of many attempts at solving this issue by means of inverse EEG/skull models (e.g., Pascual-Marqui, 1999).

4.3 Basic physiological EEG rhythms

The great majority of EEG studies to date are based on basic rhythms that have been observed to correlate with a number of states. The main rhythms are (see Figure 4.3):

- Gamma (30-80 Hz): amplitude changes related to perception and consciousness, REM sleep.
- Beta, two types, I and II (14-30 Hz): less regular activity, present in awake state, changes when eyes are opened or closed; Type I disappears during intense mental activity; Type II is elicited by mental activity.
- Alpha (8-13 Hz): Very rhythmic; normal activity in quiet and restful state; larger when eyes are closed then when opened.
- Theta (4-7 Hz): Infrequent, mostly in adolescents and in adults during stress.
- Delta (< 4 Hz): observed in deep sleep, infancy, and brain disorders.

Please note that there is no consensus for the exact cutoff frequencies for the above rhythms. For example, some authors consider the Beta band to cover frequencies up to 50Hz. There is more agreement on the frequencies for the Alpha band, though the higher cutoff is often set at 12Hz.

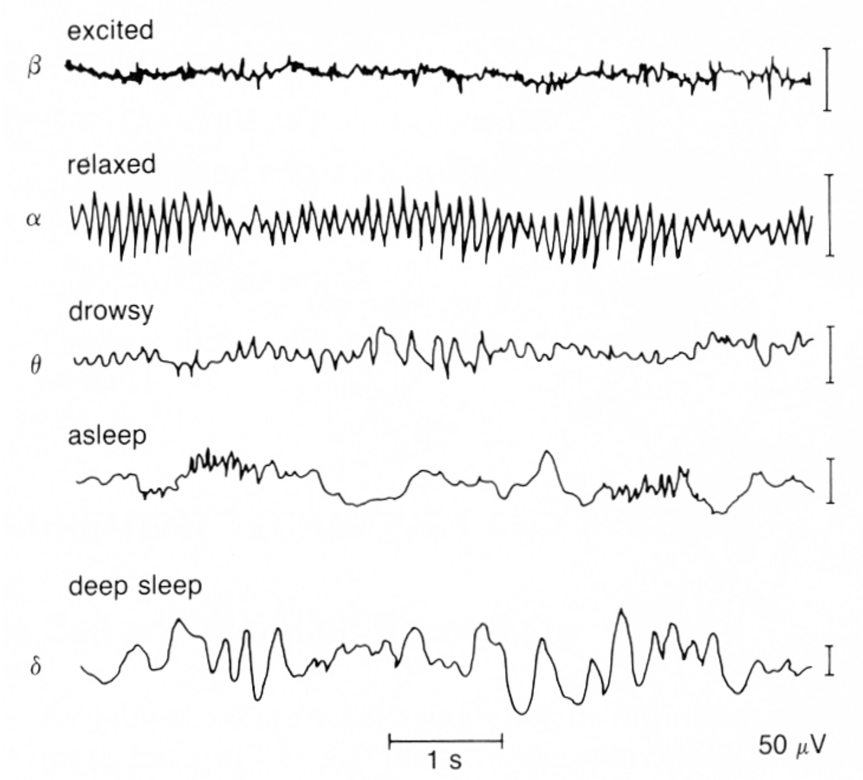


Figure 4.3: Samples of the basic rhythms observed through EEG. (Reproduced from Bronzino,1986).

4.4 The 10-20 system

The most standard location map for EEG electrodes is the internationally *10-20 system*. In this system, electrodes are located on the surface of the scalp, as shown in Figure 4.4.A. The locations for the original 21 electrodes are determined as follows (Malmivuo & Plonsey, 1995): the reference points are the *nasion* (the depression at the top of the nose, between the eyes) and the *inion* (the bony protuberance at the base of the skull, on the midline at the back of the head). From these points, the skull perimeters are measured in the transverse and median planes. Electrode locations are determined by dividing these regions into 10% and 20% intervals. Three other electrodes are placed on each side equidistant from the neighboring points, as shown in Figure 4.4.B.

In addition to the 21 electrodes, intermediate 10% electrode locations can be used for extra electrodes. The locations and nomenclature of these electrodes are standardized by the American Electroencephalographic Society (AES) (Sharbrough et al., 1991; see Figure 4.4.C). In the recommendations by the AES, four electrodes have different names from the 10-20 system. These are T7, T8, P7, and P8. These are shown in dark color in Figure 4.4.C (see Gilmore, 1994, for full guidelines for EEG electrode locations).

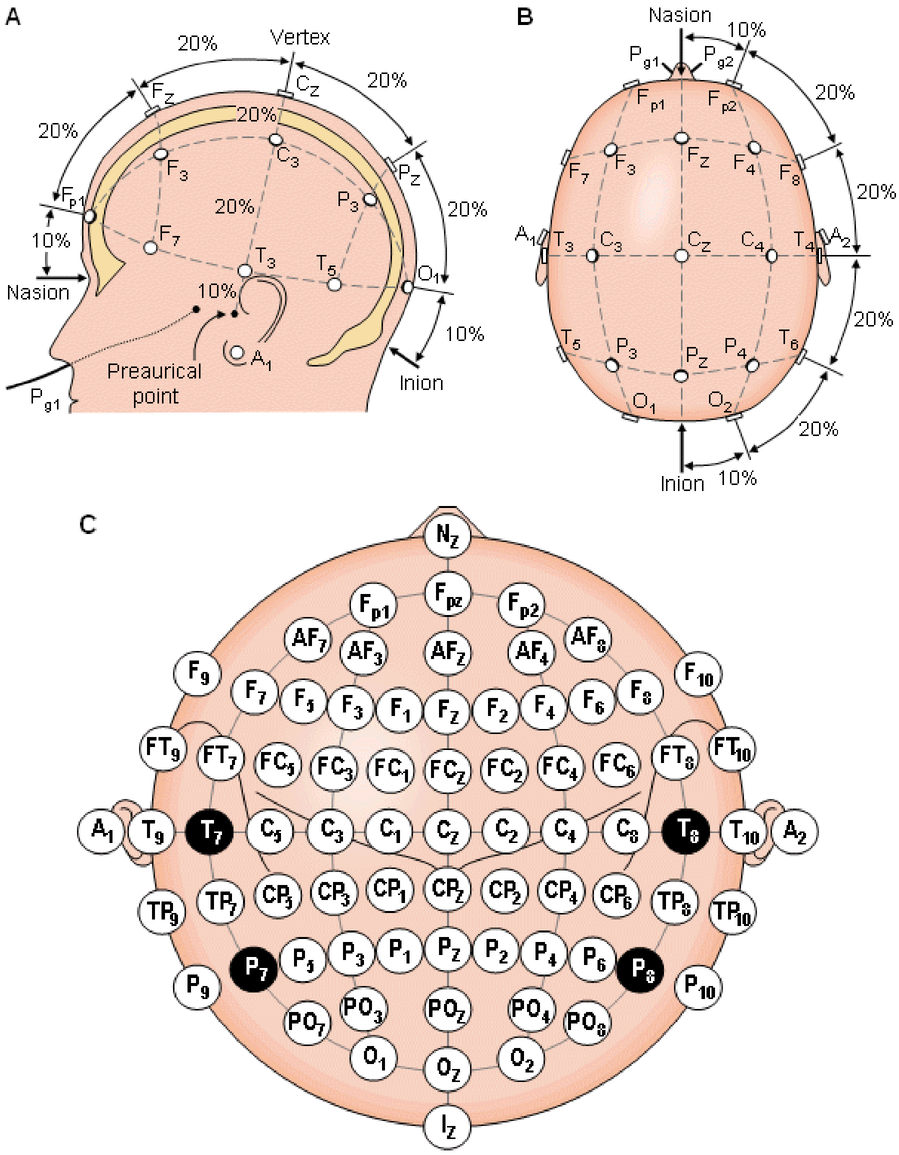


Figure 4.4: The international 10-20 system seen from (A) the left and (B) above. A = Ear lobe, C = central, Pg = nasopharyngeal, P = parietal, F = frontal, Fp = frontal polar, O = occipital.
(C) Location and names of additional 10% electrodes, as standardized by the AES. (Reproduced from Malmivuo & Plonsey, 1995).

4.5 Hardware

Electrodes

Bipolar or unipolar electrodes can be used in the EEG measurement. In the first method the potential difference between a pair of electrodes is measured. In the latter method the potential of each electrode is compared either to a neutral electrode (placed, e.g., somewhere on the body) or to the average of all electrodes. Most electrodes used today are made of Ag/AgCl. Other electrodes materials have been used in the past, but the Ag/AgCl configuration has been found to work well. Figure 4.5 below shows how well several electrodes detect a known signal in a controlled solution.

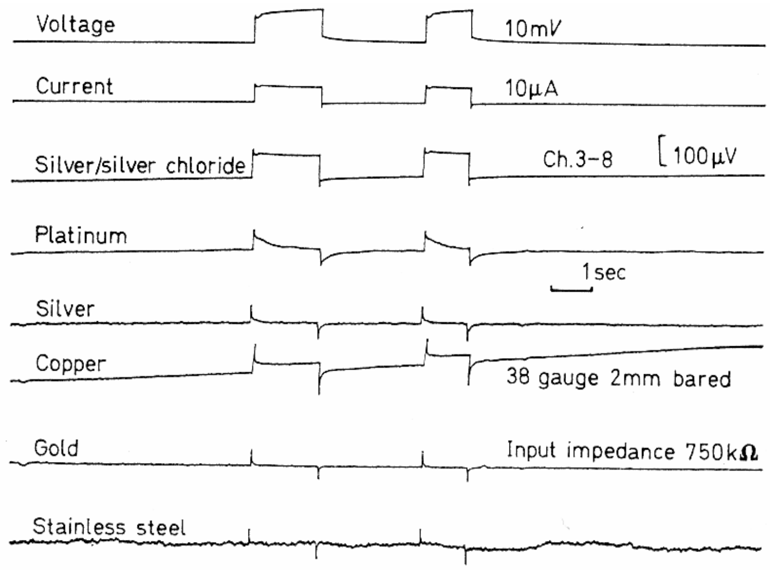


Figure 4.5: Comparison of recordings using various electrode materials. The top trace is the source signal. (Reproduced from Cooper et al., 1969).

Figure 4.6 shows the equivalent circuit representation for an electrode/skin interface. C and R_F are the capacitance and resistance values of the electrode itself, while Co is a small capacitance for so called strays and can usually be ignored. An important element in the circuit is the gel resistance R_S. This value often determines how low an impedance will be obtained between the skin and the amplifier. The lower this value (e.g., the more conductive the gel and the better the coupling between skin/gel/electrode) the better the signal to noise ratio in the recordings.

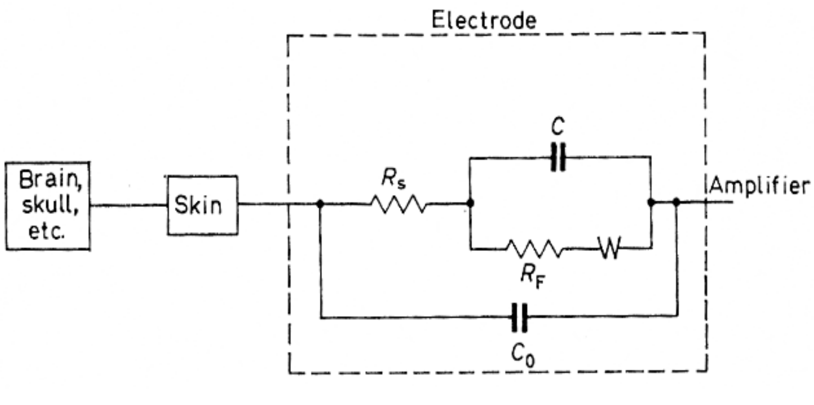


Figure 4.6: Equivalent circuit for a skin electrode. (Reproduced from Cooper et al. 1969).

Electrode Impedances and BMIs

Since the current entering the amplifier is in the order of less than 1 nanoAmpere (usually 0.01 nA), even weak artifacts can produce that is obscures the relevant signal or can even display many characteristics such that the BMI device may wrongly recognize it as a relevant signal. Electrodes polarization also usually produces artifacts in the low frequency ranges and these can be reversible or irreversible. Electrodes that undergo irreversible polarization cannot be used for slow EEG signal recordings as they have an intrinsic time constant and behave as large capacitors.

Most studies attempt at obtaining electrode/skin impedances of 7kΩ or less, although recent studies have shown that impedance as high as 40 kΩ do not significantly affect the quality of EEG signals (Ferree et al., 2001). This is very important as attempts to get lower impedances require skin abrasion, often done by means of a blunt stainless-steel needle, which causes discomfort and may cause wounds and infection if not done properly. This has also been cited as one of the main deterrents against daily use of BMIs. To address this issue, active electrodes have been recently developed (e.g., MettingVanRijn et al., 1994) and are currently commercially available from Biosemi™, a company based in the Netherlands. Such electrodes perform amplification and DC rejection, at the electrode site (Figure 4.7), while still keeping the additional amplification stages found with other electrode types.

Figure 4.7: Active electrode from Biosemi™ (left), and Ag/AgCl electrode from Nihon Khoden (right). (Source: WWW).

4.6 Signal acquisition and filtering

Once the electrodes are in place, the signals are amplified and prefiltered by analog instrumentation. The amplification factor is usually in the order of 10^6 and the filter consists of a low order low-pass with cutoff usually at 90Hz or nearby. Some instruments also include a high-pass filter near 0.1Hz and a notch filter at 50Hz (60Hz in some countries), but this is not the most common case.

Once the signal is amplified and possibly filtered by the analog instrumentation, it is converted to digital format, usually by means of a 12bit or 16bit A/D converter. The A/D conversion with 12bit resolution is suitable for EEG recordings. The typical frequency content of the amplified, filtered, and converted signal can be seen in the example in Figure 4.8, in which we see a clear strong activity in the alpha band. As A/D conversion must be done at least at twice the rate of the highest frequency of interest (the Nyquist criterion), many studies do sampling at 256 samples/s, although most studies use a 128samples/s rate and look at frequencies below 50Hz only. Further, if the instrumentation does not include a low-pass filter, 'aliasing' can occur at the A/D stage. Aliasing refers to the appearance of high-frequency components as if they were low frequency. Thus, to reduce this effect, a low-pass, anti-aliasing filter muse be used before A/D conversion.

As most instrumentation does not do all the necessary filtering, it usually necessary to use digital filters to remove high frequency noise, low-frequency artifacts, and interference from the mains. The cutoff frequency for most high-pass filters is between 0.1 to 0.5Hz, while low-pass filters usually employ a cutoff at 45Hz or less in studies that ignore frequencies above this level (this automatically removes the mains noise as well). The main filter classes are finite impulse response (F.I.R.) and in finite impulsive response (I.I.R). A popular filter for most applications is the Butterworth type, which has no ripple in the pass-band, but it often requires high filter orders to properly attenuate unwanted frequencies.

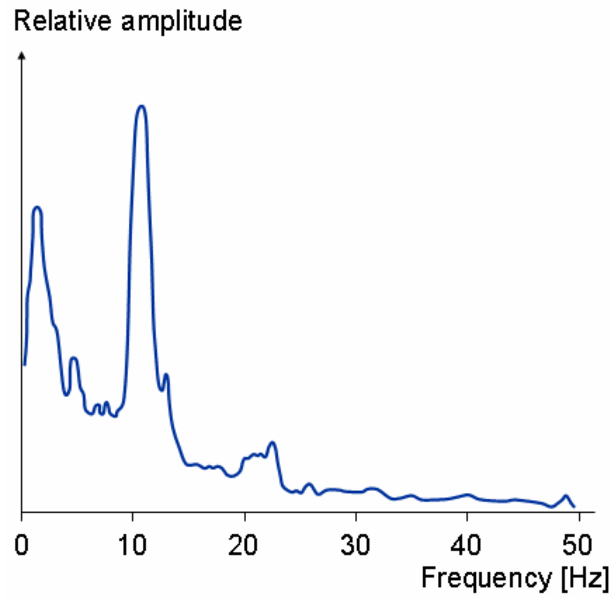


Figure 4.8: Typical frequency content of EEG recordings. (Reproduced from Malmivuo & Plonsey, 1995).

4.7 Artifact removal and referencing

There two main sources of artifacts on EEG signals that override the EEG signal itself: EMG and electro-oculogram (EOG). EMG is the electrical activity of muscles and its surface amplitude is about one thousand times stronger than EEG signals. At the location of the EEG electrodes, EMG from near (e.g., face and neck) and even not so near (upper limbs) muscles can significantly distort the recorded EEG. Unfortunately, surface EMG has significant components that cover all of the EEG range and reach up to about 500Hz. Filtering of the higher frequency components can and should be done, but little can be done to remove the effects of EMG in the EEG frequency bands, i.e., without removing significant parts of the EEG itself. The best that can be done in BMIs is to ensure that muscle activity near the head is minimized and/or that the translation algorithm be robust (i.e., be able to do proper classification of the signals in spite of the presence of EMG).

A common approach to minimize artifacts in EEG signals is to subtract a reference channel from a neutral channel near or on the head. The most common reference is the ear lobes, or the average of the recorded potential for both left and right lobes. The reasoning is that as the ear (or other suitable reference) is passive, any recorded activity is bound to be mostly noise and artifacts that are likely affecting the nearby EEG electrodes as well. Thus, subtraction of the reference signal from that of the EEG channels should lead to cleaner EEG signals. Other relatively common references are the mastoid (provided the subject does not contract jaw muscles) and the average of all EEG channels. Finally, a similar approach to reduce artifacts as well as to enhance the difference between adjacent signals is to subtract the signals pertaining to one electrode from those for the surrounding ones. This technique, only in its simplest form here, is the so called Laplacian algorithm, a spatial filter (Srinivasan et al., 1996).

EOG refers to artifacts related to eye movements and blinking. Figure 4.9 below shows the effects of EOG on the EEG signal and a comparison of artifact removal by independent component analysis (ICA) and principal component analysis (PCA). EOG can significantly affect EEG signals, especially if time domain features and characteristic waves (e.g., the P300) are to be used by the translation algorithm.

Adaptive filtering (He et al., 2005), EOG vector residual minimization (Jervis et al., 1999), PCA (Lagerlund et al., 1997), ICA (Jung et al., 2000), ARMAX modeling (Haas et al., 2003), wavelets (Bertrand et al, 1994), Gaussian smoothing (Berryman et al., 2004), Singular Value Decomposition (SVD) (Sadasivan & Dutt, 1996), among other methods.

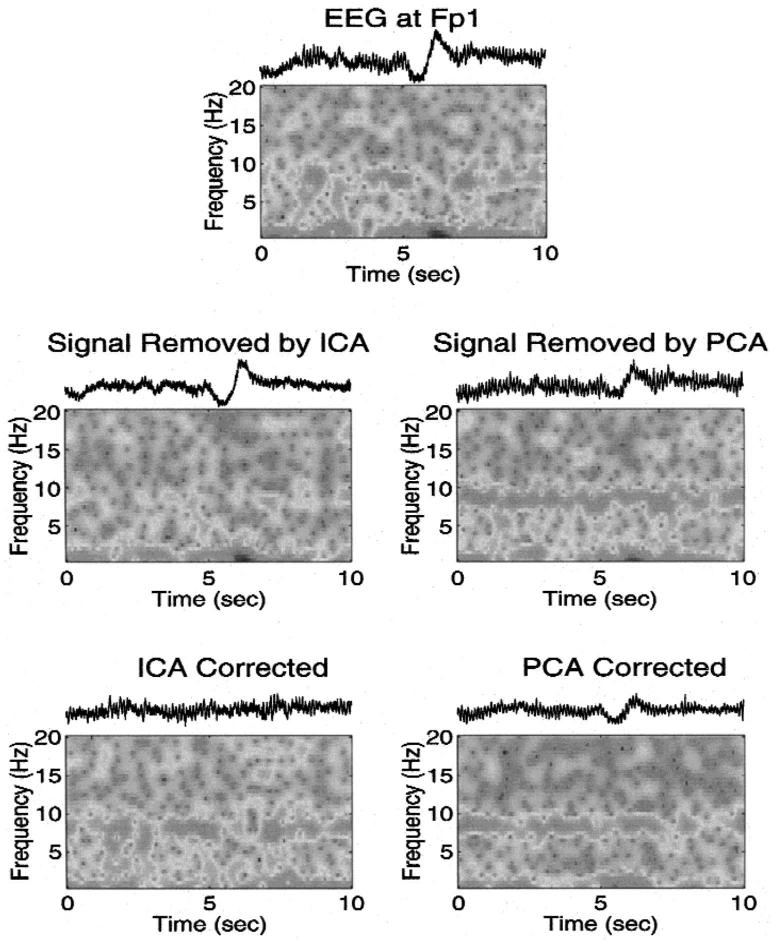


Figure 4.9: Comparison of eye movement artifact removal by ICA and PCA. Top panel: time domain and spectrograms of the EEG signals at site Fp1. Middle panels: The signals removed using ICA and PCA. Lower panels: The corrected EEG records produced by both methods. The ICA method has worked better in this case. (Reproduced from Jung et al., 2000).

Aside from EMG and EOG, other EEG artifacts are not as frequent or easy to identify, but they may be present as well. They are transient activities, high amplitude spikes caused by: (Talsma & Woldroff, 2004):

- Movement: head and body movements (e.g., breathing), wire movements.
- ECG: this can be picked up between electrodes that are far apart from each other. Small artifacts usually result from the R-wave ECG component, but the entire ECG may appear as well.
- Pulse-wave: Smooth periodic waves or triangular ones may appear near a scalp artery as a result of circulatory pulses.

4.8 Data analysis vs. specific applications

Once the data are cleaned from noise and artifacts, they can be used by the BMI in various ways. Some recent approaches (e.g,, Sepulveda et al., 2004) favour the use of an unbiased search for features that may relate to a particular class of mental task. This can be done when one wishes to maximize the class separation in the data regardless of whether or not the features and/or electrode locations have any preconceived characteristics. Features can be in the time domain (e.g., amplitude, total energy, specific shapes such as the P300 wave, low order statistics, etc.), frequency domain (energy distribution over different frequencies), or in the joint time-time domain (dynamic behaviour of the energy in various bands).

Aside from the above unbiased statistical approach, a number of other methods have been developed through the years. The discussion below is meant as a sample of some of the methods and is not intended to cover all or even most of the literature.

4.8.1 Correlation and coherence analysis

One of the important properties of EEG (as in most electrophysiological signals) is their stochastic nature. This, as the name implies, means that most important phenomena can be studied in statistical terms only, with instantaneous, single point observations having little use. As such, the analysis of EEG signals, be it in the time domain or otherwise, inevitably requires the use of statistics at various levels and using many approaches, some of which are listed below.

Correlation coefficient

Correlation analysis is a method to quantify the degree of linear fit between two or more variables. E.g., it could be used to evaluate whether individual height and weight are related to each other or whether alpha rhythm amplitude and reaction time are linearly linked as well. For EEG, one possibility is to identify signal patterns present in two signals (Shaw, 1972). If the two patterns are expected simultaneously in the two signals, the simple product point-by-point divided by the time duration (the time point number, covariance) will quantify the similarity between the two signals in the considered time interval. The correlation coefficient has the following behaviour:

- its value is +1 if the two signals have identical shapes in time and are in phase with each other;
- its value is -1 if the two signals have identical shapes in time, but are 180 degrees out of phase with each other;
- its value is always between –1 and +1.

One of the characteristics of this coefficient is that it yields high values if the two signals are very similar in shape, regardless of whether the respective amplitudes are near each other. This can be a problem as it may assign a high value to an unwanted signal. For example, if an algorithm is looking for instances when a P300 wave appears in the signal, using the correlation coefficient to find signal segments that are similar to the expected P300 shape may lead to some of the low amplitude noise yielding a false hit due to its shape.

Correlation coefficients must thus be used with caution in EEG analysis depending on what is being searched.

Auto and Cross-Correlation function

Very often, similar signal patterns occur at different time intervals in two different signals. For this reason a function of time is obtained which quantifies the correlation coefficient while translating one signal with respect to the other by the time quantity t. This resulting set of coefficients as a function of the lag t is the correlation function. In the case of EEG, the periodicity of the correlation function is not perfect (Siebert 1959, Walter 1963, Anstey 1964, Remond 1977), and the correlation function will be different from zero only in short intervals. If no similarities are present between the two signals, the values in the function will be near zero.

The autocorrelation function values (i.e., a signal compared to itself) is always 1 at $t = 0$ and is symmetric around $t=0$ for negative and positive values of t. The correlation function (both auto and cross) can be obtained though the Fourier transform as well.

Coherence analysis

A very useful description of co-occurring phenomena can be done in the frequency domain by identifying the frequencies that are present in both signals. For this purpose, the cross-spectrum is defined as the Fourier transform of the covariance function. Once again, to obtain a function independent on the signal amplitude, the cross-spectrum is "normalized" by the square root of the each signal auto-spectra; this is called coherence function. Its meaning could be described by taking two signals of wide range noise, applying the same band–pass filter and obtaining the identical signals whose coherence values is 1 in the frequency range within the band-pass filter interval, and 0 outside. By adding a different noise to one of the two signals and applying the same band-pass filters, the coherence will be less than 1.

Fourier transform analysis allows calculation of the cross-correlation function and the coherence directly from each other (Shaw & Ongley 1972, Orr & Naitoh 1976). The coherence values are calculated for each frequency bin by the following equation:

$$Coh_{xy}(\lambda) = \left|R_{xy}(\lambda)\right|^2 = \frac{\left|f_{xy}(\lambda)\right|^2}{f_{xx}(\lambda)\, f_{yy}(\lambda)}$$

which is the extension of the Pearson's correlation coefficient to complex number pairs. In this equation, f denotes the spectral estimate of two EEG signals x and y for a given frequency bin (λ). The numerator contains the cross-spectrum for x and y (fxy), while the denominator contains the respective autospectra for x (fxx) and y (fyy). For each frequency bin λ, the coherence value (Cohxy) is obtained by squaring the magnitude of the complex correlation coefficient R. For this reason, all the approximation limitations present in the Fourier analysis are present in coherence analysis as well.

As applied to the EEG signals, this measure has been used to demonstrate that the coherence between two EEG derivation signals expresses anatomical structural connections or functional coupling between two cerebral regions. E.g. Galbraith (1967) demonstrated that the evoked activity amplitude depends on the coherence of the background activity. Other examples of coherence analysis in the EEG measures are the neurophysiological investigations of epileptic seizures (Brazier, 1972; Petsche and Rappelsberger, 1973; Rappelsberger, 1978), of thalamo-cortical connections (Lopes da Silva et al., 1973 a, b), of inter-hemispheric functions (Shaw, O'Connor and Ongley, 1980; Beaumount, Mayes and Rugg, 1978). Lopes da Silva & Storm van Leuuwen (1978) demonstrated by coherence measures that topographical characteristics of mu-rhythm are different from those of alpha-rhythm.

4.9 Application specific EEG signals

4.9.1 Visual evoked potentials (VEP)

VEPs are waves elicited by a visual stimulus and are time locked to it. VEPs have bee used since the 70's in dependent BMIs. VEP signals recorded from electrodes placed over the primary visual area allow the system to recognize the user's gaze direction. In Steady State Visual Evoked Potentials (SSVEPs), a set of elements flash at different frequencies on a PC screen. In the EEG signal recorded from occipital electrodes, the harmonics at the frequency of the element the user is fixating and its multiples increase in amplitude. However VEP amplitude is also modulated by subject's attention and not only by gaze direction. Recently this characteristic has been used to realize an independent SSVEP.

In the 70's, Jacques Vidal, at UCLA, coined the term Brain-Computer Interface developed an apparatus which still satisfies the definition of dependent BMI (Vidal, 1973, 1977): this device utilized VEPs recorded from the scalp on the occiput (back of the head) and periocular (around the eyes) electrodes to determine sight direction. By defining the subject's visual focus, the device interpreted his/her will on the cursor's direction. Later Sutter (1992) developed a new system in which the subject sat in front of a monitor displaying 64 symbols (i.e., letters) in a 8 x 8 grid; groups of 8 out of these 64 symbols formed a bar grid which flashed in alternating colours (i.e., green and red). Each symbol was presented in different groups of bars and each set of groups was presented several times. After about 100 msec of each bar grid presentation, the amplitude of the VEP was evaluated and matched with the VEP's amplitudes from preceding and following groups until the system was able to select the symbol chosen by the subject via a simple act: visual fixation. If the symbols matrix was replaced by a 'virtual' keyboard, the subject could utilize a software for video-writing and could produce 10-12 words/minute.

Another method based on VEP recordings employed flashing elements on a monitor with different flashing frequencies. When such frequencies are above 4 Hz the visual system is no longer producing the typical, triphasic transient VEP, but instead produces a sinusoid containing the main frequency (fundamental) and its harmonics. This type of response is called 'photic driving' or steady-state VEP (SSVEP). This response can be identified by the BMI whenever it matches the flashing frequency of one of the elements.

SSVEP have been used for different BMIs. Middendorf et al. (2000) have trained subjects to self-regulate their SSVEP amplitude to control -online- the roll position of a flight simulator or the switch of a functional neuromuscular electrical stimulator (FES). After a half-hour of training, subjects could control both devices with more than 90% success rate. Naturally occurring SSVEPs were also studied in the group. Subjects were instructed to select a button on a screen, whose luminance was modulated at different frequencies, simply looking at it. Here again, a classification rate of 92% was achieved with a selection time of 1.24-3.02s.

Researchers at the STMicroelectronics, Agrate-Brianza, Italy, are also developing a BMI based on SSVEP (Andreoni et al., 2004). They used a simple unidimensionnal direction selection protocol and obtained classification rates of 95.7% and a speed rate of 5.3 instruction / seconds. At Aalborg University, Denmark, Cabrera and Nielsen (2004) developed a word processor based on SSVEP tested online with healthy subjects. They were instructed to focus their attention on one of the nine squares flickering at different frequencies (5-21.25 Hz) to select a number related to the square. An FFT-based power spectrum analysis applied on two EEG channels (O1, O2) was used to classify frequencies in the SSVEP and a classification rate of 92.8% was achieved using 5 seconds of EEG signal. Reasonable classification rates were thus reached to the detriment of bit rate.

Finally, SSVEPs have also been used for game control. The Media Lab Europe group in Dublin recently developed a video game called "MindBalance" (Lalor et al., 2004). In this game, the player controls the balance of a tightrope walker by focusing his/her visual attention on the desired flickering checkerboards placed on both sides of the acrobat (Figure 4.10). After a training session intended to identify the best classifier algorithm, subjects tried to avoid the character's balance loss at it walked on the tightrope. Real time performance reached 89.5% correct performance in the best cases. The authors are now working on SSVEP modulation based on focusing attention without eye movements.

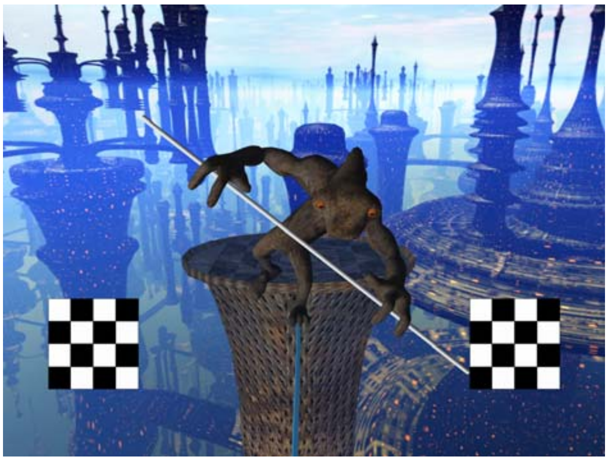


Figure 4.10 -The "MindBalance" Game developped at the Media Lab Europe group in Dublin. (Source: WWW).

VEP-dependent BMIs are entirely dependent on subject's ability to control sight direction in a way identical to BMI devices which directly measure sight direction as a relevant signal. However, VEP amplitude is also influenced by subject's attention and not only sight direction (Teder-Salejarvi et al., 1999; Chen et al., 2002).

4.9.2 Slow cortical potentials (SCP)

SCPs are generalized variations of the depolarization level of superficial cortex dendrites. The subject can learn to control the direction of this variations (positive or negative) and determine detectable changes in the EEG. The classifier is able to recognize the intended direction. Slow Cortical Potentials (SCP) have a time-constant ranging between 0.5 and 10 seconds; those of negative polarity are typically associated with movement and other function related with an increased amount of cortical activity, whilst those of positive polarity are mainly related to reductions of cortical activity. (Rockstroh et al., 1989; Birbaumer, 1997). They are employed in a BMI named "Though Translator Device "(TTD) which has been particularly employed in A.L.S. subjects (Kubler, 2000).

Recording electrodes are usually on the scalp vertex and referred to linked mastoids; after appropriate filtering and artifact removal, SCP can be extracted and the subjects gets feed-back as represented by the cursor's movement and direction. Each selection requires about 4 sec: 2 baseline seconds during which the device measures the level of the 'rest' voltage, while in the following 2 sec the subject is making his/her selection and the initial voltage wither increases or decreases (Negative or positive polarity SCP) therefore provoking cursor's movement. As previously said, there are individual cognitive/behavioural strategies -including for children- to reach the optimal level of control (Lacroix., 1981; Lacroix and Gowen AH., 1981; Siniatchkin et al., 2000). Therefore, if on one side, the negative influence of unwanted thoughts has been demonstrated, on the other it emerges that a certain amount of operational automatization and of 'dedicated' mental activities can take place also in TTD BMIs. For instance when the subject was creating 'tension' in his mind during the baseline by thinking to a bow prepared to throw an arrow he was producing a SCP of negative polarity which was favouring the production of a positive polarity SCP in the following active phase. The system can be modified also in a way to provide an acoustic or tactile feed-back (Birbaumer et al., 2000). Subjects must be trained for a period which can also be of several months and -when a level of control of about 75% is reached- it can interact with the Language Support Program (LSP, Figure 4.11) (Perelmouter et al., 1999; Perelmouter and Birbaumer, 2000) which allows the choice of one or a combination of letters with a system of two-choice selection which allows an accuracy of 65 to 90%, with 0.15-3.0 letters /min. and 2 to 36 words/hour.

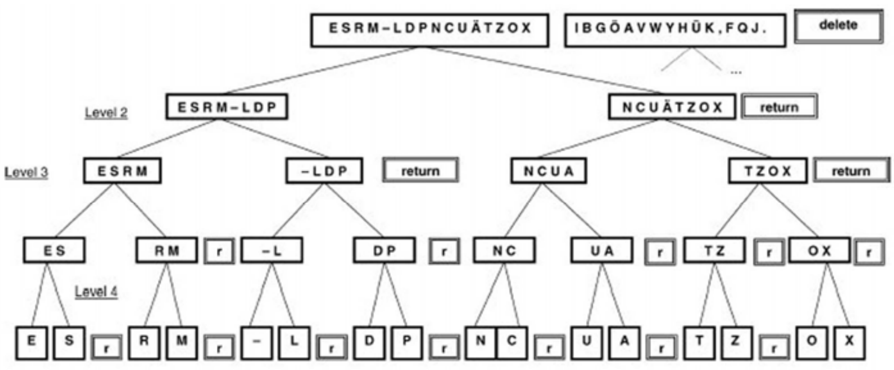


Figure 4.11: LSP. Letters are classified according to their frequency of utilization in the deutsch alphabet. Each group contains all the letters and punctuation needed for communication. At the beginning the 32 symbols are divided in two groups of 16. Selections begins when the cursor's movement exceeds a given threshold (= 7.7 microV) while the signal is discarded as an artifact whenever another amplitude threshold is exceeded. After every selection the chosen group is divided in two groups once again until reaching an individual letter. The levels to overcome for every choice are 32. (Reproduced from Neumann, 2001).

Despite the slow speed of communication, the LSP has demonstrated great utility for Subjects who cannot utile the common technologies of support.

Moreover, a predictive algorithm able to utilize the first two letters of a word in order to identify it within a personalized vocabulary (similarly to what is done by cellular phones) can increase the speed and efficacy of the apparatus which can even be implemented at a level to allow the access to internet (Birbaumer et al., 2000). By implementing the device with a stand-by condition it will be possible to maintain it on the subject in a permanent way the recording electrodes (i.e., glued with collodion) so that they can have access to the device along the 24 hours just by producing a specific sequence of SCP in order to switch the system on or off.

However, the main drawback of SCP BMIs is that some Subjects (about 30%) cannot take advantage of the neurofeedback training and are unable to gain sufficient control over their SCP amplitude changes, even after extended training. In order to solve this problem, Transcranial Magnetic Stimulation (TMS) and transcranial Direct Current Stimulation (tDCS) effect on SCP self-regulation have recently been studied in the Birbaumer's group (Karim et al, 2003, Karim et al, 2004). It is known that high-frequency TMS and anodal tDCS increase corticospinal excitability whereas low-frequency TMS and cathodal tDCS result in suppression of corticospinal excitability (Pascual-Leone et al., 1994; Cohenet al., 1998; Siebner et al., 2003; Baudewiget al., 2001). The authors have hypothesized that the two former stimulations would enhance negative SCP shift whereas the two latter would enhance positive SCP. TMS and DCS were delivered centro-frontally over the SMA while subjects tried to control their SCP to move a cursor to the top or bottom of a screen. The authors found that high frequency TMS and anodal tDCS enhanced negative SCP variation but also decreased positive SCP whereas low frequency TMS and cathodal tDCS enhanced positive SCP and reduced negative SCP, then verifying their hypothesis. New studies are now conducted to check if this effect of TMS and tDCS could be used to facilitate the learning processes of self regulating SCP shifts.

4.9.3 P300 wave

This approach uses the P300 wave elicited by a stimulus relevant to the user (Figure 4.12). The original paradigm consists of a 6 by 6 matrix of characters shown on a PC screen. Row and columns of this matrix are highlighted rapidly in a random sequence. The subject is instructed to count every time the intended letter turns on. Thus every flash is a stimulus able to produce an exogenous response but just the ones of the row and column the chosen letter belongs to, also produce an endogenous response. Identifying the endogenous response, for example the P300 wave, allows to determine the chosen character.

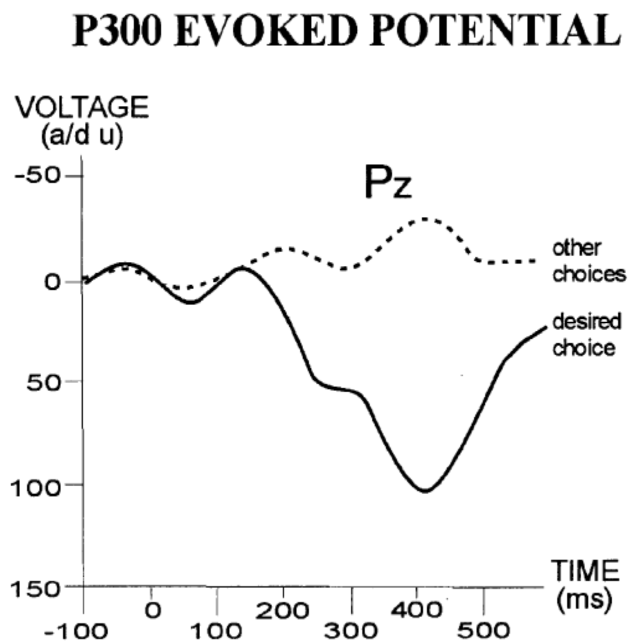


Figure 4.12: P300 wave: solid line is observed when an object catches the subject's attention. The dotted line is a typical signalin response to objects that are of no interest. The P300 wave begins about 300ms after the desired object is flashed. (Reproduced from Wolpaw et al.,, 2002).

Acoustic, visual or somatosensory infrequent and task-specific stimuli, when randomly and sporadically intermingled in a sequence of frequent stimuli are evoking on wide fronto-parietal areas a wave of positive polarity which lasts for hundred of milliseconds and have a modal peak latency of about 300 msec.. This only if the subject is able to identify the start-stimulus and is called the P300 wave (Walter et al., 1964; Sutton et al., 1965; Donchin and Smith, 1970; Farwell and Donchin, 1988; Donchin et al., 2000).

Classically, the subject sits in front of a video screen (Figure 4.13) showing a matrix of 6 x 6 letters, numbers &/or other symbols or commands. Every 125 msec a single column or strip is flashing so that in a cycle of 12 flashings each column or strip is presented twice (Wolpaw et al., 2002). The subject has to count how many times the strip or the column containing the selected letter have flashed (this guarantees the attention toward the events in the screen. The BMI must identify the P300 via different types of algorithms including the discriminant analysis stepwise, discrete wavelets transform. With healthy subjects, Farwell and Dochin reached a bit rate of 2.3 characters per min. (Farwell & Donchin, 1988). More recently, using a boot-strapping approach, Donchin et al. (2000), have reported for healthy subjects a bit rate of 7.8 characters per min. during an offline analysis with 80% of accuracy level. This bit rate dropped to 4.3 with a 95% accuracy level. No bite rate was reported for online analysis but the percentage of selected cell correctly identified was just above the chance level.

CRT Display Used in the Mental Prosthesis

MESSAGE

BRAIN

Choose one letter or command

A	G	M	S	Y	*
B	H	N	T	Z	*
C	I	O	U	*	TALK
D	J	P	V	FLN	SPAC
E	K	Q	W	*	BKSP
F	L	R	X	SPL	QUIT

Figure 4.13: Matrix of letters and symbols for a P300-based BMI. Columns and strips of the matrix are flashing in an alternate mode. The letters selected by the subjects (B-R-A-I-N) are shown on the top of the screen. (Reproduced from Farwell & Donchin, 1988).

Currently available BMIs allow a speed of about 5 words /min production, but remarkable ameliorations are possible. P300-based BMIs do not require any training stage and –therefore- are very advantageous in the early stages, but it is still unknown whether during time the P300 production is undergoing any significant change (Glover et al., 1986; Miltner et al., 1988; Sommer and Schweinberger, 1992; Roder et al., 1996; Ravden and Polich, 1999). Therefore, also in this type of BMIs it might be useful to have a third level of implementation.

Cinel et al. (2004) at the University of Essex, UK, have recently provided some experimental evidences that P300 protocols such as those proposed by the group of Donchin (P300-speller paradigm, (Farwell et al., 1988) can contain possible source of perceptual errors. These errors are typical of rapid serial visual presentation paradigms - i.e. attention related blink, repetition blindness or illusory conjunction – or attentionnal cueing tasks – i.e. automatic attentionnal shifts. The consequence of this attentionnal limits is to decrease classification rates. The same authors have proposed a new approach of feature selection and classification to improve detection of P300 signals (Citi et al., 2004). Using a *wrapper approach* which optimizes feature selection and classification together, they have suggested the importance of computing the signal difference from electrode C4 and T6 for cancelling non-P300 components et consequently increase the rate of P300 detection. It has also been suggested that letter matrix size could be an important parameter to control in order to increase the classification rate. Allison and Pineda (2003) have recently tested the performance of a P300-based BMI with different size of matrix and showed that P300 evoked component amplitude was larger with large matrix (12 x 12). It could be explained by the fact that attending to a letter in large row or column is more demanding than in a small 6 x 6 matrix.

The effect of subjects on the P300 based BMI has also been investigated. In Tübingen, Germany, the Birbaumer's group has recently tested a P300 BMI on ALS subjects (Mellinger et al., 2004). The protocol is about the same than the one described above. Bear in mind that contrary to the SCP BMIs, no training is needed for P300 BMIs, what is its main interest. However, as it can be seen in Figure 4.14, the bit rate is relatively low in most subjects who spend 10 minutes to select one letter (subject JSB). Note however that subject IBD reached a 4 letter per min. bit rate. This study shows that interface control by disable subject can be extremely problematic but it does not provide a comparison with healthy subjects. Another P300 based BMI has been tested with healthy and disabled subjects by Beverina et al. (2003, 2004) at the STMicroelectronics Lab in Agrate-Brianza, Italy. They submit the subjects to a random sequence of visual stimuli using a complex odd-ball paradigm. The subject's task was to reach a goal with the movement of a target. Left, right, up and down arrows were flashing successively and the subject focused his/ her attention on the desired direction. A learning phase was proposed for the BMI to adapt to the P300 waves of the subject. After about one day of training, healthy subjects reached a classification rate of 76.2 % with a bit rate of 7.59 bits per min., whereas subjects reached a classification rate of 68.6 with a bit rate of 7.77 bits per min.. In this experiment, results seem to be rather identical between the two groups of subjects even if subjects have a smaller classification rate. These experiments highlight the importance of testing BMIs not only on healthy subjects but also on subjects. The latter are the one for whom this technology is intended for and they clearly not have the same attentionnal and motivational capacities than healthy subjects. Moreover, as claimed by Mellinger et al., (2004), "*in severely or totally paralysed subjects, brain area(s) essential for producing and regulating a brain response used for BMI may be damaged*".

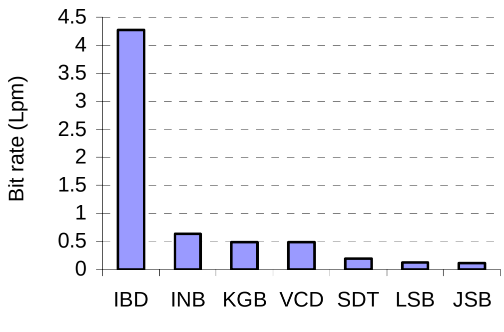


Figure 4.14: Bit rate estimates for all subjects. (Reproduced from Mellinger et al., 2004).

As mentioned in Chapter 3 above, another key point in BMIs is feedback. At Rochester Institute of Technology, the Alternative Interface Lab is studying the effect of a rich visual environment (Virtual reality) on the performance of a P300 based BMI. In a first experiment, Bayliss and Ballard (2000) used a driving environment (Figure 4.15) to check the occurrence of P300 responses in a rich virtual environment.

Figure 4.15 : The Rochester BMI. The subject is immersed in a driving environment controlling the car. (Reproduced from Bayliss & Ballard, 2000).

Subjects controlled their car using a wheel and pedals and were instructed to stop at red stop lights which occurred rarely compared to green or yellow lights. EEG signal was recorded over 8 electrodes and used correlations, independent component analysis (ICA), and a robust kalman filter to classify the P300 evoked potentials. As expected, yellow lights were classified as non-P300 and red light as P300 with respectively a 90 and 71% classification rate using the Kalman filter. In a second experiment (Bayliss, 2003), different items in a virtual room were flashing successively. P300 evoked response was elicited for items selected by the subject and this item was switched on or off by this response. The same experiment was conducted on a computer screen and on a head mounted display but with fixed image for comparison. No difference was found between the VR condition and the monitor condition but performance dropped with the fixed display. It suggest that using a richer and natural environment do not decrease the classification of brain state and then can be used for more evolved interfaces.

4.9.4 Mu rhythm

This BMI approach is based on the capability of varying the μ-rhythm of EEG. This one has about 10 Hz frequency and less than 50μVpp amplitude. It can be distinguished from a-rhythm because tightly related to the functions of sensorimotor cortex; μ-rhythm disappears after a movement execution or a tactile sensation. The subject can learn to intentionally vary μ and ß rhythms of his/her EEG through biofeedback. This approach has been used in order to allow the user to move the cursor on a PC screen.

During wakefulness the sensorimotor areas of both the hemispheres show a subcontinuous, idling EEG rhythm in the 8-12 Hz range, probably generated in the thalamo-cortical reverberating circuits, which is promptly blocked by activity in sensory processing or in motor programming and execution (Gastaut, 1952; Kozelka and Pedley, 1990; Fisch, 1999; see a review by Niedermeyer, 1999; Lopes da Silva, 1991). They are named mu rhythms when are localized over the sensorimotor cortex. Within this class of idling rhythms we might insert also the beta activity in a frequency band between

18 and 26 Hz and are distinguishable from mu and other rhythms by analysing their topography and chronology (Pfurtscheller and Berghold, 1989; Pfurtscheller, 1999; McFarland et al., 2000a).

With the BMI from Wolpaw, McFarland and Collegues (Wolpaw et al., 1991, 2000b; McFarland et al., 1997a), developed at the Wadsworth center, Albany, USA, completely paralyzed individuals can learn to control the amplitude of their mu or beta EEG rhythms to control a cursor in a bidimensional space. Figure 4.16 shows the basic phenomenon. In this example the subject increases the amplitude of mu rhythm (typically in the 8-12 Hz) to move the cursor toward the target within the screen. The frequency spectrum (Figure 4.17.a) for the two targets (top and down in the screen) shows that the “checking role” is definitively played by the mu or beta rhythms. Samples of EEG (Figure 4.16) show that the mu rhythm is maximal or minimal in relation to the lower target. For every degree of freedom of the cursor there is a linear equation which translates the mu or beta rhythms in the relative cursor’s position. The signal is recorded from one or more scalp positions, while the cursor position is refreshed 10 times/sec (Figure 4.16 and Figure 4.17.d). About 80% of subjects learn to control their mu and beta rhythms with learning sessions lasting 40 minutes each at 2-3 session / week for 2-3 training weeks. At least in the initial stages the predominant strategy is ”movement imagination”; as time is passing by, the subjects abandon ”movement imagination” and move the cursor in a more automatic way as it happens in every learned motor act (i.e. walking, bicycling).

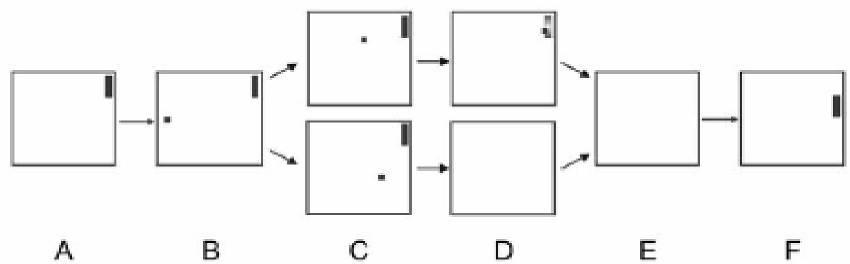


Figure 4.16 : Training method. The target is randomly positioned in one of the 4 possible positions and is moved at a constant left ➔ right speed, while the subject is controlling the vertical shift via the mu and beta rolandic rhythms amplitudes. In the two sequences C-D are shown two situations: in the 1st the subjects reaches the target, while in the 2nd is missing it. In every case the training session is starting again from F. (Reproduced from McFarland et al., 1997a).

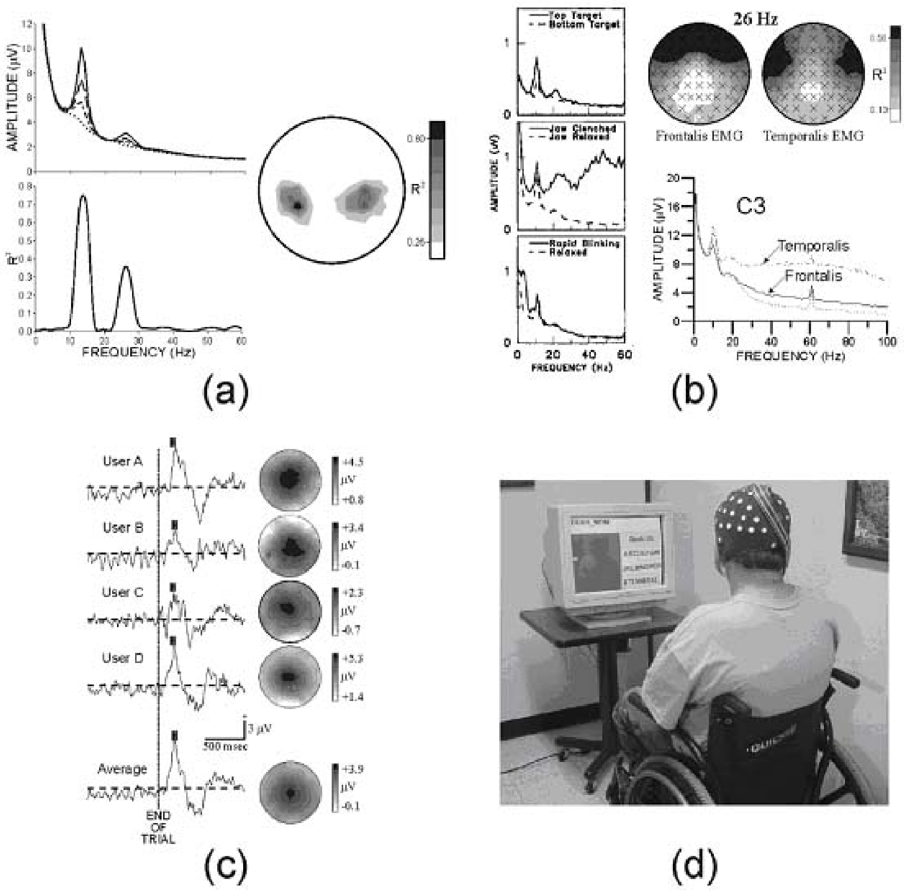


Figure 4.17: (a) Control of sensorimotor cortical EEG rhythms. The trained subject controls the cursor movement toward the targets in 4 possible vertical positions. The mu rhythm amplitude (12 Hz) from left rolandic cortex is controlling the cursor. Top left: FFT spectral analysis when the 1st target is selected (from the top, continue line), the 2nd target (long interrupted line), the 3rd target (short interrupted line), 4th target (dotted line). Bottom left: the corresponding r2 spectrum measures the amplitude variations secondary to target positioning. Right: scalp EEG topography (nose on the top) during mu rhythm control as expressed in r2). (b) Identification of non-EEG artifact. Left: FFT spectral analysis of EEG records from the sensorimotor cortex from a trained subject. Top: monitoring the 10 Hz mu rhythm for top (full graphics) or downs (interrupted) cursor's movement. In the central graphic subject is clenching the jaw (full graphic) or is relaxed (interrupted). In the last graphic the subject is blinking (full graphic) or not (interrupted). The EEG signal is easily distinguishable from artifacts. (c) Error potentials for BMI operation. (d) video writing program of the BMI2000 system. The cursor is moving from left to right with a constant speed while the subject is controlling the vertical movement. (Reproduced from McFarland et al., 1997a).

The on-line cursor control has been reached by one or two scalp sites, but recordings from 64 scalp sites have been utilized for off-line analysis (i.e., Cheng et al., 2003 and Figure 4.18). Therefore, r2 is the measure of how much the relevant signal depends from the presented target (Wolpaw et al., 1991). The analysis of r2 topography (Figure 4.18) demonstrates that the relevant signal is focused within the sensorimotor cortex and in the mu and beta frequency bands. With such a control system the cursor can be moved - in order to answer ‘yes’ or ‘no’ to questions- with more than 95% accuracy (Miner et al., 1998; Wolpaw et al., 1998). It has been demonstrated that if the subject reaches the ability to control in an independent manner the relevant signal from two different channels each producing mu and beta rhythms, the cursor movement control can be extended in two dimensions (Wolpaw and McFarland, 1994). The vertical cursor’s movement has been obtained by the summation of the weighted amplitudes of the 24 Hz beta rhythm, while the horizontal shift can be gathered by the difference between the amplitudes of the mu rhythm at 12 hz. Different components and methods for the analysis of the relevant signal have been investigated: topography and spatial filters, autoregressive frequency analysis which has a better resolution for brief EEG segments and reaches a more rapid device control, better selection of the constants in the equations transducing the EEG control to BMI device control (Figure 4.18; McFarland et al., 1997a,b; Ramoser et al., 1997).

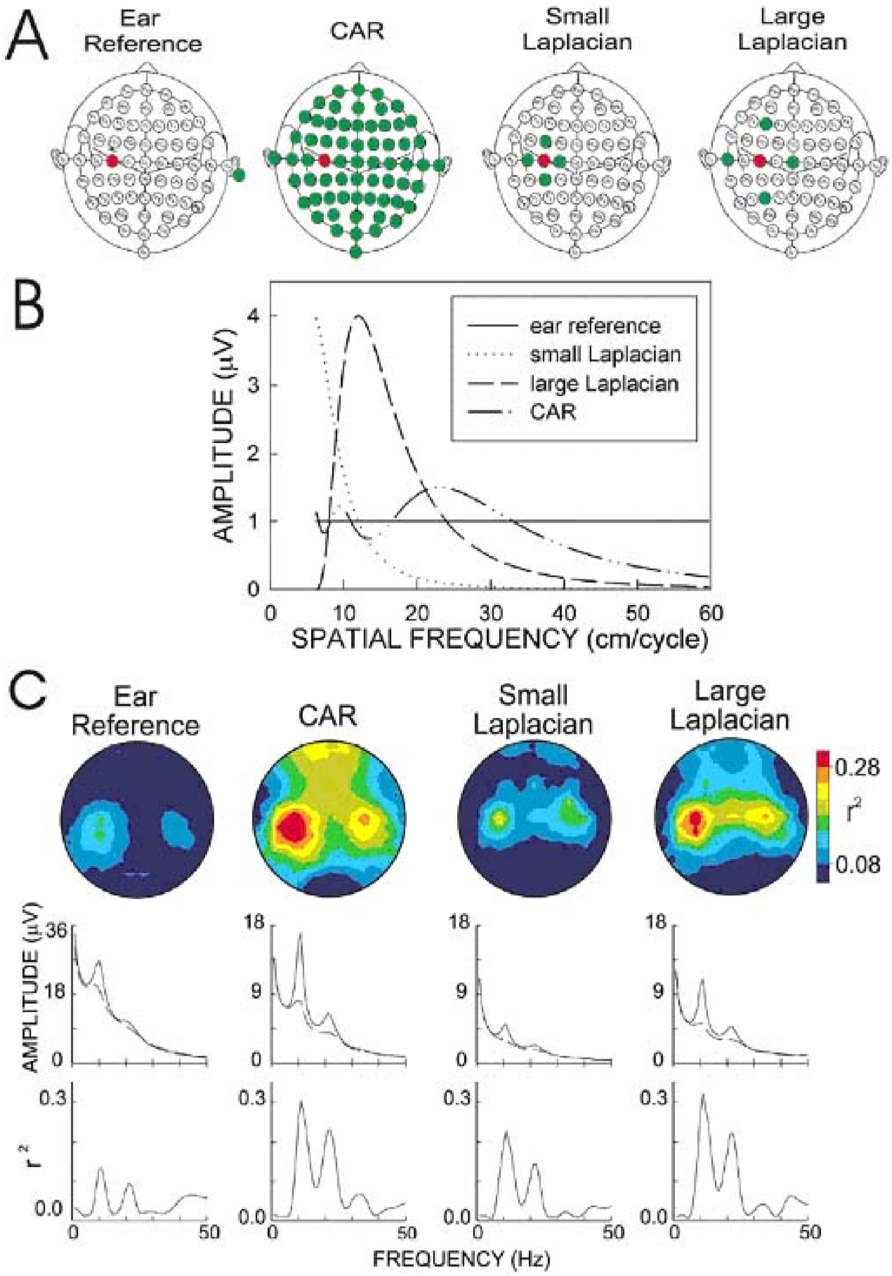


Figure 4.18: (A) Sites of scalp recordings by using 4 different spatial filters from C3 (red). During data acquisition all the 64 exploring electrodes are referred to earlobe. For obtaining the Common Average Reference (CAR) and the Laplacian methods the mean of the signal recorded from the green electrodes is calculated and subtracted from the signal recorded at C3. (B) Frequency spectrum of filters. (C) Topography of r2, signal amplitude and r2 spectrum for each spatial filter. Notice that the best results are obtained by the CAR and the large Laplacian which also provides the best resolution. (Reproduced from Wolpaw et al., 2002).

In well trained subjects errors in target selection are associated with a vertex positive potential (Schalk et al., 2000) and can be eliminated online, without the long-lasting procedure requiring the subject to confirm every choice by moving the cursor toward a direction opposite to the target one (Wolpaw et al., 1998; Miner et al., 1998). Moreover, it has been investigated if some of the EEG signals following the task could reveal whether it has been carried out according to the subject's intention (Schalk et al 2000) in the attempt of having another type of error check enabling the system to erase wrong operations without requesting time-consuming confirmation procedures. This also by knowing that the EEG during movement execution contains some components related to errors (Falkenstein et al., 1991, 1995; Bernstein et al., 1995; Gehring et al., 1995).

Every trial initiated with a one second epoch with a blank screen, followed by the presentation of two written messages to be chosen: "YES" in the top-right corner and "NO" in the bottom-left one. One second later the cursor was presented in the centre of the screen and started to move on the vertical axis, under the subject control. When the cursor reached the target (usually 2-3 seconds later) the screen became blank again. Following each choice - regardless it was correct or not- this choice was presented in the screen center for 100 msec, and again for 100 msec after one second and once again, therefore flashing thrice within about 2 seconds. Thereafter, the screen became blank again and was ready for another trial. The "error potential" cannot be ascribed to sensory feed-back for eye movements or blinking at the end of each trial (many subject never blink during the trial but do it at the end, producing an EEG contamination in an epoch overlapping the one containing the 'error potential'). However, before classifying an 'error potential' one has to exclude that it is a P300 or an oddball response to infrequent stimuli.

Whichever its origin, it has to be demonstrated whether the presence of an 'error potential' is sufficient to identify mistakes in individual trials. Despite a very low signal-to-noise ratio, the identification of an "error potential" usually (EP) helps both in implementing the accuracy and increasing the speed of information transfer.

There have been efforts for realizing practical applications of this BMI system, improving an algorithm devoted to the control of a video-writing software (Miner et al., 1998; Wolpaw et al., 1998; Vaughan et al., 2001). Moreover, in order to optimize the device's performance, Mc Farland et al. (2003) evaluated the impact of the number of target during each individual trial. Performances have then been measured both for accuracy (% of correct selections) and for the bit rate (bits/min). It has been noted that the accuracy decreases by incrementing the number of targets. In particular, for 6 out of 8 subjects, the maximal bit/rate was reached for 4 targets. The accuracy increments in parallel with the time devoted to cursor's movement, while the maximal bit/rate value was obtained for a moving time of 2-4 seconds. Therefore, such parameters are deeply affecting the device's performance and can be different across subjects.

4.9.5 Event related (de)synchroniztion (ERS&ERD)

This BMI uses EEG variations following the internal stimulus represented by the imagination of a limb movement by the user. Following a stimulus (internal or external) there can be amplitude variations of some EEG-rhythm. The percent increment of a certain rhythm after the event compared to before the event is called Event Related Synchronization (ERS) while the decrement is called Event Related Desynchronization (ERD). Electrodes placed over the motor area are able to detect ERDs on the contralateral hemisphere of the limb the subject is thinking to move. In a first stage the system is trained in order to tune the parameters of the classifier, in a later stage biofeedback allows the user improves his/her capabilities.

Several characteristics of such mu-rhythms render them good candidates for EEG-based BMIs. First, they are generated within cortical areas physiologically related to motor output where the remarkable reduction of the idling activity which is immediately preceding the motor output has been termed Event Related Desynchronization (ERD) (Pfurtscheller and Lopes da Silva, 1999b; Pfurtscheller, 1999). Interestingly, it has been recently demonstrated with Magnetoencephalography that ERD of mu and beta activity is also present in tetraplegic subjects when they attempt to produce real hand movement (Kauhanen et al, 2004). Second, there is also an increase of the idling rhythms which follows immediately the execution of the motor act as represented by a movement or relaxation of a previously contracted muscle and named "synchronization rebound" or Event Related Synchronizations (ERS) (Pfurtscheller, 1999). Contrary to ERD, beta ERS does not seems to be present in tetraplegics (Kauhanen et al, 2004). Third and more important for the BMI the ERD/ERS are not only provoked by 'real' movements, but also by movement imagination and can -therefore-support an independent BMI (Pfurtscheller and Neuper, 1997; McFarland et al., 2000a; Babiloni et al., 1999; Pineda et al., 2000).

This device, developed at the Technological University of Graz, Austria, is also based on mu rhythm ERD/ERS phenomena as the senior Scientist of this group has first described such events (Pfurtscheller et al., 1979). Studies in this direction have been focussed on the distinction amongst the different EEG components correlated with various mental counterparts of motor acts (i.e., hand vs. foot movement) in order to control a cursor or an orthotic device for opening/closing a paralyzed hand (Pfurtscheller et al., 1993, 2000a,b; Neuper et al., 1999). The relevant signal components are concentrated in the mu and beta rhythms from the sensorimotor cortex (Pfurtscheller and Neuper, 1997). According to the methods of the standard protocol, the subjects must first of all identify the most appropriate 'mental' procedure. In each of such trials (which can sum up to 160 or more, lasting 5.25 sec each) the subject is thinking to one of many possible actions (i.e. moving the hand or the right or the left foot, moving the tongue) while recording the sensorimotor cortex EEG which is then analyzed in its spectral profile in order to identify the relevant signal (i.e. the frequency bend from 5 to 30 Hz). For each imagined action an n-dimensional vector is defined; several of such vectors form a linear or non-linear classifier which subject-specific (i.e. discriminant linear analysis or neural network) and determines from the EEG which is the intended motor action (Pregenzer et al., 1996;

Pfurtscheller et al., 1996; Pregenzer & Pfurtscheller, 1999; Muller-Gerking et al., 1999). In following sessions, the device utilizes a classifier for translating the identified intended action into a continuous output (i.e. extension of a lighting bar or of a cursor) or a discrete output (i.e. letter or symbol selection) which is presented as an online feed-back on the monitor. Usually, the classifying algorithm is updated thrice a day. Recently, a robust classifier that adapt automatically to the subject as soon as his/her EEG has changed has been developed and could be implemented in an on-line BMI (Vidaurre et al., 2004). After 6-7 sessions with a double-choice trials (i.e. imagining a movement of the left hand vs the right one) the subject reaches an accuracy >90%. However, in a recent study, Guger et al. (2003) showed that on 100 naïve subjects trying to control a cursor with hand or foot imagery, only 50% yielded good performance, i.e. classification rate above 70%. Recent studies have demonstrated that some modifications can implement the device's performance. They include the use of parameters derived from autoregressive frequency analysis and by the use of alternative spatial filters, more than from the power of specific bands from the considered rhythms.

Several interfaces have been implemented in Graz, each of them insisting on the feedback given to subjects. Game-like paradigms with feedback have been implemented to enhance the subject's motivation during the training session. For example, basket or tennis games are proposed in which subjects are asked to move a cursor on a horizontal line using left or right hand in order to intercept a target.

A virtual keyboard has also been implemented that can beneficiate of the classifier training seen above. A first keyboard is based on a cue-based system with two classes (Obermaier et al., 2003): after training, the subject selects a letter using successive steps of isolation. Starting with the complete set of letters, successive subsets are selected via mental activity (right or left hand movement imagery) until the selection of the desired letter. With such a BMI, subjects can spell words with a speed of 1 letter per minute. A second spelling device has been recently implemented that allow reaching spelling rate of 2 letters per minute (Scherer et al., 2004). This is done by using multiple classes and asynchronous mode of operation. However, there are some usability limitations due to the higher cognitive load and the training requirement.

Trying to increase the motivation of subjects for training, the Graz BMI has also been implemented for navigation in a virtual reality (VR) environment (Leeb et al., 2004). Subjects were immerse stereoscopically in different virtual environment, a conference room and a city with houses and street crossing and asked to imagine left or right hand movement or foot movement to change direction. The smooth VR feedback was highly appreciated by the subject relative to the sometimes erratic feedback of the standard BMIs. Virtual reality had also been used at San Diego BMI lab to help subjects to control their mu rhythm (Pineda, 2003). Pineda et al. (2003) have trained their healthy subjects using a 3D first-person video game. Forward and backward movements were controlled on the keyboard and Left and right movements were controlled by respectively "high" and "low" mu rhythms. The authors showed that a good control of mu rhythms was gained in 3-10 hours in this environment. Finally, a BMI group in the University of Malaga, Spain, has shown that performance were better when subjects controlled their mu rhythm when controlling a car in a virtual environment than when only responding to a directional cue on a screen (Ron-Angevin et al., 2004).

In the Graz institute of technology, a further effort has been recently devoted to develop a remote control allowing the BMI to work at the subject's home, while the classifier is implemented in a research laboratory (Muller et al., 2003). This telemonitoring system has been developed to allow the subject to train at home on the BMI. A video conference system and an internet connection between the subject's home and the lab allow the expert to monitor the learning from the lab. This of great interest for subjects with reduced mobility who can train more often without leaving their home.

Presently, this remote control is used by a tetraplegic subject which drive an orthosis by means of mental imagination of hand and foot movements, enabling him to make a pinch with his 'natural' but paralysed hand (Functional Electric Stimulation, FES). The EEG characteristics from the sensorimotor brain areas are translated into outputs which open and close the fist thanks to the autoregressive estimate and to the linear discriminative classification of the EEG parameters (Obermaier et al., 2001; Guger et al., 1999; Pfurtscheller et al., 2000b; Pfurtscheller and Neuper, 2001). More recently, the same research group has shown that it is possible to obtain a holding and pinching movement. The continuous training allowed the subject the full control of the dominant EEG beta rhythm (maybe due to plastic reorganization of the neuronal circuits) which has been utilized as a relevant signal controlling the FES device.

4.9.6 Mental tasks

Spontaneous EEG recorded from subjects performing different mental tasks reveal spatial and temporal patterns that are similar across tasks and other patterns that are dissimilar. The similar patterns may be due to noise in the recording process and to mental activity common to the tasks. The dissimilar patterns form a basis for identifying the mental tasks that underlie the recorded EEG. Classification of mental tasks can be used to send different commands to a BMI. Up to five and more tasks have been successfully classified in existing BMIs.

Kostov & Pollack (2000) at the University of Alberta, Canada, have designed a BMI system able to control a cursor's movement in one or two dimensions. The EEG is recorded with a 28 electrodes montage with a binaural reference and a 200 Hz sampling rate. The autoregressive parameters extracted by 2 to 4 recording sites are translated in cursor's movement via and adaptive-logic network (Armstrong and Thomas, 1996). For this system control the training is particularly important (Polak, 2000).

Curran et al. (2003) at Keele university, United-Kingdom, recently examined which one amongst the different candidate cognitive tasks for BMI control would provide the best differentiation between the EEG patterns, allowing a faster communication. Four different candidate cognitive tasks have been selected in a way to provide the subjects with standardized instructions on the exact modalities of individual tasks execution. They were:

1. Spatial navigation in the subject's house. As in Maguire et al. (1997) the subject was required to mentally simulate to be in his/her home environment and move across the different rooms with the task of observing with attention the context besides only thinking to move (in order to avoid stimulating motor activity).
2. Acoustic imagination of familiar sounds by thinking to the preferred song or sound and listening to it in his/her head without moving lips or other body parts (Halpern & Zatorre 1999).
3. Imagination of moving the right half of the body (i.e., right fist opening and closing) without real movement of the hand).
4. Imaging movements with the left part of the body as before.
5. Results are illustrated in Figure 4.19 below. By combining visual navigation-acoustic imagination the best results were achieved. The subjects themselves reported that for them it was easier to accomplish non-motor tasks. It is quite possible that -by adopting specific tasks, chosen in view of their proximity to the subjects habits- the BMI systems could be further implemented (Curran and Stokes, 2003). For instance, logic-mathematic tasks, more than imagination of specific motor acts of a given sportive discipline or manual skill, might be adapted to individuals who already have been trained in such abilities.

CLASSIFICATION ACCURACY FROM DIFFERENT COGNITIVE TASK

correct classifications	correct classifications	p-value
navigation - auditory 74 %	navigation - right motor 69 %	$\ll 0.01$
navigation - auditory 74 %	auditory - right 71 %	< 0.01
navigation - auditory 74 %	left motor - right motor 71 %	0.013
navigation - right motor 69 %	auditory - right motor 71 %	0.02
navigation - right motor 69 %	left motor - right motor 71 %	0.026
auditory - right motor 71 %	left motor - right motor 71 %	0.40

Figure 4.19: Classification accuracy from different cognitive tasks. (Reproduced from Curran et al., 2003).

Moreover, the good results achieved by T4-P4 EEG recordings are overwhelmingly superior to all other recording positions, suggesting that it might even be possible to record from only one scalp site in order to discriminate between to non-motor intents, therefore decreasing the electrode positioning time, the bulk of the recording apparatus and an efficiency increase.

Other researchers at the Neil Squire Foundation, Canada, have investigated off-line new and different approaches never tried with on-line devices (Birch et al., 1993; Birch and Mason, 2000; Mason and Birch, 2000). They describe methods for identifying voluntary movement related potentials (VMRP) in the EEG generated within the primary sensorimotor cortex and supplementary motor area. Such an identification enabled a cursor control via a translation algorithm utilising the 1-4 Hz EEG components bipolarly recorded. These authors concentrated on VMRP recognition instead of identification of relevant signal in the EEG combined to trials driven by external stimuli. Thereafter, the attention has been focussed on the recognition of commands spontaneously generated by the subject without chronologically generated signals from structured trials. Levine et al. (1999) at the University of Michigan, USA, recorded the EEG from 17 subjects with subdural implanted electrodes (16 to 126) before neurosurgery and found potentials having a focal topography combined with specific movements and vocalizations. They might represent relevant signals for a multiple control BMI.

Pineda & Allison (Pineda et al., 2000; Allison et al., 2000) explored the relationship between individual and associative movements as they are represented in the mu rhythms and in the BRP (preparation potentials) within a simple reaction time paradigm. Babiloni et al. (2000b) developed a Laplacian EEG analysis and a dedicated algorithm for signal/space analysis in order to recognize imagined movements embedded within the ongoing EEG recorded from the sensorimotor cortex.

Millan et al. (2000) proposed a new classifier for the recognition of mental tasks from the analysis of spontaneous EEG, and included it in a portable BMI device (ABI) which has been tested on 4 young and healthy volunteers. They adapted their testing protocol to the real conditions in which the subjects would have been operating. Along this vein, the subject should be able to spontaneously take his/her decisions whenever and whatever he/she likes, and the temporal window during which the device is reading the imagination should be as brief as possible. On the basis of neuropsychological evidences the recording electrodes were concentrated on the front-parietal areas which are crucial for recognition of the investigated mental tasks (F3, F4, C3, Cz, C4, P3, Pz, P4). Performances were measured both off-line and on-line with a feed-back. The ABI system can recognize and analyze in real time up to 3 different mental tasks as identified in the spontaneous EEG with a 70% accuracy, a 5% errors and a choice rate of 0.5 sec. Moreover, since the system implements a good and flexible translation algorithm, subjects are able to learn in a short period (sometimes in 5 days training) the full interface control.

Subject	Confusion Matrix				%True Positive	%False Positive
		Relax	Left	Right		
MJ	Relax	100	0	0	52	0
	Left	0	42	0		
	Right	0	0	36		
MJR	Relax	93	0	0	63	5
	Left	0	51	5		
	Right	0	9	56		

The above table (from Millan et al., 2000) shows the results gathered with the ABI system by using two mental imagination tasks (either right or left hand movements) and a third relaxation task. It once again evidences the superiority of the non-motor imagination tasks.

4.10 Worldwide BMI research groups

Since the first attempt of Dewan (1967) to transmit Morse code messages through cerebral alpha rhythm control in 1967, and the use of visual evoked potential for cursor control by Vidal in 1972 (Vidal, 1972), research on brain computer interfaces (BMIs) has slowly evolved until the ninetieth when it exploded. As stated by Wolpaw, who leads BMI research att the Wadworth center in USA, no more than six BMI research groups were active in 1995 against more than twenty in 2000. The number of scientific publications has also greatly increased, what reveals the concrete work done in recent years. The following table presents a summary of the main current BMI groups all over the world.

Principal investigator	**Signal**	**Application / feedback**	**Location**
Austria			
Pfurtscheller , G	μ rhithm	Prosthetic arm control	Laboratory of Brain-Computer Interfaces, Graz University of Technology, Austria
Canada			
Birch, G	VMRP	Switch	Department of electrical computer engineering, University of British Columbia, / Neil Squire Foundation, Canada
Denmark			
Nielsen, K.D	SS-VEP	Word processor	Center for sensori-motor interaction; Department of health science and technology, Aalborg University, Denmark

Finland			
Sams M.	MEG β rhythm	-	Laboratory of Computational Engineering, Helsinky university of technology, Finland
Germany			
Müller, K-R.	RP	-	Intelligent Data Analysis Group, Franhaufer FIRST Institute, Germany
Birbaumer, N.	SCP	Virtual keyboard	Institute of Medical Psychology and Behavioral Neurobiology, Germany
Ireland			
Allen, R.	-	Ambiguous keyboards	Liminal Devices Group, Media Lab Europ, Dublin, Ireland
McGinnity	Information theoretic functionals - redundancies	Cursor control	Faculty of Engineering, Intelligent Systems Engineering Laboratory, University of Ulster, Ireland
Ward, T.	Motor Optical response	Ball size on a screen	Department of Electronic Engineering. Biomedical Engineering Research Group, National Univeristy Of Ireland, Maynooth, Ireland
McDarby	SS-VEP	Gaming	Mindgame Group, Media Lab Europ, Ireland
Italy			
Beverina, F.	P300	Target reaching	STMicroelectronics-Advanced system technology, Italy
Beverina, F.	SS-VEP	Direction choice	STMicroelectronics-Advanced system technology, Italy
Mexico			
Medina, V.	Electrode-wise classification	-	Department of Electrical Engineering, Universidad Autonoma Metripolitana, Iztapalapa, Mexico
Spain			
Diaz-Estrella, A.		Virtual reality	Department of electronic technologies, University of Malaga, Spain
Switzerland			
Del Millan J	Surface Laplacian	Virtual keybord, Pacman, robot navigation	Sensor Based Applications Sector, Institute for Systems, Informatics and Safety, Joint Research Center of the European Commission, Italy

Gysels, E.	Phase synchronization	-	Swiss Center for Electronics and Microtechnology, Neuchatel, Switzerland
Michel, C	Local field potentials	-	Functional brain mapping laboratory, University of Geneva, Switzerland
Pun T.	Average trial protocol	-	Computer Vision and Multimedia Lab, Computer science department, university of Geneva, Switzerland
UK			
Roberts, S.J.	μ rhythm	-	Robotics Research Group; Pattern Analysis & Machine Learning Research Group, University of Oxford. Department of Engineering Science, UK
Poli, R, Sepulveda, F Gan, J.Q.	P300, motor intentions	Selection of characters, Prosthesis/ robot control, Asynchronous BMIs	Department of computer science, Brain Computer Interfaces Group, University of Essex, UK
Curran, E.	Brain states	-	Keele University
USA			
Levine, S.P.	ERP, ECoG	-	Department of Biomedical Engineering, Iniversity of Michigan, USA
Kostov, A	μ rhythm	Environmental control device	Department of Computing Science / Faculty of Rehabilitation Medicine
Wolpaw, J.	μ rhythm	Answer Yes / No question	Laboratory of Nervous System Disorders, Wadsworth Center, NYS Department of Health, USA
Pineda, J.	mu, P300	virtual reality, virtual keyboard	Cognitive Neuroscience Laboratory, University of California, USA
Bayliss, J.D.	P300	virtual reality	Department of computer science, Artificial Intelligence and Vision Lab, Rochester Institute of technology, USA
Donchin, E.	P300	Virtual keyboard	Department of Psychology , University of Illinois at Urbana-Champaign (E. Donchin now at the University of South-California), USA
McMillan, G	SSVEP	Flight simulator/ FES	Air Force Research Laboratory, Wright-Patterson Air Force Base, USA
Sutter E.E.	VEP	virtual keyboard	Smith-Kettlewell Eye Research Institute, San Francisco

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5. Positron emission tomography (PET)

5.1 Theory of the concept

Positron emission tomography (PET) is a functional imaging technique which has undergone dramatic advances in performance in the past 20 years. From the low resolution and sensitivity, single slice designs of the early 1980s, to the high resolution and multi-slice of today, key imaging parameters have in most cases improved by at least an order of magnitude (Townsend, 2004b).

Positron Emission Tomography uses proton-rich radionuclides, as labels on tracer biological molecules, in order to image organ functions. The radionuclides used emit positrons to arrive to nuclear stability; indeed a proton in the nucleus decays to a neutron, a positron and a neutrino:

$$p \rightarrow n + e^{+} + \nu_{e}$$

The daugther isotope has an atomic number that is one less than the parent's. An important characteristic of radionuclides is the rate at which they decay, governed by the equation:

$$A = A_0 e^{-\lambda t}$$

where A is the activity at time t after a starting time, A_0 is the activity at the starting time and λ is the decay constant. Decay rates are indicates by their half-life, $t_{1/2}$, which is related to the decay constant by

$$\lambda = \frac{0.693}{t_{1/2}}.$$

In Table 5.1 some radionuclides that decay via positron emission are shown

Isotope	Half – life (min)	Maximum Energy (MeV)
^{11}C	20.4	0.960
^{13}N	10	1.198
^{15}O	2.0	1.732
^{18}F	109.8	0.633

Table 5.1: Proton-rich radionuclides used in PET.

The energy spectrum of the emitted positron depends on the specific isotope, with energies varying from 0.6 MeV for ^{18}F a 3.4 MeV for ^{82}Rb (Townsend, 2004a). The first important feature of this radionuclides is the short half-life. This involves that the particle accelerator, the cyclotron, used for the radionuclide production must be near the PET device. The second important feature is that they occur naturally in many compounds of biological interest, and can be readily incorporated into a wide variety of useful radio-pharmaceuticals.

When a radionuclide is injected into or inhalated by the patient, it decays via positron emission; the positron travels a short distance (about 1 mm) through human tissue loosing its energy and then it annihilates on contact with electrons in the tissue. An annihilation event results in two gamma photons emitted at 180 degrees and with an energy of 511 keV each (Figure 5.1) (Webster, 2001).

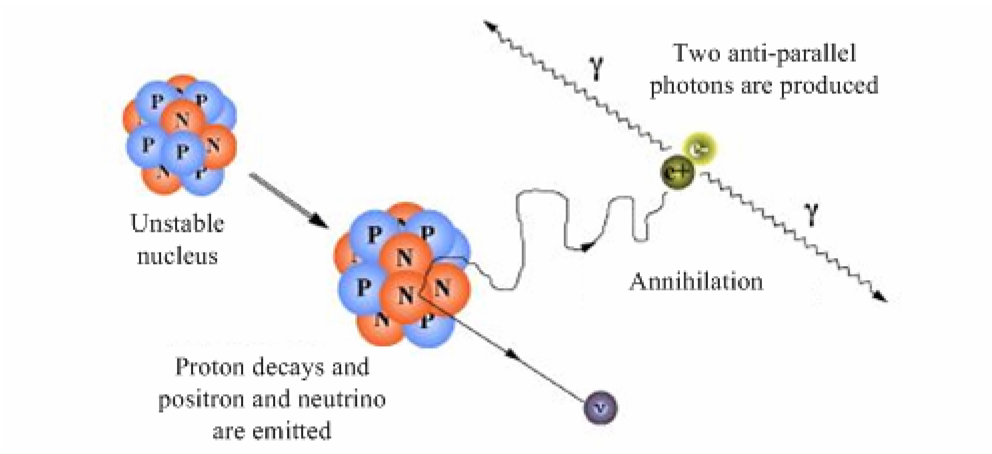

Figure 5.1: Unstable nucleus decay, positron emission, annihilation event and two gamma photons production. (Picture: depts.washington.edu).

The photons emitted via annihilation are detected with a gamma camera. These cameras consist of an cylindrical array ring of detectors, with a diameter of 80-100 cm and an axial extent of 10-20 cm, that surround the patient (Ollinger & Fessler, 1997), a crystal scintillator to convert high-energy photons to visible light, and photo-multiplier tubes and associated electronics to determine the position of each incident photon from the light distribution in the crystal.

Positron emission tomography has a poor temporal resolution, over 10 s, and a spatial resolution of about 5 mm. It’s important to underline that PET scanners attain a measured spatial resolution of around 2 mm for brain research and 4 mm for clinical whole-body studies.

The positron emission tomography is not a widely used imaging technique due to the high cost of the scanner and the need for a local cyclotron, for producing radionuclides with short half-lives, which also comes at a very high cost.

5.2 Methodologies for BMI

In positron emission tomography, radionuclides that causes the positrons emission are localized by detecting two photons, emitted in opposite directions by annihilation events, by using an array of detectors that surround the patient (PET scanner). This technique can be also used for studying the brain activity in physiological and pathological conditions and for understanding the location of the brain areas that are activated during the performance of particular cognitive tasks (Figure 5. 2).

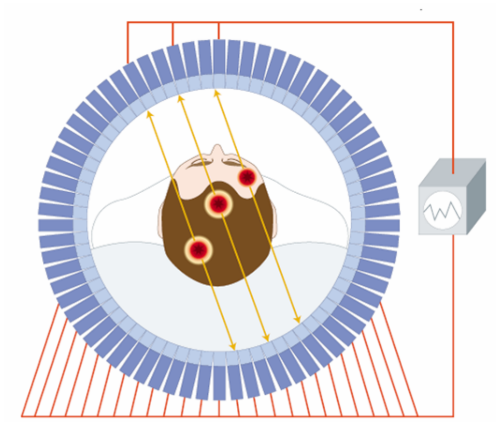

Figure 5. 2: Use of PET for studying brain activity. (Reproduced from www.biomedica.laboratorium.dist.unige.it).

This neuroimaging technique is based on the increase of the regional cerebral blood flow (rCBF) and oxidative metabolism while the neurons are enabled (Horwitz et al., 2000). Indeed the cerebral activity is linked to use the ATP (Adenosine TriPhophate) which is produced by the oxidation of glucose molecule to CO_2 and H_2O. The glucose and the oxygen, for the oxidation and ATP production, are carried by blood flow which increases where the neurons are enabled. In this case, PET uses the radionuclides as labels on tracer molecules which are in the blood flow so that the concentration of radionuclides is bigger in actived cerebral areas. In particular, the radionuclide ^{18}F is used for labeling the glucose molecule (^{18}FDG) and ^{15}O is used for labeling the water molecule ($H_2{}^{15}O$). The radionuclide ^{18}F has better properties for high-resolution PET imaging; indeed its emitted positron has a maximum energy of 0.633 MeV and a mean range of 0.6 mm.

The radionuclide for functional neuroimaging is injected into the patient. The scan by PET camera for photon detection begins after a delay ranging from seconds to minutes to transport and uptake by the cerebral area of interest. The emitted positrons annihilates with electrons; the annihilation event results in two gamma photons emitted at 180 degrees and with an energy of 511 keV each.

The annihilation position measurement depends on simultaneous or coincident detection of the pair of photons: if two photons are detected within a short timing windows (about 10 ns: *coincidence timing windows)* the annihilation is localized on the straight line (line of response – LOR) joining the two relevant detectors (Figure 5.3.A) . If this temporal condition is not respected, the emitted photons are ignored.

When two photons are detected within the coincidence timing windows but the annihilation does not occur within the LOR, the event is scattered and then it has to be rejected (Figure 5.3.B). The amount of scattering, which is primarily due to the Compton process at this energy, is characterised by the scatter fraction (SF), then by the ratio of the number of scattered events to the number of total events. In order to do this, the intensity recorded at the detectors is analyzed and compared with a particular threshold. Indeed the scattered photons loose part of their energy, so their remaining energy is below a given threshold.

Another type of event, in which only one photon is detected and the other photon is not recorded by any detector is called a single (random) photon (Figure 5.3.C). An accidental occurrence may result when two singles are recorded within the coincidence timing windows. The accidental occurrence rate increases linearly with the timing window and quadratically with the rate of single photons interacting in detectors. The radiation incident on the detectors arises not only from the radioactivity in the field of view of the scanner, but also from radioactivity outside the field of view. The random coincidence rate (R) may be reduced by shortening the coincidence timing window, and it is increased by radionuclide concentration.

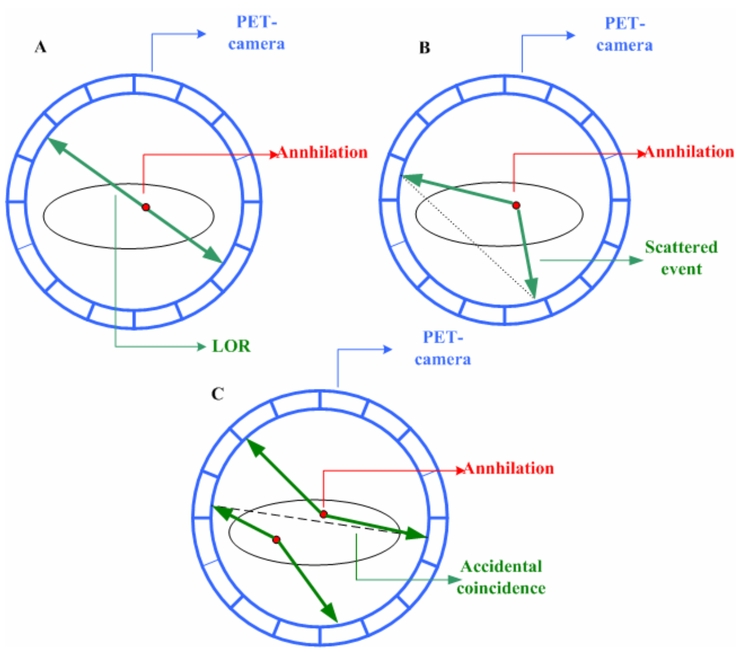

Figure 5.3: A: Annihilation position detection on Line Of Response. B: Scattered event. C: Accidental coincidence.

Only the first reported event is used for the annihilation localization. The photons emitted are detected by scintillation detectors which convert the photon energy in visible light that moreover is converted to electrical signal by a photomultiplier. The event detected is stored in matrices or sinograms where each row represents a parallel projection p(s,φ) of the activity distribution in the patient at a specific angle (φ) and axial position (z). In particular each element of the sinogram contains the number of annihilation at a specific projection direction. An image reconstruction algorithm is applied to the sinograms to recover the radioactivity distribution, thus mapping the functional process that created the distribution of positron emitter (Figure 5.4).

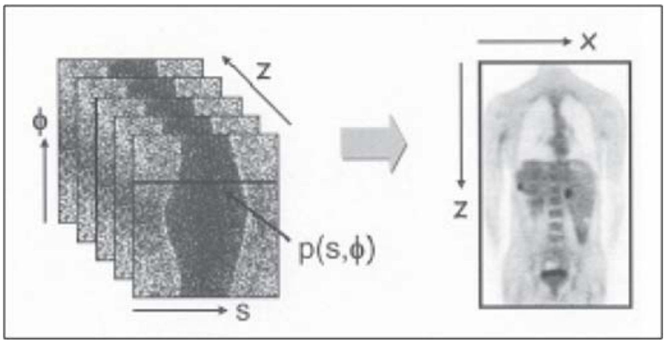

Figure 5.4: Collection of the positron annihilation events into sinograms and coronal section of the final whole-body image. (Adapted from Townsend, 2004a).

Figure 5.5 shows some examples of the brain areas activated. In pseudo-coloured PET images, the colours show the different levels of activity; in particular, the red colour represents the most active brain areas and the blue colour represents the less active brain areas.

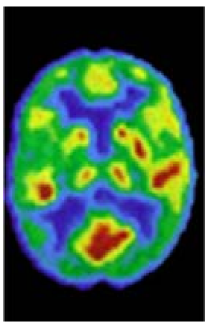

Figure 5.5: Different brain areas activated. (Source: WWW) .

5.3 Hardware

The most important hardware components in positron emission tomography are the detectors and the photomultipliers (Figure 5.6). The impressive PET progress in the last years is due mainly to developments in detector construction, to the use of new scintillators, better scanner design, in addition to an improved reconstruction algorithms.

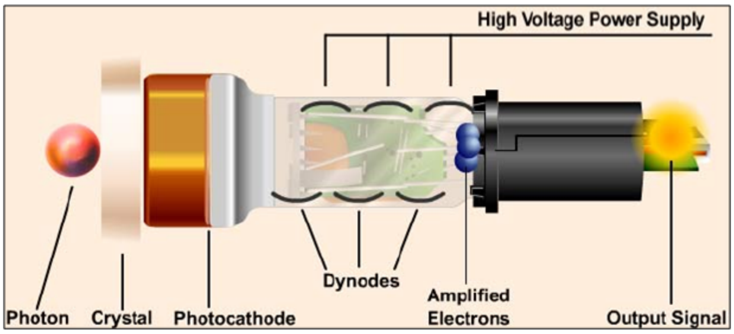

Figure 5.6 : Hardware components. (Picture: www.fisica.unipg.it).

In order to obtain the output signal, the crystal scintillator has to be linked to a photomultiplier. The first block detector developed in the mid 1980s (Casey & Nutt, 1986), used smaller scintillation detectors, each coupled to a photomultiplier tube. As this solution was very expensive, another solution was designed. In this case a block of scintillator is cut into 8 x 8 detectors and bonded to 4 photomultipliers (Figure 5.7).

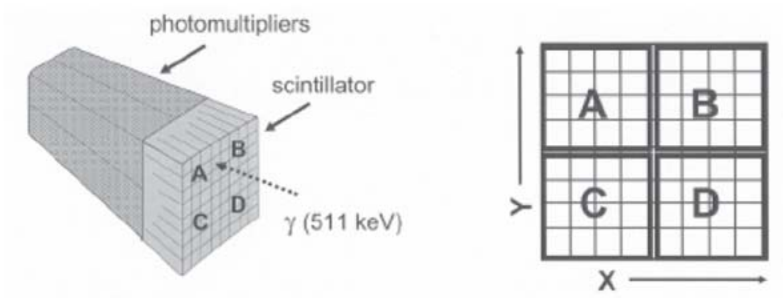

Figure 5.7: Scintillator and photomultipliers. (Adapted from Townsend, 2004a).

The first scintillator used in PET scanner was the thallium-activated sodium iodide (NaI(Tl)). The disadvantage of this scintillator is a very low efficiency at 511 keV. To improve sensitivity, it is necessary to increase the depth of the scintillator. A scintillator which offers better feature than NaI(Tl) is bismuth germanate (BGO). This material is a denser scintillator whit greater stopping power than sodium iodide. Today the most important scintillators used are gadolinium oxyorthosilicate (GSO) and lutetium oxyorthosilicate (LSO) both doped with cerium. The physical properties of all scintillators are compared in Table 5.2.

Property	NaI	BGO	LSO	GSO
Density (g/ml)	3.67	7.13	7.4	6.7
Effective Z	51	74	66	61
Attenuation length (cm)	2.88	1.05	1.16	1.43
Decay time (ns)	230	300	35 - 45	30 - 60
Photons/MeV	38000	8200	28000	10000
Light yield (%NaI)	100	15	75	25
Hygroscopic	Yes	No	No	No

Table 5.2: Physical properties of different scintillators for PET.

Photomultiplier tubes are extremely sensitive detectors of light in the ultraviolet, visible and near infrared. These detectors multiply the signal produced by incident light by as much as 10^8, from which single photons can be resolved. Photomultipliers are constructed from a glass vacuum tube which houses a photocathode, several dynodes, and an anode. The emitted photons hit the photocathode material and the electrons are produced as a consequence of the photoelectric effect. The electrons produced are multiplied by dynodes that have the feature that each dynode is held at more positive voltage that previous one. The electrons leave the photocathode and, accelerated by electric field, arrive with greater energy to first dynode. Then the electrons hit the dynode and other low energy electrons are emitted and accelerated toward the second dynode. The propagation process goes on up until the anode where the accumulation of charge results in a current pulse.

Detectors and photomultipliers compose the PET scanner. Firstly, the multi-ring scanner (Figure 5.8.A) incorporates septa mounted between the detector rings in order to shield the detector rings from scattered photons (Figure 5.8.B). In this case, only LORs with small angles of incidence are active and indeed the LORs which intersect the septa do not reach the detectors. Moreover this multi-ring scanner images a 3-D positron-emitting distribution as a set of contiguous 2-D sections.

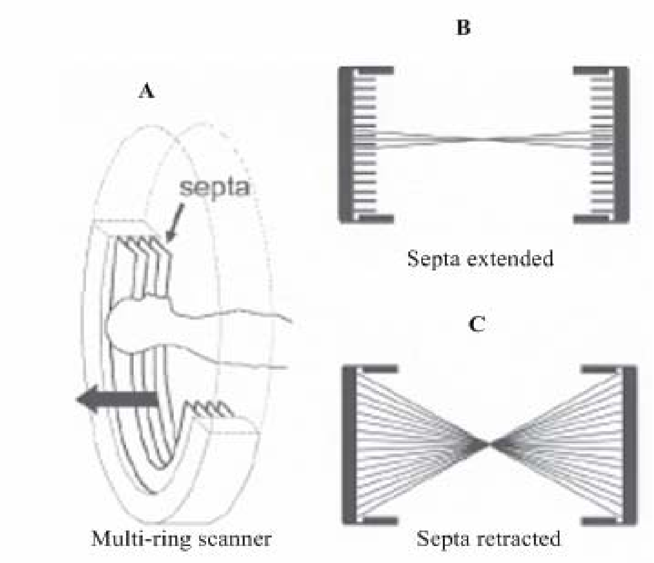

Figure 5.8: A: Multi-ring scanner. B: Septa mounted between the detector. C: Detector without septa. (Adapted from Townsend, 2004a).

The scanner sensitivity is increased by a factor of 6 or greater by septa retraction (Figure 5.8.C). In this case indeed the LORs do not intersect anything and then many more LORs are active. Moreover the septa lack allows the 3-D data set acquisition.

5.4 Current applications

The positron emission tomography is a very important functional imaging technique. The most important current application is the clinical whole-body diagnosis for detecting tumours which are distinguished by a high metabolic activity. In the neurological field, the positron emission tomography is also used for studying some diseases such as Parkinson's disease, Alzheimer's disease, epilepsy and depression. Moreover this functional imaging technique is used to explore the functional neuroanatomy of cognitive functions (Cabeza & Nyberg, 2000). Cerebral activity studies by means of PET are very important in BMIs since they allow a first localization of brain areas activated during the performance of cognitive tasks for further cerebral studies by means of the other techniques (EEG, NIRS) (Curran & Stokes, 2003) (Figure 5.9).

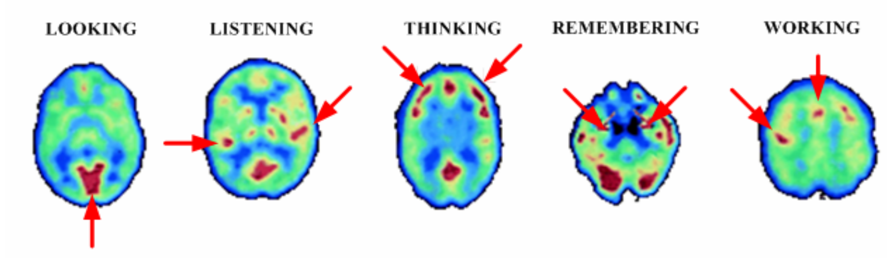

Figure 5.9: Brain areas that are actived during the performance of particular cognitive tasks. (Adapted from: WWW).

An important PET application for BCIs is the cerebral activity study while motor imagery (Pfurtscheller & Neuper, 2001, Decety et al., 1994, Decety, 1996). Motor imagery can be defined as a dynamic state during which a subject mentally simulates a given action. Several sources indicates that motor imagery pertains to the same category of processes as those which are involved in programming and preparing actual actions, with the difference that in latter case, execution would be blocked at some level of cortico-spinal flow.

5.5 Foreseen improvements

Positron emission tomography is sometimes classified as a non-invasive imaging technique, in the sense that it does not require brain surgery, but it does need radionuclide injection into the patient. For this reason and for its high cost, this functional imaging technique is replaced by functional magnetic resonance imaging (fMRI) which require not injections of contrast media. fMRI measures the change in blood oxygenation and blood volume resulting from altered neural activity; this technique is called BOLD (blood oxygenation level-dependent contrast). fMRI, covered in Chapter 6, has also other advantages with respect to PET, such as higher spatial resolution.

The foreseen improvements of PET imaging concerns the hardware components, in particular the scintillators, in order to increase the sensitivity and decrease the cost of use.

5.6 Outline on the suitability for space application (pros and cons)

Positron emission tomography is not used currently for space application and will presumably not be used even in the future because it is expensive, it needs artificial radionuclides with short half-lives and the PET scanner is bulky and heavy. Moreover, fMRI is a more effective harmless alternative technique.

5.7 Worlwide researching groups

By a careful investigation on the state of art about PET applications, we could not find any researching group worldwide who employs PET for BMIs. Instead, PET is used to understand brain activity, and nowadays it is utilized mainly for diagnostic applications.

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6. Functional magnetic resonance imaging (fMRI)

Functional magnetic resonance (fMRI, Heeger & Ress 2002) is a non-invasive method of measuring neuronal activity in the human brain. Its signals arise from changes in local haemodynamics that, in turn, result from alterations in neuronal activity, but a complex interplay relates neuronal activity, haemodynamics and fMRI signals. It has been assumed that the fMRI signal is proportional to the local average neuronal activity, but many factors can influence the relationship between the two. Much work is devoted to achieve a clearer understanding of how neuronal activity influences the fMRI signal (Logothetis et al., 2001, Huk et al., 2001).

6.1 Theory of the concept

fMRI detects changes in the concentration of deoxyhemoglobin, dependent on a complex interplay among blood flow, blood volume and cerebral oxygen consumption (Heeger et al., 2000; Heeger and Ress, 2002). When neurons increase their activity with respect to a baseline level, a modulation of the deoxyhemoglobin concentration is induced, generating the so-called blood oxygen level dependent (BOLD) contrast (Boynton et al., 1996). BOLD dynamics is characterised by an initial transient small decrease below baseline due to initial oxygen consumption (negative dip), followed by a large increase above baseline, due to an oversupply of oxygenated blood only partially compensated by an increase in the deoxygenated venous blood volume.

6.1.1 Generation of BOLD signal

The fundamental signal for BOLD of fMRI comes from hydrogen atoms, which are abundant in the water molecules of the brain. In the presence of a magnetic field, these hydrogen atoms absorb energy that is applied at a characteristic radio frequency (~64 MHz for a standard, clinical 1.5 Tesla MRI scanner). After this step of applying radio-frequency excitation, the hydrogen atoms emit energy at the same radio frequency until they gradually return to their equilibrium state. The MRI scanner measures the sum total of the emitted radiofrequency energy. The measured radio-frequency signal decays over time, owing to various factors, including the presence of in-homogeneities in the magnetic field. Greater in-homogeneity results in decreased image intensity, because each hydrogen atom experiences a slightly different magnetic field strength, and after a short time has passed (commonly called T2*), their radio-frequency emissions cancel one another out. BOLD fMRI techniques are designed to measure primarily changes in the in-homogeneity of the magnetic field, within each small volume of tissue, that result from changes in blood oxygenation. Deoxy- and oxyhaemoglobin have different magnetic properties; deoxyhaemoglobin is paramagnetic and introduces an in-homogeneity into the nearby magnetic field, whereas oxyhaemoglobin is weakly diamagnetic and has little effect (see Figure 6.1). Hence, an increase in the concentration of deoxyhaemoglobin would cause a decrease in image intensity, and a decrease in deoxyhaemoglobin would cause an increase in image intensity.

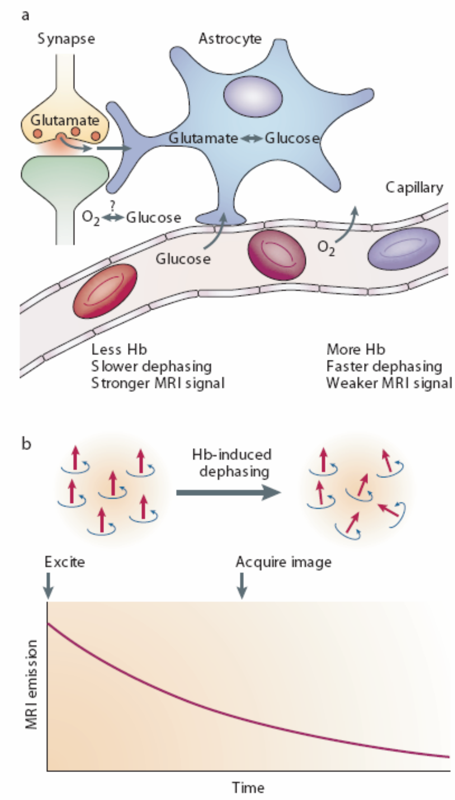

Figure 6.1: BOLD signal generation. (Reproduced from From Heeger & Ress, 2002).

Starting by the evidence that paramagnetic deoxyhemoglobin in venous blood is a naturally occurring contrast agent for magnetic resonance imaging (MRI), by accentuating the effects of this agent through the use of gradient-echo techniques in high fields, Ogawa and colleagues (1990) demonstrated in vivo images of brain microvasculature with image contrast reflecting the blood oxygen level. The called blood oxygenation level-dependent (BOLD) contrast, the signal which follows blood oxygen changes induced by anesthetics, by insulin-induced hypoglycemia, and by inhaled gas mixtures that alter metabolic demand or blood flow. They provided the suggestion, from then on confirmed by more then 150000 papers indexed in PubMed, that BOLD contrast can be used to provide in vivo real-time maps of blood oxygenation in the brain under normal physiological and pathological conditions (Ogawa et al., 1990, Bandettini et al. 1992).

6.1.2 Neurophysiological basis of fMRI signal

Logothetis and colleagues (2001, Figure 6.2) analysed simultaneous intracortical recordings of neural signals and fMRI responses. They compared local field potentials (LFPs), single- and multi-unit spiking activity with highly spatio-temporally resolved blood-oxygen-level-dependent (BOLD) fMRI responses from the visual cortex of monkeys. The largest magnitude changes were observed in LFPs, which at recording sites characterized by transient responses were the only signal that significantly correlated with the haemodynamic response. Linear systems analysis on a trial-by-trial basis showed that the impulse response of the neurovascular system is both animal- and site-specific, and that LFPs yield a better estimate of BOLD responses than the multi-unit responses. These findings suggest that the BOLD contrast mechanism reflects the input and intracortical processing of a given area rather than its spiking output.

On this basis, the BOLD signal could reflect not only the firing of local neuronal assemblies, but also the amount of their synchronized input, as well as fluctuations of the firing synchrony which can increase or decrease without affecting the net firing rate (Rees et al., 2000; Heeger et al., 2000).

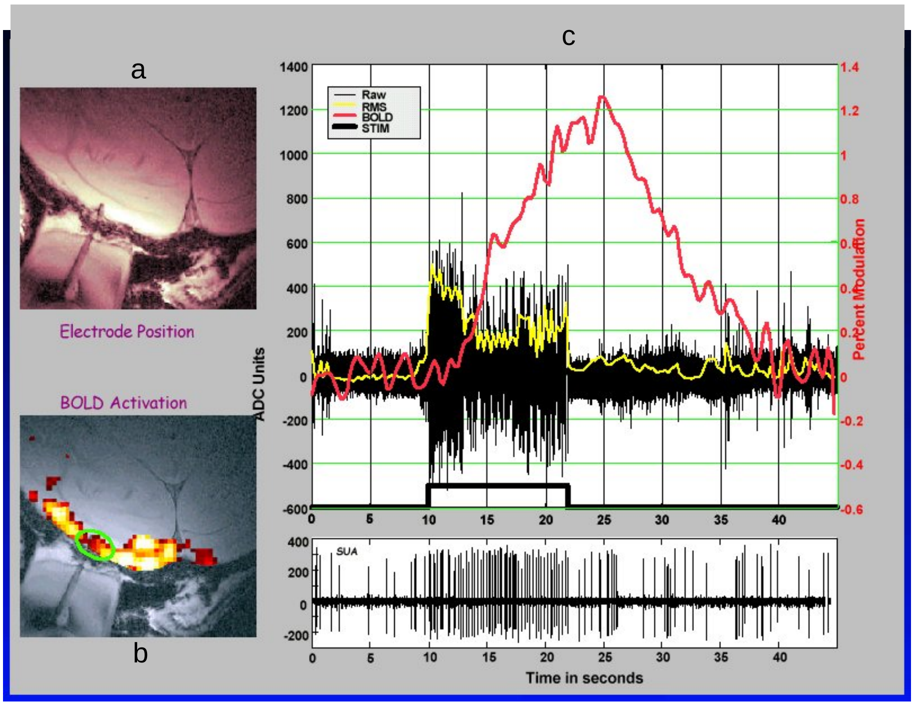

*Figure 6.2: Neural and BOLD responses to pulse stimuli. **a** Location of the electrode tip in primary visual cortex. **b** BOLD response to rotating chequerboard patterns in striate cortex. Activation can be measured around the electrode tip. **C** Haemodynamic response (red) superimposed on the de-noised raw neural signal (black). The term `de-noised raw' denotes that no other signal processing beyond the removal of gradient interference was done. The r.m.s. of the signal is indicated by a thick yellow line. (Modified from Logothetis et al., 2001)*

6.2 Current applications

The high spatial resolution of fMRI has been exploited to increase EEG-based BCIs (Hinterberger et al., 2004; Weiskopf et al., 2004a, 2004b, Yoo et al., 2004). In fact, an EEG-driven brain-computer interface combined with fMRI has been investigated (Hinterberger et al., 2004). Previously, using self-regulation of slow cortical potentials (SCPs, i.e. shifts in neuroelectric potentials lasting up to a few seconds) through the thought translation device (TTD, Birbaumer et al., 2000) aiming to training the SCP self-regulation, successful communication with completely paralyzed patients was achieved (Birbaumer et al., 1999), with a communication speed of 2-3 letters per minute which yields an information transfer rate of approximately 15 Bits/min. To enhance SCP regulation use for BCI, the TTD was combined with functional magnetic resonance imaging (fMRI). In that work, first data of SCP feedback during fMRI are presented, and technical aspects and pitfalls of combined fMRI data acquisition and EEG neurofeedback are discussed.

Capitalizing on the ability to characterize brain activity in a reproducible manner, other Authors explored the possibility of using real-time fMRI to interpret the spatial distribution of brain function as BCI commands (Yoo et al., 2004). Using a high-field (3T) MRI scanner, brain activities associated with four distinct covert functional tasks were detected and subsequently translated into predetermined computer commands for moving four directional cursors. The proposed fMRI-BCI method allowed volunteer subjects to navigate through a simple 2D maze solely through their thought processes.

6.3 Worldwide researching groups

http://www.mp.uni-tuebingen.de/mp. Eberhard Karls University, Dept. of Medical Psychology and Behavioral Neurobiology and Max-Planck-Institute for Biological Cybernetics, Dept. of Empirical Inference, Tubingen, Germany. In particular researchers Thilo Hinterberger, Niels Birbaumer.

http://brighamrad.harvard.edu/. Department of Radiology, Brigham and Women's Hospital, Harvard Medical School, 75 Francis Street, Boston, MA 02115, USA.

6.4 Outline on the suitability for space applications (pros and cons)

Above reported studies on up-dated fMRI-BCI applications, suggest that in future efforts could be planned to test the application of information obtained by fMRI, to portable system adapt to use in space environments.

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7. Near-infrared spectroscopy (NIRS)

Near-infrared spectroscopy (NIRS) provides a noninvasive, nonionizing and portable means to image brain function (Boas, 2004). NIRS offers primarily information about oxygenation based on the optical properties of hemoglobin, the protein in the blood that carries oxygen. Because oxygenated and deoxygenated hemoglobin have distinct absorption properties, the degree of oxygenation in tissue can be determined by shining light into tissue and measuring the amount of light that emerges, unabsorbed. This Blood Oxygenation Level-Dependent (BOLD) effect is also the basis of the fMRI technique. Near-infrared light affords deeper penetration into tissue, and is therefore the spectral range of choice for measuring cerebral oxygenation. Because hemoglobin is the dominant absorbing element between 700nm and 1,000nm, and because the transmission of light is relatively unaffected by water in the same region, the near-infrared region is the most favorable to the optical measurement of these parameters. Figure 7.1 shows how, by shining near-infrared light into the body and placing a detector a few centimeters away from the light source, it is possible to measure changes in the amount of light reaching the detector - and consequently changes in absorption in the same area of the body (Villringer et al. 1993). Although attempts to measure cerebral oxygenation with near-infrared light date back to the mid-1930s, when Kurt Kramer demonstrated transmission through an animal's skull (Kramer, 1935), most researchers point to the late 1970s as the beginning of the modern era of near-infrared spectroscopy (Jöbsis, 1977).

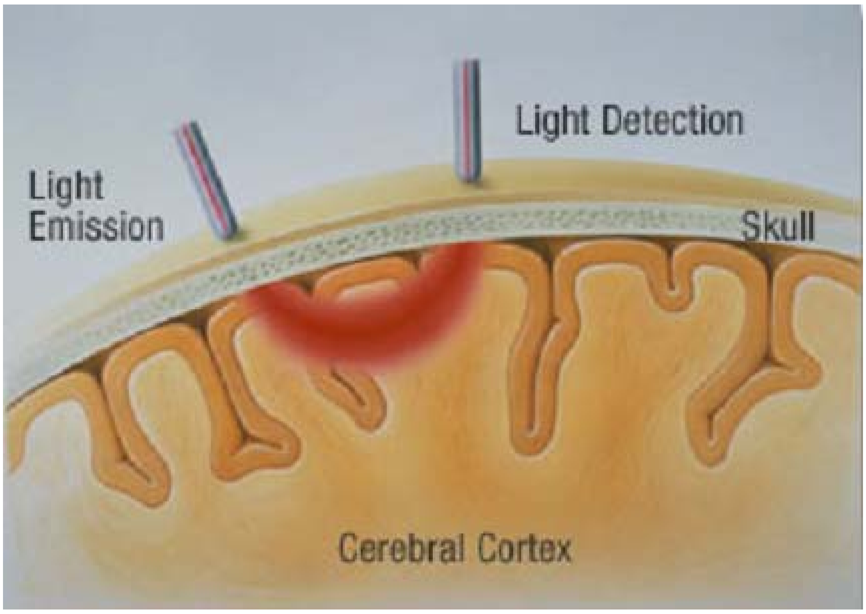

Figure 7.1: The working principle of near-infrared spectroscopy. (Source: WWW).

Developed in the 1990s, diffuse optical tomography (DOT) is used to reconstruct images of total hemoglobin concentration and oxygen saturation, based on data obtained with near-infrared spectroscopy (Yodh and Chance 1995, Villringer and Chance 1997, Boas et al. 2001). Image reconstruction consists of two parts: the forward model and the inverse solution. In the forward model, the area under study is divided into thousands of volume units called voxels. Based on the data obtained and what is known about light propagation through highly scattering medium, concentrations of oxy- and deoxy-hemoglobin in each of the voxels can be determined. Then, in the inverse solution, the voxels are simply put back together to produce an image of total hemoglobin concentration and oxygen saturation in the area under study. For a comprehensive tutorial article with an emphasis on the mathematical physics of DOT, see (Arridge, 1999)

Recently, a second signal, consisting in fast changes of the optical properties of cerebral tissue, which appears in the range of milliseconds after stimulation, has been detected (Gratton et al., 1995).

7.1 Theory of the concept

7.1.1 Brief history

In December 1977, Frans Jöbsis, a researcher at Duke University, published his seminal paper, "Noninvasive, Infrared Monitoring of Cerebral and Myocardial Oxygen Sufficiency and Circulatory Parameters," which is cited universally as the study that introduced near-infrared spectroscopy (Jöbsis, 1977). In the paper, Jöbsis described a technique with which to monitor oxygen sufficiency. His aim was to measure oxygenation of the enzyme in the brain, but because of the thickness of the skull wasn't sure whether such a thing was possible. Since measurement with near-infrared light allowed for better penetration into tissue, he eventually decided to focus on the oxidation reduction (redox) of cytochrome oxidase with an absorption peak in the near-infrared range. To test the approach, he performed an experiment in which light was transmitted from two monochromators into the head of a cat and detected with a photomultiplier tube as it exited the opposite side. The technique depends on the relatively good transparency of biological tissue in the near-infrared range, which allows for transmission of photons through the tissue. The photons can be detected when they emerge from the body, the absorption bands of oxy- and deoxy-hemoglobin and cytochrome oxidase observed and oxygen sufficiency subsequently determined.

Jöbsis later recalled how he came up with the idea behind the paper. "On December 28, 1976," he wrote in a paper presented to the First International Symposium on Medical Near-Infrared Spectroscopy, "our family menu featured a grilled chuck roast, the poor academic's substitute for steak. This very American cut of beef still contains part of the shoulder blade of the steer; a flat piece of bone perhaps 3 or 4 mm thick, about the same as the human skull. I asked my 14 yr old son Paul to clean all the muscle tissue from the bone. When he had done so we held the pink object up against the light and noticed that the shadow of a finger could easily be noted in the diffuse red light coming through the bone. If red light could, then certainly NIR light at the longer wavelengths would penetrate the human skull and provide access to the brain. Possibly other tissues could be monitored too in a minimally invasive way. We had discovered the possible existence of an optical window into the body." (Jöbsis 1999).

Initially, Jöbsis based the technique on the absorption properties of cytochrome c oxidase, but soon after the Science paper was published, he turned his attention to the absorption properties of hemoglobin. "I was trying to rid the enzyme signal of the influence of blood, which is a much stronger signal," he says. "Once I'd done that I realized that, in my hands, I had the algorithms for measuring the blood in oxygenated and deoxygenated states." Interest in the technique built slowly but surely over the following decade. In the early 1980s, several groups, as well as Jöbsis himself, reported on validation studies in which they sought to determine the efficacy and utility of what was then known variously as near-infrared spectroscopy, near-infrared spectrophotometry and niroscopy. A handful of researchers around the world picked up on the technique – particularly as it applied to the study of blood oxygenation. In Rome, Marco Ferrari and colleagues set out to explore its potential. In 1982, they presented findings from the first human studies with near-infrared spectroscopy (Giannini I et al., 1982; Ferrari M et al., 1985). The first studies to investigate possible clinical applications of the technique appeared at about the same time. In London, meanwhile, David Delpy had begun to investigate clinical applications of the technique. Delpy, who worked in neonatal intensive care monitoring, had been looking for new ways to "see" inside newborns' heads. "In 1977 or 1978," he says, "I heard Frans Jöbsis give a talk about how he'd been measuring oxygenation in the brains of cats. A cat's head is about 4.5 centimeters in diameter; the head of a premature baby is about five or six centimeters. I thought, if you can do it on a cat, with a bit of engineering you might be able to do it on the head of a baby." He was right; by the end of 1984, he and colleagues at University College, London, had designed and tested a NIRS instrument for bedside monitoring in neonatal intensive care (Wyatt et al., 1986). The group comprised of Proctor et al. conducted a series of studies in the eighties to assess the feasibility of using NIRS to monitor the effects of intracranial pressure in patients with head injuries. The researchers noted the potential benefits of using NIRS for this purpose. Later studies concluded, however, that the technique is not always suitable for the monitoring of patients with head injuries.

Further developments in the late 1980s and early 1990s helped transform NIRS into an imaging modality suitable for a wide range of applications in psychiatry and cognitive studies in general. First was the introduction of time-resolved, frequency-domain and spatially resolved spectroscopy. Originally, because they employed only continuous-wave light measured at a single point, NIRS systems could provide only relative measurements —not quantitative information about tissue oxygenation. To produce absolute measurements, researchers needed additional information, such as the length of time it takes for light to travel through the tissue being examined. Time-resolved techniques employ short pulses of light, and information about the optical parameters of the tissue is derived from the temporal distribution of the pulses. With frequency-resolved spectroscopy, the light emitted is continuous, but its amplitude is modulated – thus enabling recovery of the absorption and scattering properties of tissue. These techniques allowed for greater sensitivity and specificity of NIRS measurements, and so spurred a resurgence of interest in the modality.

Chance and colleagues hypothesized that by using picosecond laser pulses they could obtain quantitative information about the optical characteristics of the tissue (Patterson et al., 1989). Other researchers, including Delpy (Delpy et al., 1988), Enrico Gratton (Fishkin and Gratton, 1993) and Joseph Lakowicz (Sevick et al., 1992), had been working on the problem as well. The combined efforts of these researchers led to the development of time-resolved frequency-domain spectroscopy (the frequency-domain signal is the Fourier transform of the original, time-domain signal). These approaches provide for quantitative measurements of optical characteristics of the tissue and therefore offer much more robust information about oxygenation.

The second major development was the emergence of diffuse optical tomography (DOT) in the early 1990s (Arridge and Schweiger 1993; O'Leary et al., 1995). DOT enables researchers to produce images of absorption by dividing the region of interest into thousands of volume units, called voxels, calculating the amount of absorption in each (the forward model) and then simply putting the voxels back together (the inverse problem). "Light diffusion provides a mathematical formalism for imaging," says Arjun Yodh, a University of Pennsylvania researcher who, with Britton Chance, spearheaded the development of DOT. "Once one accepts the basic assumptions about transport, then it is straightforward to formulate the tomographic inverse problem."

Hundreds of studies on near-infrared spectroscopy were published during the nineties. In addition to validation studies and studies seeking to advance our understanding of how the brain works, a number of other clinical applications have been tested. The most widely investigated of these applications are monitoring of changes in oxygenation during occlusion of the carotid artery, primarily during carotid endarterectomy, and monitoring of changes in oxygenation during cardiopulmonary bypass, especially during deep hypothermic cardiopulmonary bypass and circulatory arrest. However, while a great deal of progress has been made, NIRS has not yet been widely deployed in clinical settings.

Since the late nineties, an increasing number of researchers have used NIRS in brain mapping studies, as well as in studies of clinical applications related to brain function. The former have used visual, auditory and somatosensory stimuli to identify areas of the brain associated with certain cognitive functions; other areas of investigation include the motor system and language. The latter have addressed the prevention and treatment of seizures and psychiatric concerns such as depression, Alzheimer's disease and schizophrenia, as well as stroke rehabilitation.

In addition, several groups have begun to investigate use of near-infrared spectroscopy and diffuse optical tomography in breast cancer screening and diagnosis. Optical breast imaging stands apart from other methods of breast cancer screening and diagnosis in that it focuses on the hemodynamic changes that reflect the formation and growth of tumors, as opposed to the tumors themselves. This means that it may be able to identify cancers before they are structurally evident, and therefore may contribute to further decreases in breast cancer mortality rates.

Studies such as these have been facilitated by technological advances that enable optical imaging. Until the late nineties, NIRS systems employed only one couple of source-detector pairs, enough to be able to measure hemodynamics. More recent systems have added source-detector pairs. The increased numbers of source-detector pairs have made possible imaging of hemodynamic activity.

Not only the hemodynamic response can be detected by means of NIRS. In 1997, Gratton et al. demonstrated that NIRS can also provide information regarding neural activity. They detected a new signal, termed the Event-Related Optical Signal (EROS). A fast response of the order of milliseconds that is thought to be due to changes in the scattering properties of the neuronal membranes during firing has first been measured in cultured neurons in (Stepnoski et al., 1991). Fast and localized EROSs in the human occipital cortex, elicited by visual stimuli are measured in (Gratton et al., 1997). Their results suggest that EROS manifests localized neuronal activity associated with information processing. The temporal resolution (100 ms latency) and spatial localization (sub-cm) of this signal would make it a promising tool for studying the time course of activity in localized brain areas. However, the optical response due to neural firing only yields changes of 0.01-0.1% and requires much averaging to be detected with an accuracy suitable to be used in a BMI (Franceschini and Boas, 2004).

7.1.2 Working principle: hemodynamic response

Absorption of light by colored compounds

Light passing through a solution of a colored compound (or chromophore) is absorbed by the compound and the intensity of the emerging light is therefore reduced. The relationship between the concentration of a chromophore c, its extinction coefficient α (which describes the optical characteristics of a compound at a given wavelength), the thickness of the solution d, and the ratio of incident to emergent light intensity I_0/I is given by the Beer-Lambert equation:

$$\log\left[\frac{I_0}{I}\right] = \alpha c d$$

When light of a known wavelength is used to trans-illuminate a solution of a compound of unknown concentration in vitro, the extinction coefficient and thickness of solution traversed can be substituted in the Beer–Lambert equation to derive the concentration of the substance. Spectroscopy in this form has been used for many years in colorimetric analysis and, in certain circumstances, similar principles can be applied to biological tissue.

Biological absorbers

Visible light (wavelength 450-700 nm) does not penetrate biological tissue to a thickness greater than approximately 10 mm because it is strongly attenuated as a result of powerful absorption and scattering by the tissue constituents. One of the most significant absorbers of light is water, which also has a strong absorption at wavelengths of more than 900 nm. However, there is a window of wavelengths in the near infrared region between 650 and 900 nm in which photons are able to penetrate tissue far enough to illuminate deeper structures such as the cerebral cortex (Delpy et al., 1988; McCormick et al., 1992) (see Figure 7.2).

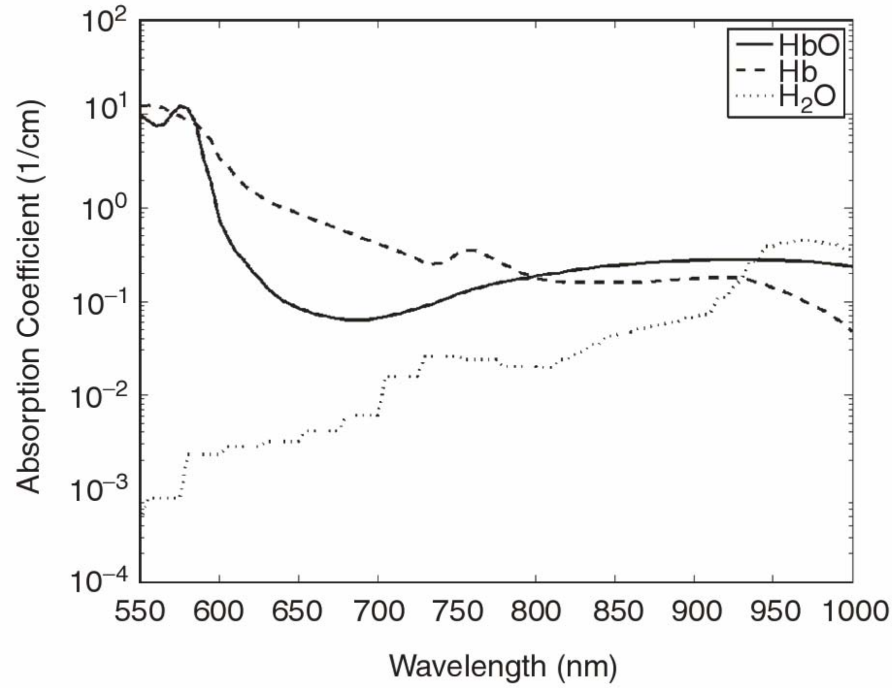

Figure 7.2: Hemoglobin and water absorption coefficients per mole as a function of wavelength. Note the relatively low absorption between 700 and 1000 nm and the crossover point around 800 nm. Data taken from (Prahl, 1999). The apparent discontinuities in the water spectrum reflect the resolution of the data when plotted at this scale and not true spectroscopic features. (Reproduced from Boas et al., 2001.)

In addition, there are compounds in the tissues whose absorption of light varies with their oxygenation status. In the near IR range, oxyhaemoglobin (HbO_2), deoxyhaemoglobin (Hb) and oxydized cytochrome oxydase (CytOx) have characteristic absorption spectra.

Effects of light scattering by tissue

The reason that the Beer-Lambert law in its simplest form cannot be applied to tissue spectroscopy is because this would require knowledge of the absolute attenuation in order to calculate absolute cromophore concentration. As tissue is a highly scattering medium, light is not only attenuated by absorption, but also by scattering away from its original linear path. The actual quantity of light lost by scattering is unknown. Total attenuation is therefore unknown and fully quantitative spectroscopy cannot be performed using conventional systems. However, it can be assumed that tissue geometry remanins unchanged during a brief NIRS measurement and because of this the degree of scattering is also unchanged. In this way, the *change* of attenuation can be calculated from the *change* in absorption, although the baseline value remains unknown.

In Figure 7.3, the light traversing the tissue sample has been both absorbed and scattered. Photon P1 still reaches the detector, though being scattered. Photon P2 passes through the tissue but is lost from the detector because of scattering.

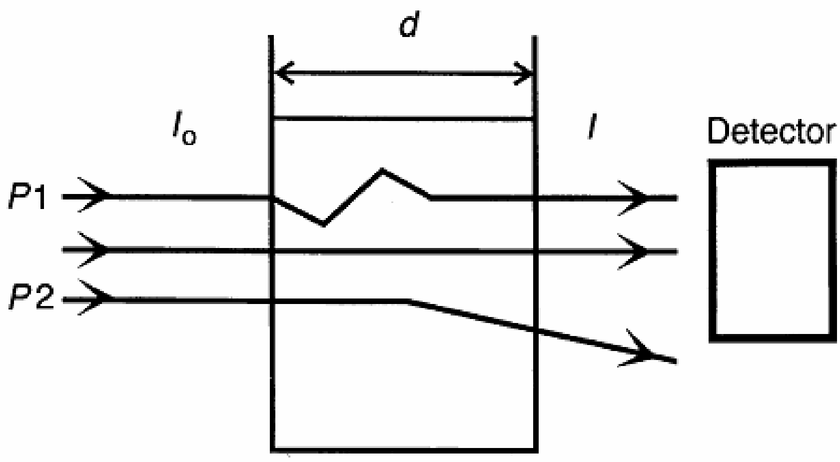

Figure 7.3: Schematic illustration of light absorption and scattering. (Reproduced from Owen-Reece et al., 1999.)

Differential pathlength factor

In addition to attenuation, tissue scattering has another significant effect. The scattered light does not reach the detector in a straight line and has to travel further through the tissue than the straight line distance *d*. In order to compute change in cromophore concentration, this additional length *d'* > *d* has to be known. The increase of distance travelled by each photon because of scattering is expressed in terms of the differential pathlength factor (DPF) (Delpy et al., 1988), which describes the *actual* distance travelled by the light. In the normal adult head, DPF is generally accepted to have a value of *d'/d*=6.3, that is light travels 6.3 times further than the straight line path. With knowledge of this pathlenght, the change in cromophore concentration can be quantified.

Knowledge of the chosen value for DPF is crucial in interpreting NIRS data. The DPF generally applied is derived from studies in healthy adults and it should be clarified that it may vary in other situations and is also wavelength dependent (Owen-Reece, 1999). DPF is 4.99 in neonatal brain, 5.51 in the adult leg and 4.16 in the adult arm, using light of 807 nm wavelength

(Duncan et al., 1995). Additionally, the effect of pathological situations, such as cerebral oedema or ischaemia, have not been investigated and clinical work to date uses one of the quoted “normal” values. DPF may also change within the same subject over a period of time if the state of the tissue (e.g. water content) or tissue geometry alters, although both are unlikely to happen during the relatively brief period during which NIRS measurements are made. New generation apparatuses may allow real-time measurements of DPF thereby removing any potential errors generated by the use of an estimated value (Delpy et al., 1988).

Quantitative methods

To summarize the considerations about optical photon transmission, Figure 7.4 visualizes the possible paths of photons through tissue and Figure 7.5 shows how probability of photon travel is distributed in a 3-D volume computational model with source and detector on the top.

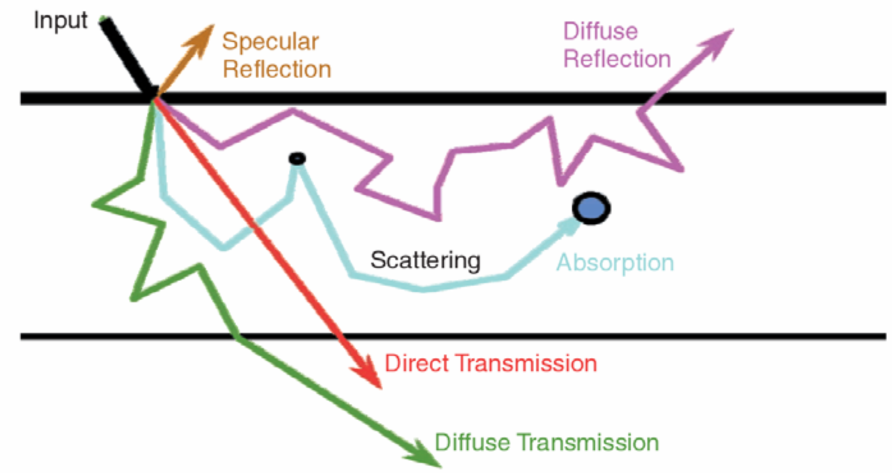

Figure 7.4: Schematic illustration of the possible path of photons through tissue. (Reproduced from Boas et al., 2001.)

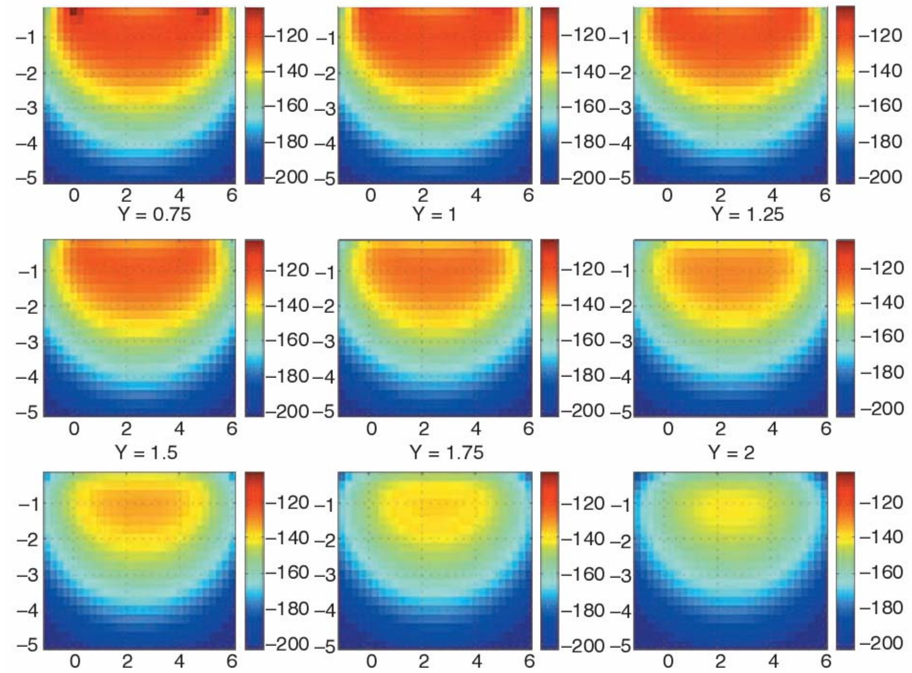

Figure 7.5: How probability of photon travel is distributed in a 3-D volume computational model with source and detector on the top. Source and detector are separated by 5 cm, each image shows a vertical slice, and distances shown are displacement of vertical slice from the line connecting the source/detector pair. (Reproduced from Boas et al., 2001.)

The description so far applies to the continuous wave approach (CW), whose major limitation, as explained, is the impossibility to compute the DPF and the need to use tabulated data for computing the differential pathlength factor. Time-resolved spectroscopy and frequency domain techniques allow to overcome these limitations, by measuring time of flight of photons or phase shift of light, respectively, the photon pathlength can be derived and quantitative measurements of chromophore concentration can be made.

Several algorithms have been published and these vary depending on the wavelengths of light used, presence of other chromophores and the precise values for absorption coefficients chosen. Recent work has applied different published algorithms to the same data set and revealed striking differences in the calculated concentration changes (Matcher et al., 1995). It is clearly important that the algorithm is known when NIRS data, collected using different equipment, are presented.

7.1.3 Working principle: neural response

The second optical signal that can be detected by means of NIRS consists of fast changes in the optical properties of cerebral tissue, which appear in the range of milliseconds after stimulation. These changes presumably are due to an alteration of the scattering properties of neuronal membranes (Gratton et al.,1995; Gratton et al.,1997; Steinbrink et al., 2000; DeSoto et al., 2001), which are simultaneous with electrical changes, cell swelling, and increased heat production (Tasaki, 1999). None of these explanations is fully satisfactory though, and there are also controversially discussed causes, like the early deoxygenation (Buxton, 2001) and some other that are summarized in (Steinbrink et al., 2005) Thus the optical signal is directly related to neuronal activity, as in EEG or MEG, which is in contrast to conventional functional NIRS, fMRI (BOLD signal) or PET, which detect only the slow hemodynamic response to neuronal activity.

Compared to the slow hemodynamic signal the fast neuronal signal is difficult to detect, because the optical changes are small and other physiological signals,such as the hemodynamic pulsatility due to systole and diastole (Gratton and Corballis, 1995) and the cerebralvasomotion at 0.1 Hz (Mayhew et al., 1996; Zheng et al., 2001), dominate. Therefore, the system has to be highly noise optimized. A recent successful attempt in detecting the fast neuronal signal by means of NIRS is described in (Wolf et al., 2002). However, more recent studies show that fast optical signals are of very low intensity and by no means robust if measured non-invasively in the human adult (Steinbrink et al., 2005). Moreover, some issues with literature are reported in that paper:

- Phase or intensity, which parameter best suits the signal detection? Despite the initial belief of phase changes being easily detectable, recent studies find that intensity changes are superior to changes in the mean time of flight due to their lower noise level.
- Optical visual evoked potentials (VEP) are smaller than first reported. Recent studies could not return a significant change in measured time of flight (or phase) after visual stimulation, whereas in the first studies the intensity of the first optical VEP reported approached the same order of magnitude as the slow response (1-25 ps).
- VEPs and SEPs share the fact that their most pronounced components have stable latencies. A retardation of the P100 in the VEP by 10 ms discriminates a healthy subjects from patients. Even when compared within individual publications, the latencies of the most pronounced peaks vary by more than 10 to 100 ms. A direct analogy of the observed optical signal changes to ERPs thus seems questionable and it cannot be excluded that they relate to motor artifacts instead.

These findings by no means doubt the existence of fast optical scatter changes in neuronal tissue (Rector et al., 1997). Moreover, a further investigation in the issue by means of invasive approaches during neurosurgical procedures is of high interest. However, the fast optical signal cannot be thought of as an alternative to EEG for measurements of fast effects related to brain activity.

7.2 Methodologies for BMI

An optical brain computer interface (OBCI) is a device, which translates physiological measures of thought processes, derived through optical interrogation techniques, into control signals capable of driving external computers independent of the peripheral nervous system. Near-infrared spectroscopy can provide information regarding both haemodynamic and neural activity. The optical response due to haemodynamic activity is a much easier signal to acquire as it leads to 1-2% changes in signal amplitude, whereas the optical response due to neural firing only yields changes of 0.01-0.1% (Fransceschini and Boas, 2004). The cerebral haemodynamic response results from an auto-regulatory process responding to the metabolic demands of neuronal firings and takes 5-8 s. The faster optical response relating to neuronal firing is of the order of milliseconds but because it is of much smaller magnitude it requires averaging techniques to achieve acceptable signal to noise ratios. Franceschini and Boas (Fransceschini and Boas, 2003) reported averaging blocks of 1000 trials and observing a 0.05% change in light intensity.

Some recent works are casting doubts on the validity of the first results reported by Gratton et al., by trying to reproduce the same experiments and measuring changes in optical properties about three orders of magnitude smaller than those reported previously by the group of Gratton and co-workers. Also they are so small that they are below the noise level of the presently available NIRS monitors (Syre et al., 2003). Also the research group in Berlin, that in 2000 published a paper with successful measurements of the fast optical signal by means of NIRS (Steinbrink et al., 2000), recently published a less optimistic view on the non-invasive detectability of these changes in the human (Steinbrink et al, 2005), motivated by an upper limit signal size estimation, predicting a signal size by orders of magnitude smaller than those previously reported. Also, they discuss the influence of small stimulus correlated movement artifacts potentially mimicking a fast optical signal.

Based on the current state of knowledge and technology, it therefore appears that millisecond-latency BMI based on NIRS are not achievable and that the only technically feasible interfaces are based on the detection of the slow hemodynamic response.

The only available publications about the real use to NIRS to build a BMI are (Coyle et al., 2003; Coyle et al., 2004). As previously pointed out, this also depends on the intrinsic delays of the slow hemodynamic response. In their BMI, Coyle et al. (see Figure 7.6) use the slow hemodynamic response, averaged over 20 s windows to achieve a bandwidth of 0.05 bps with 75% accuracy. The maximal theoretical throughput for single channel systems with improved signal processing have potential data rates which is only duble, i.e. 0.1 bps, assuming the allowance of approximately 5 s for the response to register and 5 s for the signal to return to a baseline state. Higher information transfer rates using this slow response are possible by using multiple channels.

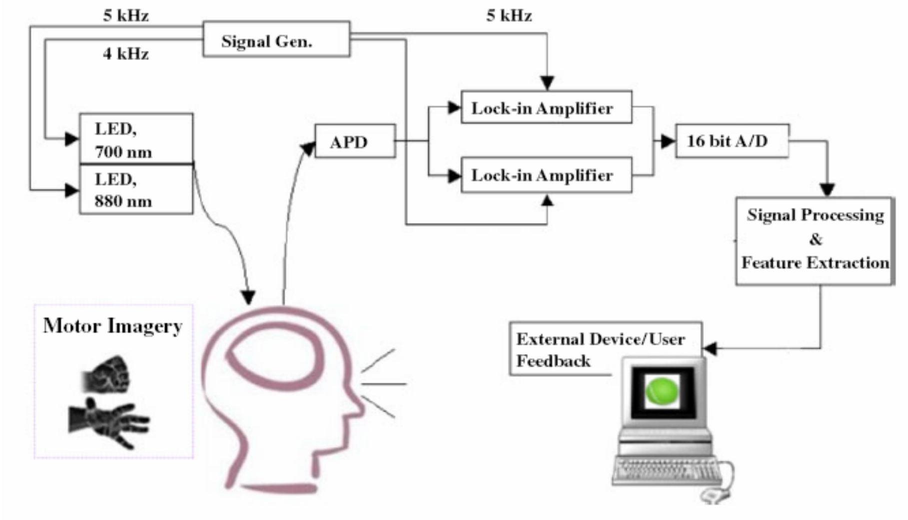

Figure 7.6: The optical BMI presented in (Coyle et al., 2004).

7.3 Hardware

There are a variety of commercially available equipment which allow tissue spectroscopy (Owen-Reece et al., 1999). It should be noted that there is a difference in the manner in which NIRS is applied to measure cerebral changes in neonates and adults. In neonates, the thin skull and small head allows light to be shone through the whole head and transmission spectroscopy is possible. In adults however, the large head and thick skull require reflectance spectroscopy where the transmitting and receiving optodes are placed a few centimetres apart on the same side of the head. The algorithms used to derive chromophore concentrations are equally valid for measurements made in both situations.

There are basic features common to all commercially available NIRS equipment Light is generated at specific wavelengths by laser photodiodes which can be detected either by a photomultiplier tube (PMT) or, in more recent equipment, by a silicon photo diode.

There are three distinct approaches to obtaining photon migration measurements (Boas et al., 2001): 1) Continuous wave illumination, 2) illumination by pico-second pulses of light, and 3) RF amplitude modulated illumination.

1. Continuous wave (CW) systems emit at constant amplitude, or are modulated at frequencies not higher than a few tens of kilohertz, and measure the amplitude decay of the incident light. As mentioned above, they do not allow to measure photon pathlength, and therefore to derive absolute chromophore concentration.
2. Short-pulse systems (Figure 7.7) detect the temporal distribution of photons as they leave the tissue. The shape of this distribution provides information about tissue optical parameters. Time-resolved spectroscopy methods then allow to make quantitative measurements of chromophore concentration.

3. In RF (Radio frequency) systems (Figure 7.8) the light source is on continuously, but is amplitude-modulated at frequencies on the order of tens to hundreds of megahertz. Information about the absorption and scattering properties of tissue are obtained by recording amplitude decay and phase shift (delay) of the detected signal with respect to the incident one. Frequency domain techniques then allow to make quantitative measurements of chromophore concentration.
4.

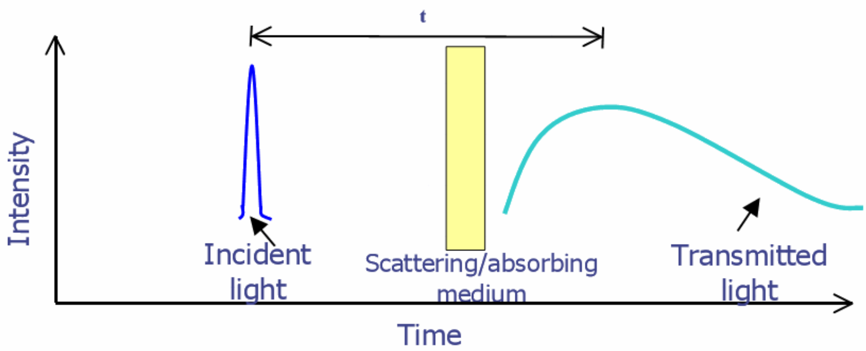

Figure 7.7: Short-pulse systems measure time of flight of the photons. (Source: WWW).

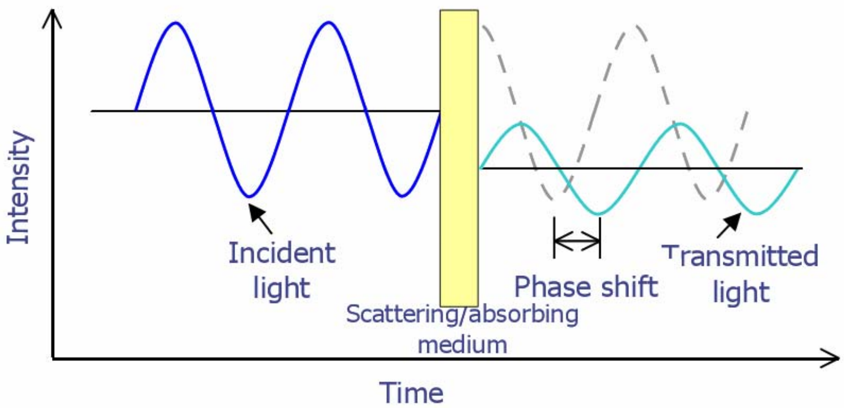

Figure 7.8: RF systems measure decay and phase shift of light. (Source: WWW).

A computer then converts the changes in light attenuation to changes in chromophore concentration. Beyond this stage, two distinct methods of data handling can be described: (1) *non-quantitative measurements – cerebral oxymetry* and (2) *quantitative concentration measurements*. They are fundamentally different but frequently confused and data from the two methods are often presented as though they were interchangeable. The performance of two commercially available spectrophotometers using these different approaches has recently been compared (McKeating et al., 1997). For more insight refer to (Owen-Reece et al., 1999).

Figure 7.9 shows a typical imaging device, together with the scheme of operation. Figure 7.10 shows a source-detector pair mounted with straps on a mockup head.

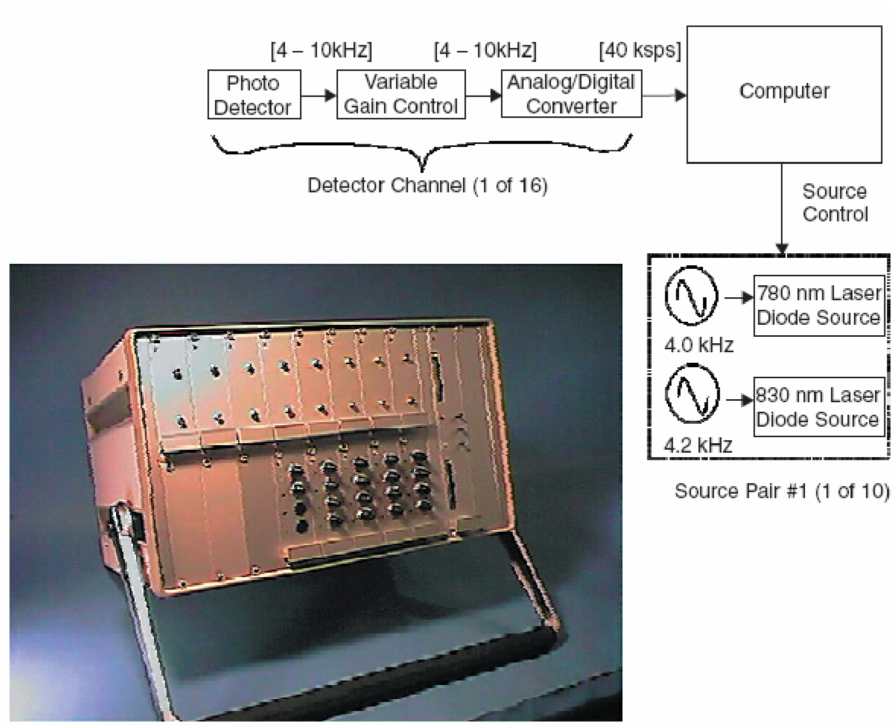

Figure 7.9: Photograph of MGH CW4 imaging device with illustration of operation. (Reproduced from Boas et al., 2001.)

Figure 7.10:Home-made source-detector pair mounted with straps on a mockup head. (Source: WWW).

Currently there are no maximum permissible exposure (MPE) for skin values specified for LEDs (Horak, 1999). Nevertheless, the MPE of skin for a laser at 880 nm, for an exposure time up to 8 hours, is 4.6 mW mm^{-2}.

For of a home made NIRS equipment to serve as a BCI, CW systems are the most accessible. They allow qualitative measurements of sufficient accuracy to investigate events of functional brain activity. For the custom design of the CW system, the following points should be observed:

- Choose light source & output power suitable for CW measurements.
- Given an attenuation of 7-9 orders of magnitude, choose a suitable detector.
- Design associated driving circuits, they must encode individual sources.
- Investigate ways of connecting source and detector to the head.

7.4 Current applications

There are a number of possible applications of NIRS. While most of these involve monitoring of oxygen sufficiency in the brain, studies published in the past several years have tested applications related to functional brain monitoring and brain mapping. We have already seen exciting results from these cutting-edge applications.

One of the most exciting of these applications is in brain mapping studies. Studies have used visual, auditory and somatosensory stimuli to identify areas of the brain associated with certain cognitive functions and to investigate hemodynamic activity in those areas. Other areas of investigation include the motor system and higher cognitive functions such as speech recognition. Studies such as these already have provided a wealth of information on brain function, and NIRS has the potential to unlock a great many more secrets about how the brain works – possibly offering direct measures of neuronal and metabolic as well as hemodynamic processes.

NIRS also has been tested in the prevention and treatment of seizures and psychiatric concerns such as depression, Alzheimer’s disease and schizophrenia, as well as stroke rehabilitation. The technique already has provided useful information on the pathophysiology of these conditions, and early studies of its clinical feasibility have shown promising results.

Another exciting application is optical breast imaging. Optical breast imaging stands apart from other methods of breast cancer screening and diagnosis in that it focuses on the hemodynamic changes that reflect the formation and growth of tumors, as opposed to the tumors themselves. This means that it may be able to identify cancers before they are structurally evident, and therefore may contribute to further decreases in breast cancer mortality rates.

The theoretical and technological advances of the past 10 to 15 years have opened the door to a range of applications, including some that involve imaging of the adult brain, which for many years had been inaccessible to NIRS. “Probably the hottest topic at the moment,” says Delpy, “is use of the system for monitoring brain activation in functional brain studies." Researchers have known for decades that performing tasks and processing various stimuli produce corresponding changes in the brain, be they neuronal, metabolic or vascular. Functional magnetic resonance imaging and positron emission tomography are commonly employed to image the changes. But these modalities are, in some ways, limited in application: FMRI requires that the subject lie relatively still in a narrow tube-like space, while PET relies on ionizing radiation dyes as contrast agents. NIRS employs no ionizing radiation and allows for a wide range of movement; it's possible, for example, for the subject to walk around a room while wearing a NIRS probe.

Since the mid-1990s, an increasing number of researchers have performed functional brain studies with near-infrared spectroscopy. They have investigated cerebral responses to visual, auditory and somatosensory stimuli, as well as the motor system and language, and subsequently begun to construct maps of functional activation showing the areas of the brain associated with particular stimuli and activities.

7.5 Foreseen improvements

<u>The drive to portability</u>

Technology has kept pace with advances in the mathematical methods to solve the problems of estimating the paths of photons. Over the years, designers of NIRS systems have added multiple sources and detectors, leading to increased coverage of areas of interest, and improved the systems' sensitivity and specificity. At the same time, individual components have become smaller and more reliable. NIRS systems today often consist of little more than a probe with fiber optic sources and detectors, a piece of dedicated hardware no larger than a small suitcase and a laptop computer. Thus, researchers and clinicians can count on a degree of portability unavailable – even inconceivable – for other imaging modalities, such as functional magnetic resonance imaging (Boas, 2004). In the future, further technological advances will lead to even smaller and more sensible systems, making NIRS, together with EEG, the leading choices for portable BMIs.

<u>The future</u>

NIRS isn't yet ready to be introduced into the clinic. Large-scale clinical trials are required to show that the technique has sufficient sensitivity and specificity, as well as predictability. In addition, clinicians need to know how to understand the NIRS signal: most have never looked at a signal that contains information about tissue oxygenation. Although it may be some time before clinical acceptance, it is already clear that NIRS can contribute to an array of applications, noninvasively, continuously and at bedside. Indeed, it seems that the history of this technique is just beginning (Boas, 2004).

The current challenge is twofold: in the near-term the challenge is to provide compelling evidence of its potential on clearly relevant applications such as detection of breast tumors and functional imaging of the brain. In parallel with this effort, in the longer-term the challenge is to develop better imaging devices, physical models, inverse reconstructions, and associated efficient algorithms, to extract the information which the multiply-scattered light is now known to possess. In particular, we believe there may be a role to play for many sophisticated image reconstruction and signal modeling techniques developed in the signal processing community for other purposes. Careful attention must be paid, however, to the integration of such techniques with appropriate models of light propagation to achieve useful and reliable results (Boas et al., 2001).

7.6 Outline on the suitability for space applications (pros and cons)

Concerning the applicability of NIRS to BMI, it must be said that the major limitation of the technique is intrinsically in the nature of the physiological process it measures: interfaces using the slow hemodynamic response are too limited for any practical application for normally-able people. They suffer from a latency of the physiological response of 5-8 s, which has to be averaged to achieve a suitable accuracy (20s of averaging for 75% accuracy) (Coyle et al., 2004), which leads to a bandwidth of 3 baud min^{-1}. The bandwidth could be improved by adding more channels and obtaining more bits per baud. However, if compared to the throughput of conventional interfaces, like keyboards and joysticks, or even interfaces to the peripheral nervous system, such as electromyography (EMG), it appears evident that, unless new methods and detectors will be able to measure the fast optical signal with sufficient robustness and without long time averaging of the order of minutes, NIRS is only theoretically suitable for real BMI applications.

7.7 Worldwide researching groups

The use of NIRS for BMI is a novel application and has not been investigated extensively yet. Its usefulness is also questionable, since NIRS at the current state of knowledge does not provide clear advantages over other portable BMI methodologies such as EEG. The known groups that have published papers on BMI using NIRS are listed below. However, due to the novelty of the application, it is likely that publications from other researching groups are currently in the review stages and will appear soon. Many other research groups, not dealing directly with NIRS for BMI, can be found in the affiliations of the papers in the bibliography.

7.7.1 Europe

- Dr. Tomás Ward, Shirley Coyle
  Biomedical Engineering Research Group
  Department of Computer Science
  National University of Ireland, Maynooth
  http://biomed.eeng.may.ie/

- Some activity, maybe only at educational level, has been spotted at
  ICT Department
  Università di Trento, Italy
  http://dit.unitn.it/research/seminario?id=DIT-SMN-06-05-179

7.7.2 Asia

- Dr. Cuntai Guan
  Institute for Infocomm Research
  Neural Signal Processing Lab
  http://psp.i2r.a-star.edu.sg/nsp/Research%20projects.htm

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8. Magnetoencephalography (MEG)

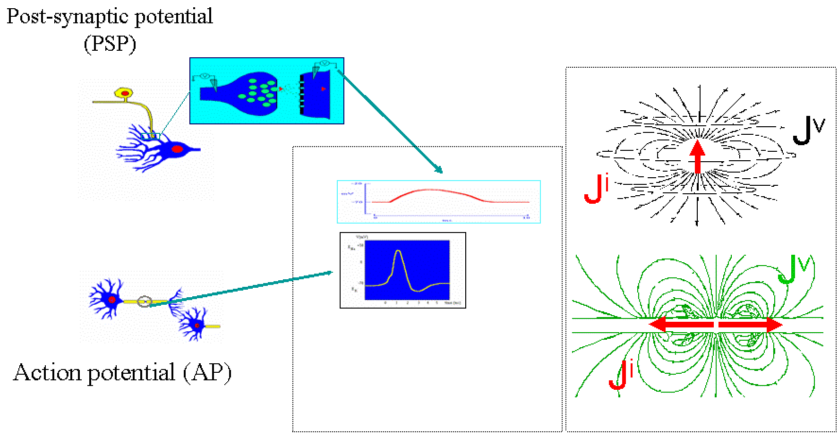
As main topics they are considered: the relationship between the magnetic field and its generators (8.1), including on one hand the neurophysiological basis and the physical theory of magnetic field generation, and on the other hand the analysis techniques for the estimation of the sources from the magnetic field measurements; moreover the instrumental techniques and the laboratory practice of neuromagnetic field measurement (Del Gratta et al., 2001). The main application of MEG for BMI is cited (8.2), with indications of signal measurement, conditioning and interpretation methods to control external machines. Worldwide active researching groups are listed (8.3). An evaluation of the suitability for space application is suggested (8.4).

8.1 Theory of the concept

Magnetoencephalography (MEG) is the technique allowing the measurement and the analysis of the tiny magnetic fields generated outside the scalp by the working human brain, mainly by post-synaptic potentials of synchronously firing neurons at rest and during processing (Del Gratta et al., 2001).

8.1.1 Generation of neuromagnetic fields

The identification of a specific electrical source configuration from a measured distribution of electric potentials and/or magnetic fields—namely the inverse problem—represents one of the most challenging aspects investigators face when trying to interpret biomagnetic signals. Indeed, the inverse problem has no unique solution, since an infinite number of source configurations can account for the measured field distribution. The introduction of some constraint, such as a specific mathematical model to be used as the signal source, permits one to solve the problem and achieve source identification. In order to understand the motivations that suggest the use of a specific model rather than some other one, it has been necessary to consider the mechanisms underlying the physiology of neural cells, in particular, the origin of action potentials and their propagation along the nervous system, and the synaptic connection as well as the generation of postsynaptic potentials. By taking into account the properties of this neuro-electric phenomena and the spatiotemporal characteristics of the induced magnetic field, it has been demonstrated that MEG signal comes mainly from post-synaptic potentials (Figure 8.1), being they excitatory (EPSP) or inhibitory (IPSP) .



	Duration time	Field intensity as a function of distance r
PSP	≈10 - 100 ms	$1/r^2$
AP	≈ 1 ms	$1/r^3$

Figure 8.1: Time duration and magnetic filed intensity as function of distance for post-synaptic potential (PSP) and action potential (AP). J^i indicates intracellular current density, J^v the volume current. Note that both longer duration and smaller reduction with increasing distance from the source render the PSP more effective than AP in MEG signal.

Moreover, a net extra-cranial magnetic field is generated only if intra-cellular currents does not sum to zero for geometrical reasons, i.e. in the case the currents flow prevalently in a specific direction. This occurs only for neuronal cells with dendrites with non-spherical geometries, i.e. pyramidal neurons (Figure 8.2.a), which are positioned in columnar structure, perpendicularly to the cortical surface (Figure 8.2.b). Taking into account that in a spherical model, a current source generates external magnetic field only if it flows in tangential direction to the sphere surface (Figure 8.2.c), we achieve knowledge that main source of MEG signal is the net effect of PSPs impinging on pyramidal neurons within the walls of cortical giri (Figure 8.2.d).

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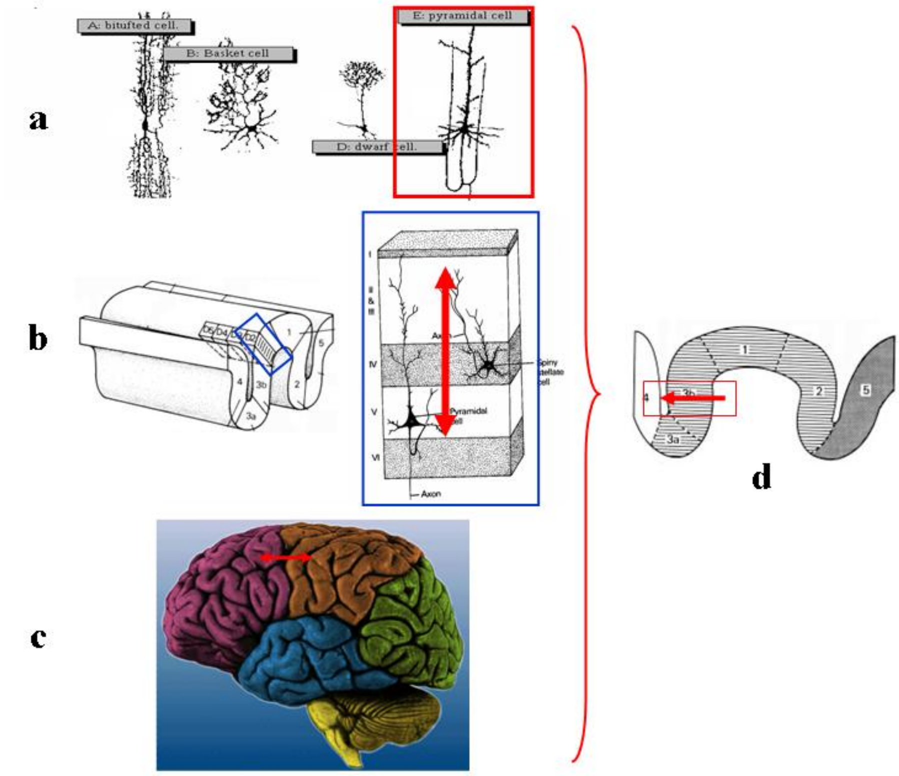

Figure 8.2: a Main kind of neuronal cells in cortical areas. b Indication of pyramidal cells positioning with respect to the cortical layer (red arrow). c Indication of current source direction generating extra-cranial magnetic field. d Indication of main source of MEG signal, i.e. activity of pyramidal neurons within the walls of cortical giri (red arrow,in the example the posterior wall of the central sulcus is shown).

8.1.2 Magnetic field source estimate

Forward problem

The bioelectromagnetic field theory that is relevant to the modelling of neuromagnetic data. The topics of this section are the statement of the assumptions that simplify Maxwell’s equations in the description of the neuromagnetic field. The subject of bioelectric and biomagnetic field theory is extensively treated in the literature. For a comprehensive description, and for related topics, the books by Gulrajani (1998), Malmivuo and Plonsey (1995) are suggested.

The quasi-static approximation of Maxwell’s equations

The assumptions adopted to simplify Maxwell’s equations will be clarified, based on the physical properties of the head as a conductor, and of the currents flowing in it as a result of neural activity. The general theoretical context in which neuromagnetic phenomena are described is that of electromagnetic theory of continuous macroscopic media. Maxwell's equations for polarizable and magnetizable media are given by

$$\mathrm{curl}\ E = -\partial B/\partial t \qquad (1)$$

$$\mathrm{curl}\ H = J + \partial D/\partial t \qquad (2)$$

$$\mathrm{div}\ D = \rho \qquad (3)$$

$$\mathrm{div}\ B = 0 \qquad (4)$$

where E and H are the electric and magnetic field respectively, D and B are the electric displacement and the magnetic induction respectively and ρ and J are the electric charge and electric current density respectively.

From equations (2) and (3) follows the law of conservation of charge:

$$\mathrm{div}\ J + \partial \rho/\partial t = 0 \qquad (5)$$

To the above equations we must add the constitutive relations that describe the macroscopic electric and magnetic properties of the media. As will be seen in the following, the bioelectric and biomagnetic fields are weak enough to justify the assumption that the constitutive relations are linear:

$$D = \varepsilon E \qquad (6)$$

$$B = \mu H. \qquad (7)$$

We shall further assume that the tissue is isotropic, so that the electric permittivity ε and magnetic permeability μ are represented by scalars. In the more general linear case, these quantities are represented by symmetric tensors of rank two. The magnetic permeability may be practically considered to be equal to the magnetic permeability of vacuum, since most living tissue is only weakly diamagnetic, with a magnetic susceptibility close to that of water ($\chi = -9 \times 10-6$), so that $\mu = (1 + \chi)\mu0 \approx \mu0$.

We are interested here in the electric potential and the magnetic field generated by bioelectric currents flowing inside the head. The latter are represented by the current source density J of equations (2) and *(5)* which is defined in some region of space—called the volume conductor—where an electric conductivity function σ is also defined. Here, again, σ will be considered to be a scalar function, implying that the conductivity is isotropic. We consider that the currents consist, on one hand, of active ion displacements related directly to electrochemical cell activity—such as ions crossing the cell membrane or flowing in a dendrite, and, on the other hand, of the passive displacement of free ions under the action of the electric field generated in the surrounding tissue by cell activity. The former are usually termed impressed currents, while the latter are called volume currents. Therefore the current density at any point in the conductor will be expressed as the sum of two terms:

$$J = J^i + J^v \qquad (8)$$

where the superscripts stand for the impressed and volume current density respectively. From the generalized form of Ohm's law:

$J^v = \sigma E.$ (9)

We obtain

$J = J^i + \sigma E.$ (10)

Let us now examine equation (2) , taking equation (10), into account:

$\mathrm{curl}\, H = J^i + \sigma E + \partial D/\partial t$ (11)

We shall now show that the intensity of the displacement current density is negligible compared with the volume current density in the usual range of frequencies of neuromagnetic fields, extending from dc to about 10^3 Hz, when we include signals due to action potentials such as those propagating in the brain stem or in the peripheral nervous system. Let us consider a sinusoidal component of the impressed current density at frequency f . Then the electric field in the volume conductor will also be sinusoidal. The second and third terms on the right-hand side of *(11)* may be expressed as

$\sigma E = \sigma E_0 \sin (2\pi f\, t)$ (12)

$\partial D/\partial t = 2\pi f\, \varepsilon E_0 \cos (2\pi f\, t).$ (13)

The displacement current term *(13)* may therefore be neglected if $f \ll \sigma/(2\pi\varepsilon)$. This condition is satisfied for frequencies lower than a few thousand hertz. In fact, to estimate a lower bound for the quantity $\sigma/(2\pi\varepsilon)$, we may consider limiting values for σ and ε. For brain tissue, $\sigma > 10^{-1} \cdot \Omega^{-1} \cdot \mathrm{m}^{-1}$, and $\varepsilon \le 5 \cdot 10^4 \cdot \varepsilon_0$, yielding $\sigma/(2\pi\varepsilon) \ge 36\,000$ Hz.

Then, we shall show that Faraday induction in equation (1) contributes negligibly to the electric field at the usual frequencies of neuromagnetic phenomena. Let us consider the integral form of this equation and use it to calculate the circulation, around a circular path of radius R, of the electric field E induced by a uniform oscillating magnetic field $B = B_0 \sin(2\pi f\, t)$ inside the head. From this circulation, the intensity of the induced electric field may be obtained:

$E = \pi R f\, B_0 \cos (2\pi f\, t).$ (14)

Typical intensities of the neuromagnetic field, measured outside the head, range from $10^{-13}\,\mathrm{T}$ for evoked fields to $10^{-12}\,\mathrm{T}$ for alpha activity. In the latter case, we may extrapolate a mean value for B_0 inside the head of $10^{-9}\,\mathrm{T}$. Taking 0.1 m for R, and 100 Hz for f, we obtain for the induced electric field $E \approx 10^{-8}\,\mathrm{V\,m^{-1}}$. On the other hand, typical potential differences measured over the scalp are about $1\times10^{-6}\,\mathrm{V}$, from which a value of $10^{-5}\,\mathrm{Vm^{-1}}$ may be estimated for the corresponding electric field. As we can see, the induced electric field is three orders of magnitude smaller than the latter figure and can therefore be neglected.

The above considerations show that the terms with time derivatives contribute negligibly to the fields. However, these terms do not act only as sources of the fields, since their presence in Maxwell's equations implies a dephasing of the fields with respect to the sources due to capacitance in the tissues, or to finite signal propagation velocity, as well as a reduced intensity of the fields in the case of capacitive impedance, with respect to pure resistance. All these effects have been shown to be negligible in the case of bioelectric and biomagnetic fields on the basis of the estimated tissue conductivity and electric permittivity values. A detailed discussion of this topic would be too long to present here, but may be found in the work of Gulrajani (1998, pg 192).

In conclusion, we may neglect in Maxwell's equations the terms corresponding to the displacement current and to Faraday induction. We are then left with the quasi-static Maxwell equations, that may be taken as the basis for a description of biomagnetic phenomena.

$$\text{curl } E = 0 \tag{15}$$

$$\text{curl } B = \mu_0 J \tag{16}$$

$$\text{div } E = \rho/\varepsilon \tag{17}$$

$$\text{div } B = 0. \tag{18}$$

The equation for the conservation of charge becomes

$$\text{div } J = 0. \tag{19}$$

Magnetic field and electric potential in an infinite homogeneous medium

To derive some basic properties of the electric potential and the magnetic field generated by bioelectric currents, we shall restrict the derivation to the simple case of an infinite homogeneous medium. This means that the volume conductor extends to infinity and its conductivity is uniform. It may be shown that

$$B(x) = \frac{\mu_0}{4\pi} \int J(x') \times \frac{x - x'}{|x - x'|^3} dv' . \tag{20}$$

It may be shown, that this formula has general validity, including the case where *(10)* is satisified but the conductivity is non-homogeneous. This formula is also known as the Ampère–Laplace law, which is the current density counterpart of the Biot–Savart law for current carrying wires.

In particular, for the most simplesource model, te so called single Equivalent Current Dipole (ECD) Q the formula *(20)* becomes:

$$B(x) = \frac{\mu_0}{4\pi} \frac{Q \times (x - x_0) \cdot e_r}{\left| x - x_0 \right|^3} . \tag{21}$$

Inverse problem

After having defined the forward-problem in MEG, we turn to a description of some of the methods for the solution of the inverse problem —i.e. the inference of neural current sources from magnetic field measurements over the scalp— which is the goal of MEG. As already mentioned, the bioelectromagnetic inverse problem has no unique solution. This was first observed by Helmholtz in 1853. Mathematically, this may be understood as a consequence of the existence of silent sources. For example, a radial current dipole in a homogeneously conducting sphere is a magnetically silent source. Thus, the addition of a silent source to a solution of a particular neuromagnetic inverse problem yields another solution of the same problem. Therefore, to find a practical solution in any particular case, the variability of the source is usually restricted.

There are principally two ways to do this. One is to assume a source model that is characterized by a small number of parameters so that the specification of the magnetic field at a sufficient number of points in space defines the source uniquely. Examples of such models are the single or multiple ECD, or the multipole expansion (Marquardt 1963; Mosher et al., 1992). The second involves assuming a more complex source model, allowing a larger variability, and then imposing constraints on the solution so that it is the unique solution satisfying a prescribed criterion. Usually, the source model used in this case is a current dipole field, i.e. an array of a large number of current dipoles with fixed position. The problem is then a linear one, since only the momenta of the current dipoles must be found. Therefore the methods of linear inverse estimation are used. To these different models correspond different techniques for the solution of the inverse problem (low-resolution electromagnetic tomography LORETA, Pascual-Marqui et al., 1995).

8.1.3 Instrumentation for MEG

The challenge for biomagnetic instrumentation is the detection of extremely weak magnetic signals (1 fT to 100 pT) in the presence of a very noisy background (~ 10 μT and above). Properly designed instrumentation must therefore be endowed with sensitive magnetic field detectors, and sophisticated noise cancellation techniques. Another aspect is represented by the suitability for clinical application of the technique, where the necessity of measuring the magnetic field over the entire area of the head is mandatory for a practical clinical use of neuromagnetism.

In the last 10-15 years several large multichannel sensors have been developed, and today about 100 institutions worldwide currently use neuromagnetic systems. Most of the systems used by the experimenters and/or clinicians are produced and sold by two companies: 4-D

Neuroimaging (9727 Pacific Heights Boulevard, San Diego, CA 92121-3719, USA— www.4dneuroimaging.com), a new company resulting from the acquisition of Neuromag Ltd by the former Biomagnetic Technologies Inc, and CTF Systems Inc. (15-1750 McLean Avenue, Port Coquitlam, B.C., Canada V3C 1M9—www.ctf.com); but other companies or single institutions have also developed their own devices. There are several published papers covering different aspects of biomagnetic instrumentation. Some of the best up-to-date documentation for biomagnetic instrumentation is the BIOMAG conference proceedings (Yoshimoto et al 1999).

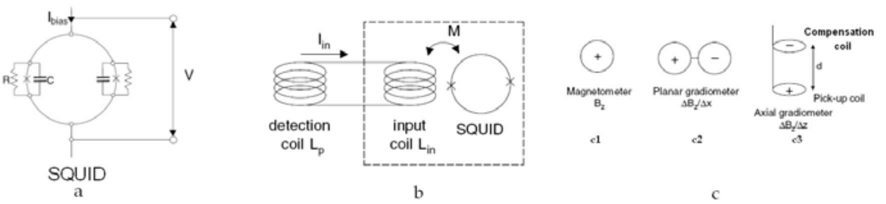

Figure 8.3: a Schematic diagram of a dc SQUID. The Josephson junction is denoted by a cross. The capacitor is due to the stray capacity of the junction, while the resistor is added to remove the hysteretic behaviour of the junction itself. b Schematic diagram of a SQUID loop with the flux transformer. The dashed box is integrated on a planar chip. The magnetic field is sensed only by the detection coil, while the SQUID loop is coupled only to the input coil. c Different types of detection coil.

Main components of a MEG system are:

1) the active sensor, called **superconducting quantum interference device (SQUID)**. SQUID devices are used in all neuromagnetic systems. Their principles of operation rely on two phenomena observed in superconductors: the quantization of the magnetic flux through a loop, that must be an integer multiple of $\Phi_0 = \frac{h}{2e} = 2.07 \times 10^{-15}$ Wb; and the Josephson effect. Indeed, the first SQUIDs were built after the prediction by Josephson (1962) that in superconductors Cooper pairs (pairs of electrons which are the charge carriers of the supercurrent) may tunnel across an insulating barrier. This phenomenon is named the Josephson effect, and the barrier is named the Josephson junction. The dc SQUID is realized by combining two junctions in parallel (see Figure 8.3.a), and its principle of operation is based on the interference of the phase of the wavefunction describing the condition of a Cooper pair across each junction. In practice, it is not convenient to use the SQUID loop to directly sense the field, mainly because the SQUID inductance must be small in order to minimize the noise of the detector. Additionally, it is convenient to use a separate detection coil to sense the external magnetic field, because in this way it is possible to change the field spatial sensitivity of the device without affecting the SQUID design. The magnetic flux sensed by the detection coil is transferred to the SQUID through an input coil

which is often built directly onto the SQUID chip (see Figure 8.3b). It is worth noting that the entire flux transformer—detection coil and input coil—is a superconducting loop. Thus, the external magnetic field induces a current in this loop which is proportional to the field itself. The simplest detection coil, namely a magnetometer, could be easy integrated within the SQUID chip, thus simplifying the construction of complex multichannel biomagnetic systems. Specific geometries for the detection coil may reduce conveniently the sensitivity to noise sources, with little loss of sensitivity for the biomagnetic sources of interest. The most used detection coil of this type is the first-order gradiometer (axial or planar, see Figure 8.3c), which is made by adding two magnetometer coils wound in an opposite sense. A room-temperature SQUID readout electronics is needed to make the sensor output a linear function of the applied flux. It varies according to different SQUID features: a more complex scheme exhibits better performance in terms of noise, dynamics and slew rate, but exhibits more integration problems; a simpler design is easily integrated but the above features are not as good. A common feature to all SQUID electronics is the flux-locked loop (FLL) configuration, where the working point of the SQUID, identified by a bias flux Φ_B and a bias voltage V_B, is maintained fixed by a negative feedback.

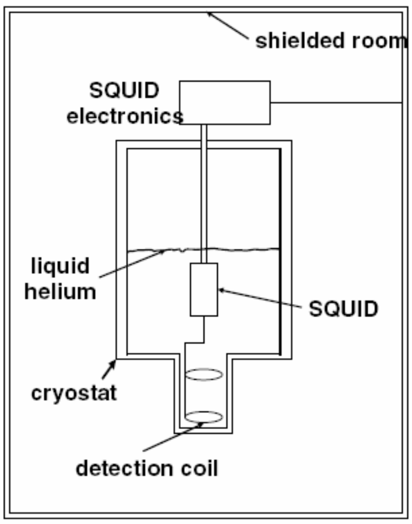

Figure 8.4: Schematic diagram of a single-channel neuromagnetic system.

2) **The cryostat**. Unfortunately, superconductivity shows up only at a very low temperature, and therefore the SQUID detector must be cooled for proper operation (Figure 8.4). All currently used large neuromagnetic systems use low-temperature superconductors materials, hence liquid helium is used as cooling fluid to reach a temperature of 4.2 K. The cryostat (dewar) enclosing the probe is a

critical part of the instrument and must satisfy severe requirements: (i) the material used for fabrication must be nonmagnetic; (ii) the magnetic noise must be less than the noise of the sensors and (iii) the distance of the detection coils from the head of the subject must be as small as possible.

3) **The shielded room** In the frequency range of interest for biomagnetic measurements, the problem of shielding can be analysed in a quasi-static approximation in terms of a magnetic circuit. The soft magnetic material (iron alloys with μ > 104) acts as a 'high-conductivity' conductor for the magnetic flux, as compared with the conductivity of the space enclosed in the shielded room. In this way a large part of the flux is concentrated in the walls and only a small part can enter the room. The total shielding factor is related to the total amount of the soft magnetic material used, and to the number and mutual distance of the layers in which the material is shaped. The shielding effect relies also on eddy current shielding (Figure 8.4).

8.2 Current applications

MEG detects brain signals more locally than EEG because neuromagnetic signals are not distorted by the concentric inhomogeneities of the tissue between the current sources and sensors. BMIs based on single-trial MEG activity detected on the sensorimotor cortex and related to the left/right finger movements are being developed and experimented. With respect to BMI efforts, usually focused on using either invasive implanted electrodes or training-extensive conscious manipulation of brain rhythms to control prosthetic devices, in a recent paper an excellent prediction of movement trajectory by real-time MEG was demonstrated (Georgopoulos et al., 2005). In healthy humans, copying a pentagon for 45 s using an X-Y joystick while MEG signals were being recorded from 248 sensors, a linear summation of weighted contributions of the MEG signals yielded a predicted movement trajectory of high congruence to the actual trajectory (median correlation coefficient: r=0.91 and 0.97 for unsmoothed and smoothed predictions, respectively). This congruence was robust since it remained high in cross-validation analyses (based on the first half of data to predict the second half; median correlation coefficient: r=0.76 and 0.85 for unsmoothed and smoothed predictions, respectively).

One of the more demanding task when developing MEG/EEG-based brain robot interfaces, is the extraction of different level values of a cerebral index in the shortest time period. Taking into account that MEG/EEG literature reports that independent component analysis (ICA) approach allow single-trial analysis (Makeig et al., 2002; Lee et al., 2003), an innovative cerebral source extraction method was developed, from MEG signals (Barbati et al., Hum Brain Mapp in press) It is obtained by adding a functional constraint to the cost function of a basic independent component analysis (ICA) model, defined according to the specific experiment under study, and removing the orthogonality constraint, (i.e., skipping decorrelation of each new component from the subspace generated by the components already found). To be noted, being the sources obtained one by one in each stage applying different criteria, the a posteriori ‘interesting sources selection’ step required by ICA procedures is avoided. Source activity is obtained along different cerebral processing states: in this way, the cerebral source can be extracted by requiring a specific behaviour during the maximal activation period, and its activity is obtained also in other cerebral states. It could be hypothesized that by this procedure, the differentiation of different levels of the cerebral source could be realized in single trials, after a setting and calibration period.

8.3 Worldwide researching groups

The Domenici Research Center for Mental Illness, Brain Sciences Center (11B), Veterans Affairs Medical Center, One Veterans Drive, Minneapolis, MN 55417, USA http://www.brain.umn.edu/index.htm. In particular Prof. Apostolos Georgopoulos (omega@umn.edu). Application to motor control.

Brain Research Unit, Helsinki University of Technology
http://neuro.hut.fi/. In particular Prof. Riitta Hari and Veikko Jousmaki.

http://www.lce.hut.fi/research/css/bci/. In particular researchers Mikko Sams and Laura Kauhanen.

http://www.mp.uni-tuebingen.de/mp. Eberhard Karls University, Dept. of Medical Psychology and Behavioral Neurobiology and Max-Planck-Institute for Biological Cybernetics, Dept. of Empirical Inference, Tubingen, Germany. In particular researchers Niels Birbaumer, Thilo Hinterberger, Hubert Preissl.

8.4 Outline on the suitability for space applications (pros and cons)

Staring in 1985, in addition to a variety of man-machine interface concepts developed in an attempt to increase the flow of relevant information between the system and operator, and alleviate the need for complex, programmer-oriented inputs through the use of user-friendly workstations, the feasibility of using brain wave sensing for computer control has been explored. In this regard, brain wave output from the human operator would serve as a machine input via an appropriate interpreter and interface device. Recently (Navin Lal et al 2005) machine learning techniques has been used to derive a classifying function for human brain signal data measured by Magnetoencephalography (MEG), for the use in a BCI. This has been helpful for evaluating quickly whether a BCI approach based on electroencephalography, on which training may be slower due to lower signal-to-noise ratio, is likely to succeed. The Authors applyed Recursive Channel Elimination (RCE) and regularized Support Vector Machine (SVM) to the experimental data of ten healthy subjects performing a motor imagery task. They demonstrated that 4 subjects were able to use a trained classifier to write a short name. Further analysis gave evidence that the proposed imagination task is suboptimal for the possible extension to a multiclass interface. The relevance of this approach is that MEG shows a better signal quality than EEG and therefore promises increased learning effects. Since the brain signals exploited by MEG and EEG are fundamentally the same, however, it could be hypothesized to transfer from an MEG-BCI to a more portable EEG based system at a later training stage. For this to work, a machine learning technique has to be established that is applicable for both types of data. A promising candidate is the EEG-based BCI described by Lal and colleagues (2004), since it shows convincing results, and it is able, due to its built-in feature selection procedure, to work with a low number of recording channels which is important for realtime scenarios.

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9. Invasive BMIs

9.1 Theory of the concept

We can think about "Invasive BMIs" as interfaces that require some kind of invasive procedure. Following this definition, also BMIs that rely upon the use of contrast agents or radioactive tracers, fall into this category.

Nevertheless in the research community the term "Invasive BMI" is commonly used to refer to "Direct BMIs" (Donoghue, 2002). These are intracortical recording systems that capture the action potentials of many individual neurons (especially those that code for movement or its intent) and decode this neural activity to infer the movement executed or imagined by the user (Figure 9.1).

The idea of directly connecting an artificial device to a living brain has always fascinated the human being. In experiments carried on in the 1950s, electrodes have been implanted in the cortex of humans and animals for recording or stimulation purposes (Delgado et al., 1952). These first attempts often allowed the spectacular "control" of an animal's motor behaviour. Since then, researchers in neurophysiology have coupled devices to the nervous system of alert primates and other animals to record its electrical activity, and thereby infer its function, or to modify its function by

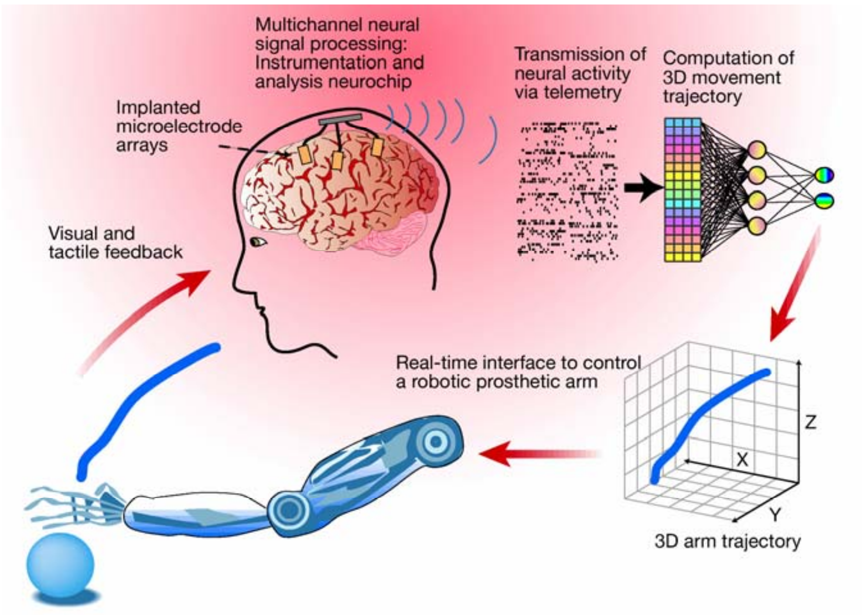

Figure 9.1. Hypothetical BMI for the control of a robotic arm. A set of chronically implanted microelectrode arrays gathers the activity of ensembles of neurons. The neural activity is fed to a computational algorithm that reconstructs a 3-D trajectory to control the prosthetic arm. A closed loop is established by providing the user with both visual and tactile feedback. (Reproduced from Nicolelis, 2001).

stimulating it electrically.

Today, physical devices are implanted in the human brain for therapeutic purposes for the treatment of neurological disorders in people for whom the available drugs have failed to work. Deep brain stimulator implants are often effective to relieve the tremor, rigidity and bradykinesia of Parkinson's disease by altering basal ganglia activity (Benabid et al., 2001). While these and other uses of electrical stimulation allow physicians to alter brain function by injecting a signal, they do not establish a communication channel for the subject.

With the exponential evolution of computing systems and algorithms, several research groups have started to look into the potential applicability of cortical interfaces for this more demanding application: to establish a communication channel between the subject and an artificial device. Such BMIs, BCIs, or neural prostheses might help to restore abilities to patients who have lost sensory or motor function because of disease or injury by extracting signals directly from the brain (Friehs et al., 2004). The artificial device can serve as a substitute for the damaged region (e.g., the spinal cord in quadriplegic patients). Otherwise, as in the case of a neuromotor prosthesis, it allows the user to drive the appropriate effector (e.g., a robotic arm) by thought.

Probably the most widely accepted neural prosthesis in human use is the cochlear implant (Parmet et al., 2004). It by-passes damaged parts of the ear and directly stimulates nerve fibres of the auditory nerve. Sound waves are converted into electrical signals the brain can learn to interpret. Other research has focused on restoring vision for the blind (Hetling & Baig-Silva, 2004) with implantable systems to inject the visual information on the retina or even directly on the visual cortex (Schmidt et al., 1996; Fernandez et al., 2005). One other possible application is the restoration of motor control for patients with movement disorders. In a tragic situations, brain stem stroke, degenerative disorders (amyotrophic lateral sclerosis or Lou Gehring disease, multiple sclerosis, muscular dystrophy), brain or spinal cord injury, cerebral palsy, can leave patients in a locked-in state with minimal or no movement (and consequently no speech), but full cognitive functions.

In most non-invasive BMIs the information rate poses a hard constraint on how the desired action is coded. Often the user can select a choice among a reduced discrete number of high level commands (e.g., Yes/No, Up/Down/Left/Right, alphanumeric characters, ...). On the contrary, direct interfaces can allow continuous movement in a three-dimensional coordinate system. Following the first pioneering works (Evarts, 1966; Humphrey et al., 1970), it was shown that the linear combination of electrical signals simultaneously recorded from 3-5 firing neurons could provide a relatively good estimate of the joints angular movements. Until now, a number of procedures have been tested in order to extract information from groups of recorded neurons about the movement aims (Reviewed in Schwartz et al., 2001).

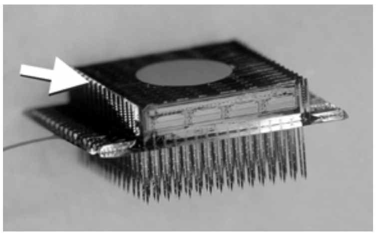

Figure 9.2: Thin film 256-shank array of 1024 multiplexed sites. Signal processing electronics on board (arrow). Developed at the University of Michigan. (Reproduced from Donoghue, 2002).

9.2 Methodologies for BMI

In order to capture the action potentials of many individual neurons and decode the neural activity to infer the movement executed or imagined by the user, demanding neural interface, sophisticated signal processing and computationally intensive interpretation algorithms are essential.

9.2.1 Signal measurements

Directly recording the neural activity of the cortex is challenging because some physiological and technological issues have to be addressed.

The recording of action potentials of individual neurons requires a close proximity between the microelectrode and the signal source. For a successful and reliable signal, countermeasures are needed to deal with shifting populations of neurons (Suner et al., 2005). At the current stage recordings of few hundreds of neurons can provide useful signal for months.

Miniaturization is necessary to place the recording device inside the skull. Telemetry is needed to move signals to remote processors and effectors (Nicolelis, 2001; Maynard et al., 1997).

The more commonly used electrodes are microwires, multiple electrode arrays (MEAs) and neutotrophic electrodes.

Microwires are aggregates of small wires and have been used for many years for chronic cortical recordings (Marg & Adams, 1967; Palmer, 1978).

More advanced multiple electrode array systems (e.g. Figure 9.2) are being developed using advanced manufacturing and design methods (Bai & Wise, 2001; Maynard et al., 1997; Rousche et al., 2001).

Neurotrophic electrodes are also being tested. These electrodes consist of implanted glass cones filled with a substrate containing nerve growth-stimulating substances (Kennedy, 1989; Kennedy et al., 1992). This extracellular recording electrode is bioactive and requires nerve fibres to sprout into the glass cone, a process which occurs over a period of several weeks.

9.2.2 Conditioning

The recorded neural signals are buffered, amplified, and filtered by electronics. Most researchers recommend early pre-amplification and digitization of the analog recording data to minimize the signal deterioration. The numerical signal can be moved to remote processors and effectors with telemetric techniques in order to reduce infections due to wires coming out of the skull.

9.2.3 Interpretation

After recording neural signals, one must derive a useful command signal from them. The digitized brain signal has to converted into a code that best represents the desired action. For a neuromotor prosthesis, this could be the movement of a cursor or the specification of a complex arm trajectory. Several research groups were able to extrapolate with good approximation 2-dimensional and 3-dimensional arm or hand movement (Lauer et al., 1999; Kennedy et al., 2000; Taylor et al., 2002; Serruya et al., 2002; Shenoy et al., 2003; Pfurtscheller et al., 2003; Graimann et al., 2003).

From a computational point of view, multiple neuron recordings represent a significantly more challenging decoding problem than EEG signals. Electrical activity recorded from, e.g., MEAs, must be digitized at high rates (>20 kHz) for hundreds of channels. This huge amount of data must be processed and action potentials must be sorted from noise and one from each other (spike sorting). Later, decoding algorithms must decode neural activity into a command signal within a reasonable time frame (on the order of tenths of second).

The firing rate of motor cortex populations can provide a good estimate of movement commands or even motor intentions, including force and direction (Evarts, 1966; Humphrey et al., 1970; Georgopoulos, 1994).

The interpretation procedure can be composed of the following stages:

- preprocessing;
- feature extraction;
- interpretation.

The preprocessing is often performed by a filter or a Kalman filter in order to remove components of the recorded data whose spectral distribution or dynamics allow them to be recognized as noise (e.g., noise from the power line).

The feature extraction stage processes the data and extracts relevant features to feed the classifier. Feature often used for cortical interfaces are the firing rate of different neurons or populations. Algorithms for spike detection and spike sorting extract and classify different spikes classes. Here the spike waveform is used to decode multi-unit activity into single neuron spikes. Spike events of each cell are time binned in a frames of about 100 ms to estimate the spike rate. Information about the spike rates is gathered in a vector where each dimension of the vector corresponds to a particular neuron and the value or magnitude of each dimension is proportional to that cell's firing rate.

The purpose of the interpretation algorithm is to discover and use a consistent relationship between the vector in the neural space and the corresponding vector in movement space. Interpretation algorithms can be divided into two broad categories: inferential and classifiers (Schwartz, 2004). Inferential methods are model based and depend on some understanding of underlying mechanisms. An example of inferential mehod is the "population vector algorithm" (Moran & Schwartz, 1999; Schwartz, 1993) that uses the assumption that each neuron codes for a preferred direction and pulls towards it; the actual direction is evaluated as combination of the contributions of the different cells. Differently from inferential methods, classifiers do not require prior knowledge about the model underlying the phenomenon. After a learning phase where the classifier is given a set of examples constituted of neural vectors and the related movement vectors, the relationship found is used to infer the movement vector given the neural vector.

All the different machine learning techniques used for direct BMIs, such as linear regression, population vector and neural network models, are themselves not new. Nevertheless, it is a significant achievement to identify approaches and modify them to deal with large neural data sets (Donoghue, 2002).

Both the quality and form of movement reconstructions may be further improved when interactions among neurons (Maynard et al., 1999) or additional signal features (Wu et al., 2006) are considered.

A completely different approach is to record a more degenerate, but also more easily obtained, signal from local field potentials (LFPs). Some studies (Donoghue et al., 1998; Pesaran et al., 2002; Mehring et al., 2003; Rickert et al., 2005) demonstrated that LFPs carry substantial information about a planned and/or executed movement. The recording of LFPs is simpler and expected to have a better long-term stability than the recording of single-unit activity (SUA). Moreover, the decoding of LFPs can be performed directly on the raw signals, as opposed to the decoding of single-unit activity in which previous spike sorting is inevitable.

9.2.4 Output

After the neural data is translated by the interpretation module into movement coordinates, it can be used to drive different output devices. The movement information can be used to control a computer cursor, to control a robotic device (as a substitute for a moving human limb or for augmentation purposes), or injected back into the patient's own limb to activate muscles (for example, through a functional electrical stimulation).

Besides the actuation itself, the output is also useful during the training. The subject generates a neural signal, watches the device move and tries to change the activity to advance the device to the target. Such a closed control loop can dramatically improve prosthetic performance (Serruya et al., 2002;

Taylor et al., 2002; Camena et al., 2003) compared to open-loop decoding (in which the subject does not observe movement of the device).

9.3 Foreseen improvements

Future improvements in the field are linked to a few key questions to be addressed.

Concerning to the cortical interface itself the following key topics will be important:

- better understanding of electro-physiological activity of the cortex;
- biocompatibility of electrodes for chronic implants;
- multi electrode arrays conforming to sulci and gyri of the cortex;
- nanodevices to obtain a finer resolution in the recording of neural activity.

As for the interpretation stage, the key points will be:

- more advanced modelling methods able to deal with large amounts of data gathered by arrays of thousands of electrodes;
- models able to use the additional information from spike timing (Stein et al., 2005) instead of just rates.

Concerning the output devices, the key issues to address will be:

- enhance dexterous manipulation by providing the user with feedback;
- working on actuator technology, component miniaturization, energy storage to allow end effectors and prostheses to be lighter and suitable for human wereability.

9.4 Outline on the suitability for space applications

At National Aeronautics and Space Administration (NASA), a research group called “Extension of the Human Senses Group” is investigating the use of some bioelectric signals, Electromyogram (EMG) and Electroencephalogram (EEG), to eliminate the need for mechanical joysticks and keyboards. As an example they have flown a Class IV simulation of a transport aircraft to landing with an EMG based "joystick" (Wheeler et al.). The goal is to improve performance of NASA missions by developing brain-computer interface (BCI) technologies for augmented human-system interaction. BCI technologies will provide powerful and intuitive modes of interaction with 2-D and 3-D data, particularly for visualization and searching in complex data structures, such as geographical maps, satellite images, and terrain databases.

Until now we found no report concerning the development of invasive brain-machine interfaces for space applications. In general invasive BMIs (as many other invasive methodologies) are for now considered only justifiable for restoration of severe impairments. For augmentation purposes non-invasive methodologies are obviously preferred.

Anyway Alan Rudolf, the former head of the DARPA brain-machine research program, once said “Implanting electrodes into healthy people is not something we’re going to do any time soon, but 20 years ago, no one would have thought we’d put a laser in the eye either. This agency leaves the door open to what’s possible.” (Horgan, 2004).

9.5 Worldwide researching groups

In the Nicolelis group at the Duke University Medical Center, USA, chronically implanted monkeys allowed simultaneous recordings from hundreds of individual neurons. This helped to investigate the time dynamics of neural circuits during learning procedures (Nicolelis, 2003). From the acquired data, it has been possible to gather information for the knowledge of basic mechanisms of the visuo-motor control, such as hand movement direction, grip force, hand angular speed and acceleration in relation to its space position. Such a bulk of information have been utilized for the control of a multi-joint robotic arm, with a comparative on-line analysis between natural movements carried out by the animal arm-hand and the artificial robotic arm-hand movements. In the same study (Nicolelis, 2003), another problem concerning the amount of information needed (i.e. from how many neurons information should be acquired simultaneously in order to have a sufficiently faithful estimate of the coded parameters for correct execution of a planned motor action) has been approached.

Chapin and colleagues (Chapin et al., 1999) at the State university of New York, USA, trained rats in a way that they received water supply by pressing a lever controlling a robotic arm movement. The firing activity of 21-46 neurons simultaneously recorded via implanted microelectrodes within the primary motor cortex was used as relevant signal for a device controlling the robotic arm. Researchers noted that many animals learned to perform the task by only using their brain signals without moving any body part. Rats probably developed the ability to control the neuronal firing, previously used to generate limb movements for lever pressing, without actually dispatching it down through the spinal cord relays to the relative target muscles. Following studies confirmed such a finding (Wessberg et al., 2000; Taylor et al., 2002; Serruya et al., 2002). In these experiments about 100 electrodes were implanted in the monkey cortex and the animal control was based on firing of 10 to 100 neurons.

Andersen group in Caltech, USA, has implanted monkeys in their posterior parietal cortex (Meeker, 2005), a region which is believed to participate in movement planning. By decoding the signals from 96 electrodes the researchers were able to predict 67 per cent of the time where in their visual field trained monkeys were planning to reach. They also found that this accuracy could be improved to about 88 per cent when the monkeys expected a reward for carrying out the task. After 50 trials, monkeys learned to modulate their neuronal firing frequency and reached the selected target without any actual movement.

At Brown University researchers have been able to take advantage of the implantation of deep brain stimulators for improvement of motor disorders to explore the ability of patients to control their neural signals. The activity of 4 to 6 neurons in the premotor and prefrontal regions has been recorded simultaneously during visuo-motor arm movement tasks. With a few minutes of practice, patients have been able to control their neural activity to bring a cursor to a target (Donoghue et al., 2003). Off-line decoding using a maximum likelihood estimator revealed that small, pseudo-randomly selected neuronal ensembles in the human cortex contain information about movement direction and intent (to move or not to move) (Ojakangas et al., 2003).

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10. Multi-modal integration

The multi-modal integration of data obtained with several neuroimaging techniques allows a coherent modelling of human brain higher functions. In fact, large bulk of updated evidence underlines the values added of integration of different brain imaging techniques. Integration allows to overcome the inherent limits of each technique, both in terms of spatial and temporal sensitivities (Figure 10. 1, Table 101), as well with respect to the physical/neuro-metabolic mechanisms subtending sensed signal (Figure 10. 2).

Technique	Resolution	Advantages	Disadvantages
SPECT	10 mm	Low cost Available	Invasive Limited resolution
PET	5 mm	Sensitive Metabolic studies Receptor mapping	Invasive Very expensive
EEG	poor	Very low cost Sleep and operation monitoring	Not an imaging technique
MEG	5 mm	High temporal resolution	Very Expensive Limited resolution for deep structures
fMRI	3 mm	Excellent resolution Non-invasive	Expensive Limited to activation studies

Table 10.1: Spatio-temporal characteristics of different imaging techniques

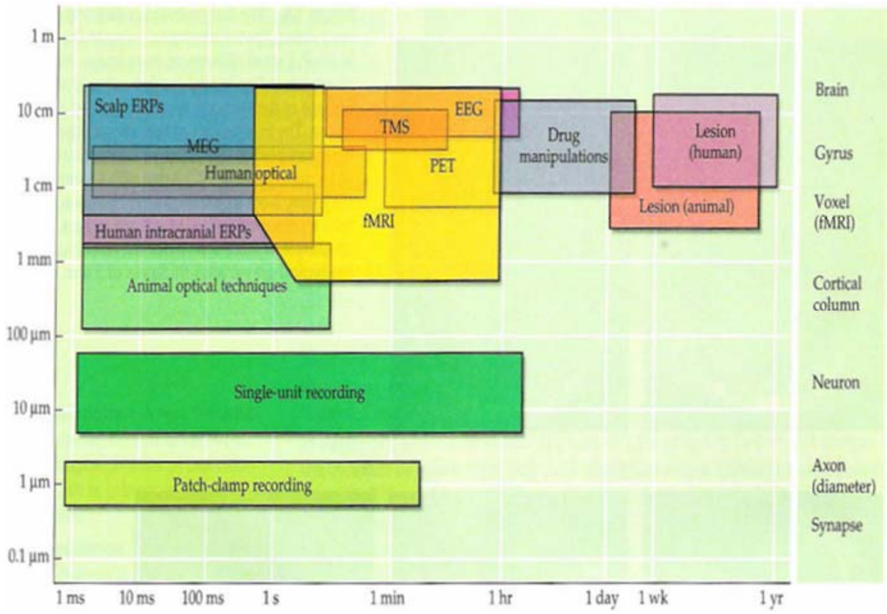

Figure 10. 1: Schematic drawing of spatio-temporal characteristics of different imaging techniques. (Reproduced from Huettel et al 2004).

10.1 Different imaging techniques

A strong international effort has been devoted to create inter-disciplinary teams able to understand and exploit different information coming from the techniques above represented (Rossini & Pauri 2000; Riera et al., 2005; Babiloni et al., 2004a, 2004b). Also, ad-hoc courses are built up covering the theoretical basics of multimodal imaging to examine brain activity in real time coming from magnetic resonance imaging (MRI), functional magnetic resonance imaging (fMRI), magnetoencephalography (MEG), electroencephalography (EEG), transcranial magnetic stimulation (TMS) and optical imaging (near infrared spectroscopy, NIRS; diffuse optical tomography, DOT), positron emission tomography (PET) equipment and data analysis tools (see Figure 10.2). TMS has not been described so far but is presented in Section 12.2.2 in the context of the feedback problem. Single-photon emission computed tomography (SPECT) is is a nuclear medicine tomographic imaging technique using gamma rays that is not useful for BMIs. fMRI provides fine spatial details (millimetres, Table 10) of the brain responses; MEG and high density EEG technique (hrEEG) are able to study brain areas by analysing cortical electric/magnetic fields generated during cerebral processing. Their high temporal resolution allows to detect relatively restricted functional neuronal pools activated during cerebral processing of external stimuli. With respect to the hrEEG, the MEG technique allows a more precise localisation of the sites of neural activity buried into the cortical sulci, but it is unable to detect the response of the crown of the cortical giri because of its poor sensitivity to radially oriented dipoles, which can be sensed by EEG/hrEEG. Motor cortex topographical mapping of different body districts could be obtained by TMS. PET is

sensitive to signal generated by isotopes decay of different molecules, making possible receptor mapping.
The integration of functional and anatomical information provides cues on the relationship between brain activity and anatomic sites where this takes place, allowing the characterisation of the physiological activity of the cortical brain layers in physiological and pathological conditions.

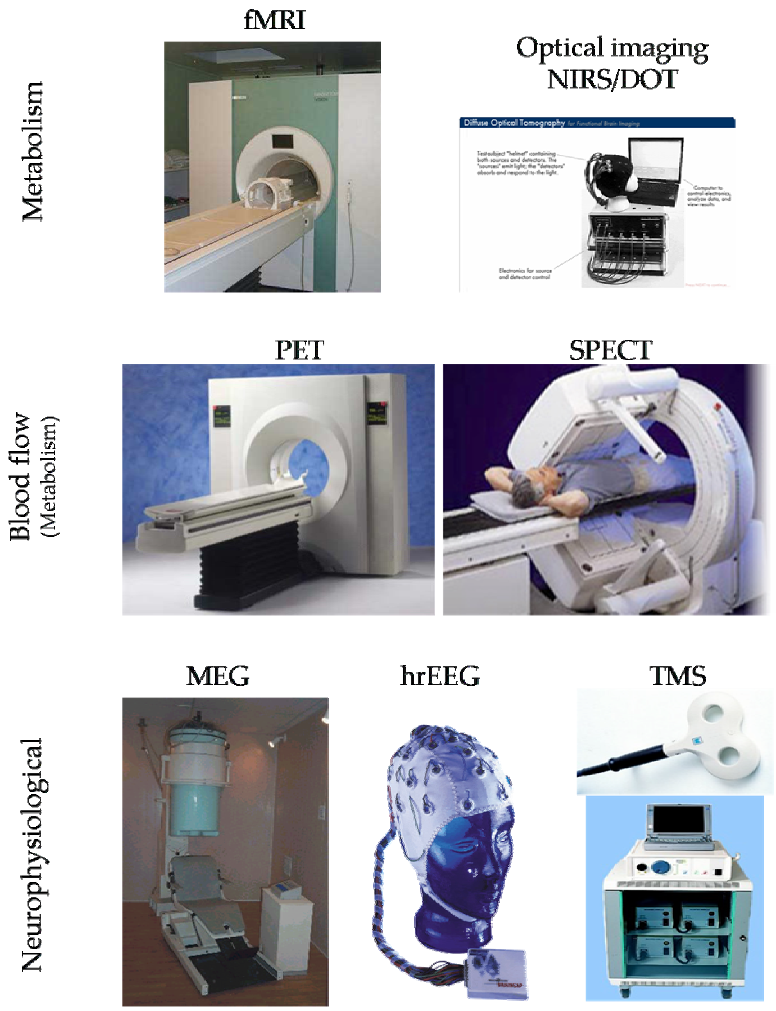

Figure 10. 2: Different imaging techniques, providing information about brain function, using different nature properties: metabolism (fMRI, optical imaging), cerebral blood flow (PET, SPECT), neuronal activity (MEG, hrEEG, TMS). (Source: WWW).

10.2 Integration and/or fusion?

Integration has to be intended in two different meanings: the use of information coming from one technique to interpret/extract information obtained from another technique; more simply, accurate overlapping of

information coming from two or more different techniques by defining a common coordinate reference system. The latter, i.e. the fusion of data coming from independent equipments, although completely resolved from a theoretical point of view -with zero error-, involves a great effort to be solved from a technical point of view. Up to now, main experience comes from fields were stereotactic procedures are required, i.e. stereo-EEG and radiosurgery. In particular, gamma Knife (GK) radiosurgery presents the highest requirements in terms of imaging accuracy as the treatment is applied in a single high-dose session with no other spatial control than medical imaging. Moreover, clinical application could include, in addition to the morbid tissue characterization via MRI, the stereotactic PET. This, applied to GK procedure, represents an example of application of modern multimodality imaging in radiosurgery (Levivier et al., 2004).
Other kinds of co-registrations allow integration of anatomical and functional data (MRI-EEG, MRI-MEG, MRI-TMS, MRI- PET, MRI-SPECT). Functional information of different nature (fMRI-EEG, fMRI-MEG, TMS-EEG, Riera et al., 2005, Babiloni et al., 2004a, 2004b) also provide deeper understanding about the brain organization, in particular in pathological conditions (Rossini et al., 2004).

10.3 Worldwide researching groups

http://www.kyb.tuebingen.mpg.de/lo/ Max-Planck-Institute for Biological Cybernetics, Tubingen, Germany.

http://www.nmr.mgh.harvard.edu/martinos/aboutUs/index.php The Martinos Center's dual mission includes translational research and technology development. The core technologies being developed and used at the center are magnetic resonance imaging (MRI) and spectroscopy (MRS), magnetoencephalography (MEG) and electroencephalograpy (EEG), near infra-red spectroscopy (NIRS) and diffuse optical tomography (DOT), Positron Emission Tomography (PET), electrophysiology, molecular imaging, and computational image analysis. A particular area of innovation at the Center is Multimodal Functional Neuroimaging which involves the integration of imaging technologies. We are also world leaders in the development of primate neuroimaging techniques. Major areas of research at the center include, psychiatric, neurologic and neurovascular disorders, basic and cognitive neuroscience, cardiovascular disease, cancer and more. With an extensive and expanding inventory of state-of-the-art imaging facilities, a world class team of investigators and collaborators, and important government, industry and private supporters, the Martinos Center is leading the way to new advances and applications in biomedical imaging.

http://brighamrad.harvard.edu/ Department of Radiology, Brigham and Women's Hospital, Harvard Medical School, 75 Francis Street, Boston, MA 02115, USA.

http://www.mit.edu/research/ Massachusetts Instute of Technology, 77 massachusetts avenue cambridge, ma 02139-4307

http://www.itab.unich.it Istituto di Tecnologie Avanzate Biomediche, Università G. D'Annunzio, Chieti, Italy

10.4 Outline on the suitability for space applications (pros and cons)

Above reported studies on up-dated fMRI-BCI applications, suggest that in future efforts could be planned to test the application of information obtained by fMRI, to portable system adapt to use in space environments.

10.5 References

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11. BMIs and space applications

In this chapter we will try to outline the possible current and future uses of brain/machine interfaces applied to space applications. Currently, apart from (Trejo et al., 2006), which is not an independent BMI, we are not aware that such applications already exist and there are a few constraints of BMIs that limit their usability for practical space applications. In order to identify possible applications, we first describe and identify the requirements of applications, both in space and rehabilitation. Then we compare those requirements with the performance of available interfaces, both BMIs and standard human-computer interfaces. This comparison allows us to identify some demonstrators that are can be realized with currently available technology. From the comparison, other possible uses of BMIs that could be suitable for demonstrators emerge. With future technology improvements, these demonstrators could become real applications.

11.1 Potential advantages

11.1.1 Potential advantages for general applications

From a control system viewpoint, we can summarize the information processing that happens in everyday life, as we interact with the outside world, as depicted in Figure 11.1. Our intention to interact with an object (e.g. grasp it), which resides in some cognitive network inside our brain, is translated into motor commands in the motor cortex and then sent to our limbs through the efferent pathways. The results of our action is then gathered by our sensing system (eyes, touch, etc.), translated to sensory signals and sent back to the central nervous system (CNS) through the afferent pathways.

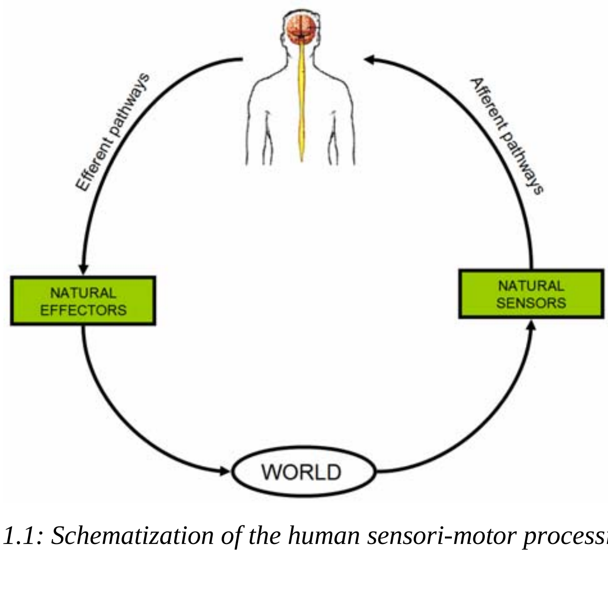

Figure 11.1: Schematization of the human sensori-motor processing loop.

This representation is very simplistic, since feedback is believed to occur at various levels, but it allow us to clarify the potentials of direct brain-robot communcation: in an *ideal* brain-machine interface, the motor commands, instead of being sent to the natural effectors in the musculo-skeletal system (e.g. the limbs), will be sent to an artificial actuation system (a robot) and its action on the environment will be measured by a sensing system composed by artificial sensors and fed back to the nervous system as they were natural signals (see Figure 11.2).

The artificial system can be hooked in at various levels in the system above, e.g. intercepting efferent EMG signals or using the peripheral nervous system (PNS) for feedback, but for a true BCI, only the CNS will be interfaced; the BCI will be therefore independent from the functioning of the PNS and will be usable also by people with various levels of inabilities.

BMIs have so fare been extensively studied as a communication means for people that are affected by most severe disabilities, such as amyotrophic lateral sclerosis (ALS) and, as a result of the disease or injury, have no voluntary control of muscles (Donoghue, 2002; Mussa-Ivaldi and Miller., 2003). In this case, they possess no communication means with the outside world and a BMI may represent their only way to interact with other people and objects. For these people, also very inefficient BMIs will represent an improvement with respect to their actual situation, so even interfaces with low bitrates can be considered as prosthetic applications. The most performant BCI typewriters achieve only bitrates of a few letters per minute (Wolpaw et al., 2002).

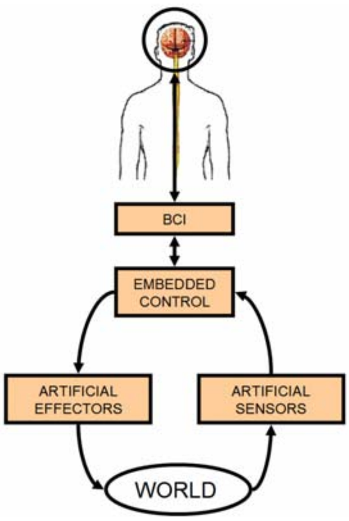

Figure 11.2: Schematization of the brain-robot interaction loop.

On the other end of the spectrum are able-bodied users. For these users, the use of a BCI as an alternative communication device is not useful, due especially to their low bandwidth and the fact that current BCIs require a high cognitive load from the user, long trainings, and do not allow the user to perform activities besides interacting with the BCI, to avoid artifact signals that are not directly related to the driving of the BCI. For these users, BCI would only be practical if conceived as an *augmenting interface*, i.e. an interface that allows them to perform actions *in addition* to what they already can do with their normal abilities. Figure 11.3 shows the human augmentation scenario, in which a user both exploits his natural neural pathways *and* a BCI.

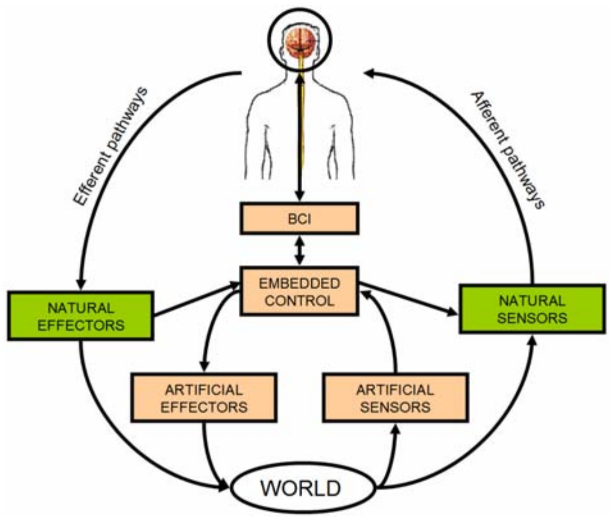

Figure 11.3: Schematization of the human augmentation interaction loop.

11.1.2 Potential advantages for space applications

For space applications, the most important scenario among those described in the previous section, in the scenario of *human augmentation*. Astronauts are not only able-bodied, but also specially-trained people, therefore it makes little sense for astronauts to avoid using conventional interfaces, such as keyboards and joysticks, which we will show to have a higher *throughput* (i.e. information transfer rate) than BMIs, in favor of BMIs that currently require a high cognitive load and offer a poor throughput. Only if astronauts or technical people from Earth will be able to use BMIs *in addition* to conventional interfaces, or to achieve some goals for which conventional interfaces are *not suitable*, it will make sense to introduce BMIs into space applications. This is why we believe that, for space applications, augmenting interfaces will have a dominant role. We identify such situations and sugest possible uses and demonstrators based on BMIs for space applications in the next sections of this chapter.

11.2 Environment effects on BMI

11.2.1 Human physiology in space

Human anatomy and physiology are the result of the evolution through time to adapt the human being to life on Earth. The space is a completely different environment and the human body undergoes some key modifications when in space (Lujan & White, 1995).

The cardiovascular system changes the way it operates, even on a short journey into space. On Earth, gravity pulls the various body fluids down towards the feet. In the absence of gravity these fluids redistribute upwards towards the chest and the head. The body perceives it as an increase in fluid volume in the upper part of the body and multiple physiologic changes in the kidneys, in the cardiovascular system, and in the red blood system, take place.

The muscles of astronauts undergo deep changes as they adapt to the absence of the natural gravitational pull. The bone formation and calcium metabolism also change in microgravity.

Our brain and overall nervous system work together to provide us with the direction, guidance, and impulses necessary to move about and function day to day. The removal of gravity affects the way the sensory and balance centres within our brains perceive the outer environment and the position and the orientation of the body within it.

11.2.2 Effects of microgravity on the brain

In the virtual absence of gravity the brain must re-adapt internal models of the laws of dynamic. Gravity dictates the laws of motion of our body and limbs, as well as of the objects in the external world with which we interact. In order to, e.g., catching a flying ball, the central nervous system must quickly perform complex considerations starting from internal models, to generate coordinated motor actions in response to incoming sensory information (McIntyre et al., 1998). In absence of gravity the brain has to re-adapt this models to the new environment.

In a microgravity environment the brain must change the strategies it uses for spatial orientation. Gravity is essential for spatial orientation on Earth. Contact forces of support opposing the acceleration of gravity (g) indicate the “down” direction. The otolith organs also provide information about head orientation with respect to the gravitoinertial acceleration (Lackner & DiZio, 2000).

In reduced gravity, the brain receives afferent proprioceptive signals different from what it is used to on Earth. In the presence of gravity, the head orientation in relation to the gravitoinertial resultant modulates muscle spindle sensitivity (Lackner & DiZio, 2000). In microgravity environments, these constant signals the body is so used to are transformed. There are many anecdotal reports that limb proprioception is affected by exposure to weightlessness.

All these changes in what the brain receives and how it process the information can lead to modifications that can reflect on the functioning of a Brain-Machine Interface. The signals and patterns a BMI is based upon, can be disrupted, reduced, enhanced or changed by the different environment and its consequences. Therefore we could not exclude that a BMI developed and tested on Earth could stop working in space or need a new tuning of the parameters of the algorithm to adapt to the psycho-physiological modifications of the CNS.

Some study seem to confirm that gravity can affect some aspects of the brain functioning even if apparently not related to orientation or proprioception. At the Institute of Space Medico-Engineering, Beijing, China, studies have been carried on to assess the effect of head-down tilt (HDT) in the event-related potentials (ERPs) related to selective attention to stimuli from left and right visual field. The outcome (Wei et al., 1998) is that the mean amplitude of P400 (a late positive component) decreased during HDT and more significantly at posterior and central brain regions. As the P400 component probably reflects the active inhibition activity during attention process, these results suggest that the higher brain function was affected by the simulated weightlessness.

11.2.3 Effects of radiations

Weightlessness is not the only factor affecting the human body in space. The absence of the protection of the atmosphere exposes astronauts to a steady flux of cosmic particles. Long permanence in orbit results in a dose of radiation many times that of the same period spent on Earth. This can lead to higher risk of developing cancer or immunodeficiency.

Cosmic-ray particles also interact with our visual system and give rise to the phenomenon known as a "light flash". More than 80% of the astronauts have experienced visual sensations of white flashes of light, with different shapes, moving across the astronaut's visual field or towards the astronaut. The flashes, technically known as "phosphenes", are unusual visual phenomena observed in space and caused by the interaction of energetic cosmic-ray particles impinging on the retina (Pinsky et al., 1974). On board the Mir space station, the Sileye-2 protocol of experiments has been carried on (Avdeev et al., 2002). This allowed researchers to identify two separate components of cosmic rays that cause these flashes: one due to heavy nuclei and one due to protons (Casolino et al., 2003).

We cannot a priori exclude that these phenomena could interfere with the operating of a Brain-Machine Interface. They could in principle act as external stimuli and trigger the activation of specific areas. Nevertheless their impact could be limited because they are quite rare. The measured rate of occurrence of light flashes (LF) varies for different missions: from a minimum of 0.18±0.02 LF/min-1 on Mir to a maximum of 1.3±0.1 LF/min-1 on Skylab (Casolino et al., 2003).

11.3 Technology readiness

Prior to the definition of demonstrators and solutions for using BMI for space applications, we will analyze the readiness of the technologies that are needed both for BMIs and for the applications. Rather than suggesting out-of-the-box solutions, we derive the definition of possible demonstrators by merging the needs of space applications to the current performance of BMIs. To analyze technology readiness and help pointing out possible demonstrators, in the following Section 11.3.1 we first define scenarios and contexts for the use of BMIs in rehabilitation applications, the only field where the use of BMIs has been truly investigated so far. Subsequently, in

Section 11.3.2, we define the scenario of domotic applications and environmental control, a context where BMIs, given their characteristics, have good perspectives to be applied. Then, in section Section 11.3.3, we define possible scenarios for the use of BMIs for space applications. In Section 11.3.4 we summarize the requirements, in terms of *throughput* and *latency*, of the all applications listed in the previous scenarios. In Section 11.3.5, we list the main types of available human/machine interfaces, both standard human-computer interfaces and BMIs, and characterize them also in terms of throughput and latency. This characterization allows us, in Section 11.4.1, to merge the performance of the interfaces with the needs of applications and to derive currently feasible space applications for BMIs. In Sections 11.4.2-11.4.4, we identify and describe three of these applications that we have chosen as demonstrators.

11.3.1 Rehabilitation applications

11.3.1.1 Communication devices

Restoring communication is a top priority for people with severe disabilities such as locked-in syndrome, in which the person is completely paralyzed and unable to speak. Consequently, BCI researchers have experimented with several methods of assistive communication, ranging from simple binary (yes/no) capabilities (Wolpaw et al., 2000) and iconic selection applications such as TalkAssist (Kennedy et al., 2000), to virtual keyboards that support spelling. Several approaches to spelling have been developed. (Perelmouter & Birbaumer, 2000) describe a binary speller, dividing the alphabet in successive halves until the desired letter is selected. This speller has been used by a locked-in person to compose letters in a real-world home environment. (Wolpaw et al., 2000) describe a similar speller, dividing the alphabet into successive fourths instead of halves. (Donchin et al., 2000) have developed a method based on the P300 component of event-related potentials, which allows the user to select a letter by flashing rows and columns of a two-dimensional (2-D) alphabet grid to determine the desired letter. Kennedy et al. have provided locked-in subjects with 2-D cursor navigation to select letters from a WiViK virtual keyboard (Kennedy et al., 2000). Although each of these spellers has been shown to work, communication is still slow, averaging three letters per minute. The spellers have largely been used for training by providing prepared words or phrases for the subject to spell, called copy-spelling. Several of these spellers have also been used for free-spelling, although measuring the accuracy of BCI output is difficult and relies on user self-reporting.

Also, for space applications, silent speech methods can be envisaged, based on similar technology, for reliable communication under compromised conditions, such as in pressurized suits or noisy environments. However, at the current state of technology, subvocal speech systems seem to be more promising and have a long research history that dates back to the late 1970s (Garrity, 1977) and has been recently demonstrated in (Larkin, 2004). In particular, for space applications, Chuck Jorgensen et al. at the NASA Ames Research Center are investigating how to interpret nerve activity that happens near the throat when humans speak in order to gain information about what a person is saying. The system discerns words from the electromyelogram/electropalatogram (EMG/EPG) readings of nerve signals that control vocalization in larynx and tongue muscles. The system learns to match features in the waveforms of the readings to the six words and 10 digits. The nerve signals are measured by sensors attached to the skin on the side of the throat to pick up signals bound for the larynx, and on the soft tissue under the chin to pick up signals bound for the tongue. A user is able to speak silently using the method because the signals are tapped at a point before they are used to vocalize speech. The method picks up signals when a person is speaking silently using almost no muscle movement. Two prototype applications have been demonstrated. The first uses subvocal signals to allow a user to browse the Web. A user silently speaks numbers to spell out two-digit codes that represent each letter of a search term. The search results are numbered, and a user silently speaks the numbers to choose Web pages. The second application allows a user to silently control a Mars rover. "We have a real-time control demo of a Mars rover which we can sub vocally move around terrain," said Jorgensen them. The prototype uses the words stop, go, left, right, alpha, and omega. Alpha and omega are general control words that represent pairs of functions like faster/slower or up/down depending on context. More details are available at:

http://www.nasa.gov/centers/ames/news/releases/2004/04_18AR.html.

11.3.1.2 Rehabilitation Robotics

During the last 10 to 15 years, robots have become more and more common in non-industrial environments such as private homes and hospitals. These robots are often called “human-centered” or “human-friendly” systems because the presence of the robot involves a close interaction between the robotic manipulation system and human beings. The close interaction can include a contact-free sharing of a common workspace, or a direct mechanical human-machine interface (Riener et al., 2005). In comparison to the traditional metrics of performance, human–centered robot interaction implies a totally different set of requirements than for industrial robots that are operated in structured environments. Such requirements include safety, flexibility and mechanical compliance of the robot, gentleness and adaptability towards the user, ease of use, communicative skills of the robot, humanoid appearance and behaviour.

An important application of human-centered or human-friendly robots is rehabilitation where the safety is the most important feature. Indeed rehabilitation robots are used close to users and they have to avoid injury to the user (Tejima, 2000).

Rehabilitation robotics advances are required by growing elderly population, for the decrease of hospitalization time, for the increase of healthcare quality and for diseases that were previously incurable. The rehabilitation is not linked only to motor deficits of elderly or disabled people following stroke, but it becomes more and more important for the healing of neurological diseases.

Neural Prosthetics, i.e. restoring movement for people with motor disabilities, is indeed another key application for BMI technology. Cortical signals have been used to control a hand orthosis (Pfurtscheller et al., 2000), essentially restoring the connection from the brain to a paralyzed arm. A locked-in subject has also used neural signals to control a virtual hand (Kennedy et al., 2000) in the hopes that simulation would provide clues to potentially incorporating functional electrical stimulation (FES) into a BMI system to restore movement.

The goal of this section is the description of the most important rehabilitation systems, providing a classification according to their peculiar application.

Rehabilitation robotics can be classified in:

- **assistive technologies**: robots and machines that improve the quality of life of disabled and elderly people, mainly through increased personal independence both in social and working fields.
- **neuro-rehabilitation robotics**: robots and mechatronic tools for clinical therapy in neuromotor rehabilitation.

11.3.1.3 Assistive technologies

Prosthetic devices

The basic goal of a prosthetic device is to provide a disabled person an aid that can perform the function of one or more limbs. Concerning to upper limb, the hand prosthetic device is the most important because the hand is not only a motor organ but also a very sensitive and accurate sensory receptor. Current hand prostheses can perform grasping and grasp maintenance, but they can not perform manipulation tasks with a stable grasp which involves high dexterity, a lot of sensors and a complex control system. At present, there are at least five different ways to restore the functionality of an amputated patient (Laschi et al., 2000). A still valid option is the use of a cosmetic prostheses, generally made by duplication of the contralateral arm (Figure 12.4.A). Conventional body-powered prostheses are powered and controlled by gross body movements, usually of the shoulder (Figure 121.4.B). Myoelectrically controlled prostheses are just one degree-of-freedom (DoF) grippers controlled by one or two channels of electromyographic signals (EMG), either in proportional or switching mode (Figure 121.4.C). Hybrid prostheses combine a body-powered with a myoelectric prosthesis an case of shoulder disarticulation level amputation. Another approach consists in designing prostheses specifically for some activities (Figure 121.4.D). But at present the best way to partially restore the functionality of an amputated limb is use myoelectrically controlled prostheses, in particular the OttoBock SUVA Hand.

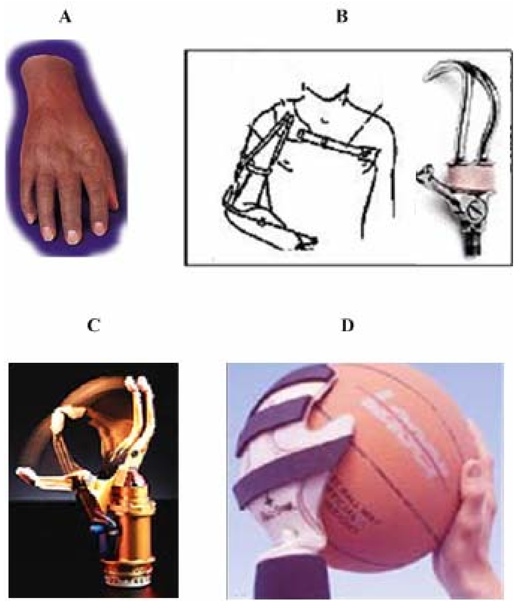

Figure 12.4:Different ways to restore the functionality of an amputated patient. (Photos: A: www.livingskin.com. C: Otto Bock HealthCare GmbH. B&D: WWW).

The OttoBock SUVA Hand has 1 DoF to object grasp but a further DoF can be included by an actuator on the wrist. Two sensors, force and slippage, allow to perform a stable grasp (Figure 11.5). Some features are: supply power 6 V, maximum opening 10 mm, opening-closing speed 15-130 mm/s and weight 460 g. This prosthetic hand can be covered by a silicon glove.

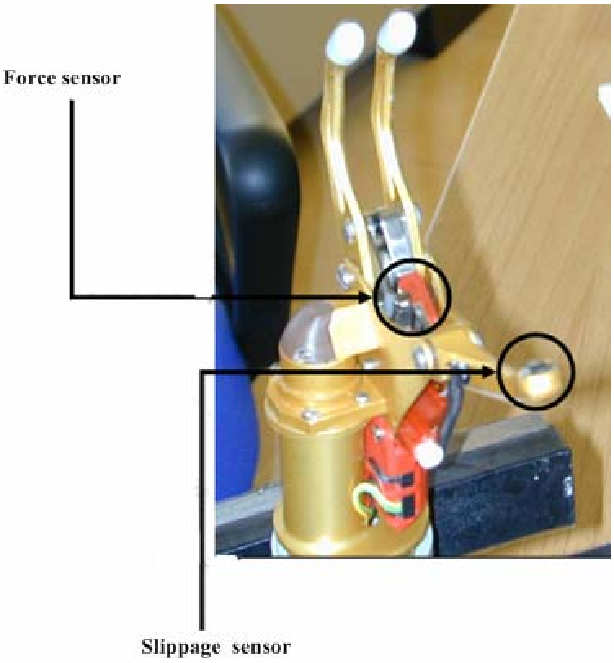

Figure 11.5: Sensors of OttoBock SUVA Hand. (Photo: Otto Bock HealthCare GmbH).

Some myoelectrically controlled prototypes are shown in Figure 11.6 and the most important feature are shown in Table 12.1.

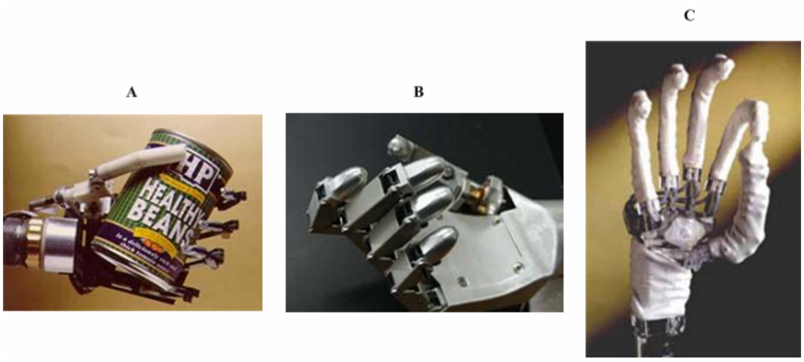

Figure 11.6: A: Southampton-Remedi (Reproduced from Light et al., 2002). B: Hokkaido University (Reproduced from Fujii et al., 1998) . C: Karlsrushe University (Reproduced from Schultz et al., 2001).

	DoF	**Max Force**
OttoBock SUVA	1+1	10-100 N
Southampton-Remedi	6	100 N
Hokkaido University	10	156 N

Karlsrushe University	18	12 N

Table 12.1: The most important features of prosthetic hands.

Robotic mobility aids

The most important robotic mobility aids are wheelchairs (Figure 11.7).

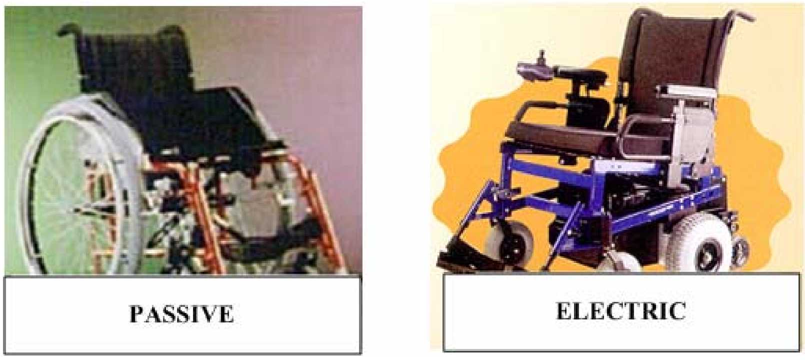

Figure 11.7: Some example of wheelchairs. (Source: WWW).

There is a considerable research and development activity focused on them in order to design wheelchairs whit a certain degree of customization to ensure comfort, safety and ease of control. Conventional wheelchairs are difficult to manoeuvre in constrained spaces because they only have two degrees of freedom (forward/backward movement and steering). But wheelchair systems with customized user interfaces, sensors and integrated controllers, can make the operation of a wheelchair much simpler and make it more accessible to people with disabilities. Such chairs may use a wide variety of sensors ranging from ultrasonic range sensors cameras, encoders, accelerometers, and gyroscopes and any desired input device (communication aids, conventional joysticks, sip and puff switches, pressure pads, laser pointers, speech recognition systems and force reflecting joysticks). Suitable control algorithms assist the user in avoiding obstacles, following features such as walls, planning collision-free paths and travelling safely in cluttered environments with minimal user input. An important example is the TIDE-OMNI wheelchair (Figure 11.8); it is an electrical and omnidirectional wheelchair with intelligent navigation system based on ultrasonic and infrared sensors for obstacle detection (Hoyer, 1995, Hoyer et al., 1997).

Figure 11.8: TIDE-OMNI wheelchair. (Photo: www.dinf.ne.jp).

The very important goal of research is to overcome all obstacles like steps and curbs. One innovative wheelchair that can go up and down any flight of stairs proposed by Professor Shigeo Hirose (Hirose et al., 1991) is shown in Figure 11.9.A. A novel remote centre mechanism moves the seat on an elliptical arc as the attitude of the chair changes and maintains the posture of the user independent from the wheelchair posture.

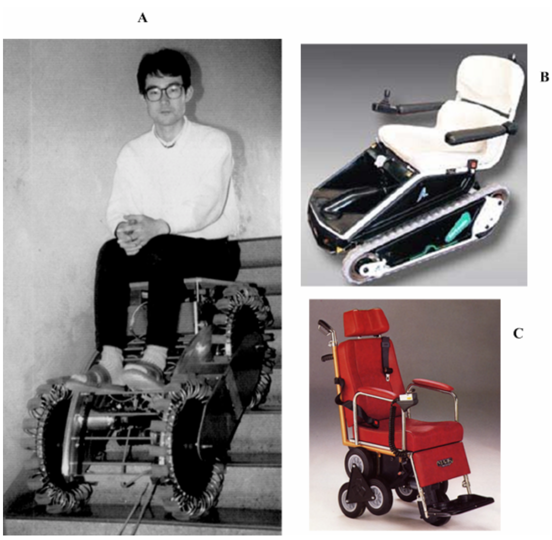

Figure 11.9: Wheelchair used to go up and down flight of stairs. (A: reproduced from Kumar et al., 1997. Photos B&C : WWW).

Moreover, stand-up wheelchairs (Figure 11.10) afford better seating and reaching, relief from pressure sores, and better health. They also allow users to operate equipment that is designed to be operated by standing people and improves the quality of social interaction with non-disabled standing people.


Figure 11.10: Stand up wheelchair. (Source: WWW).

Robots are important also for the elderly. Indeed they can assist them in standing up and in sitting down, can support their weight in walking and also robots to avoid their falls were proposed. An important example is the Guido^{TM} smart walker (Rodriguez-Losada et al., 2005), shown in (Figure 11.11), used to develop a mobility aid for people who are both frail and visually impaired. 75% of the visually impaired are elderly and they often have related mobility problems that severely limit their independence.


Figure 11.11: The smart walker Guido^{TM}. (Reproduced from Rodriguez-Losada et al., 2005).

Guido aims to provide a mobility aid with makes taking independent exercise a safer and more enjoyable experience. Guido is a 4-wheel robust walking frame or rollator provided with two motors to steer the front wheels, but is has to be pushed by the user. It has a SICK laser to sense the environment, and a force sensor in the handle to sense the steer command.

<u>Robotic manipulation aids</u>

One the most important examples of robotic manipulation aids is wheelchair robots. Indeed one of the major aims of rehabilitation robots is to pick and place objects. If the robots can be mounted on a wheelchair, this will be convenient for the wheelchair users. A manipulator mounted on a wheelchair should have at least 6 DoF for manipulation. Operating those degrees of freedom is sometimes complex for users and some robots were designed to be operated by task-oriented commands. The most famous robot arm mounted on a wheelchair is the Manus (Kwee, 1995, Kwee, 1997, Verburg et al., 1996) (Figure 11.12.A) which has more than 100 users worldwide and it is used as a base system in many research projects.

A robot arm used for manipulation aid is Tou (Dallaway et al., 1995). Tou (Figure 11.12.B) is a robot arm developed at the Polytechnic University of Catalunya, Spain**.** The robot is designed to be intrinsically safe due to a structure which is both soft and highly compliant. Tou is constructed from cylindrical segments of foam rubber. Each segment may be deformed in two degrees of freedom, using cables pulled by motors in a base unit. The arm is intended to complement rather than replace the assistance provided by carers. Operators may use Tou to carry out tasks such as page turning and scratching where great strength and precision are not required. The arm is normally controlled directly, however, a number of basic motion sequences may be programmed into the controller.

Dexter (Figure 11.12.C) is an anthropomorphic arm developed by Scienzia Machinale s.r.l. (Pisa, Italy) (Zollo et al., 2002). It has eight degrees of freedom and can be used for aid in home or hospital.

Another important example is MOVAID (Figure 11.12.D) (Dario et al., 1999). The objective of the MOVAID project is to give disabled and elderly users more comfortable access to and control of non-specialized consumer products, such as food preparation or house cleaning equipment. For severely disabled or bedridden users, the solution is a modular mobile robotic assistance system that interacts with activity workstations. For other users, this consists of a range of user interfaces for appliances. Explicit in the MOVAID approach is that the user continues to play an active role in the control of the environment through mediation of the robotic system. The modular robotic system features a mobile base equipped with an innovative eight degrees-of-freedom robot arm with a low level controller and the MARCUS gripper, sensory systems for navigation and obstacle avoidance, a docking capability to activity workstations, off-line local control sequences, and remote control, optionally with video inspection. The activity workstations can be adapted by users who already own a robot arm and facilitate the high-level control of the arm. A major component of the project is the design of the user interfaces for the workstations and for the control of the robotic system.

Some features of manipulator arms are shown in Table 11.2.

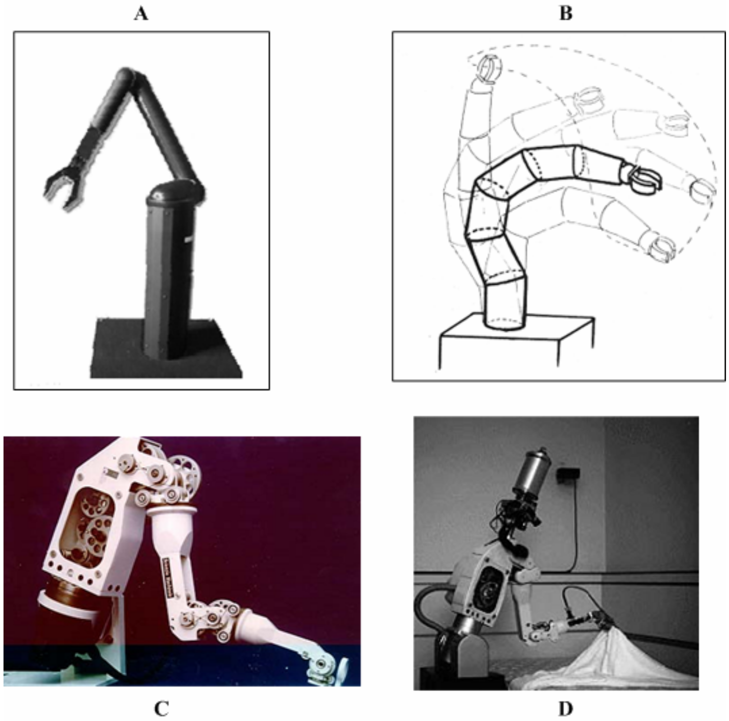

Figure 11.12: Examples of robotic manipulation aids. A: Manus. B: Tou. C: Dexter. D: Movaid. (Photos: A: www.exactdynamics.nl. B: WWW. C&D: www-arts.sssup.it).

	DoF	Workspace	Max Speed
Manus	6	800 mm x 360°	0.5 m/s
Dexter	8	1200 mm x 350°	0.2 m/s
Tou	6	>1000 mm x 360°	< 0.1 m/s

Table 11.2: Features of manipulator arms.

In general a robot for a single task can be used more easily and be cheaper than a multipurpose robot. In this case, feeder robots are the most important examples. The Handy 1 (Topping & Smith, 1999) (Figure 11.13.A) is a robotic aid conceived and developed at Keele University, U.K. The aid features a five DoF robotic arm and a food tray mounted on a wheeled base unit. The arm is controlled by a single switch input device, in conjunction with a number of LEDs which illuminate in sequence. The Handy 1 has been shown to improve the eating skills of regular users over time due to the consistency with which food is presented. But the aid has been considered for other activities including drinking, shaving, and teeth cleaning and making up. Other feeder robots are MySpoon (Ishii et al., 1995) (Figure 11.13.B) and Neater Eater (Figure 11.13.C).

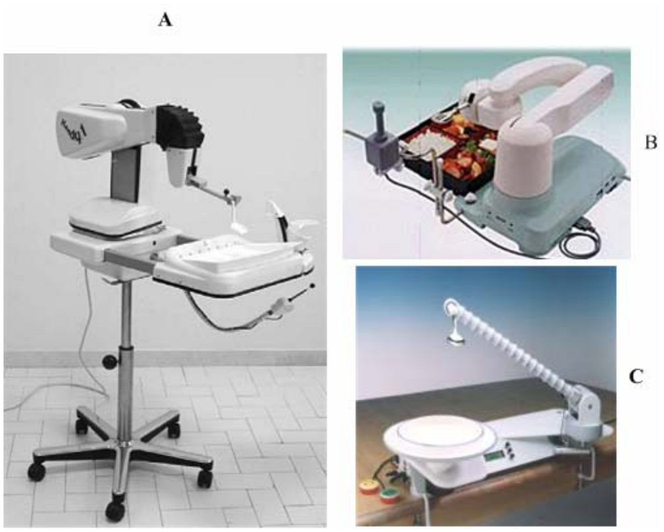

Figure 11.13: Feeder robots. A: Handy 1. B: MySpoon. C:Neater Eater. (Source: A: WWW. Photos: B: www.cems.uvm.edu. C: www.neater.co.uk).

11.3.1.4 Neuro-rehabilitation robotics

In this section we provide some information about neuro-rehabilitation robotics, to complete the scenario of rehabilitation applications. However, this class is not relevant for this particular study.

Robots for physical and occupational therapy

Neuro-rehabilitation robotics originates by application of rehabilitation robots to physical and occupational therapy following brain injury like stroke. Indeed the effects of stroke can be devastating, resulting in deficits of cognitive, affective, sensory and motor functions. Motor deficits persist chronically in about one-half of stroke survivors (Krebs et al., 2000). Moreover stroke rehabilitation is labour-intensive, relying on one-one, manual interaction with therapists. The demand for physical and occupational therapy for stroke survivors is expected to increase because improvements in medicine and healthcare will continue to increase the life expectancy of the population, and the incidence of stroke is more prevalent among older adults. Rehabilitation robots allow the patients to perform the therapy autonomously and more frequently. Indeed recent studies have shown that intensive therapeutic intervention can contribute to significantly reduced motor impairment and improved functional use of the affected arm (Fasoli et al., 2003). Robots moreover can provide quantitative information about patient's movement and improvements. This can allow an objective rehabilitation assessment.

The most studied neuro-rehabilitation robots are for upper limb but there are also a few robots for lower limb rehabilitation.

Some examples of neuro-rehabilitation robots for the upper limb are:

- MIT-Manus: developed by Massachusetts Institute of Technology (Cambridge, MA, USA) (Krebs et al., 1998).
- MIME (Mirror Image Movement Enhancer): developed at Stanford University & Veterans Administration R&D, Palo Alto, CA, USA) (Lum et al., 1997).
- MEMOS: developed at Scuola Superiore Sant'Anna (Pisa, Italy).

For lower limb rehabilitation, the most important example is:

- Lokomat: developed at Balgrist Hospital (Zurich, Switzerland) (Colombo et al., 2000).

11.3.2 Domotic and environmental control applications

Domotics is the household application of modern technologies. It is a word formed from domus (Latin, meaning house) and informatics (DOMus infOrmaTICS). These applications aim at the achievement of a unitary management for building installation and for outside connections, ensuring optimisation and reduction of power consumption and also some services like security, comfort, and information exchange. The household appliances and installations have a high automation degree, which ensures their work at optimum parameters without human presence, but also the possibility for the user to view and change these parameters from home and from outside.

In general, domotics can contribute to a better quality of life, but in particular it can be used by disabled and elderly people to be more independent and autonomous. Then an intelligent (smart) house can be considered as a comprehensive and intelligent aid, adaptable to the functional possibilities of the user and to the desired actions.

Some categories where domotics can be applied are:

- **Safety** like burglar alarm, fire alarm, gas and smoke detector, medical alarm.
- **Closing/Opening** i.e. for doors and windows.
- **Light control** to turn it on and off.
- **Temperature control**
- **Remote control** of household appliances, curtains and electronic devices like TV, radio.
- **Housekeeping** like adjustable bed, kitchen and cupboard, adapted toilet.

The general scheme of a domotics house is shown in Figure 13.14.

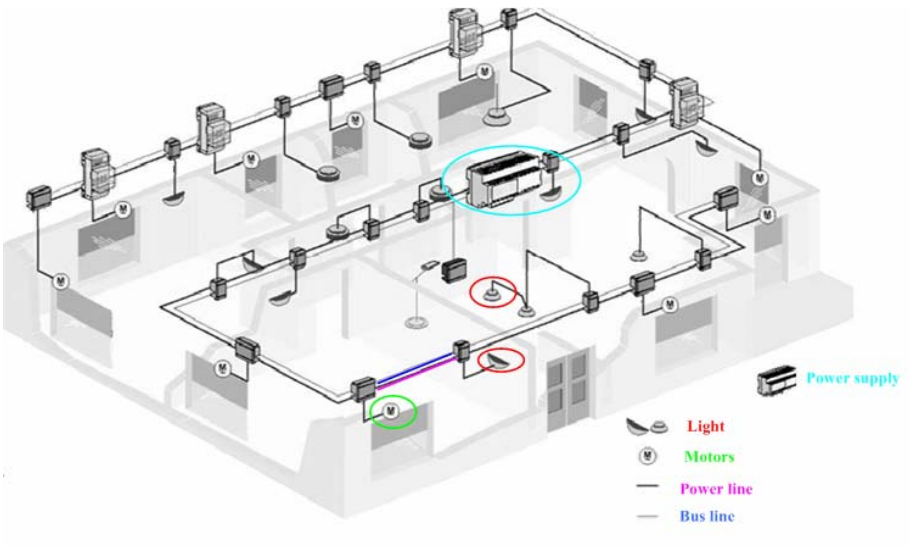

Figure 13.14: General scheme of a domotics house.

All controlled elements are connected to the same wiring, the BUS line (Binary Unit System), and each one has its own specific “address”. The most important elements of domotics house are sensors and actuators connected to the bus.

Sensors, like switches, temperature-meters, infrared-cells, motion-detectors, wind-detectors and light-cells, generate signals which are sent to the actuators by wireless connection (infrared or radio waves). They can be motors for doors, windows, curtains, rolling shutters. Sensors, actuators, supply and communication are components of a home network which is controlled by the coordination-system.

Another important part of the domotics house is the user interface for controlling the system or to send movement command to the actuators. The most important interfaces utilized by users are universal remote controls and touch screens (Figure 11.15).

Figure 11.15: The most important interfaces utilized by users. (Photos: A: www.s-o-h.de, www.gewa.se, www.sicare.de. Source: B: WWW).

In Figure 11.15.A the remote controls (form left to right : James II, Prog III, Sicar Pilot) are shown, while in Figure 11.15.B a touch screen (Siemens) is shown. Both interfaces have different programmable push buttons, in order to adapt the functions of the domotics house to the personal needs of the users.

The research in domotics field is very important and continuously growing, in particular in rehabilitation field, because it represents a good solution to improve the autonomy and the quality of life of disabled and elderly people.

Virtual reality has been employed in BMI training systems because of its relative safety and motivational factors. Bayliss and Ballard describe a virtual driving environment that tested P300 responses when subjects encountered a stoplight (Bayliss & Ballard, 2000). Later work includes a virtual apartment which allows the user to interact with virtual people and objects (Bayliss, 2003). Mason et al. have used the LS-AFD device to allow users to navigate a maze by making turning decisions at intersections

(Mason et al., 2004). Pfurtscheller has used online analysis and classification of single EEG trials during motor imagery for navigation in an immersive virtual environment (Pfurtscheller et al., 2006), see also Figure 11.16. Virtual reality can provide a safe environment for training and tuning neurally controlled interfaces to real-world devices, such as a power wheelchair. More experimentation is necessary to determine if skills learned in a virtual-reality setting transfer to real-world scenarios.

The concept of environmental control is interesting also for space applications, where it can be applied for the monitoring and regulation of all sorts of environmental parameters like light, temperature and other devices inside a spaceship or space station. Spaceships pervasive computing is another possible application to which BCIs could give a direct interface.

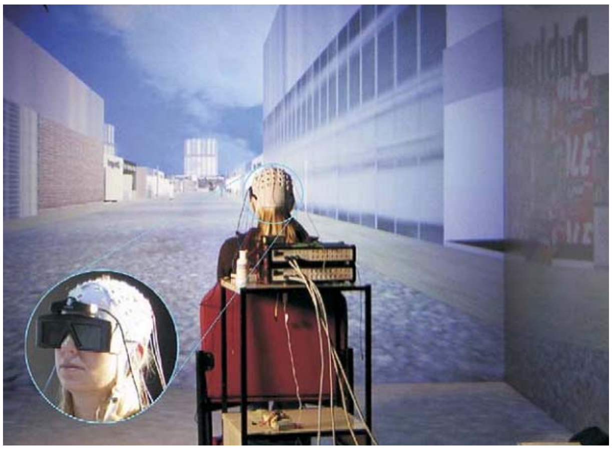

Figure 11.16: Picture of one participant during the experiment in an immersive virtual environment. (Reproduced from Pfurtscheller et al., 2006).

11.3.3 Space robotic applications

Besides alternative communication (see Section 11.3.1.1) and environmental control (see Section 11.3.2), space robotics is another field where BMIs could be tested and applied with success. We here briefly review the main devices of space robotics. Our aim is not to be exhaustive, but rather to offer a classification of space robots to help the decision of which among those can be potentially driven by a BMI. This will be discussed in Section 11.4.1.

11.3.3.1 Introduction

After four decades of manned space flight one might forget that the space environment continues to be extremely hostile to human beings. They have to be encapsulated in vehicles (for intra-vehicular activities, IVA) or special, extremely expensive suits, which protect them from the hazard of the space environment (for extra-vehicular activities, EVA) (Hirzinger et al., 2000). For this, automation and robotics (A&R) is become one of the most attractive areas in space technology; it allows to develop machines that are capable of surviving the rigors of the space environment, and performing exploration, assembly, construction, maintenance and servicing whit a very limited amount of highly expensive manned mission, especially reducing dangerous extravehicular activities. Space robots are important to operate in space because they can perform tasks less expensively or on an accelerated schedule, with less risk and occasionally with improved performance over humans doing the same tasks. They can operate for long durations, often “asleep” for long periods before their operational mission begins. They can be sent into situations that are so risky that humans would not be allowed to go (Bekey et al., 2006).

There are four key issues in space robotics:

- mobility: moving quickly and accurately between two points without collisions and without putting the robots, astronauts, or any part of the worksite at risk;
- manipulation: using arms and hands to contact worksite elements safely, quickly, and accurately without accidentally contacting unintended objects or imparting excessive forces beyond those needed for the task;
- time delay: allowing a distant human to effectively command the robot to do useful work;
- extreme environments: operating despite intense heat or cold, ionizing radiation, hard vacuum, corrosive atmospheres, very fine dust, etc.

In this section we provide a classification of space robots, together with some examples, in order to understand the possible applications of BMIs to space.

11.3.3.2 Classification

First, space robots can be classified according the control distance between humans and robots. In this case, there are two kinds of control:

- local: humans control space robots from a “local” console, as astronauts inside the pressurized cabin, with essentially zero speed-of-light delay;
- remote: humans control space robots from a “remote” console, as humans operators on Earth, with non-negligible speed-of-light delays.

Space robots can be also classified, according the specific application, into:

- rover robots;
- manipulator robots;
- “astronaut-equivalent” robots;
- free-flyer robots.

11.3.3.3 Rover robots

Rover robots are vehicles launched by a lander over a planet or a satellite. They are designed to move in tortuous areas and to ride out obstacles; for this they have a lot of wheels and they have solar panels for power. The most important tasks of rovers is the exploration of planet or satellite and the characterisation of a wide range of rocks and soils.

The first rovers was used on the Moon (Lunar Roving Vehicle - Lunar rover – LRV) on July 31, 1971 during the *Apollo 15* mission (Figure 14.17). LRVs were used for greater surface mobility during the Apollo program J-class missions (*Apollo 15*, *Apollo 16*, and *Apollo 17*). The Apollo LRV was an electric vehicle, with maximum speed of 13 km/h, designed to operate in the low-gravity vacuum of the Moon and to be capable of traversing the lunar surface, allowing the Apollo astronauts to extend the range of their surface extravehicular activities. These NASA's rovers have been abandoned on the Moon.

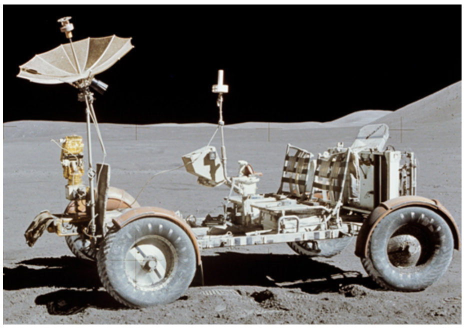

Figure 14.17 : Lunar Roving Vehicle (NASA). (Photo: nssdc.gsfc.nasa.gov).

Also on that list are the Soviet Union's unmanned rovers named Lunokhod 1 (1970) and Lunokhod 2 (1973).

The rovers are also used for Mars exploration. The first robotic roving vehicle to be sent to the Mars is Sojourner (JPL – launch December 4, 1996) (Figure 11.18) which explored Mermaid Dune in the summer of 1997. Sojourner had six wheels and could move at speeds up 0.6 meters per minute. It was controlled remotely by an earth-based operator (with a 10 minute time delay), but the rover also had some autonomous control, and could negotiate obstacles with a set of laser pointers and some insect-like artificial intelligence. The first function of Sojourner was to demonstrate that small rovers could operate on Mars.

Figure 11.18: Sojourner. (Photo: mars.jpl.nasa.gov).

Two MER (Mars Exploration Rover) rovers, Spirit and Opportunity, created by the JPL (Jet Propulsion Laboratory), were sent to explorer the Martian surface in 2003.

Figure 11.19: The rover Spirit. (Picture: science.nasa.gov).

These robotic geologists are equipped with a robotic arm, a drilling tool, three spectrometers, and four pairs of cameras that allow them to have a human-like, 3D view of the terrain. Each rover can travel as far as 100 meters in one day to act as Mars scientists' eyes and hands, exploring an environment where humans cannot yet go. The most important feature of the two rovers is autonomy of movement: the human operators from Earth give the end-point for mobility and/or manipulation, then the robot plans the better paths through the obstacles field eliminating the need for moment-to-moment interaction with humans on the Earth.

11.3.3.4 Manipulator robots

Telerobotics technology has been developing within the Space Program since the start of the Space Transportation System. The first and most famous robot manipulator in space is the Remote Manipulation System (RMS) (Hannaford et al., 1995) of the Space Shuttle or Canadarm (Figure 11.20).

Figure 11.20: Space Shuttle's Remote Manipulator System or Canadarm. (Source: WWW) .

It is an electromechanical arm that manoeuvres a payload from the payload bay of the space shuttle orbiter to its deployment position and then releases it. It can also grapple a free-flying payload, manoeuvre it to the payload bay of the orbiter and berth it in the orbiter. he RMS has six joints that correspond roughly to the joints of the human arm, with shoulder yaw and pitch joints; an elbow pitch joint; and wrist pitch, yaw, and roll joints. The end effector is the unit at the end of the wrist that actually grabs, or grapples, the payload.

The movement of the RMS is controlled by the Space Shuttle General-Purpose Computer (GPC). The hand controllers used by the astronauts tell the computer what the astronauts would like the arm to do. Built in software examines what the astronauts commanded inputs are and calculates which joints to move, what direction to move them in, how fast to move them and what angle to move to. As the computer issues the commands to each of the joints it also looks at what is happening to each joint every 80 ms. Any changes inputted by the astronauts to the initial trajectory commanded are re-examined and recalculated by the GPC and updated commands are then sent out to each of the joints. The RMS control system is continuously monitoring its "health" every 80 ms and should a failure occur the GPC will automatically apply the brakes to all joints and notify the astronaut of a failure condition. The control system also provides a continuous display of joint rates and speeds, which are displayed on monitors located on the flight deck in the orbiter. As with any control system, the GPC can be over-ridden and the joints can be operated individually from the flight deck by the astronaut.

Another important example of arm manipulator, is ROTEX (Roboter Technologie Experiment) (Figure 11.21) developed by the German Aerospace Center (DLR) which flew in a cabinet on the SPACELAB module in the Space Shuttle in 1993. ROTEX is an experiment which has successfully proved for the first time that a robot in space could be remotely controlled. Its gripper was provided with a number of sensors, especially two 6-axis force-torque wrist sensors, tactile arrays, grasping force control, an array of 9 laser range finders and a tiny pair of stereo cameras to provide a stereo image out of the gripper. In addition a fixed pair of cameras provided a stereo image of the robot's working area (Hirzinger et al., 1994). It could be controlled in three modes: teleoperation on board (astronauts using stereo-TV-monitor), teleoperation from ground via human operators, sensor-based off-line programming.

Figure 11.21: The Rotex arm. (Photo: www.dlr.de).

11.3.3.5 "Astronaut-equivalent" robots

An "astronaut-equivalent" robot is designed specifically to work with and around humans. The robot's considerable mechanical dexterity allows it to use EVA tools and manipulate flexible materials much like a human astronaut would. Moreover, space suits often do not allow free dexterous movement, a limitation which can be overcome by using a robot manipulator.

The most important example of "astronaut-equivalent" robot is Robonaut (Johnson Space Center) (Figure 11.22).

Figure 11.22: Robonaut performing dexterous grasp. (Reproduced from Wilcox et al., 2006).

The central premise of Robonaut is that a robot that is about the same size, strength, and dexterity as a suited astronaut will be able to use all the same tools, handholds, and implements as the astronaut, and so will be able to “seamlessly” complement and supplement human astronauts. The robot closely resembles the form of a suited astronaut except that it has only one leg instead of two, moreover the robot incorporates more than 50 coordinated degrees-of-freedom and physical capabilities approaching those of a human in a spacesuit (Figure 11.23) (Rehnmark et al., 2004).

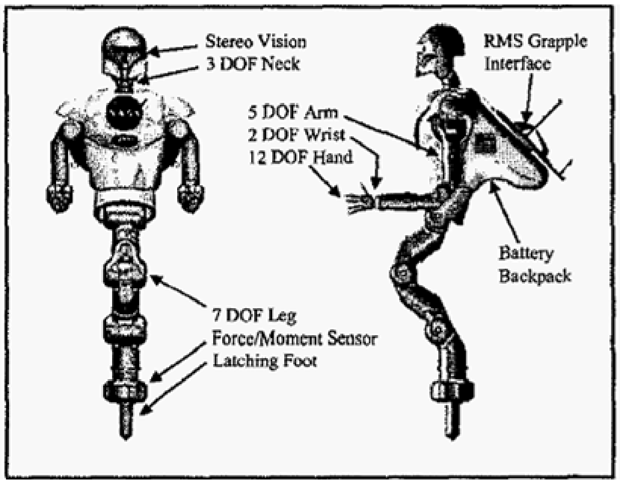

Figure 11.23: Robonaut. (Reproduced from Rehnmark et al., 2004) .

Robonaut is a teleoperated master-slave system in which a human teleoperator becomes the robot master (Figure 11.24) . Because Robonaut is designed to work with and around humans, the human-machine interface is central to the high-level control system design, which also incorporates distributed autonomy and learning modules.

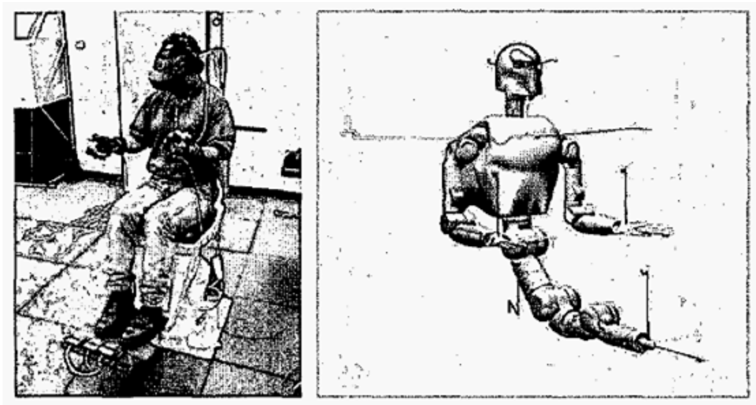

Figure 11.24: Master-slave system to control Robonaut. (Reproduced from Rehnmark et al., 2004) .

The fundamental control methods for Robonaut are Cartesian position control of the arms, neck and leg and joint position control of the hands. For relatively small forces, Robonaut uses an impedance control law.

The Robonaut Hand has a total of fourteen degrees of freedom. It consist of a forearm motors and drive electronics, a two degree of freedom wrist, and a five finger, twelve degree of freedom hand. The hand itself is broken down into two sections: a dexterous work set which is used for manipulation and a grasping set which allows the hand to maintain stable grasp while manipulating or actuating a given object (Laschi et al., 2000, Lovchik & Diftler, 1999).

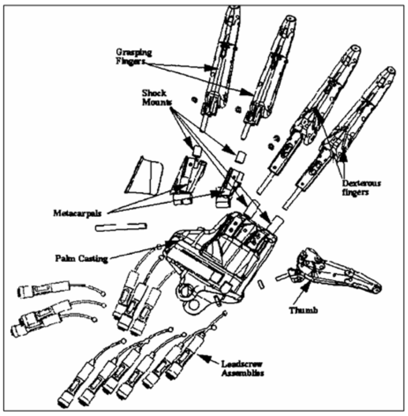

Figure 11.25: Robonaut Hand. (Reproduced from Laschi et al., 2000).

Another robotic hand for space application is developed by DLR (Deutsches Zentrum fuer Luft- und Raumfahrt). It is a multisensory four-finger hand with twelve total degrees of freedom.

Figure 11.26: DLR's hand. (Reproduced from Laschi et al., 2000).

11.3.3.6 Free-flyer robots

One relatively straightforward use of robotics in space is free-flying inspection. The first free-flying space robot is the Japanese ETS-VII (Engineering Test Satellite VII) (Hirzinger et al., 2002) launched in 1997. It consists of a pair of satellites, a "Chaser" satellite and a "Target" satellite (Figure 5.27) (Oda et al., 1996). Each satellite was separated in space after launching and a rendez-vous docking experiment was conducted twice, where the Chaser satellite was automatically controlled and the Target was being remotely piloted. Then the system consist of the on-board segment and the on-ground segment. The on-ground robot control station will be located at NASDA (National Space Development Agency of Japan) space centre where the satellite tracking control centre is located. The onboard robot system is mounted on ETS-VII Chaser satellite. In addition, there were multiple space robot manipulation experiments which included manipulation of small parts and propellant replenishment by using the robot arms installed on the Chaser as ETS-VII Robot Arm. This arm is a 6-degrees-of-freedom manipulator whose length is approximately 2 m).

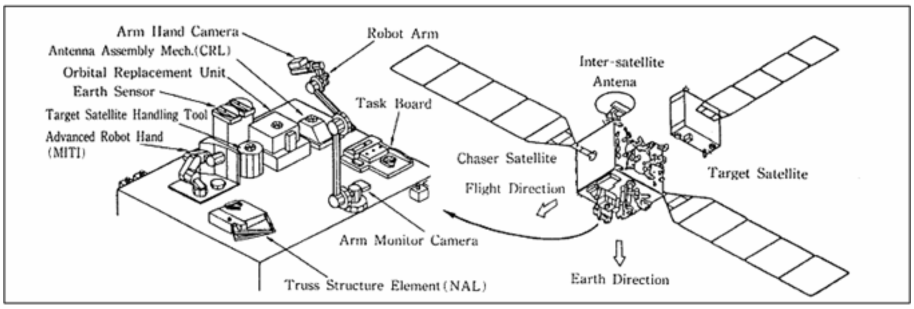

Figure 5.27: ETS-VII: Chaser satellite and Target satellite. (Reproduced from Oda et al., 1996).

ETS-VII robot arm works in three operation mode: the telemanipulation mode, the pre-programmed execution mode, and the real-time execution mode.

Another example of robot for free-flying inspection is AERCam Sprint (Activity Robotic Camera Sprint), developed by JSC (Johnson Space Center), that was flown as part of a space shuttle in 1997. This spherical (14" diameter) (Figure 11.28.A) vehicle was remotely controlled from within the Space Shuttle cabin, and was able to perform inspection of the exterior of the Space Shuttle. Sadly, the vehicle has not been flown since, and in particular was not on-board during the final mission of the Shuttle Colombia, where in-flight inspection might have changed the outcome.

Figure 11.28 shows the Mini-AERCam, which is a small (8" diameter) successor to the AERCam-Sprint that has been funded subsequent to the Colombia disaster for routine operational use on future missions (Figure 11.28.B).

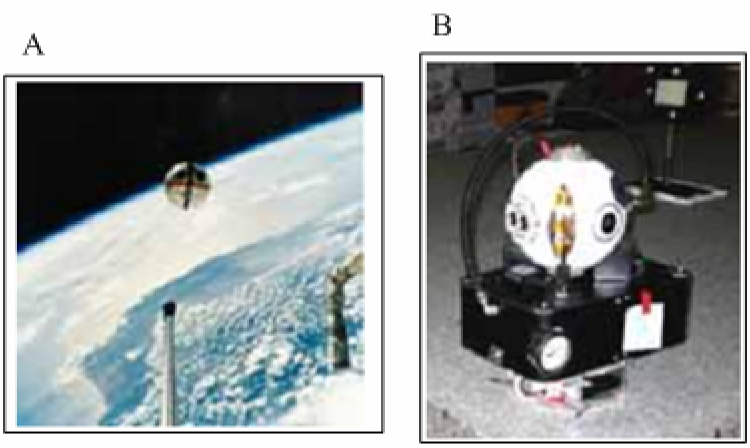

Figure 11.28: A: AERCam Sprint. B: Mini-AERCam.(Reproduced from Wilcox et al., 2006).

11.3.4 Throughput and latency needs of applications

In the last sections we have described the main space applications of robotics, environment control and communication. We also listed rehabilitation robotics applications and domotics. In this section, we will decscribe the needs of these applications in terms of two important numerical parameters that will allow us to select appropriate interfaces for driving those applications, namely *throughput* and *latency*.

- Throughput (also called *bitrate*, *bandwidth*, or *information transfer rate*) is the rate at which a computer or network sends or receives data. It therefore is a good measure of the channel capacity of a communications link, and connections to the internet are usually rated in terms of how many bits they pass per second (bit/s).
- Latency is a time delay between the moment something is initiated, and the moment one of its effects begins. The word derives from the

fact that during the period of latency the effects of an action are latent, meaning "potential" or "not yet observed".

The difference between throughput and latency is that latency is measured from the time a request (e.g. a single data packet) leaves the client to the time the response (e.g. an acknowledgment) arrives back at the client from the serving entity. The unit of latency is time. Throughput on the other hand is the amount of data that is transferred over a period of time. For example if over ten seconds twenty packets are transferred then the throughput would be 20/10=2 packets per second. Throughput can have many units (for example: bits/s, bytes/s, or packets/s), but it is always measured in a volume-per-time ratio.

However it is a very bad measurement of perceived speed, which is mostly based on how quickly it responds to you. Responsiveness has far less to do with throughput than latency. As the classic example goes, a station wagon full of magnetic tape has excellent throughput and horrible latency. It may take a week to deliver data from California to New York, but can carry so much that the throughput is better than broadband. Yet a user who has to wait a week to see a web page will complain that they preferred their much faster dialup connection!

Normally throughput and latency are opposed goals. To improve latency you typically want to increase how much the computer checks to see if you are trying to interact. This checking overhead slows you down. However, there is one very common exception to this rule. Network protocols and programs tend to synchronize both ends regularly. If these synchronizations are slow, then throughput can suffer horribly.

In the following, we will introduce one table for every class of applications listed in the previous sections. For every class, we define a range for both throughput and latency. Concerning throughput, we analyzed several ways to control the applications and their communication needs. We computed the throughput in b/s (bits/second) as the products of the number of bits per unit command (bit/command) and the number of commands per second (command/s) that have to be sent to the device to be able to control it interactively.

The required value of throughput depends on the control system of the device:

1. A low-level controller with no autonomy will leave all decisions to the users and will require many simple commands to be driven interactively, like in driving a car, where the user has to control almost everything by theirself, apart from the combustion of the engine, he/she has to steer, to accelerate/brake, to shift gears, etc. In this case, the commands will be simple (few bits/command) but frequent (many commands/s).
2. On the other hand, high-level controller with a high degree of autonomy will accept complex commands from the users and then do lots of things autonomously, like a CNC machine or a computer-aided manufacturing robot, where the commands usually are: fabricate part number 304832. Such a controller will require

complex commands (many bits/command) but less often (few commands/s).

The value of latency, depends on how interactive the system is intended to be and how much a feedback is needed to close the control loop. Latency is especially important for space applications, since latency will increase according to the distance of the user to the controlled devices, which can be also very far apart (in terms of light speed). It is clear that there is some connection between of commands/s and latency: if an application requires N commands/s and latency (for a round trip) is T seconds, the user will get feedback about its intended action every T seconds, but in the meantime, TN commands will have been sent to the device. Therefore, to ensure that feedback can affect the subsequent command, $NT<1$ is required. On the other hand, it might be possible to send several commands without affecting the stability of the control loop, e.g. because the commands refer to different degrees of freedom or because of internal control loops or control strategies that might rely on data coming from device-mounted sensors. It is often difficult to say which is the biggest acceptable latency for communicating with the user, so that he/she still feels interacting with the device and not frustrated by the long waiting time. We will discuss this issue further when identifying which interfaces satisfy specific application needs (Section 11.4.1). In the meantime, in this section, we list approximate but likely values for the different applications.

Rehabilitation

Hand	**bit/command**	**command/s**	**bit/s**	**latency (s)**
Worse	2	0.2	0.4	5
Best	36	3	108	0.3

Table 11.3: Bandwidth and latency from the worse to the best rehabilitation hand.

Wheelchair	**bit/command**	**command/s**	**bit/s**	**latency (s)**
Worse	2	0.3	0.6	3
Best	10	3	30	0.3

Table 11.4: Bandwidth and latency from the worse (digital) to the best (analogical) wheelchair (mobility aid).

Manipulation aid	**bit/command**	**command/s**	**bit/s**	**latency (s)**
Worse	12	0.6	7.2	2
Best	22	3	66	0.3

Table 11.5: Bandwidth and latency from the worse to the best manipulator arm (manipulation aid).

Feeder	bit/command	command/s	bit/s	latency (s)
Worse	1	0.03	0.03	10
Best	3	0.2	0.6	1

Table 11.6: Bandwidth and latency from the worse to the best feeder robot (manipulation aid).

Manipulator + Hand	bit/command	command/s	bit/s	latency (s)
Worse	-	-	7.2 + 0.4 = 7.6	2
Best	-	-	66 + 108 = 174	0.3

Table 11.7: Bandwidth and latency from the worse to the best system manipulator arm + hand.

Manipulator + Hand + Wheelchair	bit/command	command/s	bit/s	latency (s)
Worse	-	-	7.2 + 0.4 + 0.6 = 8.2	2
Best	-	-	66 + 108 + 30 = 204	0.3

Table 11.8: Bandwidth and latency from the worse to the best system manipulator arm + hand + wheelchair.

<u>Domotics</u>

Domotics	bit/command	command/s	bit/s	latency (s)
Worse	1	0.1	0.1	10
Best	6	1	6	0.3

Table 11.9: Bandwidth and latency from the worse to the best environmental control application.

<u>Space</u>

Rover	bit/command	command/s	bit/s	latency (s)
Worse	2	0.03	0.06	30
Best	10	3	30	0.3

Table 11.10 Bandwidth and latency from the worse to the best rover robot for space application. A space rover can be compared to a wheelchair (2 translation dof and 1 rotation dof), except that it does not need to be very interactive, since it can move very slowly or be provided with embedded sensors for autonomous movement control. Therefore the worst-case values are lower.

Manipulator arm	**bit/command**	**command/s**	**bit/s**	**latency (s)**
Worse	12	0.6	7.2	2
Best	22	3	66	0.3

Table 11.11: Bandwidth and latency from the worse to the best manipulator arm for space application. Concerning interactivity, even with movement scaling, a manipulator arm for space applications has requirements similar to a manipulation arm for rehabilitation.

Hand	**bit/command**	**command/s**	**bit/s**	**latency (s)**
Worse	2	0,2	0,4	5
Best	36	3	108	0.3

Table 11.12: Bandwidth and latency from the worse to the best robotic hand for space application.. Concerning interactivity, even with movement scaling, a robot hand for space applications has requirements similar to a prosthetic hand for rehabilitation.

Astronaut Equivalent Hand	**bit/command**	**command/s**	**bit/s**	**latency (s)**
Worse	2	2	4	2
Best	24	3	72	0.3

Table 11.13: Bandwidth and latency from the worse to the best astronaut-equivalent robotic hand. In case of the astronaut-equivalent hand, figures differ than from the generic robot hand for space applications, since fine manipulation capabilities are required.

Astronaut Equivalent Arm	**bit/command**	**command/s**	**bit/s**	**latency (s)**
Worse	14	2	28	2
Best	20	3	60	0.3

Table 11.14: Bandwidth and latency from the worse to the best astronaut-equivalent robotic arm. In case of the astronaut-equivalent hand, figures differ than from the generic robot arm for space applications, since fine positioning capabilities are required.

Astronaut Equivalent Leg	bit/command	command/s	bit/s	latency (s)
Worse	12	0.1	1.2	10
Best	20	1	20	1

Table 11.15: Bandwidth and latency from the worse to the best astronaut-equivalent "leg", i.e. the positioning of the trunk. Trunk movements for positioning can be performed with lower throughput and higher latency than for hand/arm movements. The figures in this table allow a fair range of interactivity levels.

Astronaut Equivalent Head	bit/command	command/s	bit/s	latency (s)
Worse	4	0.1	0.4	5
Best	9	2	18	0.5

Table 11.16: Bandwidth and latency from the worse to the best astronaut-equivalent head. Head movements for changing camera orientation can be performed with lower throughput and higher latency than for hand/arm movements. The figures in this table allow a fair range of interactivity levels.

Astronaut Equivalent	bit/command	command/s	bit/s	latency (s)
Worse	-	-	4x2 + 28x2 + 18 = 82	2
Best	-	-	72x2 + 60x2 + 111 = 375	0.3

Table 11.17: Bandwidth and latency from the worse to the best astronaut-equivalent robot. These figures are the overall requirements of the whole astronaut-equivalent robot.

Free-flyer	bit/command	command/s	bit/s	latency (s)
Worse	12	0.1	1.2	30
Best	18	1	18	1

Table 11.18: Bandwidth and latency from the worse to the best free-flyer robot for space application. Free-flyer robots, as rovers, do not need to be very interactive, since they can move very slowly or be provided with embedded sensors for autonomous movement control. Unlike rovers, they have 3 translation and 3 rotation dofs, so they require more complex commands. Minimum latency has been slightly increased.

The following figures plot the same throughput-latency requirements, grouping all applications in domotics and rehabilitation (Figure 11.29) and space (Figure 11.30).

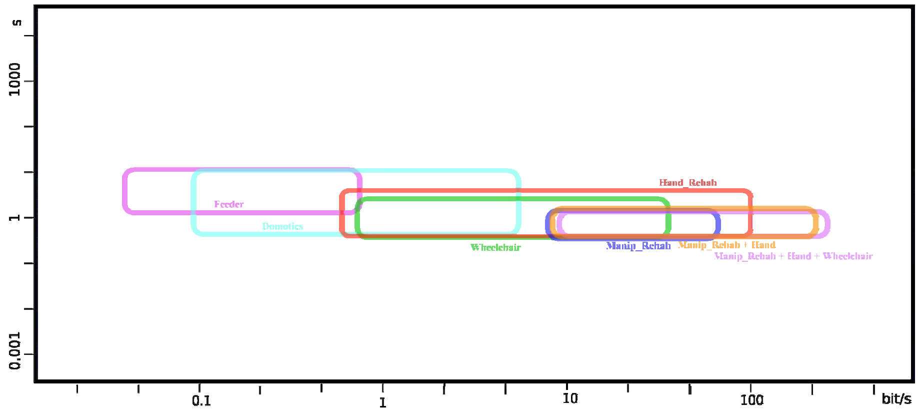

Figure 11.29: Throughput and latency requirements of domotics and rehabilitation applications.

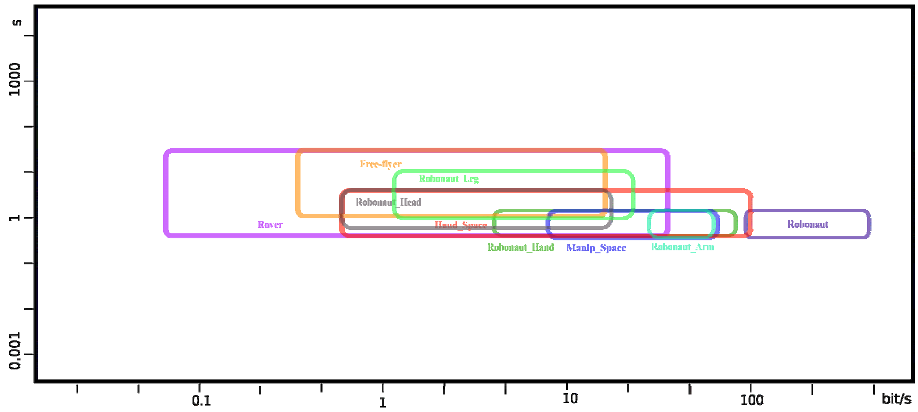

Figure 11.30: Throughput and latency requirements of space applications.

11.3.5 Performance of available interfaces

In this section we will list and plot the performance of various types of interfaces, in terms of throughput (b/s) and latency, as measured from various works found in literature. The problem here is to get a uniform measure of throughput, since different authors usually define them differently. The approximate ranges for the latency and throughput presented in the chart are averages and extrapolations from the different papers in literature, especially the ones referred above for each interface. Concerning throughput, the Shannon information rate is meant (Shannon, 1948). In most papers it is not reported but the number of symbols, the error probability and the transfer rate (symbols/s) is stated or can be inferred. In these cases a symmetric N-symbol channel with symbol rate R and error probability (1-P) is hypothesized. Therefore the throughput has been calculated as:

$$B = R \cdot \left(\lg_2 N + P \lg_2 P + (1-P) \lg_2 \frac{(1-P)}{(N-1)} \right).$$

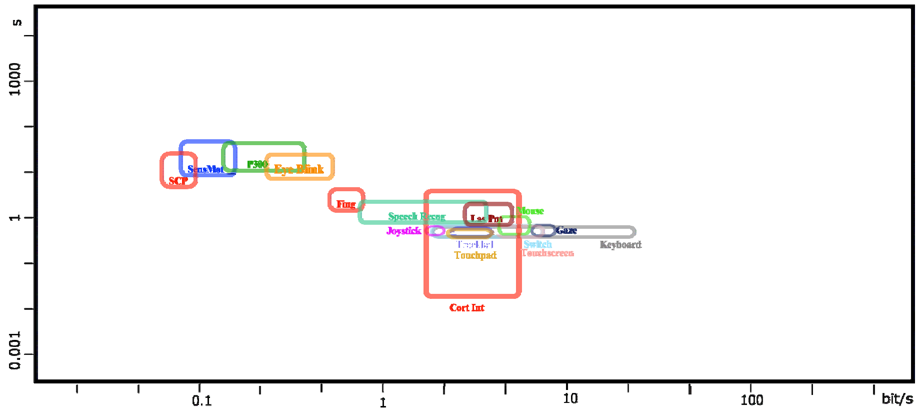

Figure 11.31: Throughput and latency of various HCIs

In Figure 11.31, latency and throughput are reported for different Human-Machine Interfaces (HCIs). The plot is not meant to be an exhaustive coverage of all the different interfaces available nor to reproduce the performance of the interfaces in a quantitatively rigorous way. Nevertheless it can be useful to sketch qualitatively the performance in terms of throughput and latency of the interfaces available in order to determine which one can be adequate for a specific task and which cannot.

Interfaces labelled in *italic* font are Brain-Machine Interfaces while the others are not and are somehow dependent on muscular intermediation.

The reported BMIs are:

- *SCP*: Slow Cortical Potentials (Birbaumer et al., 2000; Kronegg et al., 2005).
- *SensMot*: Sensorimotor cortex rhythms (McFarland et al., 2003; Obermaier et al., 2001; Kronegg et al., 2005).
- *P300*: P300 evoked potentials (Donchin et al., 2000; Kaper et al., 2003; Kronegg et al., 2005).
- *Cort Int*: Cortical interfaces (Serruya et al., 2002; Santhanam et al., 2005).

While examples of other HCIs are:

- *Eye Blink*: a camera based speller using eye blinks (Grauman et al., 2001).
- *Fing*: a camera based finger counter (Crampton & Betke, 2002).
- *Speech Recog*: Tiny and small vocabulary automatic speech recognition systems (Urban & Bajcsy, 2005; Axelrod et al., 2005).
- *Las Pnt*: Laser pointer (Oh & Stuerzlinger, 2002).

Concerning the performance of several standard HCI interfaces, as mice, trackballs, keyboards etc, we used comparative interface studies of HCIs (Fitts, 1954; Card et al., 1978; Plaisant and Sears, 1992; Hyrskykari, 1997; MacKenzie et al., 2001; Oh & Stuerzlinger, 2002; MacKenzie & Soukoreff, 2003;), the ISO Standard 9241-9 (ISO 9241-9, 2000) and inferred some data from average speeds of touch-typists (for keyboards) (Smith and Cronin, 1992; Khurana & Koul, 2005) and telegraphers (for a single switch). From the comparative studies, we report throughput measured for mouse, joystick, trackball, touchpad, and touchscreens. We also report data on gaze-based interfaces (Jacob, 1990; Sibert and Jacob, 2000; De Silva et al., 2003 ; Xiao et al., 2005).

Those are listed in the Tables 11.19-11.26 below.

Mouse	**bit/s**	**latency (s)**
From	4.5	0.3
To	5.3	1

Table 11.19: Bandwidth and latency for mouse interface.

Trackball	**bit/s**	**latency (s)**
From	2.8	0.3
To	3.2	0.5

Table 11.20: Bandwidth and latency for trackball interface.

Touchpad	**bit/s**	**latency (s)**
From	2.6	0.3
To	3.2	0.5

Table 11.21: Bandwidth and latency for touchpad interface.

Joystick	**bit/s**	**latency (s)**
From	1.6	0.3
To	2.0	0.5

Table 11.22: Bandwidth and latency for joystick interface.

Keyboard	**bit/s**	**latency (s)**
From	15	0.3
To	23	0.5

Table 11.23: Bandwidth and latency for keyboard interface.

Touchscreen keyboard	**bit/s**	**latency (s)**
From	4	0.3

To	8	0.5

Table 11.24: Bandwidth and latency for touchscreen keyboard interface.

Switch	bit/s	latency (s)
From	2	0.3
To	8	0.5

Table 13.25: Bandwidth and latency for morse code interface.

Gaze control	bit/s	latency (s)
From	5.9	0.3
To	8.5	0.5

Table 14.26: Bandwidth and latency for gaze control interface.

11.4 Possible demonstrators

In this section we first match the tables of interface performance and application needs that we have presented in the previous section. This allows us to identify realistically which applications can be driven by means of a BMI and also which type of BMI is required for a given application. Next, based on this analysis, we define a few demonstrators among those possible applications, choosing them also according to other factors, such as responsiveness and autonomy. The demonstrators have been defined for applications both in intra-vehicular activities (IVA) and in extra-vehicular activities (EVA) and are the following:

1. BMI-driven rover (EVA);
2. Hands-free control of cameras and maps (IVA or EVA);
3. BMI for spaceship environmental control (IVA).

We describe the applications here in Section 11.4 and will further focus on the details of their possible implementation in Section 11.5.

11.4.1 Merging performance and needs

Here we present and discuss the overlap, in terms of throughput and latency, of the needs of various applications in rehabilitation, environmental control and space with the performance of brain-machine interfaces.

In Figures 11.32 and 11.33 we show the overlap of application needs and interface performance. In order to reduce the complexity of the figures, we have split the plots in two parts. The upper part of the figures focuses on applications, i.e. it show the requirements of each single application, superimposed on the overall interface performances that is drawn as a single uniformly-coloured area to represent all available interfaces. On the other hand, the lower part of the figures focuses on interfaces, i.e. it shows the opposite: on a background, uniformly-coloured area that represents the overall requirements of all applications, the performance of the single interfaces are draws. Matching the upper and the lower part of the figures, it is possible to point out whether the performance of a single interfaces matches the needs of a single application. Drawing all interfaces and application on one graph would have resulted in a too confused and unreadable figure. It is worth noting that in the upper parts of the figures, the background area representing the interfaces has been drawn with no upper limits on latency, i.e. the background area is reaching the top of the plot. This is because interfaces, according to the technology they are based on, have a minimum latency which limits their performance. In principle, it is always possible to wait for a command to be received by a remote location with an high latency; of course, high latency limits responsiveness, but this is not an intrinsic limitation of the interface itself, but rather of the whole system.

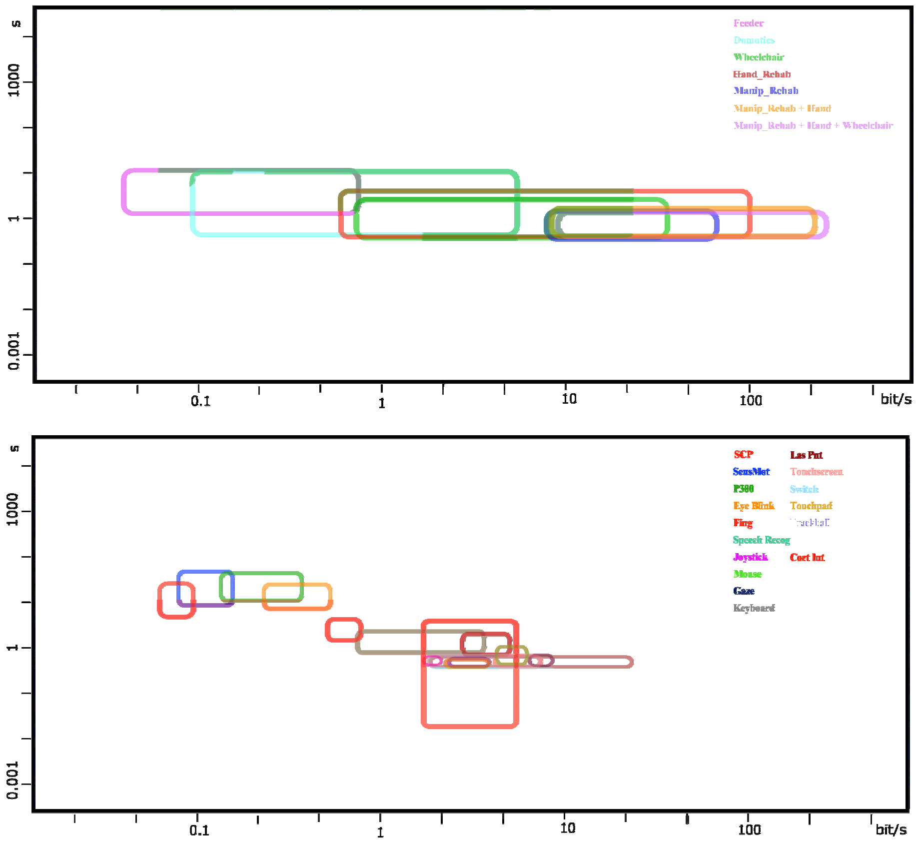

Figure 11.32: Overlap between rehabilitation applications needs and interface performance.

Concerning rehabilitation application, we see that there is an overlap for low throughput non-invasive BMIs (SCP, SensMot, P300) with robotic feeder and domotics applications. For these application, several studies have already been published (Bayliss & Ballard, 2000; Bayliss, 2003; Mason et al., 2004; Pfurtscheller et al., 2006). All other rehabilitation applications require higher throughputs that are currently feasible with non-invasive BMIs. Concerning invasive interfaces (CortInt), since they provide throughputs comparable with standard human-computer interfaces (HCI) as joysticks and mice, they could be used successfully for many rehabilitation applications, including wheelchair and prosthetic hand control, with even greater interactivity than standard HCIs. Of course, all interfaces can also be used for applications with lower throughput and higher latency requirements…

BMIs can successfully be used for some other rehabilitation applications, like word spelling, i.e. typewriting (Wolpaw et al., 2000; Kennedy et al., 2000; Perelmouter & Birbaumer, 2000; Donchin et al., 2000; Kennedy et al., 2000), hand orthosis control (Pfurtscheller et al., 2000; Kennedy et al., 2000), and wheelchair control (Millán et al., 2004). Nonetheless, it is worth noting that these are sub-optimal implementations of the applications: these applications are useful because for some patients there are no other alternative devices. However, the systems provided are not responsive enough, i.e. not as much as the user would expect to be able to use them interactively. E.g. EEG-based spellers reach a maximum throughput of 0.4 b/s (Wolpaw et al., 2002) which allows to type about 3 characters per minute. Writing can be sped up with incorporation of statistical language models (Ward & MacKay, 2002), or other techniques for word prediction such as T9 in cellular phones (Inverso et al., 2004), but this affects how the commands are formed, i.e. the requirement of the application, and not the interface throughput itself. Future advances in non-invasive BMIs will probably increase their performance and make these BMIs better suitable for rehabilitation, even if it will not be possible to achieve the performance of cortical interfaces.

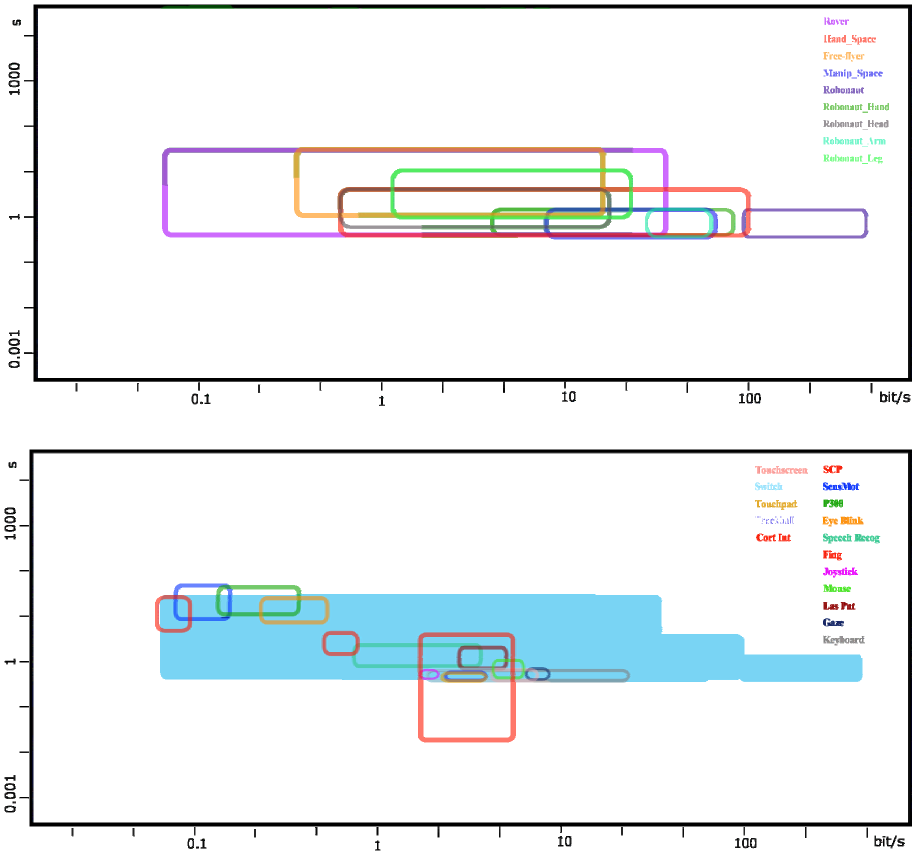

Figure 11.33: Overlap between space applications needs and interface performance.

Concerning space applications, we see that non-invasive BMIs have better potential than in rehabilitation. This is because of the higher latencies that are necessary (or that can be accepted) e.g. for moving space rovers or free flyers. It is worth noting, however, that systems with a high latency cannot interact rapidly with the user, therefore, to achieve stable controls, the systems must either move very slowly, or have a high degree of autonomy, i.e. it has to rely on an embedded controller which interacts with local sensors at interactive rates and receives, from time-to-time, some higher-level commands from the user, such as “move to the rock over there”, or “dock to the base station”, which will be interpreted by the embedded controller and transformed into lower-level commands. Also in these cases, however, the high cognitive load necessary to use non-invasive BMIs makes them less suitable than other conventional HCIs with higher throughput and lower latencies. E.g. it will be easier, more intuitive, more ergonomic and less tiring to drive a distant rover by means of a joystick than by means of a BMI, even if the use of a BMI will be feasible, e.g. for a demonstrator. On the other hand, again, cortical interfaces are suitable for a wide range of space applications, but their development will have to go through experimental validation first on primates, then on patients that underwent neurosurgery, and finally, maybe future, can be applied to healthy people for use as a BMI. For application with even greater latency, in the order of minutes or more, interactivity is not possible and BMI usage, although possible, would be senseless.

Concerning the driving of astronaut-equivalent robots (AER), it is worth noting that no *single* interface among those listed (not even conventional HCIs) is able to drive *all* degrees of freedom of the AER. However, this comparison in unfair: we should rather compare *single* components (arm, hand, trunk, etc.) of the AER to *single* interfaces. In this case, it is possible to drive them e.g. by means of joysticks or keyboards. In the following section, we will propose to control an astronaut-equivalent head by means of a BMI. There is no direct overlap between the application requirements and the interface performance: however, as in the case of the previously-mentioned rehabilitation applications, we are "almost there" and by means of a smart control, and by sacrificing some responsiveness, the application is feasible.

Moreover, there is another type of interface which has not been listed among the conventional interfaces in Section 11.3.5, namely *motion analysis systems*. The reason for this omission is the difficulty of computing throughput, since it is directly related to the human transfer function, which is not univocally defined and rather difficult to determine experimentally. Master systems based on optical, electromagnetic or electro-mechanic tracking systems allow high acquisition rates (frame rates of several hundred Hz are not uncommon). Therefore those systems are highly indicated for master/slave control of an AER, since the required throughput for movement does not exceed the one that can be produced by the human body, which we were not able to quantify at this stage but which are certainly lower than those measurable with full-body motion analysis systems or sensorized exoskeletons like NDI Optotrak, ViconPeak or MetaMotion Gypsy (see Figure 11.34).

Figure 11.34: Optical, electromagnetic and electro-mechanic motion capture systems. (Photos: www.metamotion.com).

11.4.2 D1: BMI-driven rover

This demonstrator is a quite-straightforward porting of an existing demonstrator for rehabilitation applications, namely a BMI-driven wheelchair, to a space application, by substituting the wheelchair with a space rover. In their work, Millan et al. show that “brain activity recorded non-invasively is sufficient to control a mobile robot if advanced robotics is used in combination with asynchronous electroencephalogram (EEG) analysis and machine learning techniques” (del R. Millán et al., 2004). They show how a Khepera robot, mimicking a wheelchair, can move through a maze, by using BMI commands and embedded IR obstacle detectors. The robot was controlled by an internal 6-states model, and the EEG input was classified according to a 3+1 states model (3 known states + 1 unknown state). In their experiment, mental control at a maximum obtainable bitrate of about 1 b/s, in which however real values were lower due to loss of attention by the user, was comparable to manual control on the same task with a performance ratio of 0.74.

The feasibility of the rover demonstrator in terms of BMI performance is shown in Figure 11.35. As also stated in the previous section, BMIs may not be the best choice for driving a rover: there is no direct need to use a BMI for controlling the rover, and that it has been proven that using another type of conventional interface, such as a joystick, yields better results with almost no training and user fatigue at all in using the interface. However, the application is feasible and a BMI-driver rover is currently a technologically-ready demonstrator.

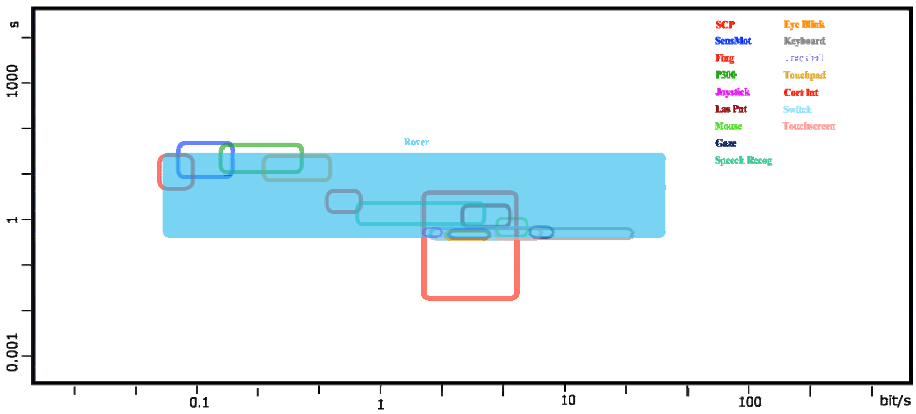

Figure 11.35:Suitability of BMI interfaces for the rover demonstrator in terms of throughput and latency.

11.4.3 D2: Hands-free control of cameras and maps

The demonstrator described here is an augmenting application, i.e. an application that could not be performed in the same way by one person alone. The typical situation for which the demonstrator is meant is the hands-free control of two degrees-of-freedom, in order to allow the user to control additional interfaces with his/her hands. Practical scenarios include:

- The steering of a camera (e.g. a rover-mounted camera, the robonaut head) while the user's hands are controlling the robot arms, by means of joysticks or exoskeletons (see Figure 11.36), for exploration or spaceship maintenance;
- The navigation through a map (scrolling the map or an image on a display) while the user's hands are controlling a keyboard and/or a mouse or are being used gesture recognition, e.g. by video or EMG (see Figure 11.37);
- The control of the grasp opening/closing and the grasp type of a robotic hand while the user's hands are controlling the robot arm by means of joysticks.

For an easy but still visually effective practical implementation of this demonstrator, the Robonaut could be simulated in a virtual environment instead of using a real robot.

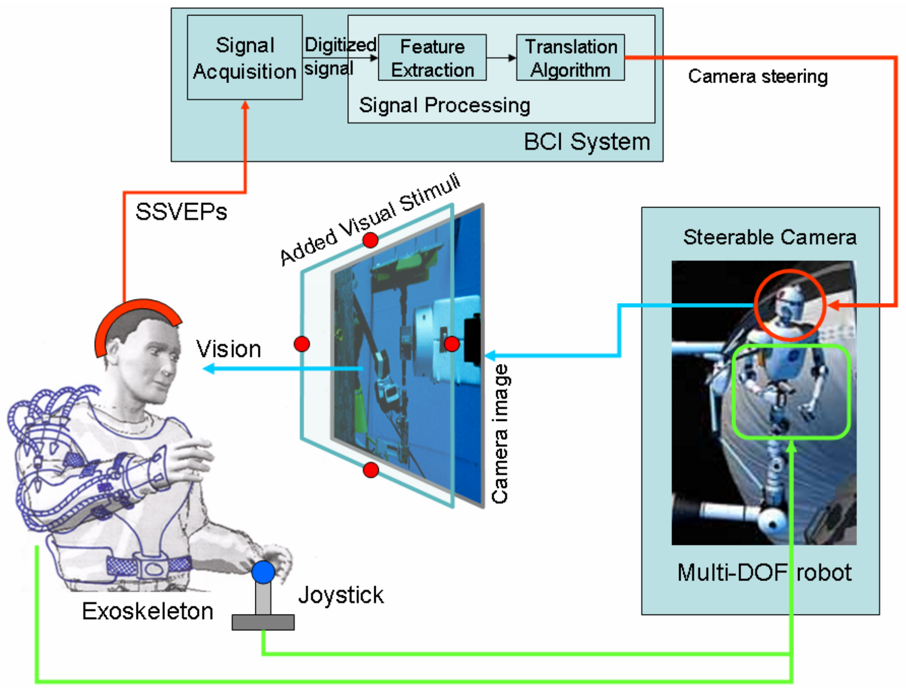

Figure 11.36:one of the possible scenarios for the proposed demonstrator: the user is moving the robot head by means of a BCI while his hands are using joysticks or an exoskeleton to control the arms of Robonaut. By shifting his/her attention to the added visual stimuli, whithout moving his gaze point, the elicited SSVEPs are used to control the steerable camera for EVA maintenance.

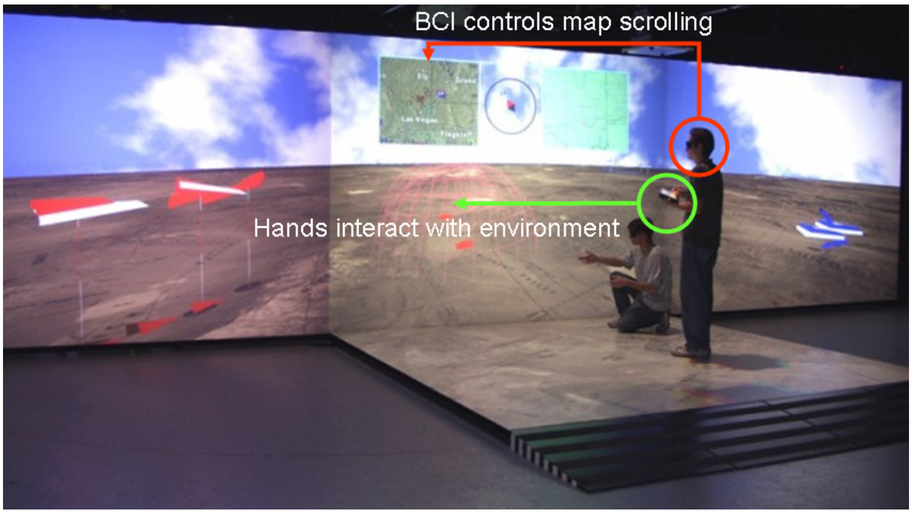

Figure 11.37:a second scenario for the proposed demonstrator: the user is interacting with the map by means of free hand gesture recognition, while map scrolling is controlled by means of a BMI. In this case, gaze direction is important to keep the attention on the scenario and the map and should not be used for scrolling. An independent BMI, as those proposed based on SSVEPs, can be used.

Concerning the feasibility of the application in terms of thoughput and latency, it must be noticed that the robonaut head does not intersect any of the non-invasive BMIs (see Figure 11.38). This excludes to be able to move the camera in a fluid, interactive way. However, it will be still possible to move the camera incrementally, in steps, as it were controlled by means of switches and sliders. The feasibility of this approach in terms of interface performance is shown in Figure 11.40 in the next section.

A related application has been very recently investigated by NASA: (Trejo et al., 2006) have developed and tested two EEG-based BCIs for 1-DoF and 2-DoF cursor control on a computer display. The 2-DoF application, named Think Pointer, allows hands-free navigation of moving maps and other displays. However, the difference with the approach that we propose here is that our approach is based on an *independent BMI*, i.e. a BMI that does not require voluntary muscle movement, whereas the BMI developed by Trejo et al. is a *dependent BMI* that requires changing of the gaze fixation point. In the scenario illustrated in Figure 11.37, the gaze fixation point is used to keep the attention on the scenario and should not be used for interacting with the map. Moreover, the approach of Trejo et al., from the user viewpoint, does not require a BMI: the same result could be achieved by means of a gaze tracker. Therefore we feel that our proposed approach is more suitable for a BMI demonstration.

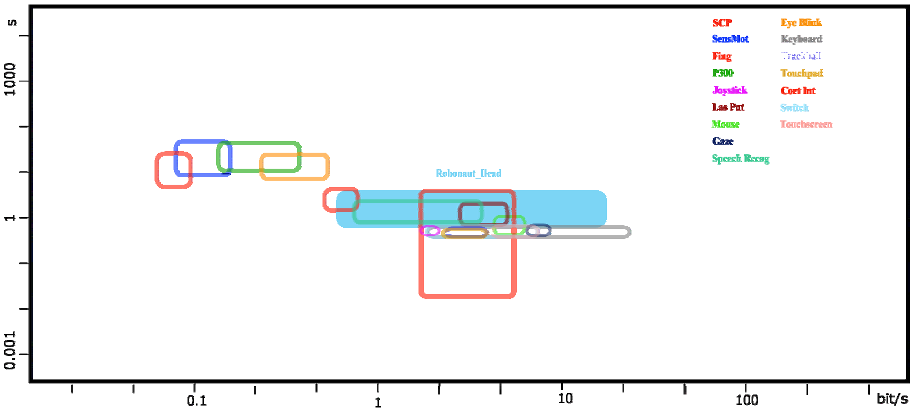

Figure 11.38:Suitability of BMI interfaces for hands-free control of steerable cameras and dynamic maps control in terms of throughput and latency.

11.4.4 D3: BMI for spaceship environmental control

The concept of environmental control is interesting also for space applications. Indeed, the control panel of a BMI is usually a simple interface composed of switches and sliders, which are controls that are easily implemented by means of a BMI. The feasible demonstrators, here, are the same than in domotics, ported to space application (see Figure 11.39). Again, for maximum visual effect, a virtual environment could be used to simulate a spaceship or space station instead of a real home.

As can be seen from Figure 11.40, several BMIs can be suitable for driving domotics and environmental control applications, even if they are not the best option. It is obvious that switches and sliders are the most intuitive way to control switches and sliders, but EEG-based BMIs have sufficient trhoughput and acceptable latency to be used for demonstrating BMI-based environmental control as a demonstrator.

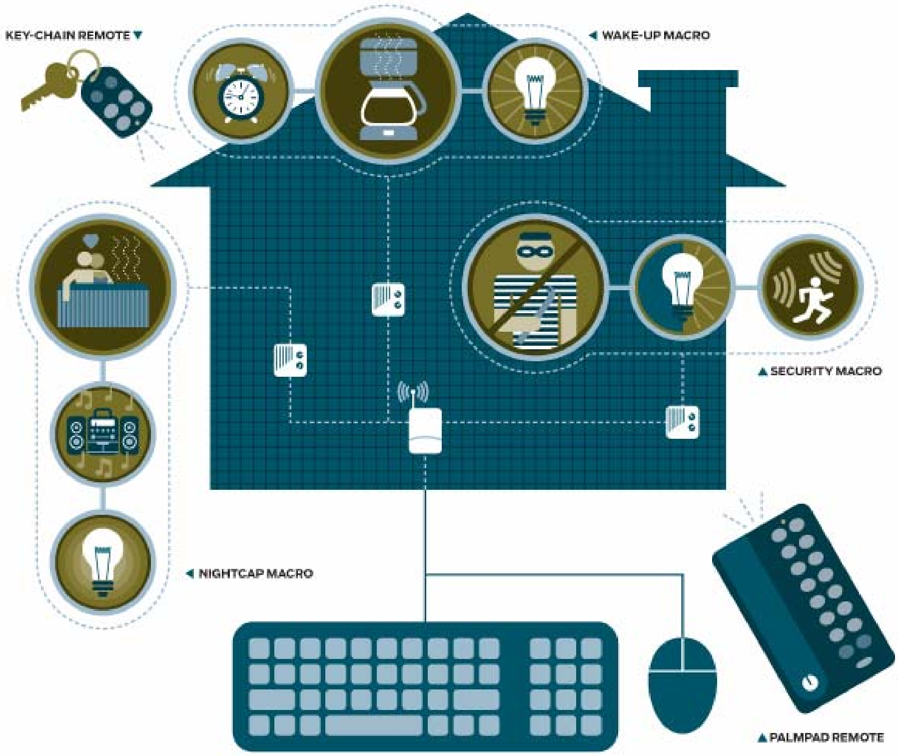

Figure 11.39: Home automation concept. Be means of a suitable centralized control center, the same result can be achieved by means of a BMI as a demonstrator for automation of spaceship or space station. (Source: WWW).

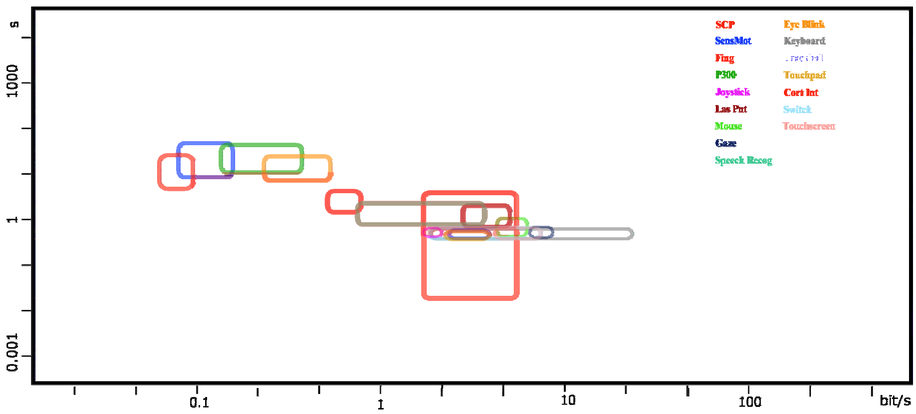

Figure 11.40: Suitability of BMI interfaces for domotics and environmental control in terms of throughput and latency.

11.5 Possible showstoppers

Possible showstoppers concerning specifically BMIs in space applications are hard to predict. Possibly they would be the same as on Earth plus some additional ones due to the environmental effects. Yet showstoppers on Earth are just partially known because the topic is mostly still at a research stage and has not yet reached clinical nor everyday applications. Therefore experiments are carried on in a controlled environment and not in their final working scene where further possible problems can arise.

Nevertheless, focusing on non-invasive EEG based BMI, we can identify a few key points:

- Electrical artifacts (probably invalidating some data but not necessarily ending the session):
    - artefacts from non-EEG biosignals (EMG, EOG, ...);
    - EEG artefacts (distracting events, drowsiness, anxiety, ...);
    - interference from the surrounding electrical equipment (fluorescent lights, ...).
    - shifting signals due to changes in conductive gel (or other materials) in prolonged situations – this can lead to useless signals due to a very low signal-to-noise ratio as the conductive gel dries,
    - transmission failure and/or noise if wireless systems are used,
- Mechanical artefacts (these apply to nIR systems as well):
    - discomfort with sensor array in confined spaces and in prolonged use (possibly days),
    - electrodes improperly attached or in poor condition may lead to variable impedances;
    - sweating can affect, for example, the impedances of the electrodes, cause the electrode to detach, or short-circuit two adjacent electrodes;
    - wires coming out from electrodes can interfere with the task the user is supposed to carry on and hamper their movements;
    - at the same time the user can inadvertently run up against a wire, pull it, and affect the electrical contact or even the electrode integrity.

The above issues are even amplified by the fact that, in the usual common reference configuration, all channels are recorded with respect to a common ground electrode. Therefore any problem concerning that electrode would affect all channels.

Concerning additional specific problems related to on space use of the interface, we can identify the following:

- sensor motion in high-g and abrupt motion situations - this can cause the pattern recognition system to lose track of the signal and may even lead to injury,

- additional interference related to environmental effects (see Section 11.2), such as disturbances from radiation in deep space (e.g., solar winds, etc.),
- the electrodes and the wiring must be protected because of the subject floating or the possibility that other floating objects collide with the electrodes or wiring;
- the set-up and initiating procedures could reveal to be difficult in zero gravity or when wearing gloves,
- power shortage in prolonged use.

As can be seen from the above, critical problems relate to hardware/material issues. Thus, the basic robustness of the system will require rethinking the engineering of currently available systems, almost all of which have in mind on-earth clinical and home environments only. This means that the development of BCI systems for space must include testing under the conditions listed above and the necessary redesigning that will imply. This will also likely require the use of different materials from the ones currently in use.

11.6 Possible solutions for implementation

In this section we provide further details about the implementation of one of the demonstrators proposed in the previous section. We have chosen **demonstrator D2 “Hands-free control of steerable cameras and dynamic maps”** because this system has a great potential for being an *augmenting BMI*. The underlying approach requires some visual attention of the user, but not the *complete* attention, therefore it should be possible for the user to **carry out other tasks while using the BMI**.

The implementation of this demonstrator is based on an independent BMI for general-purpose two degrees-of-freedom control, which is being investigated by the authors in the context of the “NEUROBOTICS: the Fusion of Neuroscience and Robotics” project, funded by the European Commission in the IST FET Programme (http://www.neurobotics.info). We here describe the approach underlying the augmenting BMI, since the possible applications have been discussed previously in Section 11.4.3.

Introduction

Steady-state visual evoked potentials (SSVEPs) are signals non-invasively recorded on the scalp of the subject while looking at a visual stimulus flickering at a certain frequency.

SSVEPs detected by means of Electroencephalography (EEG) have been used, e.g., in (Müller-Putz et al., 2005), to implement a Brain-Machine Interface (BMI). A set of two or more light sources flickering at slightly different frequencies is presented to the user. Each light is associated to a command the user can select by shifting the gaze to the corresponding light. The elicited SSVEPs have the same fundamental frequency as the stimulating frequency but they can also include higher order harmonics and sub-harmonics (Herrmann, 2001). Whenever the user fixates a certain flickering stimulus, a classification algorithm can infer the selected choice by frequency domain analysis.

This approach relies on a fine control of the gaze by the user. For certain impairments this can hard or even impossible to achieve. Even for able-bodied people, the need to shift the gaze to select a command can represent a heavy limitation to the possible applications of the system. All situations were the user is required to devote high attention to another task and to focus the gaze on it, are ruled out. A BMI where the user can covertly pay attention to a cue (with peripheral vision) to control the machine is therefore desirable and this study will focus on it.

The underlying dynamics of SSVEPs are not well understood but several studies among which (Müller et al., 1998) show relations with cognitive variables such as attention, stimulus classification and memory search. SSVEPs have been reported to behave as index of visual spatial selective attention (Morgan et al., 1996). This mechanism (also referred as “spotlight of attention”) allows the brain to focus on discrete locations in visual space for the allocation of processing resources.

The Multimodal Signal Processing group at University College of Dublin used the considerations and the results above as starting point to develop a pilot version of what they called visual-spatial attention control brain-computer interface (V-SAC BCI) (Kelly et al., 2005a). They used a paradigm with bilateral stimuli and provided the user with feedback. Six out of eleven subjects were able to devote visual spatial attention to the selected cue therefore engendering the required SSVEP modulations while gazing at a fixation cross.

In another experiment (Kelly et al., 2005b) they used the same protocol to record signals for later offline analysis. They recorded high spatial resolution EEG data (64-channel by means of active electrodes) in order to attempt to classify the left/right attention by extracting SSVEPs at optimal channels selected for each subject on the basis of the scalp distribution of SSVEP magnitudes. The accuracy was approximately 71% across ten subjects and increased up to 79% by combining SSVEP features with attention-dependent parieto-occipital alpha band modulations.

Aim

For the proposed demonstrator D2 “Hands-free control of steerable cameras and dynamic maps”, we plan to implement an independent brain-machine interface for two degree of freedom (DoF) control of a robotic device. At the state of the art the major issues reside in the interface itself rather than in the peculiar application. Therefore the demonstrator study should focus on the development of a general-purpose 2 DoF interface employable for a broad range of usages, among which are those proposed as D2 above. Once sufficient precision and reliability are eventually reached, peculiar aspects of a the single application (e.g. camera-steering, map navigation) should be addressed in order to make the interface best suitable for it.

In order to make the interface easily usable to drive whichever tool to perform whichever operation, the interface itself must not demand too much attention from the user in order to allow her/him to devote the required concentration to the main task. This is why we require the interface to be independent, i.e. controllable without the need to gaze in a particular direction. This interface should try to extract commands while the user is naturally looking at things related to the task (the robot, the object to grasp, a camera display, etc.).

Implementation

A visual-spatial attention control brain-machine interface (V-SAC BMI) is under development. A set of flickering stimuli are located in the field of view of the user (but without hindering her/his view of the task). The stimuli flicker at slightly different frequencies eventually making it possible to infer the attended one by frequency analysis of the recorded SSVEP.

Three ways to control the switching on and off of the lights have been considered:

- stimuli shown on a PC screen;
- hardware-generated clock to light LEDs;
- software-generated clock to light LEDs.

All these three solutions offer both advantages and disadvantages. Using stimuli presented on a PC screen the shape and content of stimuli is highly customizable but the refresh rate of the screen poses constraints on the values of frequencies to choose from. The use of a hardware generated clock to light LEDs does not use resources from the PC and allows to freely choose the frequencies but these (once chosen) are fixed and so is the shape of the stimuli. Using the PC to generate via software the timing of the lights is a bit more resource demanding and requires a real-time operating system or board, but allows to freely choose and change the frequencies even during the operation. In particular, with this method generated frequencies can have a minimum common multiple much higher than the refresh rate of the PC screen.

Finally the third option has been chosen since the freedom to change the frequencies of the stimuli while the interface is operating can help to infer the stimulus attended and therefore the command the user intends to send the machine.

Architecture of the system

Stimuli are implemented by means of high intensity blue LEDs. Among different similar parts, L-7104QBC-D by Kingbright has been chosen for its high intensity and high directionality. Figure 11.41 depicts some relevant technical data. The LEDs are controlled with the parallel port by means of the current driver A5801 by Allegro. A small printed circuit board have been designed and realized.

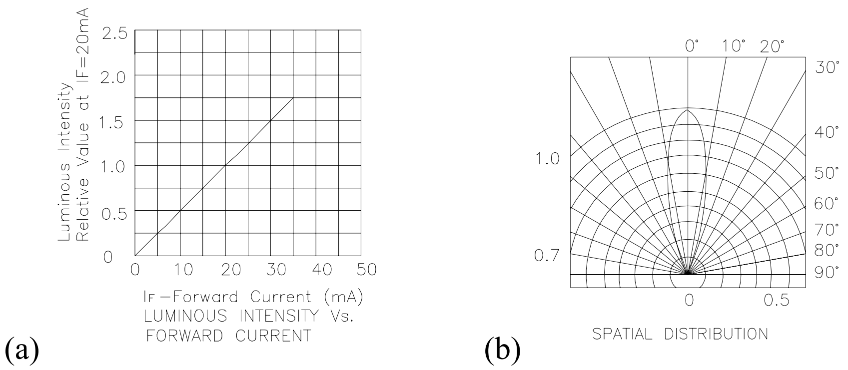

Figure 11.41: Technical data for the L-7104QBC-D LED: (a) luminous intensity vs. current chart relative to the nominal value of 1500 mcd at 20 mA; (b) luminous intensity polar plot. (Source: Kingbright, Inc.).

For the timing to be accurate and reliable a real-time operating system can be a good choice. Furthermore the real-time architecture can be also useful for the control of the robotic device. We decided to use the well known and widespread RTAI system developed and maintained by the Aerospace Engineering Department of Politecnico of Milano. This operating system (OS) is based on Linux and allows a PC to be used for hard/soft real-time applications.

As most EEG devices available have no drivers nor support for the Linux operating system it was difficult to have one single PC performing stimuli timing, acquisition, data storage for offline use, data analysis, classification, and control of the robotic device. Therefore the acquisition and the data storage for later offline analysis have been moved to a different PC running Windows XP operating system. The PC running Real Time Linux is then devoted to stimuli timing, data analysis, classification and control of the robotic tool. The whole system is depicted in Figure 11.42.

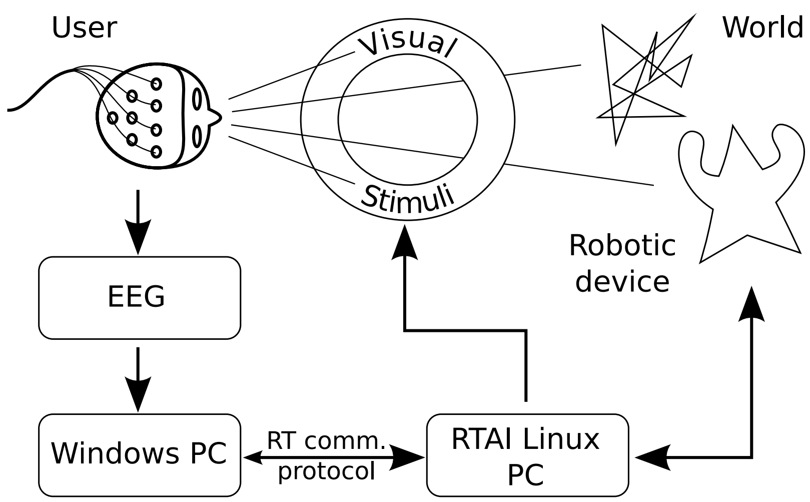

Figure 11.42: Overall diagram of the interface.

In this system a key point to address is the communication between the two PCs. The one devoted to acquisition must provide the other one with the recent samples of the recorded data. This process must take place in real-time. This means not only that data must be sent as soon as it arrives but also that samples arriving too late are completely useless. Therefore a reliable protocol like TCP is not appropriate because it can persist, in case of communication delays, trying to send old useless data with the risk of eventually jamming the whole communication.

Another protocol is under study for our specific task. It will be built on top of UDP in order to avoid unconditional retransmission of undelivered data. Nevertheless retransmission will be performed for data with a certain threshold of age. This can help reducing the already rare data misses in a ethernet crossover cable without crippling the system even if the cable is unplugged for a short period of time.

11.6.1 Possible challenges and practical problems

Apart from the specific implementation provided in the previous sections and chapters, there are a few general considerations that can be made about existing and future challenges for BMIs in space applications, which makes their successful implementation and use much more difficult than for applications in rehabilitation.

In particular, space BMIs should meet the following basic design criteria:

- should not affect avionics function
- user friendliness
- robustness against different noise conditions
- robustness against motion
- chronic or at least prolonged-use noninvasive recording systems
    - limit human encumbrance (discomfort) problems
        - these decrease probability people will want to use it
        - users do not behave naturally
        - the body unconsciously reacts against it
- deal with multi-sensory information.

Issues concerning interference on avionics relate to the fact that user-friendly technology will most likely use wireless communication protocols. Cleaner transmission channels such as fiber optics add encumbrance to the system and are know to break very easily as well. Thus, any wireless systems used in space (BMI or otherwise) will need to use **very well defined frequency bands (even if spread-spectrum is used)**.

Other factors such as channel and subject specific addresses are not an issue even using today's technology, but care must also be taken to ensure that **signals are not distorted between the emitters and the receivers** either.

Thus, interference and information loss must be considered when designing BMIs for space. This includes possibly significant from amplifiers at various stages.

Further, if BMI signals are to be transmitted wirelessly, care must be taken to ensure the standard **confidentiality issues on data** from humans. To this end, the overall system must include strong encryption and other measures to address legal and ethical issues.

BMI Sensors Related Issues

The most important aspect of technology to be tackled with regard to many of the above problems is the type of sensors to be placed on the human subject. Current electrode caps, even the most advanced ones such as Biosemi's, require elaborate procedures for placement, taking at best 20min in most systems with many channels. Once a device is in place, however, any motion of the sensors with regard to the skin can render the signals useless. In a space environment, there can be many situations in which sensor motion/displacement may occur, especially during take-off and landing. The mere occurrence of high-g situations can lead to displacement as sensors have different inertial properties from that of human tissue (at least to date).

Whether EEG, NIR, or another technology is used for transduction of the brain signals, the sensors to be used in space will have to be easy don and doff while being stable on a particular skin site. In order for that to happen, **entirely new non-invasive sensor technologies will have to be explored**, possibly through the use of conductive polymers or similar.

Suitable non-invasive sensors do not yet exist to address these issues. A simple question to ask as a gauge is: will users be able sleep, shower, etc., while still wearing the BMI, or will we be satisfied with systems that can be worn on occasion only? The former is of course the ultimate aim, but the latter is large enough a challenge for the next years. Even so, we must address the issues raised in this section if 1) BMIs are top work well in space, and 2) people will not be adverse to its frequent use.

Intelligent Software as a Possible Solution

Should the interface stability problems persist for non-invasive technology over the next decade, intelligent software may handle some of the problems. Adaptive algorithms are already taking an integral part in BMIs as the observed signals shift in behaviour in as little as a few seconds. In space and other motion-prone chronic situations, the **algorithms will need to include mechanisms to track location-related changes**, as well the resulting changes in signal features. This has not been considered in current BMI research. Possible approaches may include the finding of a robust, well localized brain signal that can be tracked periodically by the BMI, thus making adjustments accordingly. Should such brain signal fail to be found (which seems very likely), **non-invasive technology may require a semi-**

implanted (placed just under the skin) signal source for tracking purposes.

Aside from software related solutions, there may be the need for occasional execution of mental tasks for location tracking purposes. For example, a specific repetitive motor imagery exercise may be executed (e.g., imaginary finger flexion) thus yielding relatively well known features on specific locations. This would allow the software to re-label channel numbers as needed. Another possibility is to use subliminal (non-noticeable) evoked responses, such as to occasionally evoke known visual or auditory (or other) responses that are well localized. This would allow for tracking of location shifts without disturbing normal human operation of the BMI.

Multi-Sensory BMIs

Of necessity (i.e., we are in the early stages of development of the technology), all BMIs developed to date use signals from specific sensory channels in separate. In a realistic setting, this cannot be guarantied. Normal operation of any non-BMI device requires that the brain use many sensory channel types. This cannot expected to be any different for BMIs. For some tasks, e.g., robot manipulator control, visual information alone may not be enough, also possibly requiring touch and proprioceptive feedback. Thus, future BMIs will need to not only be robust under multisensory information but they will also need to make use of properly designed feedback protocols and translation algorithms to use that information to its advantage.

11.7 Prospective applications

11.7.1 Real-world applications

To be effective in real-world applications, there are many challenges inherent in employing BCI control, which must be addressed and overcome. These challenges are common to both space and rehabilitation applications and can be generalized in several categories (Moore, 2003):

1. Throughput (or information transfer rate) – Even the best average information transfer rates for experienced subjects and well-tuned BCI systems are relatively low, in the vicinity of 24 b/min (roughly three characters per minute) (Wolpaw et al., 2002). This is too slow for natural interactive communication, so, in order to effectively use BMIs as an alternative to conventional interfaces, it is necessary to research ways of optimizing selection techniques and incorporating prediction mechanisms to speed up communication.
2. High error rate – A significant complicating factor in the slow information transfer rate of BMI users is the high probability of errors. Brain signals are highly variable, and this problem is exacerbated in severely disabled users by fatigue, medications, and medical conditions such as seizures or spasms. Self-reporting errors is also extremely difficult, particularly if the subject has little or no

communication channel outside of the BMI system itself. Devising methods of quickly resolving or preventing errors is critical to successful BCI interaction.

3. Autonomy – Ideally, a communication system for a person with severe disabilities should be completely controlled by its user. Unfortunately BMI systems require extensive assistance from caretakers who need to apply electrodes or signal-receiving devices before a user can communicate. Also, the set-up and initiating procedures should be made easy for usage by everyone even in difficult conditions, like in zero gravity. Furthermore, most BMI systems are system-initiated, meaning that the user cannot turn them on and off independently. This results in what is termed the "Midas touch" problem – the BMI system interprets all brain activity as input, so how can the user communicate the intent to control the system? A BMI user may be able to perform a selection to turn the BMI system off, but turning it back on again is an issue. It is possible to use hybrid systems, combinations of different BCI techniques, and other biometric interfaces to solve this problem (Moore, 2003).
4. Cognitive load – Most BMI systems are tested in quiet laboratory environments, where users are able to concentrate on the task at hand with minimal distractions. BMI users in the real world have to deal with much more complex situations, including the cognitive load of the task being performed, emotional responses, interactions with other people, and possibly even safety considerations. Careful study of the effects of cognitive load on the efficacy of BMI controls is necessary in order to determine whether BMI's could be used for rather "quiet" in-home everyday living situations up to challenging living situations of space ships or stations.

Typical tasks intended for subject training include positioning a cursor, tracking a moving object, or selecting a target. Once these skills are acquired, the subject can progress to applications that perform real-world tasks such as communication, controlling the environment, or moving robotic limbs. Concerning the ability of healthy people to use BMIs, Guger et al. (2003) have performed a study in which 99 healthy people participated in a BCI field study conducted at an exposition held in Graz, Austria. Subjects were instructed to imagine a right-hand movement or a foot movement after a cue stimulus depending on the direction of an arrow. Roughly 93% of the subjects were able to achieve classification accuracy above 60% after two sessions of training.

For the sake of completeness, another recently published review paper draws a picture of the continued progress in the field of Brain Interface (BI) research over the last two decades. Indeed, as the number of BI researchers and organizations steadily increases, newer and more advanced technologies are constantly produced, evaluated, and reported. Though the BI community is committed to accurate and objective evaluation of methods, systems, and technology, the diversity of the field has hindered the development of objective methods of comparison. Jackson et al. (2006) introduce a new method for directly comparing studies of BI technology based on a theoretical models and taxonomy proposed by Mason, Moore, and Birch (Mason et al., unpublished).

11.7.2 Future scenarios for space applications

For defining which novel space applications will be possible in a more distant future, it is useful to recall that BMIs are only a part of the more general concept of Hybrid Bionics Systems (HBS). In a HBS (see Chapter 1 for the definition), natural and artificial sensors and actuators interact symbiotically under the joint control of the human nervous system and one or more artificial control systems, as illustrated schematically in the example of Figure 11.43.

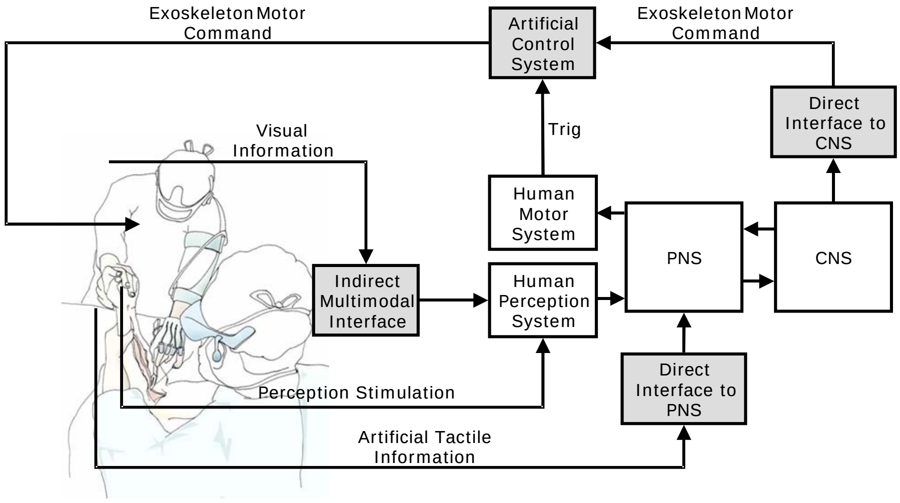

Figure 11.43: An example of different direct and indirect interfaces adopted on an HBS: direct (peripheral) neural interfaces transmit artificial tactile signal to the PNS. Direct (brain) interfaces capture and transmit user intention to the control system of the HBS. Artificial stimulation (thermal or tactile) are generated by the artifical system and captured by the human perception system (skin of the hand). Visual information is displayed on a special visor (indirect multimodal interface) and projected on the human retina.

Research and development on HBS, after solution of the more evident problems of interfacing with the human body and in particular with the nervous system, will eventually allow the rising of completely novel and breakthrough applications in many scenarios. Here, we envisage and briefly describe three basic scenarios in which HBS can be applied:

<u>Beyond teleoperation</u>

Teleoperation is concerned with the remote control of robotics artefacts by human beings in environments that cannot be accessed directly (too small, too big, too distant). In this scenario BMIs can be used to increase the sensation of immersive tele-presence and 'natural' interaction between the human being and the artifact.

We envisage three different direct interface technologies whose application can be experimented within the scope of the "Beyond tele-operation" scenario: novel interfaces implanted at the PNS level first in rats or cats, then in primates and finally in humans, non-invasive BMI interfaces (such as EEG, MAG, or fast-optical NIRS) and maybe an array of microelectrodes implanted in the brain cortex in primates and subsequently in humans.

Figures 11.44 and 11.45 illustrate the "Beyond Tele-operation" scenario, in two possible cases of a planetary rover (Figure 11.44) and of a biomorphic artefact for navigating inside the human body (Figure 11.45). These two scenarios exemplify the scalability of the proposed concept.

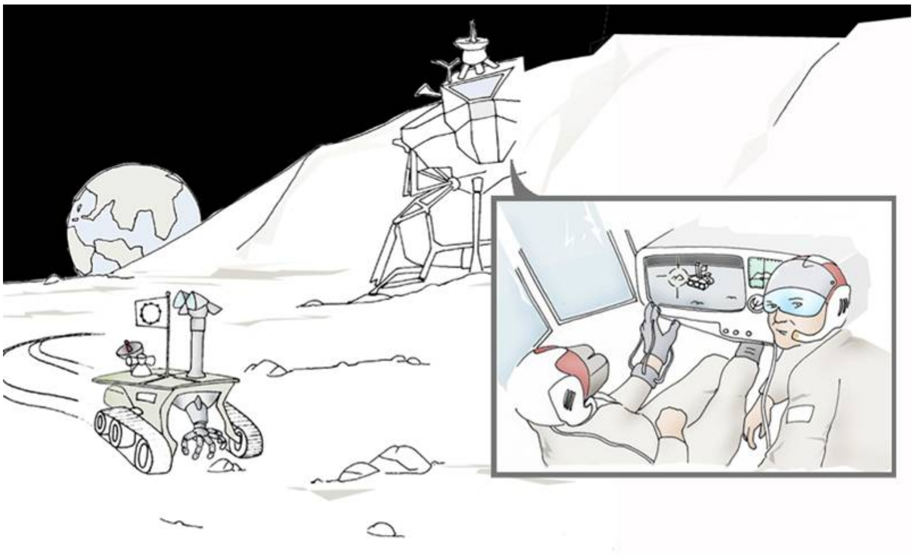

Figure 11.44. A typical "Beyond Tele-operation" scenario: the arm-hand system of a planetary rover is remotely controlled by a human operator through a natural bidirectional interface conveying both efferent and afferent signals.

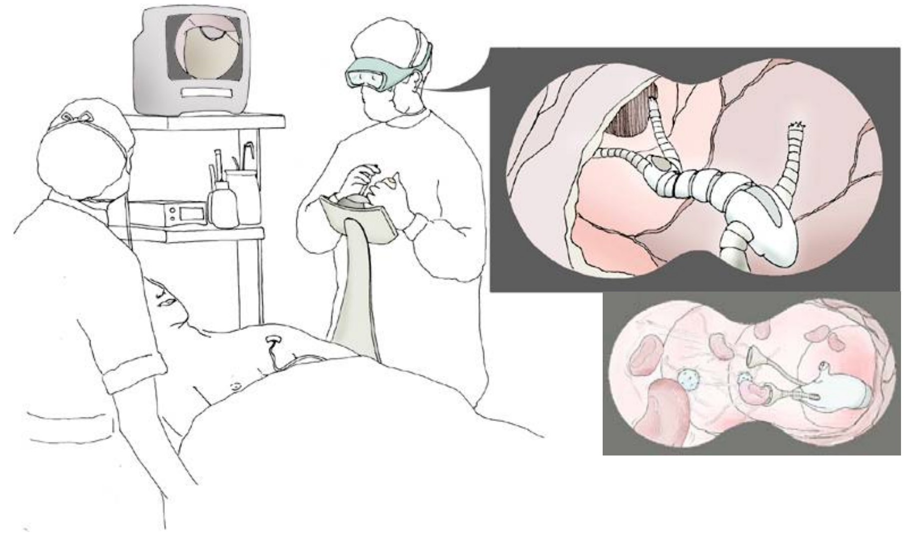

Figure 11.45. A typical "Beyond Tele-operation" scenario: a biomorphic artefact equipped with miniaturized arm-hand systems is operated by an endoscopist (or surgeon) for internal exploration of the human body or for catching moving cells. In this case, too, a natural interface provides immersive tele-presence in the environment explored by the artefact so that the operator can effectively control the micro-manipulators for locomotion and grasping purposes.

Beyond ortheses

In this scenario, BMIs can be used to more efficiently and naturally control devices that act as assisting or augmenting devices for human senses and actions. In the field of robotics, an example is the development of exoskeletons for human limbs intelligent enough to detect the user's motor intentions, to dynamically monitor/copy movements of the limbs and to augment performance accordingly in terms of accuracy, strength, endurance, reactivity, etc.

In this context, we define ortheses as devices which are externally attached to a limb for the support or for the improvement of its function. Exoskeletons, on the other hand, are wearable machines that give human limbs enhanced strength, speed and endurance (DARPA, http://www.darpa.mil/baa/baa00-34.htm). The origin for this field of research can be traced back to the 1960s when the U.S. military developed exoskeletons to increase the capacities of soldiers in combat (Kazerooni, 1993). Unfortunately, significant gains were not achieved due to the design limitations in controls, power sources, actuators and structural materials prevalent during that period. Current advances in these components (Sanchez et al., 2000; Kobayashi et al., 2002; Caldwell et al., 1999) now allow improvements in exoskeleton design that are envisaged to be commercially viable in the near future. With the advent of these developments, there have been intensified activities among research groups in the application of exoskeletons for teleoperation, virtual reality, rehabilitation, and materials handling in manufacturing and sea/air cargo

(Bergamasco et al., 1994; Giuffrida et al., 1996; Lee et al., 1990; Kazerooni, 1993).

Figures 11.46 shows typical “Beyond Ortheses” scenarios. Left part of Figure 11.46 envisages the application of an intelligent exoskeleton in a fine manipulation task, in order to improve human accuracy and endurance in micro-surgery operations. Right part of Figure 11.46 proposes application to recovering of human performance, in case of motor impairment.

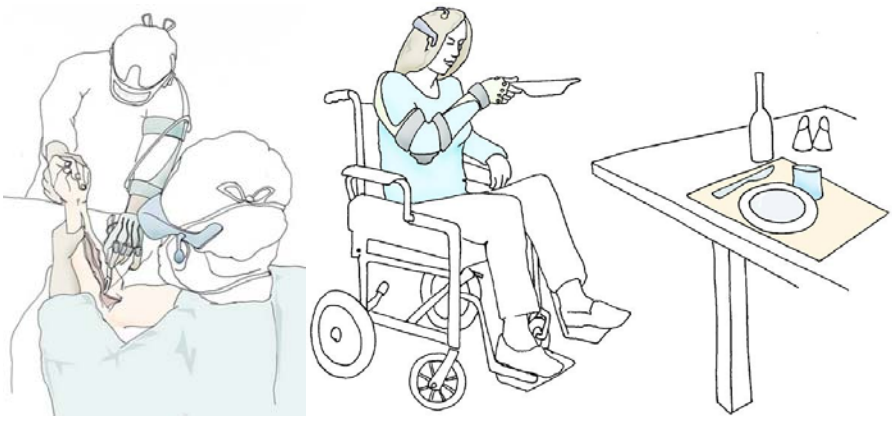

Figure 11.46. Left: the “Beyond Ortheses” scenario, in the case of enhancing human performance. The example concerns micro-surgery, in which improvement of accuracy and endurance may be needed. Right: the “Beyond Ortheses” scenario, in the case of recovering human performance. In this example, an intelligent exoskeleton is worn by a motor disabled person, in order to re-gain the use of the upper limb.

Beyond prostheses

This scenario concerns the possibility of developing new prostheses, by means of artificial body parts substituted or added to the human body. It will be possible to control these prostheses also by means of BMIs, although interfacing with the PNS will probably be preferable for the feedback of proprioceptive signals. The related problems to be solved are the generation of motor commands for additional limbs or body parts as well as the selection of additional multiple sensory inputs, including novel afferent proprioceptive data generated by the additional limbs.

Active arm and hand prostheses have been available from leading prosthesis manufacturers for several years. Using a myoelectric interface, such arms can be used to make one-dimensional pinch grasps, thus aiding the patient in performing basic manipulation tasks. On the downside, the coarseness of the myoelectric interface prohibits the use of more complex prosthetic devices requiring exact positioning, such as the use of an active elbow or shoulder joint. Also, current devices do not exhibit more complex grasp strategies than “open hand” / “close hand”. The “beyond prostheses” scenario will evolve in two directions: 1) to investigate functional replacement of limbs (mainly the arm and hand) with complete restoration of proprioceptive and exterocpetive feedback by means of neural interfaces; and 2) to study the possibility of augmenting human abilities by means of an additional arm and hand that will extend the performance of the human body.

The interface technologies used in researching in this scenario will be fast non-invasive interfaces in humans and primates. The use of microelectrodes arrays implanted in the brain cortex in primates will be needed as a first step to finally move to human implants.

Figure 11.47 illustrates a scenario for "Beyond Prostheses", consisting in the augmentation of human limbs. Additional arms are envisaged to be physically interfaced to the human body, in order to provide the user with additional manipulation and grasping capabilities.

Figure 11.47. A few illustrations of typical "Beyond Prostheses" scenarios. Additional limbs are connected to the human body, providing additional manipulation capabilities, as well as additional sensory (tactile and haptic) feed-back.

11.7.3 Tentative timeline

We would like to finish this future perspectives section with a tentative timeline of future technologies. Based on studies performed at BT Exact

Technologies (Pearson & Neild, 2001), we have selected some technologies and dates relevant to the future of BMIs for space applications and list them below. As clearly results, the dates are not always consistent, but it might be fun to speculate about how our future will look like:

Anthropomorphic robots used for factory jobs	2008
Artificial Nervous System for autonomous robots	2010
Home manager computer	2011
Machine use of human-like memorising, recognising, learning	2012
Artificial senses, sensors directly stimulating nerves	2012
Alpha-wave induction sets	2012
Some implants seen as status symbols	2012
Helium 3 mining on moon	2012
Holographic displays for continuous video	2015
Thought recognition used in sleep enhancement	2015
First manned mission to Mars	2015
Highly integrated biosensors	2017
Artificial brain cells	2017
Human knowledge exceeded by machine knowledge	2017
Computer link to biological sensory organs	2018
Actuators resembling human muscles	2019
Use of free space holograms to convey 3D images	2020
Artificial insects and small animals with artificial brains	2020
Electronic memory enhancement	2020
Computer enhanced dreaming	2020
Remote control devices built into pets	2020
More robots than people in developed countries	2025
Artificial peripheral nerves	2025

Emotion control devices	2025
Network based telepathy	2025
Thought recognition as everyday input means	2025
Creation of “The Matrix”	2025
Learning superseded by transparent interface to smart computer	2025
Production, storage and use of antimatter	2025
Space factories for commercial production	2025
Robots physically and mentally superior to humans	2030
Full direct brain link	2030
Dream link technology	2030
Start of construction of manned Mars laboratory	2030
Use of human hibernation in space travel	2030
Brain 'add-ons'	2033
Artificial brain	2035

Addendum: Wild cards. Events that could happen almost anytime, listed by earliest potential occurrence:

Asteroid or comet hits earth	BC*
Massive solar flare wipes out life on earth	BC*
Human Mutation	BC*
Space exploration creates superbug	2000*
The hostile arrival of ETs detecting our transmissions	2010*
Computers and robots become superior to humans	2015*
Self-aware machine intelligence	2015*
Computers/Robots think like humans	2015*
Hybrid nanotech-organic creatures	2020*

Nanotechnology takes off	2020*
Humans access net directly, become an integral part of global information system	2030*
Human genetic engineering creates hostile super-race	2070*
Humans assimilated into net	2075*

Also on the sci-fi side is the opinions of the futurologist Ray Kurzweil about the future of menkind. We quote some interesting passages of (Kurzweil, 2002): “By around 2030, we may have the technology to directly link our brains to the ultra-smart computers that will be around then, giving us so much extra brainpower that we deserve a new name, Homo Cyberneticus. Furthermore one of the most important application of circa 2030 nanobots will be to literally expand our minds. We're limited today to a mere hundred trillion interneuronal connections, which we will be able to augment by adding virtual connections via nanobot communication. This will provide us with the opportunity to vastly expand our pattern recognition abilities, memories, and overall thinking capacity as well as to directly interface with powerful forms of nonbiological intelligence. It's important to note that once nonbiological intelligence gets a foothold in our brains (a threshold we've already passed), it will grow exponentially, as is the accelerating nature of information-based technologies. Note that a one inch cube of nanotube circuitry (which is already working at small scales in laboratories) will be at least a million times more powerful than the human brain. By 2040, the nonbiological portion of our intelligence will be far more powerful than the biological portion. It will, however, still be part of the human-machine civilization, having been derived from human intelligence, i.e., created by humans (or machines created by humans) and based at least in part on the reverse engineering of the human nervous system.”

According to these considerations by futurologists, our future may look bright, but what is certain is that if we want brain interface technology to be on par with this timeline, a lot of effort and funding has to be devoted to research on BMI.

11.8 Worldwide researching groups on BMI for space applications

Europe

- Dr. Carlo Menon
  ESA Advanced Concepts Team
  ESTEC
  European Space Agency (ESA)

  ESA has funded three short studies on “Non invasive brain-machine interfaces” within the context of the ADIADNA program (study ID

05/6402). This document is the final report of one of those three studies.

Americas

- Dr. Leonard Trejo
  Intelligent Systems Division
  NASA Ames Research Center
  National Aeronautics and Space Administration (NASA)
  Extension of the Human Senses Project
  http://www.nasa.gov/centers/ames/research/technology-onepagers/human_senses.html

  At National Aeronautics and Space Administration (NASA), a research group called "Extension of the Human Senses Group" is investigating the use of some bioelectric signals, Electromyogram (EMG) and Electroencephalogram (EEG), to eliminate the need for mechanical joysticks and keyboards. As an example they have flown a Class IV simulation of a transport aircraft to landing with an EMG based "joystick" (Wheeler et al.). The goal is to improve performance of NASA missions by developing brain-computer interface (BCI) technologies for augmented human-system interaction. BCI technologies will provide powerful and intuitive modes of interaction with 2-D and 3-D data, particularly for visualization and searching in complex data structures, such as geographical maps, satellite images, and terrain databases.

  Recently, they have developed and tested two EEG-based BCIs for 1-DoF and 2-DoF cursor control on a computer display. The 2-DoF application, named Think Pointer, allows hands-free navigation of moving maps and other displays (Trejo et al., 2006). A demonstration video is available at:

  http://ti.arc.nasa.gov/story.php?id=265&sec=

- Dr. Alan S. Rudolph
  Defense Science Office
  Defense Advanced Research Projects Agency (DARPA)
  Department of Defense (DoD), USA
  http://www.darpa.mil/dso/programs.htm

  The Defense Science Office at Darpa is funding a "Brain Machine" Research Program, with the declared aim to use BMI for controlling unmanned aircrafts and vehicles on the battle field. This field of research closely resembles the space applications, apart from the delay issues due to increased distances for space applications. The delay problem in space applications, however, can be compensated due to looser real-time requirements of space applications. In some sites, the program is referred to as "Neuromics". In the context of the Brain Machine Interface Program, they have invasively recorded brain signals of a monkey to make it control a robot arm. The research group at Duke University has received fundings from DARPA, so the experiment cited in DARPA documents could be the one in (Nicolelis, 2003). Latest available DARPA documents refer to results obtained within the year 2003, but financial documents show that the budget for the Human Assisted Neural Devices (formerly Brain Machine Interface) Program was 12 Million $ for FY (financial year) 2003, 7 Million $ for FY 2004, 12 Million $ for FY 2005, 15 Million $ for FY 2006, and 15 Million $ for FY 2007.

This program will develop the scientific foundation for novel concepts that will improve warfighter performance on the battlefield as well as technologies for enhancing the quality of life of paralyzed veterans. This will require an understanding of neuroscience, significant computational efforts, and new material design and implementation. Closed-loop control of peripheral devices using brain signals will be examined. Examination of different brain regions will be accomplished in order to generate coded patterns to control peripheral devices and robotics. Techniques will be examined to extract these signals non-invasively. This effort will be conducted with the Veteran's Administration to ensure approaches are compatible with prosthetic requirements. Program plans are:

- Extract neural and force dynamic codes related to patterns of motor or sensory activity required for executing simple to complex motor or sensory activity (e.g., reaching, grasping, manipulating, running, walking, kicking, digging, hearing, seeing, tactile).
- Determine necessary force and sensory feedback (positional, postural, visual, acoustic, and other) from a peripheral device or interface that will provide critical inputs required for closed-loop control of a working device or prosthetic.
- Explore new methods, processes, and instrumentation for accessing neural codes non-invasively at appropriate spatiotemporal resolution to provide closed-loop control of a peripheral device.
- Demonstrate real time control under relevant conditions of force perturbation and cluttered sensory environments (e.g., recognizing and picking up a target and manipulating it).

- Dr. John Main
  Defense Science Office
  Defense Advanced Research Projects Agency (DARPA)
  Department of Defense (DoD), USA
  http://www.darpa.mil/dso/thrust/matdev/ehpa.htm

  Closely related although not dealing with BMIs, it is worth mentioning the DARPA initiative that is currently trying to develop exoskeletons for human performance augmentation (EHPA). Focussed on military applications, its results could be useful in aerospace as well. In particular, four EHPA projects work on the development of small actuators, lightweight structures, and control technology to be integrated in devices 'wearable' by a human and able to augment his/her physical capabilities.

- Melody M. Moore
  BrainLab
  Georgia State Universiry, GA, USA
  http://www.cis.gsu.edu/brainlab/

  The BrainLab at Georgia State University is not specifically involved in researching space applications for BMIs. It is, however, devoted to researching and developing interaction techniques which will allow BCIs to be effective in real-world applications (Moore, 2003).

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12. Future technologies and roadmaps for BMIs

According to previous argumentations we can now accept the idea that non-muscular communication is no more a mere speculation and that the brain can interact with the external world via a machine, even if in a way completely different from the one foreseen in science fiction movies and books (Thomas, 1977). The present non-invasive systems, in fact, reach – at their best – 25 bits/min (Wolpaw et al., 2002). Even a minimum capacity can be of paramount importance for those who cannot communicate, such as locked-in patients. In all those Patients missing any voluntary control on musculature, a BMI system is the only one enabling them to react to questions requiring simple answers (with a bit rate of 20/min it is possible to give 20 ‘yes’ or ‘no’ answers), to control somehow the environments (i.e. lights on/off, air conditioning on/off or up/down, TV switch) and to utilize the word processing software programs (with a predictive function software and a 25bit/min rate it is possible to write 2 words/min) or control a prosthesis.

For able-bodied people, however, this communication capacity is too low to result in any usefulness, especially since most of the interfaced designed so far require too much concentration and user isolation to filter out any unwanted noise due to the environment or to other, concurrent, brain activity.

BMI system implementation will require to solve several open issues like:

- the independence from the usual neuromuscular channels for communication;
- the dependence from physiological mechanisms regulating brain function;
- the improvement of signal acquisition and relevant signal identification and extraction;
- the improvement of transduction algorithms, output devices and operational protocols;
- the development of learning and behavioural strategies weighted on the subjects motivations and success rates;
- the adoption of scientific methods and standards for the evaluation criteria, applications and groups of subjects;
- the development and training of new non-muscular channels for communication which are nowadays barely known.

12.1 System roadmaps

Before being applicable to able bodied subjects, research in BMI will be carried out for rehabilitation purposes. In this case, the following considerations have to be made for a correct choice and design of the BMI system as a whole.

12.1.1 Independence from neuromuscular output channels

While a BMI dependent system simply reflecting the activity of the physiological neuromuscular output channels can be useful (e.g. Sutter, 1984; Sutter, 1992), the future interests for the BMI will be largely based on its independence from such types of output. The interest raised by the use of slow cortical potentials as relevant signal in Patients entirely paralyzed due to an advanced stage of ALS is paradigmatic (Birbaumer et al., 1999; Birbaumer et al., 2000). Similarly, BMI systems based on wave P300 generation seem to be independent (Donchin et al., 2000). Such a wave, in fact is probably reflecting the attentional/motivational drive of a subject toward a target stimulus, which in a BMI is the selection intended by the subject. Meanwhile, the visual stimuli needed to elicit a P300 might be partly dependent by the sight direction (Michalski, 1999; Teder-Salejarvi et al., 1999; Nobre et al., 2000) or from the interface configuration (Bayliss et al., 2004). It has been shown that mu and beta rhythms generated in the sensorimotor cortical areas can support independent BMI since they are sensible to motor planning or mental simulation without any real motor output (e.g. McFarland et al., 2000). Moreover mu or beta-based cursor control is independent from skull or limb musculature activity (Vaughan et al., 1998). Finally, an efficacious mu-based BMI has been obtained in a ALS patient (Miner et al., 1996).

12.1.2 Dependence on the physiological brain activity

While the BMI systems based on slow cortical potentials, P300, mu or beta rhythms and neuronal firing recorded with invasive electrodes do not require any muscular control, they certainly depend on some degree of normal CNS physiological activity. Brain deficits inherently due to the background disease, as well as deprivation of sensory feed-back can actually affect the subject ability to generate such relevant signals. This indicates how important is to ‘tailor’ the choice on the relevant signal according to the subject.

12.2 Hardware roadmaps

12.2.1 The problem of feedback

The ways of providing feedback to the user of a BMI have already been presented in Section 5.3.2. Here we discuss the feedback problem in more detail, starting with a quotation from Graimann et al., (2006), which gives an excellent short introduction of the feedback problem: "Although BCIs provide alternate communication channels that bypass traditional neuromuscular channels, learning to operate a BCI successfully is similar to learning tasks that involve muscular control. Just as walking or speaking requires training and practice, the operation of a BCI is an acquired skill that involves many of the same learning mechanisms. The most important element of such learning is the presence of feedback. During the learning process, whether it be walking, speaking, or using a BCI, the subject makes adjustments based on the outcomes produced by their efforts in order to eventually hone their skills appropriately. The observation portion of this cycle of observation and adjustment is known as feedback, and is crucial to the learning process.

The consequence of this is that BCI systems must be designed to adapt to the user during the learning processes while the user in turn adapts to the BCI system. The BCI and user then form two adaptive controllers in which successful operation is the result of adequate adaptation of each system through the use of feedback.

The types of feedback involved may be continuous or discrete. In the former, feedback is provided immediately and smoothly usually by a visual cue which may grow and shrink, or may move in one direction or another to capture some aspect of the BCI system being monitored. For example, a cursor on a screen might move up and down, or a vertical bar may change in height. By contrast, discrete feedback, which is generally delayed by its nature, involves an on/off indication of success such as a light that glows only when a particular brain state is achieved.

Feedback may also be classified as realistic or abstract. In the forgoing examples, the feedback would generally be viewed as abstract as opposed to the realistic feedback of a picture of a hand opening and closing as the subject imagines his own hand executing these movements.

Although it is well known that feedback is very important in the learning process, it remains unclear which type of feedback is best. This appears to be a subject dependent issue, as one subject may have the best success with one type of feedback, whereas another subject might find that particular type of feedback to be distracting.

In a BCI system, the skill developed by the user involves proper control of specific electrophysiological signals. The brain has the ability to adapt and modulate various electrophysiological signal features and the better the feedback provided to the user during training, the faster will this adaptation take place."

12.2.2 Direct feedback to the CNS

The type of feedback provided to the user is of utmost importance. Currently, only invasive methods can be theoretically used to provide direct feedback to the CNS. Apart from the ethical problems and from the practical problems related to complexity of the implantation surgery, post-operative consequences and maintaining the interface functionality despite cicatrization of neuronal tissue, there are also safety-related problems.

“Implanting electrodes into healthy people is not something we’re going to do any time soon,” says Alan Rudolf, the former head of the DARPA brain-machine research program. “But 20 years ago, no one would have thought we’d put a laser in the eye either. This agency leaves the door open to what’s possible” (Horgan, 2004). If “tapping the brain” using electrodes only for reading is risky and its long-term effects on the brain is unknown, direct brain stimulation by means of invasive methods is a largely unknown field. A few things we know about this comes from neurosurgery, where electrodes are directly applied to the exposed brain in order to identify what areas are responsible for different cognitive tasks, like counting, speaking, vision, etc., prior to brain surgery. In this section, we further concentrate on the problem of feedback and discuss the future developments on invasive interfaces below.

A non-invasive technique for directly stimulating the CNS exists: *transcranial magnetic stimulation* (TMS). TMS is a neurophysiologic technique that allows the induction of a current in the brain using a magnetic field to pass the scalp and the skull safely and painlessly. In TMS, a current passes through a coil of copper wire that is encased in plastic and held over the subject’s head. This coil resembles a paddle or a large spoon and is held in place either by the investigator or by a mechanical fixation device similar to a microphone pole. As the current passes through the coil it generates a magnetic field that can penetrate the subject’s scalp and skull and in turn induce a current in the subject’s brain.

Technical developments in the devices used for TMS made it possible in the late 1980’s to apply TMS in trains of multiple stimuli per second. This form of TMS is called repetitive TMS or rTMS. In rTMS, stimuli are applied to the same brain area several times per second during several consecutive seconds. Repetitive TMS is an exciting tool in research on brain function, but it remains experimental at this point. Repetitive TMS can be used to study how the brain organizes different functions such as language, memory, vision, or attention. In addition, rTMS seems capable of changing the activity in a brain area even beyond the duration of the rTMS application itself. In other words, it seems possible to make a given brain area work more or less for a period of minutes, hours, days or even weeks when rTMS is applied repeatedly several days in a row. This has opened up the possibility of using rTMS for therapy of some illnesses in neurology and psychiatry.

TMS is not an inherently safe technique. The main concern when using rTMS is its potential to induce a seizure or epileptic convulsion, even in subjects without any predisposing illness. This risk is low, in the order of 1 in 1000 studies or less. It is important to note that experiencing a seizure induced by rTMS has never led to the development of epilepsy or posed any risk for subsequent unprovoked seizures. In addition, rTMS induced seizures would occur during the rTMS study or immediately after. Overall, less than 10 seizures caused by rTMS have been reported in the world’s literature and most of them occurred in the setting of early studies designed to evaluate the safety of rTMS. Nevertheless, a seizure is a possible adverse effect of rTMS and the laboratories in which rTMS is conducted are fully equipped for the emergency treatment of such an adverse effects. Repetitive TMS can also cause memory problems and other cognitive deficits. These adverse effects appear to be very rare, mild, and very transient. However, chronic effects are unknown. In summary, all these risks, related to the fact that the throughput of rTMS, if considered as a output BMI (data flow from machine to brain), would be anyway too low for any practical use. We can anyway speculate that in the future it will be possible to concentrate TMS signals in a very specific brain region, affecting very localized cortical networks and therefore yielding any perceptible cognitive effect on the used. This achievement, however, is predictable in a far future, about 20-25 years from now, according to the BT Exact Timeline (Pearson & Neild, 2001).

12.2.3 Feedback not directed to the CNS

In the meantime, we better focus on alternative feedback methods for BMIs. What is today commonly used is visual or auditory feedback. However, visual attention is selective, and paying attention to the BMI feedback will not allow the user to carry out other tasks in the meantime, preventing augmentation applications. In some cases overlay of BMI feedback information on the users natural vision with hybrid (or mixed) reality techniques, by means of head-mounted displays or see-through displays, can allow the user to still use the visual channel.

Other sensory substitution techniques could allow to use the auditory channel or the haptic/tactile sensory system for feeding back information to the CNS. Both tactile displays od electro-tactile sensation could be explored. Electro-tactile dispays do not provide natural sensation as haptics does, but signals can be coded and the user can be trained to interpret different feedback signals. A discussion of all the psychophysics effects connected to sensory input and sensory substitution techniques is out of scope of this report.

Another feedback method, which is feasible, is to use the peripheral nervous system (PNS), as a bidirectional machine interface. Interfacing with the PNS can be both invasive or non-invasive, where the invasive techniques yield the better performance both in terms of throughput and latency, because of the same reasons that determine the superiority of cortical interfaces for BMIs. Again, the discussion of interfacing with the PNS is out of scope of this report.

12.2.4 Invasive BMIs

By means of direct BMIs, machines and devices could be incorporated into the “neural space” as an extension of one’s muscles or senses. This could lead to unprecedented augmentation in human sensory, motor, cognitive, and communication performance.

A major goal is to record and simulate processes from the single neuron level and then to develop interfaces to interact with the neural system.

As also stated in Chapter 9, concerning the cortical interface itself the following key topics will be important.

Better understanding of electro-physiological activity of the cortex. The increasing number of laboratories with the capability of simultaneously recording the extracellular activity of hundreds of single neurons in both anaesthetized and awake animals could change the face of systems neuroscience. New neuroscientists can visualize the function of entire neural circuits at work and it seems fair to state that the next generation of systems neurophysiologists will be formed almost exclusively of neural ensemble physiologists (Nicolelis and Ribeiro, 2003):

- *Biocompatibility of electrodes for chronic implants*. Several problems need to be solved before making invasive technologies feasible for human implants. Already, promising results have been achieved with electrodes on cats and rats where signals from electrodes can remain detectable for over a year (Tyler & Durand, 1997; 2003). Experiments on human patients have been carried out successfully, with signal stability of over one and a half year using electrodes doped with growth hormones (Kennedy et al., 2000; 2004). Stimulation of specific motor neurons has been shown to elicit the desired motor output, expanding our understanding of the different functional areas of the brain.
- *Multi electrode arrays conforming to sulci and gyri of the cortex*. The planar design of Multi-Electrode Arrays restricts their application to outer surface structures of the cortex. However, it may be possible to design ways to insert the array in sulci or to design new custom shaped arrays conforming to the highly folded cortical surface.
- *Nanodevices to obtain a finer resolution in the recording of neural activity*. It has been hypothe sized (Llinás & Makarov, 2003) the acquisition of brain activity through the vascular system, by means of of nano-wire technology coupled with nano-technology electronics. It would allow the nervous system to be addressed by an extraordinarily large number of isolated nano-probes via the vascular bed. The basic idea consists of a set of n-wires tethered to electronics in the main catheter such that they will spread out in a “bouquet” arrangement into a particular portion of the brain’s vascular system. Such arrangement could support a very large number of probes (in the millions) used to record, very securely, electrical activity of a single or small group of neurons without invading the brain parenchyma.

Concerning hardware enhancement of the EEG signal-to-noise ratio, in a presentation on BMIs (Rudolph, 2001), DARPA speculates about targeting magnetic particles to specific brain regions that would interact with the magnetic field fluctuations introduced by neuronal activity. This could create a local signal (e.g 500 micron, 500-1000 neurons) that would be read by a non-invasive technique.

12.3 Software roadmaps

12.3.1 Extracerebral biological artefacts

Muscle contraction on the cephalic district as well as eye movements produce electromagnetic signals which can be recorded from scalp electrodes with amplitudes which can easily overwhelm the brain generated signals, particularly on frontal, temporal and occipital regions (Anderer et al., 1999; Croft & Barry, 2000; McFarland et al., 1997, Goncharova et al., 2000). More important, the electromyographic (EMG) signal from frontal muscles can imitate the frequency of the mu and beta rolandic rhythms and the electrooculographic (EOG) signal and blinking can resemble the fronto-central theta rhythms. They must be treated as artefact, identified and discarded (Goncharova et al., 2000). Spectral frequency topographic distribution analysis help in revealing extracerebral artefacts and in avoiding the risk of a BMI misinterpreting – for instance – a frontal EMG signal as the relevant one for the BMI control (Lauer et al., 1999; 2000; Wolpaw et al., 2000b). Research in this respect is very active, aiming to develop algorithms for online identification and elimination of extracerebral artefacts, in particular for those having amplitude, frequency and topographic characteristics mimicking those of the relevant signal.

12.3.2 Relevant signal components

The main characteristics of the relevant signal components are largely determined by the limits and nature of their utility.

For instance, Slow Cortical Potentials develop in a temporal window between 300 ms and few seconds after the event they are related to. Therefore, in a BMI system based on these signals if the subject wants to increase the bit-rate above 1-2 bit/s, he/she would have to learn to produce 2 or more levels of SCP at a given recording site and/or to control SCP in different areas independently of one another. There have been studies showing that this is possible (Kotchoubey et al., 1996, 1997; Hardman et al., 1997).

While the mu and beta rhythms have frequency ranges of 8-12 Hz and 18-26 Hz respectively, the modulation of their amplitude takes place within half a second (Wolpaw et al., 1997; Pfurtscheller, 1999; Pfurtscheller and Lopes da Silva, 1999a). On the other hand the subjects are certainly able to provide more than two degrees of amplitude modulation and can learn to control different rhythms (Wolpaw and McFarland, 1994; Vaughan et al., 1999). A mu/beta-based BMI can select amongst 4 or more choices every 2-3 seconds (McFarland, 2000b; McFarland et al., 2003).

It is still unexplored the possibility of producing two ranges of amplitude for VEP or P300, but it it proven that they can be independently generated in partially overlapping trials therefore increasing the selection rate (Donchin et al., 2000). As an alternative it could be possible to increase this rate if the subject would be able to control Evoked Potentials with a shorter latency (e.g. Finley, 1984).

The firing frequency of individual cortical neurons could allow an information transfer rate significantly higher, but it is still unproven that they can be controlled independently from the motor output and of the sensory feed-back which physiologically are associated to their activity. Key elements in defining the useful level of a signal are its correlation with the subject's intent, besides the level of voluntary control that the subject can reach on the signal itself.

Experiments with 3 ALS patients with "locked-in syndrome" using an SCP-based BMI, revealed that each one was using a different strategy: one used a positive polarity SCP, the second a relatively rapid decrement of the SCP, and the third the P300 wave (Kubler, 2000). Once an individual strategy has been developed, this is quite resistant to any change; therefore, at least in the early learning stages, the BMI systems should be able to identify, adapt and extract in an optimal way the components of the relevant signal which are best controlled by each subject.

12.3.3 Signal analysis: extraction of components

The target of the BMI system is to track the subject's intent which is embedded in his/her brain activity. Like any other communication channel, also BMI system performance heavily depends on the signal-to-noise ratio. What should be considered noise and what signal, depends on the relevant characteristic of the brain activity the BMI is based on. For instance, in a BMI based on motor cortex mu rhythms, the biological "noise" includes the alpha activity from other brain areas (i.e. the visual cortex) while in a cortical BMI the relevant signal is the firing rate of individual neurons and the biological noise is the firing of the adjacent neuronal pools. It is worth noting the importance that BMI systems identify and eliminate signals generated outside the CNS, like the EMG from scalp and face muscles and EOG. A further and difficult step is the discrimination of signal from noise if they have similar topography, amplitude and frequency content. For instance, the EOG is more problematic than EMG for those BMI systems operating on the basis of SCP (Birbaumer et al., 1990) because of their frequency overlap; similarly beta-dependant BMI systems are more sensible to EMG artefacts (Goncharova et al., 2000).

There are several techniques that might be able to improve the signal-to-noise ratio, including: spatial and temporal frequency filters, signal average, on-line individual trials artefact recognition. Spatial filters identify the components of relevant signal by combining data from 2 or more recording sites as that they can focus on a given activity selectively generated in a certain scalp region. The simplest spatial filter is the typical bipolar recording in which the 1st spatial derivative is calculated and then increases the differences of a current (tension) gradient in a certain direction. Laplacian filter is the 2nd derivative of the instant spatial current (tension) distribution and emphasizes the radially oriented sources activity immediately beneath the recording site (Zhou, 1993; Nunez et al., 1997). It can be calculated by combining the recorded potentials from the exploring electrode with those from the adjacent electrodes (e.g., Hjorth, 1991; Nunez et al., 1994). As the exploring-reference inter-electrode distances decrease the Laplacian derivative becomes progressively more sensitive to sources of EEG potentials have higher spatial frequencies (small and localized) and less sensitive to lower spatial frequencies (i.e. largely distributed sources). Laplacian derivative and the spatial filters with average reference apply a fixed set of weights and a linear combination of channels (i.e. recording electrodes sites), both using weights which when summed equal zero so that the difference is the final result and the spatial filter results a high-pass one.

Other spatial filters are those utilizing principal components (PCA) or independent component analysis (ICA). In these methods, weights are determined by the measured data. Principal components analysis produces orthogonal components but might be inappropriate for the separation of signals coming from two different sources because it does not consider statistical dependence that only emerges in higher order moments. Independent component analysis uncover the independent sources among recording sites and can, at least in principle, discriminate between mu rhythms and other sources (Makeig et al., 2000). Such methods still need to be compared with simpler Laplacian filters in which the weight of channels is independent from data they record.

An adequate temporal filter can improve the signal-to-noise ratio (e.g. McFarland et al., 1997). Oscillating signals, like the mu rhythms can be extracted with a fitted filter (Pfurtscheller and Aranibar, 1979) or can be measured by the amplitude of the corresponding peak in FFT spectral analysis (Marple, 1987). Methods of frequency analysis like band-pass filters require relatively shorter time frames while FFT methods require longer ones. Therefore the former can be preferred when the relevant signals themselves are transients (e.g., P300) and when the BMI system is requested to provide an immediate feed-back to the user.

12.3.4 Signal analysis: transduction algorithms

The performance of a transduction algorithm is determined by a series of factors including the appropriateness with respect to the specific signal components, the level of encouraging and reward provided to the subject in controlling such components, and the effectiveness in translating them in commands for the BMI device. If the subject is unable to control the signal, the algorithm is useless and the system cannot correctly operate. If the subject has some control, the algorithm can more or less infer the subjects' intents and drive accordingly the device.

The initial choice of the relevant signal components on which the algorithm should be applied, can be based on standardized guidelines (i.e. the knowledge of the recording sites and of the spatial and temporal frequencies of mu and beta rhythms) properly modified after the initial topographic and spectral findings extracted from each subject (Rockstroh et al., 1984; McFarland et al., 1997). They can then be further implemented into automated procedures. In example Pregenzer et al. (1996) have employed the learning vector quantizer (LVQ) to define the optimal recording sites and frequency bands for their subjects.

Currently available systems utilize different transduction algorithms, from linear equations, to discriminant analysis and to neural networks (e.g., Wolpaw et al., 2000b; Pfurtscheller et al., 2000; Kostov and Polak, 2000). In the simplest case, in which only one component is utilized, the transduction output algorithm might simply be a linear function of the component. The algorithm must use appropriate values for the intercept (McFarland et al., 1997). In the case the command for the vertical cursor movement, the intercept must allow the patients both for up and down movements. Ramoser et al. (1997) have found that the average value of the signal component within a time interval preceding the command execution allows a good estimation of the most appropriate intercept. The steepness determines the command gain, like for the cursor speed. When a single components is chosen between more than 2 options, the steepness also affects the choice accessibility (e.g., McFarland et al., 1999, 2000b). It is also possible to apply several highly complex transduction algorithms which allow a supervised learning approach, like the discriminant analysis (e.g., Jain et al., 2000) and the non-linear discriminant analysis, i.e. the logic adaptive network described by Kostov and Polak (2000).

Until now, the majority of evaluations have concentrated on simple BMI-subject adaptive level: the body of on-line recorded data have been utilized as a test for the efficacy of the various algorithms under examination.

A second adaptive level, which allows continuous adjustments reacting to spontaneous fluctuations of the relevant signal components, can be evaluated also in off-line tests, but only if there is a simulation of the on-line condition and under continuous monitoring that the algorithms adjustments are based on previous data and apply to following data (e.g., Ramoser et al., 1997). Such an analysis requires a consistent bulk of data from on-line recordings along a prolonged time epoch in order to include all the possible sources of signal variability. The need for such a second level of adaptation allows the adoption of simplex algorithms, since the parameters for adaptation are much more complex and vulnerable to the instabilities for complex algorithms like those in the neural networks and non-linear equations.

The third level of adaptation, which manages the interface between the subject and the device, cannot be evaluated via off-line analysis, since it replies to the continuous interactions between the subject and the devices and participates to such interactions. Since the transduction algorithms adaptation must conform to subject's adaptations and because of the inter-subject variability, the choice of a 3rd level of adaptations needs a large control population as much representative of the general populations as possible, together with long epoch of data recordings. This condition might help also to afford the artefact problem due to EMG and EOG or to neuronal firing when using invasive, single-neuron recordings. Being artefacts an obstacle to the correct performance execution, it would be probably possible to autonomously decrease or eliminate them.

12.3.5 Operative protocols

In an ideal condition, a BMI system should be continuously operative in search of a relevant signal. However, a continuous condition of signal's transduction might be dangerous, for instance provoking the identification of involuntary signal not addressed to the BMI. A possible solution concerns the implementation of a pattern of signals which operate as ”on”, ”off”’ switching signals which should be purposefully generated without the risk of taking place spontaneously (Birbaumer et al., 2000; Kaiser et al., 2001).

12.3.6 Smarter control

In order to make the robotic artefact follow a desired trajectory it is necessary to determine the position or speed of each actuator at each time step. Obviously, this is impossible with the current bitrates of BMIs, especially non-invasive ones. A key idea is that the user’s mental states are associated to high-level commands (e.g., “turn right at the next occasion”) that the robot executes autonomously using the inputs of its on-board sensors (Millán et al., 2004).

Therefore the high-level commands received from the user through the BMI must be integrated by an intelligence layer in order to guarantee a safe and efficient task execution.

It is necessary to address a few major theoretical and technological issues:

- perception of the world: the robotic device should be able to use its sensors to reconstruct a local map of the environment;
- proprioception: the robot should maintain an estimate of its location and its configuration in a world coordinate frame;
- collisions avoidance: the robot should be able to operate in a dynamic environment avoiding moving obstacles and people;
- motion planning: the robot should plan its movements considering the high-level command from the user, the map of the environment, its own position, and the position of all other actors.

12.4 Novel applications

Until now it has not been created a BMI system able to satisfy the different categories of potential users, since different types of handicap need different approaches and solutions to the problems. It is therefore necessary to classify different devices according to the clinical problems they should address. It is possible to build-up a hierarchy of potentials users, having at its base healthy subjects and at its top patients with “locked-in syndrome” deprived of any sensory feed-back (except for the visual one) and of all the motor outputs (including eye movements).

With regard to healthy subjects, BMI systems (either invasive or non-invasive) could represent the cornerstone for what are called “augmentative technologies”. Studies from Nicolesis’ group have shown that recordings from few hundreds of neurons in the motor cortex are sufficient to control a robotic arm up to a level that such neurons can be detached from their usual functions and learn the new one, namely the control of a peripheral (robotic) device. Such future applications open an avenue of old and new implications, non only on the scientific grounds, but also on the ethical ones bordering the dream of creating a Superman with interfaces enlarging sensori-motor and memory capabilities.

As previously stated, the present BMI systems are of little if any utility to paralyzed Patients still able to control few muscles. They, therefore, are mainly restricted in the application to completely paralyzed subjects still controlling the head and eye muscles. In cases in which even this last motor control is absent or excessively variable in time, they might integrate the presently available non-BMI systems for communication and control, with, e.g., BMI based on photic driving of VEPs. However, when the muscular control is missing or too fatiguing the BMI systems represent the only mean able to re-establish a minimal ability of communicating with the external world. But even in this case it is possible to make some distinctions.

If, for instance, the physiological sensory pathways are working (including those mediating tactile and proprioceptive sensations) it would be possible to use a system driven by the brain EEG to control an electric stimulator connected to one or more limbs of the subject. In this way, by managing hand fist opening and closure it could be possible to restore the ability to catch objects, utilizing the visual and sensory feed-back for performance completion (Pfurtscheller et al., 2003).

If only the cephalic sensory pathways are functioning (head tactile sensation, vision, hearing) sensory feed-back is mainly restricted to the visual one with some limitations. For applications like a cursor movement or the use of a word processor, the visual feed-back is sufficient, but it is quite inadequate for prosthetic or orthesic control. In such cases it can be hypothesized the use of systems based – at least in part – on residual sensory pathways like those of the head.

Vibrating devices stimulating the face or neck skin might decrease the time lag for perception, i.e. of the contact between the prosthesis and an object. Even the auditory pathways can be used to expand the sensory feed-back. However, they share similar time constants with the visual ones so that they are useless except for very specific situations (in the blind).

12.5 System roadmaps (reprise)

BMI research activities involve and integrate several disciplines including neurobiology, neuropsychology, engineering, applied mathematics, domotics, informatics and bioethics. Despite that, all the research projects utilizing BMI have a similar target (i.e. to reach and accurate and rapid way of communication), they widely differ not only for the choice of the various components of the system, but also in their immediate aims. In fact, some projects are focused on specific applications like the control of neuroprostheses or of a word-processor, while others are devoted to more generalized solutions. In brief, research projects have up to now pointed to demonstrate that a given brain signal recorded in a particular way and transducted in a command via certain algorithms can control a given device for some specific subjects. Therefore, it is clear that in order to reach significant milestones, research projects will have to follow more general principles concerning planning and evaluation of the gathered data. Moreover, various BMI systems will have to be validated on larger subjects populations covering different types of clinical applications. Besides inter-individual variability also intra-individual variability will have to be checked solving the problem of the wide oscillations (minutes, hours, days, weeks, months) in performance of the subjects utilizing the BMI. Therefore, data records will have to be repeated several times in a relatively long time epoch in order to exactly describe the range of variability of the tested BMI parameters. Offline analysis of such data are not per se sufficient to compare the different components of the relevant signal, the extraction and analysis of relevant signal methods and the transduction algorithms due to the fact that they cannot precisely predicts their short- and long-term effects. Therefore, promising techniques for offline analysis will have to be validated also online for sufficiently long sessions and on a sufficient large number of subjects. Until now, the vast majority of the BMI-based studies have utilized as a qualitative parameter the accuracy and/or the speed in carrying out a given performance. Despite the importance of such an approach, this is intrinsically dependent from the characteristics of the application and by the efficacy of the system to interface with the ability of the subject to control the relevant signal. It is understandable on this frame why it is so difficult to compare each other different BMI system. The standard method for the communication systems evaluation is represented by the bit-rate (i.e. the flow of information transfer) which is the amount of exchanged information per time unit and incorporates into a unique index both the speed and accuracy of the investigated system. Recently, a general-purpose BMI platform for research and development has been accomplished (BCI2000 by Schalk et al., 2004) which can use every type of brain signal, signal analysis, output devices and operative programs. Figure 12.1 shows the design of BCI2000. It has been already tested on the majority of the existing systems reaching performances very similar to those obtainable with ad hoc platforms of individual systems. By reducing the time, the efforts and the expenses necessary for testing new designs and by providing a standardized data format for offline analysis and allowing to research groups missing a high-performing software to afford research on BMI systems, the BCI2000 instrument can speed-up the research impetus in this field. For this reason BCI2000 has been designed to combine two basic principles: being a modular system and maximizing independence, interchangeability and scaling of each module and each module components. There are four modules for executing the basic functions of every BMI system: 1) signal acquisition, 2) signal analysis, 3) output control, 4) operative protocol.

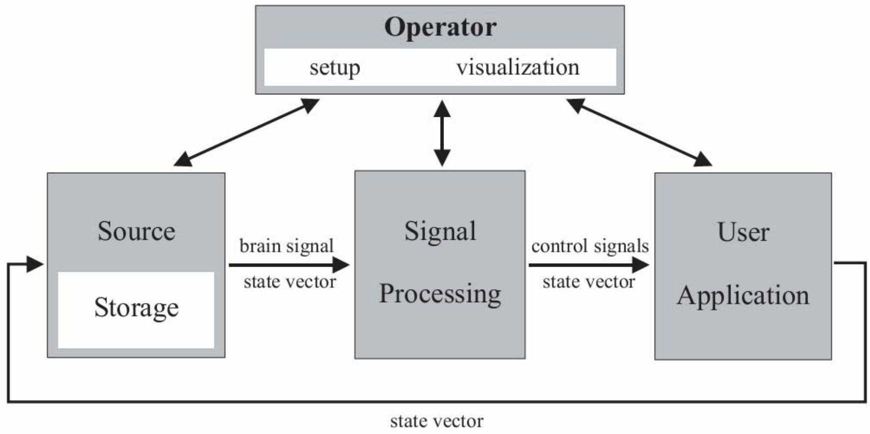

Figure 12.1: BCI2000 design. BCI2000 consists of four modules: operator, source, signal processing, and application. Operator module acts as a central relay for system configuration and online presentation of results to the investigator. It also defines onset and offset of operation. During operation, information (i.e., signals, parameters, or state vectors) is communicated from source to signal processing, to user application, and back to source. (Reproduced from Schalk et al., 2004).

Modifying one or more modules requires little – if any – changes in the remaining modules. With easily available and cheap software it is therefore possible to satisfy the major requirements of new methods of signal acquisition and analysis. BCI2000 has already shown to be able to manage the signals from different sources (i.e. EEG signals from the scalp and from microelectrodes, SCP and wave P300) and to provide the different output for cursors as well as from word-processor control. From the online operations, whatever the final design, BCI2000 extracts a complete data-set in a standard format of routine analysis. For every different application, software developers will have the possibility to exploit the general BCI2000 functions and to finally concentrate only on the aspects which are specific for that particular method. The numerous BMI methods born in recent years and the rapid implementation of the system from a growing body of labs (more than 20 within the early part of this year) testifies the ease and practical advantages of the BCI2000 approach.

12.5.1 Invasive methods

Invasive interfaces record a huge amount of data. Processing algorithms are demanding and require power computers to extract the desired end effector trajectory from thousands channels sampled at high frequency. In order for these interfaces to be used in real applications, all the subsystems devoted to processing should be moved inside the skull. The implant would ideally consist of a few thin film multi-electrode arrays implanted in the motor cortex, with filters, amplifiers and telemetry circuitry embedded.

As also stated in Chapter 9, concerning the interpretation stage for cortical interfaces, the following key topics will be important.

More advanced modelling methods able to deal with large amounts of data gathered by arrays of thousands of electrodes. One area of research that is gaining more and more interest is the large-scale analysis of data generated by biological systems (genomics, cortical recordings) . For this task, a broad range of fields are involved: applied mathematics, statistics, signal processing, control theory, nonlinear dynamics, spatio-temporal pattern formation, complex systems, artificial intelligence, data mining techniques, just to cite the main ones.

Models able to use the additional information from spike timing instead of just rates. Current neuroprostheses assume that the intensity of a stimulus is coded as a rate of impulses over time (“rate code”). It has been questioned whether rate is the only parameter that encodes information about sensory and motor events. The exact timing of spikes from one neuron or the relative timing of spikes in a population of neurons (“temporal coding”) could convey further information that can turn out to be important in the feats of pattern recogniti on (Stein et al., 2005).

12.6 Conclusions

To conclude this extensive review of BMI applications, we would like to summarize in Table 12.1 the expected benefits that can be result from the use of BMIs for different categories of users. As previously stated, the field of human augmentation is not only the most fascinating, but also the most challenging. Many advances in the understanding of how the human brain works will be needed to achieve human augmentation and the most promising approaches to these goals, at the current state of knowledge, are based on invasive neuronal recordings, a technique that, on the other hand poses severe ethical and practical limitations to research in this field, especially for able-bodied people. We therefore expect to see advances in the use of invasive methods first on tetraplegic people, which will eventually, if ever practically feasible, be ported to normal subjects for investigating human augmentation. Until then, EEG appears to be the most practical, portable, and feasible alternative.

Apart from the technical discussions on which technology bears the greatest potential to be applied to BMIs, a lot of effort has to be devoted to research on BMIs to transform these potentials into reality.

User	Current benefits	Prospective	Time
Tetraplegic without brainstem lesions	Restore basic communication ability	Restore basic motor abilities	Near future
Tetraplegic with brainstem lesions	Restore basic communication	Restore basic motor abilities	Future

	ability		
Paraplegic, triplegic	Poor	Restore lost abilities	Future
Healthy	None	Human augmentation	Far future

Table 12.1. Timeline of current and future benefits of BMIs for different categories of users.

12.7 References

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