Brain-computer interface controlled neuromuscular electrical stimulation of the upper limb for stroke patients

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**BRAIN-COMPUTER INTERFACE CONTROLLED
NEUROMUSCULAR ELECTRICAL STIMULATION OF
THE UPPER LIMB FOR STROKE PATIENTS**

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List of Symbols

J	Inertia
V	damping coefficient
θ	angle
$\dot{\theta}$	angular velocity
$\ddot{\theta}$	angular acceleration
M	moment
m	mass
r	radius
y	control vector for BCI output
α	amplitude of arm swinging
ω_d, ω_n	natural frequency, damped natural frequency

List of Abbreviations

EEG	Electroencephalogram
EMG	Electromyogram
BCI	Brain-Computer Interface
NMES	Neuromuscular Electrical Stimulation
AP	Action Potential

Abstract

The human nervous system is susceptible to injury from both extrinsic and intrinsic factors such as trauma or disease. Particularly devastating injuries include stroke and spinal cord injury, where a tragically localized lesion greatly impairs motor function. Unfortunately, the central nervous system is unable to repair itself, and Man has lived with the permanent effects of paralysis, which can only be mitigated with effective rehabilitation or assistive devices. A promising method that has surfaced for stroke rehabilitation is the use of neuroprostheses, which transmits information from the brain to peripheral nerves and muscles by bypassing the damaged neural pathways.

The neuroprosthesis developed in this dissertation targets motor function, and comprises of two sub-systems: sensing of motor imagery with a brain-computer interface (BCI), and activation of muscles with a neuromuscular electrical stimulation (NMES) system. This dissertation puts forth the idea of how paralysed users can control the movement of one upper limb joint by using an EEG-based BCI coupled with a muscle model for NMES movement.

A phenomenological and physiological approach is used to develop the muscle model for the upper limb, enabling the limb to be flexed or extended to a specific angle. Preliminary trials with two healthy subjects showed that the muscle model was successful in moving the limb to within $\pm 5^\circ$ from the desired angle.

As it takes a considerable amount of concentration and focus to operate a BCI, one question that arises is whether stroke patients are able to use a BCI, especially in the post-acute phase when recovery is believed to be maximal. To answer that question, the first ever study on BCI-NMES usage by post-acute (<3 months) stroke patients was performed, and results were encouraging – 4 out of 6 hemi-paretic patients who completed the study were able to use it to perform movements of their wrists. With that, various BCI-NMES protocols can be explored to facilitate neurorehabilitation during the post-acute phase of stroke, where rehabilitation is thought to be more effective. Though functional improvement was not yet proven, it will be the focus of future multi-centre studies with the developed BCI-NMES neuroprosthesis.

Chapter 1 – Introduction

1.1 Background

As you pick up this dissertation and flip through the pages to read it, you probably did not consciously plan and think through each and every movement required to perform this task. Most able-bodied people probably take these movements for granted, and thus do not give it a second thought. However, even a simple movement such as flipping a page, for example, involves very complex processes of planning, execution, feedback, and communication between body parts. These processes occur in various parts of the body, originating from the brain in the central nervous system, to the peripheral nervous system and musculo-skeletal parts of the body.

The intention to move a body part starts with the firing of thousands of neurons in the motor cortex of the brain. The signals, or ‘instructions’, are then propagated down the efferent nerves via action potentials to the motor end plates of the desired muscle. Myosin and actin filaments within the muscle fibres pull against each other, causing the muscle to contract. The muscle then pulls against the tendons which are connected to the bones, resulting in movement of that particular segment of the limb.

The process does not end there; through proprioceptive feedback that is sent back to the brain via afferent nerves, the brain is able to determine the position of that body part. This communication between the brain and peripheral body parts allows the brain to know *if* and *when* the desired movement has been completed, or if the resulting movement deviates from the original intended movement. With this information, the brain is then able to plan and execute the next movement. All these processes happen continuously to enable voluntary motor function to perform tasks. Figure 1.1 illustrates these processes, albeit a simplified version. More detailed descriptions follow in the later chapters.

Figure 1.1 – Processes that occur to perform a voluntary movement

The human body is susceptible to injury from both intrinsic biological pathologies as well as extrinsic factors such as trauma or disease. Particularly devastating injuries include stroke and spinal cord injury, where a tragically localized lesion can inflict great impairment to most aspects of an individual's functioning by interrupting one or more of the processes described above. Unfortunately, the central nervous system is unable to repair itself, and Man has lived with the debilitating, permanent effects of paralysis. Thankfully, efforts have not been spared to discover means to recover from or mitigate paralysis.

To date, one of the most promising treatments for such pathologies is the use of stem cells to regenerate existing cells, and grow new nerve cells to replace the diseased or damaged ones. Studies in rats have already shown that neural stem cells injected into stroke-induced brain cavities are able to grow and integrate efficiently to form primitive neural tissue [Bible 2009]. It is hypothesized that this will enable the actual recovery of damaged parts of the central nervous system, where new neural tissue assumes the respective function. The first ever study involving the use of stem cells for stroke patients was started in January 2009, at the Southern General Hospital,

Glasgow, UK. It is still undergoing feasibility and safety trials using relatively low doses of stem cells. Involving the harvesting of stem cells from aborted human foetuses, this method is thus shrouded in controversy with some groups calling it 'cannibalism'. This trial has only been approved in the UK and was rejected by the Food and Drug Administration for trials in the US [Ghosh 2009]. Thus, it is also unlikely that this method will be widely available in the near future.

Although the damaged parts of the brain do not repair themselves, other parts can assume the function of the damaged cells. The cortical rearrangement of neurons is termed *neuroplasticity*, and it is believed to be responsible for motor function recovery. The extent of neuroplasticity is unfortunately limited and recovery of motor function has been inadequate, leaving many stroke survivors with chronic disability [Hallett 2002].

The main cause of decreased well-being among stroke patients was found to be arm motor impairments [Wyller 1997]. In another survey among quadriplegics, reanimating the paralysed limb has been identified as the most desired outcome [Stein 2005]. Various options must then be explored for the restoration of arm function. In rehabilitation engineering, one such approach is the use of neuroprostheses that directly reads brain activity and acts on peripheral parts of the body in order to improve or replace impaired functions. Popovic [Popovic 2001] suggests that neuroprostheses that use functional electrical stimulation to activate paralysed muscles are the most promising. To this end, researchers have in mind a system that restores or replicates movement [Kübler 2005].

Over the past few decades, numerous attempts have been made to enhance motor recovery; methods such as the neurodevelopmental technique [Bobath 1959], sensorimotor integration [Flanagan 1967], proprioceptive neuromuscular facilitation [Knott 1968], biofeedback [Basmajian 1982], and functional utilization of evolving synergies [Brunnstrom 1970] have been proposed. However, controlled studies have yet to demonstrate the superiority of any one of these methods in improving motor function for stroke survivors [Stern 1970, Lord 1986, Basmajian 1987, Wagenaar 1990, Dickstein 1996].

While the definitive method for stroke rehabilitation is not known, it is widely understood that motor and functional recovery involves active, repetitive and intense exercises of the paretic limb [Wolf 1989, Taub 1993, Butefisch 1995, Loureiro 2004, MacClellan 2005]. Recent years saw the advent of robot-assisted therapies to deliver the higher levels of intensity and repetitiveness required. To name a few, among the robots are the MIT-Manus [Krebs 1998], the Mirror-Image Motion Enabler (MIME) [Lum 2006], the Simulated Environment for Arm Therapy (SEAT) [Johnson 1999], and Gentle/s [Loureiro 2003]. Early studies with robot-aided therapies have shown promising results [Krebs 1998, Volpe 1999, Hesse 2005, Daly 2005, Prange 2006, Krebs 2008], and it has been suggested that robotic paradigms may eventually enhance motor learning and rehabilitation beyond the levels possible with conventional training techniques [Reinkensmeyer 2004]. However, as further trials have yet been performed to determine the best method, the standard of care currently still revolves around the tried and tested methods of conventional physical and occupational therapy.

Another promising method that has surfaced for stroke rehabilitation is the use of neuroprostheses. Neuroprostheses are artificial systems that bypass diseased or damaged neural pathways from the brain to the peripheral nerves and muscles. Research in this field indicates that neural signals can be used to control artificial prosthetic devices, such as robotic arms or electrical stimulation devices. Preliminary findings have also demonstrated that paralysed patients can learn to regulate their brain signals to interact with computers [Kennedy 1998]. Nicolelis further suggests that in the near future, hybrid brain-machine interfaces could be used to restore various aspects of motor function in patients severely paralysed by strokes, spinal cord injuries, or peripheral degenerative disorders [Nicolelis 2001].

Recently, Daly & Wolpaw put forward the idea of using a brain-computer interface (BCI) to give stroke survivors more effective motor control, as regulation of their electroencephalogram (EEG) may guide activity-dependent plasticity. They also suggest that by using brain signals to supplement impaired muscle control, BCIs may be able to improve efficacy of rehabilitation protocols and thus restore muscle control. One of their proposed methods involves using brain signals to activate functional electrical stimulation [Daly 2008a]. On the afferent side, it is hypothesized that

proprioceptive feedback that arise from repetitive movements will induce long-term potentiation in the motor cortex and modify the excitability of specific motor neurons, thus enhancing motor learning [Asanuma 1991]. It is thus hypothesized that learning to regulate brain signals, coupled with the long-term potentiation induced through repeated proprioceptive feedback, will lead to restoration of motor function.

Most BCI studies thus far have involved chronic stroke patients. In a study by Buch *et al* [Buch 2008], it was demonstrated that 6 out of 8 chronic stroke patients with hand plegia were able to learn to operate a binary magnetoencephalography (MEG)-based BCI after 13-22 sessions, and to voluntarily open as well as close a prosthesis attached to their paralysed hand. In another study, 5 chronic (>6 months) stroke patients with severe upper limb paresis managed to regulate their EEG to gain control of a binary BCI after 9 training sessions [Daly 2008b]. As most motor recovery occurs within 5 months of stroke onset [Jørgensen 1995], interventions to facilitate recovery, including BCI-based therapy, should ideally occur during this timeframe. However, there is currently still little data on the use of an EEG-based BCI in patients less than 6 months post-stroke.

Brain-computer interfaces and neuromuscular electrical stimulation hold promise for restoration of motor function, but remain a long way before they can become commonplace neuroprostheses for performance of complicated movements. Challenges faced include the limited control from non-invasive BCIs, the amount of training required to use a BCI, its efficacy in providing any therapeutic effects, the complexity of stimulating specific muscles in the upper limb for task performance amidst a multitude of other factors.

1.2 State of the Art of BCI-controlled Neuroprostheses for Motor Function

Neuroprostheses for motor function can be categorized into implanted and non-invasive systems, each of them with their respective pros and cons. Nicolelis [Nicolelis 2002] pioneered the implanted systems by demonstrating how a monkey with implanted electrodes in the brain could tele-operate a robot arm to move exactly

as its own arm did. Velliste *et al* [Velliste 2008] went further and astonished the world with an implanted system that allowed a monkey to control a robot arm as if it were its own, enabling the monkey to use the robot arm to feed itself. In humans, quadriplegic Matthew Nagel became the first human recipient of an implanted BCI, with a microelectrode array implanted in his primary motor cortex, which he used to control cursor movements, operate devices, as well as opening and closing a prosthetic hand [Hochberg 2006].

For non-invasive systems, Pfurtscheller *et al* [Pfurtscheller 2000a] were the first to demonstrate a hand orthosis operated by an EEG-based brain-computer interface in 2000 to assist the user with hand grasp actions. In 2003, Pfurtscheller demonstrated the use of non-invasive brain-computer interface coupled with surface functional electrical stimulation to restore hand grasp function. This system enabled a tetraplegic patient, with incomplete spinal cord injury below C4, to hold and drink from a glass [Pfurtscheller 2003]. Their non-invasive BCI was later combined with the implanted Freehand® system to enable a tetraplegic patient with complete motor and sensory lesion below C5 to grasp and release objects in order to perform pick and place tasks [Müller-Putz 2005]. Figure 1.2 below illustrates these two systems.

Figure 1.2 – Non-invasive brain-computer interface and electrical stimulation facilitate hand-grasps in tetraplegic patients. Top: surface electrical stimulation [Pfurtscheller 2003]. Bottom: implanted electrical stimulation [Müller-Putz 2005].

1.3 Motivation for this Project

Stroke remains one of the major causes of disability worldwide. It has been estimated that out of the 75% of patients who survive the first month after a stroke, more than half will require specialized rehabilitation [Pollack 2002]. Even after completing conventional rehabilitation, many patients still face persistent and disabling upper limb motor deficits [Daly 2005]. With the increasing aged population typical of developed countries combined with the chances of stroke doubling with each decade after 55 years of age [Winters 2000], there is a need to improve methods for stroke rehabilitation. Upper limb weakness and loss of function is a significant problem in stroke survivors. A number of longitudinal studies indicate that 30% [Heller 1987] to 66% [Wade 1983, Sunderland 1989] of hemiplegic stroke patients will have a functionally useless arm, whereas only 5% to 30% demonstrate recovery of dexterous hand function [Heller 1987, Nakayama 1995, Kwakkel 2003].

This prospect of direct brain control of the paretic limb opens up many options for rehabilitative or assistive applications. Using a brain-computer interface (BCI) is, however, not easy; both Man and machine must undergo a certain amount of training in order to use it, and high levels of concentration must be maintained during its use. Thus, when using a BCI neuroprosthesis in stroke, one question that has surfaced is, whether stroke patients are able to elicit a significant change in EEG that can be used as a control signal, and whether this would be repeatable.

Furthermore, if BCI-NMES is to be used for restoration of motor function in other joints of the upper limb, it should ideally be able to produce gradated movement of the limb, for which a muscle model must be developed to study the movement produced by electrical stimulation. At present, there are no clinically viable hand neuroprostheses for hemiplegics. Sheffler has identified specific requirements for its development: i) It should provide proximal and distal control, ii) Utilize control paradigms that produce effortless movement of the impaired upper limb without compromising the function of the healthy limb [Sheffler 2007]. The research work carried out for this dissertation aims to provide control of the proximal joint, i.e. elbow joint, by using a BCI combined with an NMES model to achieve that movement.

1.4 Scope

This dissertation has two distinct sub-systems: the brain-computer interface (BCI), and neuromuscular electrical stimulation (NMES) system. Both systems are of non-invasive type and come together to form a neuroprosthesis for motor function. This dissertation details the integration and implementation of both systems, and presents laboratory and clinical experiments of their usage.

Since the desired application involves motor function, EEG changes in the μ (8-14Hz) band shall be used for BCI operation because this phenomenon is a direct consequence of motor imagery. While this dissertation is not intended to further develop BCI technology, a method to improve BCI usage is implemented.

The application of this neuroprosthesis is targeted at the paretic upper limb of stroke patients in the post-acute phase. The focus will be on muscles that act on the elbow and wrist joints, as stroke survivors often face wrist extension problems, and elbow flexion/extension movements are required to place the hand in appropriate positions. The muscle model will be based on a phenomenological approach as the parameters are more easily measurable and thus more practical.

1.5 Objectives

This project entails the development of a BCI-NMES neuroprosthesis targeted at rehabilitation of motor function. For spinal cord-injured patients, the lesion does not affect the brain and EEG elicited by motor imagery can be expected to remain the same; but the same cannot be said of stroke patients who have sustained some damage to the brain. A necessary step would thus be to determine if stroke patients can use a BCI.

NMES systems that enable a user to perform arbitrary movements conventionally require the user to control the amount of stimulation manually, using residual functions to manipulate input devices such as a joystick. Alternatively, constant stimulation parameters are used to induce full range movements, for example, a full hand grasp/release. In order to develop a BCI-NMES system that allows the user to move his/her arm to any specific point without the need for manual user input, a muscle model must be developed to determine the amount of electrical stimulation needed to move the arm autonomously.

Considering the above problem statements and scope, there are three objectives of this dissertation:

- i To integrate the brain-computer interface and electrical stimulation sub-systems to enable users to move their arm by thinking about it;
- ii To determine whether post-acute stroke patients elicit sufficient changes in μ rhythm EEG during motor imagery in order to operate a brain-computer interface, and if they do, to facilitate their training to use the BCI;

- iii To develop a phenomenological model of the biceps and triceps in order to induce specific, controlled movements of the elbow joint using neuromuscular electrical stimulation.

1.6 Organization of this Report

The following chapters are organized as follows:

- Chapter 2 offers essential information pertaining to parts of the human body that interact with the brain-computer interface, and explains the mechanisms of neural rehabilitation.
- Chapter 3 describes in detail the brain-computer interface used in this research, as well as the integration of the brain-computer interface and neuromuscular electrical stimulation systems to build a neuroprosthesis.
- Chapter 4 introduces neuromuscular electrical stimulation, lays out the challenges faced, and proposes a method to produce specific movement of the elbow joint.
- Chapter 5 presents the first ever clinical trial with post-acute stroke patients.
- Chapter 6 summarizes the contributions of this dissertation and proposes future directions for this research.

Chapter 2 – Pathologies and Rehabilitation of the Human Nervous System

The motor neuroprosthesis interacts continuously with the human body by sensing motor intent from the brain (in the form of changes in μ -rhythm EEG), and acting on peripheral nerves to produce muscle contraction and hence movement. The system thus encompasses both Man and machine. This chapter describes parts of the human anatomy which interact with the neuroprosthesis and briefly describes the neural rehabilitation process.

2.1 *The Nervous System*

The nervous system consists of the central nervous system (CNS) and the peripheral nervous system (PNS). The CNS consists of the brain and the spinal cord, while the PNS consists of all other nerves leading to and from the CNS. The PNS can be further subdivided into the autonomic, enteric and somatic nervous systems, of which only the last one comes under voluntary control.

2.1.1 Motor Cortex

Of particular interest in the development of a neuroprosthesis for motor function is the motor cortex, where signals for voluntary movement originate. The motor cortex is located in the rear portion of the frontal lobe, just before the central sulcus that separates the frontal lobe from the parietal lobe. Figure 2.1 illustrates the position of the motor cortex, and Figure 2.2 shows the regions of the motor cortex associated with motor function of various body parts.

Figure 2.1 – Location of the motor cortex and relative locations of the cortical regions responsible for the planning and execution of voluntary motor function [Kandel 2000]

The motor cortex plans the execution of each movement – from which muscles to activate and how strongly to activate the muscles. Billions of neurons within the motor cortex coordinate the various parameters of movement, such as the direction and speed of movement, as well as the force exerted by the muscles. The firings of these neurons make up the electrophysiological activity that sums up on the scalp, and can be recorded as electroencephalography (EEG). These ‘instructions’ are then carried down the cortico-spinal tract to the motor circuits of the spinal cord, before branching out to the respective peripheral nerves. The neural pathway from the motor cortex to the limb is illustrated in Figure 2.3. Each hemisphere of the brain controls movement on the contralateral side of the body, i.e. the left brain controls movement on the right side of the body, hence damage to the left motor cortex would result in paralysis to the right side of the body and vice versa. Anatomical details are described more comprehensively in [Horch 2004].

Figure 2.2 – Regions of the motor cortex associated with motor function of various body parts [Penfield 1950]

The region of the motor cortex responsible for movement of the elbow, wrist and hand, is located slightly lateral to the sagittal plane, as shown in the above figure. Activity from this area is picked up over electrodes C3 (for right limb movements) and C4 (for left limb movements).

Figure 2.3 – Signals originating in the motor cortex are carried down the cortico-spinal tract to the peripheral body parts [Kandel 2000]

The brain is capable of imagining a rehearsal of a particular set of movements, without any actual movement. This is a mental process known as motor imagery. It is widely accepted that such imagination of movements share similar brain regions and functions as the actual movements [Jeannerod 1995], and this was proven using fMRI [Porro 1996]. Decety [Decety 1994] explains that the difference between mental imagination and actual movement is that the execution signal is blocked at some cortico-spinal level, while the signal that originates in the motor cortex remains the same. Beisteiner [Beisteiner 1995] suggested that by simulating the movement in both time and space, images of sensation associated with the actual execution are produced. Pfurtscheller [Pfurtscheller 1997a] also found similarities in EEG patterns related to imagination of a movement and planning of that particular voluntary

movement. The specifics of these EEG patterns will be discussed in greater detail in the following chapter.

These findings play an important role in the development of a neuroprosthesis for restoration of motor function. It implies that paralysed persons could be capable of learning to regulate their motor imagery in order to control an external device, or neuromuscular electrical stimulation of their own limbs. Indeed, Pfurtscheller demonstrated this concept by using an EEG-based BCI to control a hand orthosis and functional electrical stimulation of the paretic hand in patients with spinal cord injury [Pfurtscheller 2000a, Pfurtscheller 2003].

2.1.2 Peripheral Nerves

In the healthy nervous system, movement-related signals that originate in the motor cortex are transmitted via action potentials through efferent nerve fibres that descend from the brain to the motor neurons, which then cause the muscles to contract and produce movement. The motoneurons that constitute the motor peripheral nerves run from the spinal cord to the muscles, are easily located and hence stimulated with NMES. Their positions, however, may shift a little when the arm is constrained or constricted, making it more challenging to deliver constant electrical stimulation.

Action potentials (AP) are electrophysiological signals that transmit information by propagating through the nerves. An AP is triggered by the depolarizing of a nerve. Under inactive conditions, the different ionic concentrations create an electrical potential between the interior and exterior of the nerve membrane, ranging from about 70 to 90 *mV*, with the interior of the nerve being electrically negative. When an AP is triggered, this potential is inverted and the inside becomes electrically positive for a short duration of approximately 400 μ s. The depolarization disturbs the resting regions ahead of the nerve and allows it to propagate. This electrophysiological signal can be detected as electromyography.

When NMES is applied, the excitability depends on factors such as the distance of the cathode to the nerve, the diameter of the nerve, and the amount of electrical charge flowing through. The larger the diameter, the greater the amount of electrical charge

that flows through it, and the easier it is to excite. These larger nerve fibres innervate Type II muscle fibres, and will be elaborated on, under the section on motor function.

In the opposite direction, the ascending afferent nerves run from the peripheral parts of the body back to the cortico-spinal tract, and up to the somatosensory system. They carry sensory information to the brain, such as the position and speed of the limb. For example, healthy people will be able to close their eyes and gently touch their noses because they know exactly where their hand is, relative to their noses, and how fast their hand is moving. Such information is acquired from proprioceptive mechanoreceptors in the joints, muscles, tendons and ligaments, and fed to the CNS continuously to establish a closed control loop between the brain and peripheral parts of the body.

2.2 Motor Function

When the action potential reaches the motor nerve axon terminal, at the mid-point of the muscle fibre, it causes the muscle fibres to contract symmetrically on both sides. Anatomical details of the motor units are available in [Keller 2001].

There are two types of muscle fibres:

- Type I: Smaller force, smooth contraction, fatigue-resistant
- Type II: Larger force, fast and twitching contraction, fatigue-prone

The smaller nerve fibres are connected to the Type I muscle fibres, whilst the thicker nerve fibres are connected to the Type II muscle fibres. As mentioned earlier, the thicker nerve fibres are more easily stimulated with NMES. As a result, the Type II muscles get fatigued faster, which is a major drawback of NMES.

An artificial 'action potential' can be created by inducing the change of potential between the inside and outside of the cell by altering the extracellular potential, a method known as electrical stimulation. This artificial means of excitation achieves the same effect as that of a voluntary action potential generated by the brain, and it cannot be differentiated by the muscle [Rattay 1990, Horch 2004].

The torque produced by a muscle is dependent on factors such as joint angle, contraction velocity, viscosity, and elastic properties. Details of the muscle contraction and electrical stimulation method will be discussed together with the muscle model presented in Chapter 4.

2.3 Paralysis Due to Stroke

A cerebrovascular accident, or stroke as it is more commonly known, is a sudden disruption in blood supply to the brain that causes damage to brain tissue and hence partial loss of brain function. The disruption could be due to a blockage in blood flow, or due to a rupture of blood vessels in the brain; these are termed ischaemic and haemorrhagic strokes respectively. As a result of destruction of cortical tissue, generation and integration of neural signals are distorted and interrupted. When these affected areas include the sensorimotor cortex, there is a reduced or absent ability to activate muscle tissue, which ultimately impairs motor performance. Motor function impairment is commonly measured with the Medical Research Council (MRC) motor power grading scale from 1 to 5, as shown in Table 2.1.

A stroke affects only the CNS, leaving skeletal muscles intact and functioning normally. The only thing lacking is the appropriate input signal to these muscles. The contraction of skeletal muscles can thus be triggered by artificially introducing electrical pulses to the nerves surrounding and leading to the respective muscle, otherwise known as electrical stimulation.

Table 2.1 - Medical Research Council (MRC) motor power grading scale

Score	Description
5	The part moves through full range of motion against maximum resistance and gravity. "Normal" differs for each muscle group and in individuals of different age, sex and occupation.
4	The part moves through full range of motion against gravity and moderate resistance.
4-	The part moves through full range of motion against gravity and less-than-moderate resistance.
3+	The part moves through full range of motion against gravity, takes minimal resistance, and then "breaks" i.e. relaxes suddenly.
3	The part moves through full range of motion against gravity with no added resistance.
3-	The part moves less-than-full range of motion against gravity.
2+	The part moves through full range of motion in a gravity-eliminated plane, takes minimal resistance, and then "breaks" i.e. relaxes suddenly.
2	The part moves through full range of motion in a gravity-eliminated plane, with no added resistance.
2-	The part moves less-than-full range of motion in a gravity-eliminated plane.
1	Tension is palpated in the muscle or tendon but no motion occurs at the joint.
0	No tension is palpated in the muscle or tendon.

The effects of stroke include (but are not limited to) diminished senses, loss of perception, impaired cognition, slurred speech, difficulty in swallowing, loss of bladder and bowel function, and impaired motor function. Damage to neural areas is responsible for controlling movement and concomitant disuse and persistent abnormal posture of the impaired limb cause a host of centrally and peripherally-based sensory motor impairments. Such impairments include decreased passive range of motion, weakness, hyperactive reflexes and incoordination; these are manifested partially as an inability to independently coactivate muscles [Winters 2000]. As the central

nervous system is unable to undergo neither regeneration nor repairs, parts of the brain damaged by the stroke remain dead.

Fortunately, some of these impairments may not be permanent. The brain has the natural ability to reorganize to compensate for lost function or new environmental requirements [Horch 2004]. It has also been shown that, despite age and neurologic deficit, a comprehensive rehabilitation can improve functional abilities of the stroke survivor [Feigenson 1979]. This process is termed as neuroplasticity which involves the sprouting of new dendrites, synthesis of new proteins, and changes in synaptic contacts with other neurons.

2.4 Neural Rehabilitation

Treatment of stroke typically includes medications, hospital care and rehabilitation. The first three treatments focus on the minimization of damage caused by the stroke while the fourth, rehabilitation, focuses on recovery. The severity of paralysis or loss of bodily functions depends on the extent of damage to the brain caused by the stroke. In severe cases, one side of the body is paralyzed (hemiplegia) and the patient loses control and sensation of that side of the body. Severe paralysis or lack of voluntary control of distal parts of the upper limb has been estimated to afflict about 30 percent of stroke survivors [Hesse 2005].

The recovery of motor function after stroke tends to follow a certain pattern [Zorowitz 1999]. Muscle stretch reflexes in the limbs become more active on the paralysed side within 48 hours post-stroke, starting from distal parts of the limb. Spasticity develops soon after, prior to the restoration of volitional movement, but subsides as volitional movement improves. Prognosis is poor when there is a prolonged flaccid period, volitional movement is absent for more than 2 weeks, lack of voluntary hand movement for more than 4 weeks, or when there is severe proximal spasticity. These cases usually make up about 10 percent of stroke survivors. Conversely, approximately 10 percent of stroke survivors will recover completely and spontaneously within 12 weeks. This leaves the 80 percent majority of stroke survivors who are left with some form of disability and to possibly benefit from stroke rehabilitation.

Rehabilitation, however, must be administered intensively within 6 months post-stroke, as it has been observed that the majority of motor recovery occurs within this period [MacClellan 2005].

There are two theories behind the recovery of motor function following brain damage. The first theory suggests that the surrounding healthy cells will sprout collaterally to reactivate the damaged cells to participate in motor activity, while the second theory suggests that neural pathways and synapses that are not normally used for a particular function can be called upon to take over the effects of remaining input and replace the function of damaged ones [Zorowitz 1999]. The physiologic mechanisms of plasticity have also been demonstrated through functional magnetic resonance imaging, which show higher levels of activation in the sensorimotor and pre-motor cortices on the same side, as well as the dorsolateral prefrontal cortex and the perimeter of the infarcted area during rehabilitation activities [Cao 1998].

Daly [Daly 2008] suggests that BCI technologies can significantly aid people with devastating neurological disorders, and might restore more effective motor control for stroke patients. He posits that the use of brain signals to supplement impaired muscle control could increase the efficacy of rehabilitation protocols, since the afferent and efferent loops are closed, thus improving activity-dependent plasticity in the CNS. To this end, this dissertation documents the development and use of a BCI and NMES to enable hemi-paretic stroke patients to move their upper limb.

Chapter 3 – The Brain-Computer Interface (BCI)

This chapter starts with an introduction to the various types of brain-computer interfaces, and then explains the rationale for using an EEG-based BCI that uses μ rhythm changes that result from motor imagery. The specific methods used in this BCI are then presented in detail.

3.1 Introduction to Brain-Computer Interfaces

Brain-computer interfaces (BCI) enable their users to act on the environment without going through the normal intermediaries of the peripheral nerves and muscles [Wolpaw 2000b]. BCIs have been used for various applications, such as a spelling device [Birbaumer 1999], moving a cursor [Wolpaw 1991], controlling a robot around a room [Millán 2004], controlling an orthosis [Pfurtscheller 2000a] or prosthesis [Hochberg 2006], playing games and controlling smart homes [*g.tec – Guger Technologies*]. A widely accepted definition of a BCI is a direct communication pathway between the brain and an external device that bypasses the normal output pathway of the peripheral nerves or muscles. Nicolelis offers a more detailed definition, by referring to these devices as ‘hybrid brain-machine interfaces’ (HBMI), reflecting the hybrid nature of continuous interactions between the brain and external devices [Nicolelis 2001]. He then further distinguishes between HBMI that stimulate the brain in order to transmit information (Type 1) or samples brain activity to control external devices (Type 2). An EEG-based HBMI falls into the latter category, and is also commonly referred to as a BCI.

BCIs operate on the various types of measurements of brain activity. These include electroencephalogram (EEG), functional magnetic resonance imaging (fMRI), magnetoencephalography (MEG), near infrared spectroscopy (NIRS), and electrocorticography (ECoG). Some of these methods are invasive and require surgical implantation of devices, while others are non-invasive.

One of the objectives in this project was to develop a neuroprosthesis for motor function. As such, it should be minimally obtrusive, and preferably wearable and portable. Methods such as fMRI, MEG and NIRS require bulky equipment, while ECoG and other more invasive methods pose a higher risk to the subject due to surgical implantation. The fMRI scanners are huge, occupying a whole room, while the subject is pretty much immobilized on a horizontal bed with his head in the machine. The MEG requires a magnetic shielding room to be constructed, and the subject is confined to the room.

On the other hand, the entire EEG setup consists of only an EEG amplifier which is the size of a small laptop, a laptop computer, and a wearable electrode cap. It can be taken off just as easily as it is put on, and can be used almost anywhere. It also offers high temporal resolution in the order of milliseconds. As EEG is non-invasive, there is no risk of complications arising from the surgical implantation of devices into the brain. Its convenience has led Wolpaw to conclude that it is the only practical possibility for a non-muscular and non-invasive communication channel [Wolpaw 2000a]. Therefore, the EEG approach is perhaps the most suitable.

The use of EEG, however, is not without its drawbacks. As EEG is measured on the scalp, it reflects the aggregated electrical activity of millions of neurons from a large area of the brain, which may or may not be related to motor activity [Chapin 2000]. During volume conduction of electrical activity from the neuron within the brain to the scalp, the skull acts as an insulator which attenuates neural signals and filters out high-frequency signals, thus lowering the signal-to-noise ratio and spatial resolution of EEG. Despite these drawbacks, EEG still offers a sufficient information transfer rate to operate a neuroprosthesis.

Electroencephalography (EEG) is the recording of electrical signals originating from post-synaptic potentials that aggregate at the cortex and transmit through the skull to the scalp, with surface electrodes. EEG can come in many forms as a result of different mental states. There are two general categories – endogenous and exogenous electrophysiological activity [Wolpaw 2000b]. Endogenous forms are the result of the user intentionally regulating the amplitude of specific frequency bands,

such as the μ and β rhythms over the sensorimotor cortex [Pfurtscheller 1997a, Pineda 2000]; whereas exogenous forms are the result of the user's natural response evoked by an external stimuli, such as the P300 signal produced after the flashing of a desired target [Sutton 1965, Polich 1998, Donchin 2000]. These two forms have also been classified asynchronous and synchronous respectively. In the former the user is free to generate a mental state at will [Müller-Putz 2006], whereas the latter is cue-based, meaning that the user can only respond in a predefined time-window depending on the external stimulus. While the asynchronous BCIs offer the user more flexibility, it requires substantially more training to use [Allison 2003].

For the purposes of a neuroprosthesis for motor function, it would be ideal to utilize an endogenous EEG signal that is a direct result of the user's intention to move his/her paralysed limb. This phenomenon of event-related synchronization (ERS) and desynchronization (ERD) of the μ (8-14 Hz) rhythm has been well-documented, and it has been shown that people can learn to regulate their μ rhythms. The amplitude of the μ rhythm is largest when the subject is not moving or not imagining any movement (i.e. resting), and attenuates when the subject is moving or imagines movement [Beisteiner 1995, McFarland 1997, Pfurtscheller 1997a, Pfurtscheller 1997b, Pineda 2000, Neuper 2006]. The next section explains how this phenomenon is used to operate the BCI.

3.2 The Brain-Computer Interface

EEG is acquired through a *NuAmps* EEG amplifier and sampled at 250 Hz. The EEG acquisition was mono-polar with the right earlobe as the common reference point. Conducting gel is applied between the electrodes and scalp surface to reduce impedances to below 5 k Ω . The area above the motor cortex corresponds to electrode positions FC3, FC4, C3, C4, CP3, and CP4 of the international 10/20 montage for EEG electrodes [Jasper 1958], as shown below in Figure 3.1.

Figure 3.1 – EEG electrodes over the motor cortex

EEG power in a specific band (see next section on customization for each subject) is calculated over a 250 millisecond window, at 100 millisecond intervals. Typically, this band ranges from 8-14 Hz. This gives a joint feature vector of EEG powers:

$$\hat{x}_t = \{x_{t,FC3}, x_{t,C3}, x_{t,CP3}, x_{t,FC4}, x_{t,C4}, x_{t,CP4}\} \quad (3.1)$$

where x_t is average power over the most recent window at time t and the subscripts denote the respective locations.

In order to measure the attenuation in the respective EEG rhythms, the baseline levels must be recorded. To do this, subjects were seated comfortably in a chair and told to relax, not to move, or even think of moving. EEG was then recorded for 3 minutes, and the average power of each channel is taken as the baseline. The vector of baseline powers is thus:

$$\hat{x}_0 = \{x_{0,FC3}, x_{0,C3}, x_{0,CP3}, x_{0,FC4}, x_{0,C4}, x_{0,CP4}\} \quad (3.2)$$

where x_0 is the average power over the 3-minute calibration period and the subscripts denote the respective locations.

Due to differences in conductance between the electrodes and the scalp, as well as variations in EEG at the various locations, different weights must be assigned to

different channels to get an unbiased output. The weight array, denoted as w , measures the power difference between the various channels during rest, is learnt empirically and normalized during calibration.

With the current EEG power, the baseline power and weight array, the control vector, y , can be found:

$$y = \hat{w}^T (\hat{x}_t - \hat{x}_0) \quad (3.3)$$

Equation 3.3 above is simply the difference in EEG power between the current state and the resting state, multiplied by the weight array.

The control vector y is then used to control the position of an on-screen cursor; this will be described later in Section 3.4 on the graphical user interface.

3.3 Customization for Each Subject

As each person is unique, the BCI must be customized for each and every subject. Although it is well established that EEG in the mu rhythm that spans 8-14 Hz attenuates the most, the most active frequencies vary from person to person.

Since the power over a range of frequencies is averaged to determine the vector y (see Equation 3.3), inclusion of inactive frequencies (frequencies that show little change in amplitude) will reduce the amount of attenuation seen over the entire band, rendering the BCI less sensitive. It is thus important to identify and use only the most active frequency range. Before going into the specifics of identifying the most active frequencies of each signal, the various EEG signals shall be described.

Customization of the BCI starts with recording EEG during various actions. Subjects were seated comfortably in a chair, leaned back on the back rest, and placed their arms on the table top. They were instructed to follow on-screen instructions, which included hand-grasping and foot-tapping actions interspersed by periods of rest. In performing the hand grasping, subjects rested their forearms on the table and

repeatedly closed and opened their hands. If subjects could not perform the required actions, they were told to try their best, and to imagine that particular movement.

The sequence and timings are shown in Figure 3.2. In order to prevent subjects from pre-empting the next action, they were not told the sequence of actions, nor were they told the duration that each action had to be performed. Furthermore, each particular action was performed for 45 seconds. However, only the 25-second interval in the middle was used for analysis.

Figure 3.2 – Sequence and durations of actions performed during EEG recording

To avoid EMG and EOG artefacts, subjects were instructed not to clench facial muscles or look around by moving their eyes during the recording. Recordings that were contaminated with EMG artefacts were discarded, and the recording process repeated. EMG artefacts are easily identified as they are many times larger in magnitude than EEG.

After the EEG was recorded, the mean was removed, and filtered offline to between 8–13 Hz (zero-phase digital filtering with MATLAB 'filtfilt' function). The amplitudes of each frequency component was then found using fast Fourier transform, and averaged over each window. The resulting output is the variation of EEG against time. Figure 3.3 shows an example of the filtered EEG for each action. Figure 3.4 shows the variation of EEG against time for each electrode position C3 and C4.

Figure 3.3 – EEG from positions C3 and C4, filtered between 8-14 Hz, during various actions: left hand grasping (L Hand), left foot tapping (L Leg), right hand grasping (R Hand), right foot tapping (R Leg), and resting. This chart shows that EEG amplitude is higher during resting than during motor intent.

Figure 3.4 – Variation of EEG against time for various actions. Average power of EEG is higher during resting (black line) than hand grasping (blue line) and foot tapping (green line).

The above sample was recorded from a stroke patient 12 days post-stroke. The 48-year-old male suffered a haemorrhagic stroke to the basal ganglia, as confirmed by a CT scan. He experienced weakness on the left side of the body with a Medical Research Council (MRC) power grading of 4- for his wrist extensors, which meant that he could extend his wrist through the full range of motion against gravity and less-than-moderate resistance.

From the above data sets (refer to Figure 3.4), the effects of each action can be compared against the resting state; e.g. Data A1 can be compared against Data A0 to see the effects of motor intent on EEG. The graphs show that EEG in the 8-14 Hz band attenuates during motor intent. Although the attenuation is evident over the entire band, the response of the BCI could be made more sensitive by analysing only the most active frequencies of each subject.

To do this, the EEG signals (as shown in Figure 3.3) are decomposed into individual frequencies ranging from 8-14 Hz with a step size of 0.5 Hz. The weights of these frequencies are then estimated using the Bandlimited Multiple Fourier Linear Combiner (BMFLC) [Veluvolu 2007]. Following that, the weights of each frequency are averaged over the duration of the signal, and compared against the resting EEG, as shown in Figure 3.5.

Figure 3.5 – Weight of each frequency component during resting (solid line) and movement (dotted line). This plot shows a pronounced event-related desynchronization [Wolpaw 1991] in the 8 to 12 Hz band.

After the most active frequencies of the μ band that attenuate during motor imagery are determined, the BCI can be customized to focus only on those frequencies. For example, as shown in Figure 3.5, the amplitudes of frequencies 8, 8.5, 9, ... 12 Hz were averaged and used to determine the x_t for each electrode position (as per Equation 3.1).

3.4 The Graphical User Interface

The graphical user interface (GUI) employs the ‘basket paradigm’ [Krausz 2003], in which a ball (the cursor) drops from the top of the screen to the bottom of the screen at a constant speed. The ‘baskets’ are targets at the bottom of the screen, and when the ball falls into a particular basket, that target is selected. The user only controls the horizontal position of the ball, i.e. move the ball left/right. These movements are dependent on the control vector y , as mentioned in Equation 3.3 earlier. Figure 3.6 illustrates the GUI.

Figure 3.6 – GUI of the BCI showing the ‘basket paradigm’ [Krausz 2003]. The control vector moves the ball in the horizontal direction while the ball drops at a constant speed into a ‘basket’ that represents a selection.

The left target triggered electrical stimulation to move the paralysed limb to the left, and vice versa for the right target. Details of electrical stimulation are further elaborated in Chapter 4.

3.5 Training to use the BCI

Training to use this BCI is an operant conditioning approach, whereby the consequences of one’s actions are used to modify the performance of those actions. In this case, the BCI user’s imagination of limb movement results in changes in μ -rhythm EEG, which is then translated into horizontal movement of cursor [Krausz 2003]. The user is unable to sense the outcome of his/her motor imagery, and hence needs feedback through a more tangible form – visual feedback of the cursor movement – illustrated in Figure 3.7. Observation of those movements will aid the subject to modify his/her motor imagery in order to move the ball as desired.

Figure 3.7 – The visual feedback loop aids the user in the operant conditioning approach required to train to use the BCI. The user attempts various types of motor imagery to move the cursor to the desired target.

The user will then have to try out various forms of motor imagery to achieve that goal. As each individual is unique, different users will require different types of motor imagery to regulate their μ -rhythms. For example, one user may find that motor imagery of wrist extension may produce the greatest change in the μ rhythm (as reflected by appropriate cursor movement), while another user may find that motor imagery of hand grasping produces has a better effect. Some subjects have described the motor imagery that they used as likening it to the “shifting the manual gear stick of a car”, or “ironing”, while another subject described himself as “turning to the left while walking”. It typically takes 1 or 2 hours for users to train to use the BCI.

Chapter 4 – Neuromuscular Electrical Stimulation of the Upper Limb

Once the user's intention to move his/her paretic arm has been sensed through the brain-computer interface, the next step would be to assist the user to materialize that movement. This can be achieved through neuromuscular electrical stimulation (NMES). This chapter starts with an introduction to NMES, and then details how a controlled movement of the arm is achieved with a phenomenological muscle model for NMES.

4.1 Introduction to Neuromuscular Electrical Stimulation

Earlier in Section 2, it was mentioned that the action potentials could be artificially created to excite the nerves so as to induce muscle contraction. This is exactly what electrical stimulation does.

Common terminology includes functional electrical stimulation (FES), neuromuscular electrical stimulation (NMES), transcutaneous electrical nerve stimulation (TENS or TNS), and electrical stimulation (ES). These names essentially refer to the same thing, which is the passing of electric current through the efferent nerves to alter the extracellular potential, thereby changing the potential between the inside and outside of the nerve cell, thus creating an artificially induced action potential. In this report, this process shall be referred to as neuromuscular electrical stimulation (NMES) as it does not directly accomplish any specific functional task, but may lead to specific effects that could enhance function. An in depth review can be found in [Sheffler 2007].

4.1.1 Principles of NMES

Electrical stimulation involves sending very small current pulses through the nerves. The magnitude of each pulse is typically in the order of a few milli-amperes and lasts less than 250 micro-seconds. Pulses are typically sent at a frequency of 20-25 Hz. Figure 4.1 illustrates the setup for stimulating one muscle using surface electrodes.

Figure 4.1 – The basic setup for neuromuscular electrical stimulation. The stimulator sends small current pulses to the nerves. [Cleveland FES Center, FES Resource Guide]

The intensity of NMES is characterised by three parameters: amplitude, pulse width, and frequency. These parameters are shown in Figure 4.2. The amplitude and pulse width determine the number of muscle fibres activated, while the frequency of pulses determines the temporal summation of muscle fibre contractions [Sheffler 2007]. With additional muscle fibres contracting more often, it is apparent that all three parameters, within certain ranges, are proportionate to the amount of force produced. The strength of the muscle contraction can thus be controlled by modulating these parameters.

Figure 4.2 – Illustration of electrical stimulation parameters: amplitude, pulse width, and frequency.

The contractile force produced by a muscle in response to NMES is highly non-linear, making its application complicated. The specifics of each factor are covered in detail in Section 4.3.

Electrical stimulation is applied to the body through electrodes, which may be applied to the skin surface (non-invasive) or implanted in the body (invasive). Surface electrodes, also referred to as transcutaneous electrodes, are easily applied and taken off, and pose little risk as they are applied externally. They are the simplest and thus widely used for rehabilitation purposes. The cathode, which is usually the active electrode, is placed directly over the motor point of the muscle while the indifferent electrode is placed distally over the tendon. Surface electrodes measuring 5 x 5 cm were used in this study.

Implanted electrodes are surgically implanted into the body, over the specific nerves they are intended to stimulate. These are semi-permanent, meaning they cannot be attached or detached on a daily basis. Since implanted electrodes deliver electrical current directly to the specific nerves, they allow better muscle selectivity even if the muscles are located deeper in the limb. However, surgery is required to insert, replace or remove electrodes. Furthermore, electrical stimulation systems that are not

completely implanted, i.e. those with percutaneous electrodes, may also pose a risk of infection. [Keller 2001]. Thus, the option of using implanted systems may not bode well for users, especially those undergoing rehabilitation.

Surface electrodes also do pose some risks, such as skin irritation from the electrode gel or discomfort due to electric currents passing through other sensory nerves. This sensation is likened to pins and needles. Fortunately, most users adapt to this sensation after a while. The use of surface electrodes poses a few challenges. Perhaps the biggest drawback of surface electrodes is that, since it is applied on the skin, the current must pass through the skin, fat, tissue, as well as other nerves and muscles which were not intended for stimulation. Thus, when multiple muscles and nerves are located near each other, for instance in the forearm, it is not possible to only target specific muscles for stimulation. This problem is exacerbated when the skin and hence electrodes are rolled over different muscles, such as during pronation/supination of the forearm. As electrodes are applied and taken off for every session, the placement of electrodes will differ between sessions, and subsequently affect the resulting movement.

Regulation of stimulation can be done by controlling either the voltage or current. Due to the abovementioned impedances which may vary with movement, the voltage across the nerve may vary. As a result, muscle contraction will also vary. Current regulated stimulators offer a more stable muscle response as the output impedances are very high, making them less susceptible to fluctuations in impedances and providing better control of muscle contractions. However, if the impedance between the electrode and skin become very high as a result of poor contact, there could be a very high current density at that location which may cause skin burns. This risk is mitigated by limiting the stimulation voltage. Current regulated stimulators can produce voltages of several hundred volts [Keller 2001]. A current regulated stimulator, the *Complex Motion*, was used in the work done for this dissertation.

At low stimulation intensities, electrical stimulation preferentially recruits Type II muscle fibres with lower stimulation thresholds [Sheffler 2007]. Natural and fine voluntary contractions with weak forces, such as a precise and well controlled grasp, primarily uses Type I muscle fibres which are small and fatigue resistant. FES,

unfortunately, starts exciting the large and fast Type II muscle fibres at lower stimulation intensities, and excites the Type I fibres only at higher intensities. These Type II fibres produce high twitching forces but fatigue easily [Keller 2001].

4.1.2 NMES for Upper Limb Neurorehabilitation

It is a common belief that NMES is an effective method of neurorehabilitation, and various groups have sought to demonstrate its effectiveness. Chae administered NMES to acute stroke patients to perform wrist and finger extension exercises and found significantly improved gains in Fugl-Meyer (upper limb) scores, indicating that NMES enhances recovery of the upper extremity in acute stroke survivors [Chae 1998]. Francisco studied the effects of EMG-triggered FES on the paretic wrist of acute (<6 weeks) stroke patients, and found significant improvements in Fugl-Meyer and Functional Independence Measure scores over the control group which underwent wrist strengthening exercises without FES [Francisco 1998]. Daly's study on chronic (>12 months) stroke survivors found that functional neuromuscular stimulation and motor learning produced significant gains in Arm Motor Ability Test for the wrist and hand (AMAT) and Fugl-Meyer upper limb coordination [Daly 2005]. Kimberly studied the effects of intensive NMES use on the hemiplegic forearm, and found that subjects improved in measures of strength and hand grasps. The use of fMRI showed an increased index of cortical intensity, leading her to suggest that intensive FES plays a crucial role in stimulating cortical sensory areas, thus improving function [Kimberly 2004]. Ring supported this hypothesis with his study of FES on the wrist and hand of sub-acute stroke patients, and concluded that supplementing conventional rehabilitation with intensive use of FES at home does improve upper limb outcomes [Ring 2005]. He offers an insight: The central nervous system is sensitive and reactive to stimuli on the peripheral nerves, and it responds by temporal and topographical reorganization [Ring 2007].

Although these studies may require larger sample sizes, multi-centre double-blinded trials, and long-term follow-up evaluations to further prove the efficacy of NMES for neurorehabilitation, the numerous studies and opinions provide a strong basis to believe that NMES is indeed beneficial for neurorehabilitation. Keller believes that FES training is crucial in the reorganization of the remaining intact pathways and

promoting neuroplasticity in the central nervous system [Keller 2001]. Sheffler posits that if active, intensive and repetitive movement training facilitates motor relearning, then NMES-mediated repetitive-movement training should also produce similar results [Sheffler 2007]. Daly recognizes the substantial influence that activity-dependent neuroplasticity of the CNS has on the effects of rehabilitation [Daly 2008].

4.2 The NMES system

There are few stimulators that allow customizable electrical stimulation for research purposes. Perhaps the only two commercially available devices capable of research use are the *Complex Motion* [Keller 2002] and *Motionstim 8* [www.medel-hamburg.de]. The *Complex Motion* was used in this project.

The *Complex Motion* facilitates fast testing of stimulation methods, as stimulation parameters and sequences are easily programmed through a graphical user interface. It has two input channels that measure either analog or digital TTL signals, through which stimulation amplitude can be adjusted in real time, or stimulation sequences can be selected. These features facilitate integration with the BCI system. More detailed specifications of the *Complex Motion* can be found in [Keller 2001 and 2002].

4.3 How the BCI-NMES Prosthesis Works

In Chapter 3, the brain-computer interface (BCI) which provided the sensing system was described. Chapter 4 described the neuromuscular electrical stimulation (NMES) that made up the actuation system. Together, these systems detect the user's motor intent and activate the muscles to achieve that movement. The flowchart in Figure 3.8 shows the operation of the BCI-NMES neuroprosthesis.

Figure 4.3 – Flowchart for operation of the BCI-NMES neuroprosthesis

4.4 Integration of the BCI and NMES systems

Both the EEG acquisition and NMES systems were integrated with the laptop computer. The *NuAmps* EEG amplifier was connected to the laptop through a USB interface, while the NMES system was connected to a data acquisition card (*National Instruments DAQ Card 6036E*) which was in turn connected to the laptop through a PCMCIA interface.

Joint angle signal from a *Biopac TSD130B* goniometer was acquired by the DAQ card and processed using *NI LabVIEW*. Joint angle was differentiated to obtain angular velocity and angular acceleration. As a second derivative was used to gather information on acceleration, a high sampling rate of 2000 Hz and a moving window average was used in order to reduce noise. A digital-out channel from the DAQ card was connected to the analog-in channel of the Compex Motion stimulator to coordinate the electrical stimulation of either the biceps or triceps. The BCI application was developed in *C++* and interfaced with the *NuAmps Scan* software to acquire EEG. The GUI and communication with the NMES system were developed

using *Visual C#.NET*, while the control of NMES stimulation and acquisition of joint angle from the goniometer was done with *NI LabVIEW*.

Figure 3.9 illustrates the hardware components of the BCI-NMES system and shows the interaction between the system and user. Figure 3.10 shows a photo of a subject donning the complete BCI-NMES setup.

Figure 4.4 – Components of the BCI-NMES neuroprosthesis and interactions with the user

Figure 4.5 – A subject donning the complete BCI-NMES setup

4.5 A Physiology-based Phenomenological Model for NMES

For any movement to be useful, it must be controlled. Producing controlled movements of the limb through artificial means such as NMES is a challenging problem, given the highly non-linear characteristics of the plant, which consists of the agonist-antagonist muscle pair coupled to the joint.

The study of muscle contractions, either artificially by NMES or naturally by brain signals, date back a long way to two prominent works by Hill in 1938 [Hill 1938] and Huxley in 1957 [Huxley 1957]. Hill's research described muscle behaviour with a non-linear ordinary differential equation of a system comprising of contractile elements in series and parallel with elastic elements. His approach was a phenomenological one, where various empirical observations of phenomena are related mathematically and consistent with theory despite not being directly derived from theory. Huxley's fundamental research was independent of Hill's, and he described muscle characteristics with partial differential equations of the underlying

biochemical processes. The main difference was that Hill's approach was a 'systems' approach that adopted an input-output perspective, while Huxley's was a more fundamental approach. Models based on biophysical contractile mechanisms are complex, and the parameters involved are extremely difficult to measure. The motivation to use such biophysical models is further undermined by the insignificant advantages that they provide over the Hill-based model during normal human movement [Winters 1987]. These differences led to Hill's approach being more palatable for most groups.

In order to move the arm artificially with NMES, a model had to be built to estimate the relationship between the various stimulation parameters (inputs) and the resulting movement (output). A phenomenological approach was favoured for use here, as this approach made use of parameters that are relatively easier to identify. A phenomenological approach relates a particular phenomenon to the input that caused it, without the need to understand the intermediary processes. Phenomenological approaches are best used when explicit relationships between all the sub-systems cannot be determined. In this study, the 'phenomenon' is that the muscles produce a force when an electric current (the input) is applied. The exact mechanisms, of how the stimulation depolarizes the nerve membrane and propagates, of how much the individual muscle fibers contract to produce a certain force, etc, are not studied.

The model should thus make it possible to use NMES to move the arm by a specific amount, within a few degrees of the desired angle. This will be useful for users to position their hands in an appropriate position to perform other tasks. This model shall be limited to that of a single-muscle activation, and shall initially be applied to muscles of the elbow joint.

Such a model would be useful for slow movements, where the antagonist muscle need not be used to decelerate the movement. For patients with little or no function, stimulating just one muscle will produce the movement that they are otherwise unable to perform. Although the degree of dexterity and control may not be as good as that of a healthy person, it still is a significant gain over paralysis. Furthermore, a single-muscle model will enable users to use the NMES system for a longer period of time,

as muscles are not fatigued by the co-contraction of the antagonist muscles for every movement.

One such phenomenological model was developed by Ferrarin [5], who applied NMES to the quadriceps muscles to control the movement of the freely-swinging shank. This model extends Ferrarin's model of one muscle of the lower limb [Ferrarin 2001], to two muscles of the upper limb. In order to move any joint, two muscles must be activated – one for flexion and the other for extension. For the elbow joint, the biceps brachii ('biceps') and triceps brachii ('triceps') effect the flexion and extension movements respectively. The same model is applied to both muscles, but the characteristics of each muscle must be determined individually. The plant (muscle) is non-linear, and can be modeled in 3 parts: i) Muscle activation, ii) Force and power characteristics, and iii) Passive properties of the musculoskeletal system. These parameters and the methods to estimate them are described in the following sections.

For illustrative purposes, this model was built based on the physical properties of a healthy male subject (i.e. the author himself).

The model developed here was implemented for muscles controlling the elbow joint, namely the biceps brachii ('biceps') and triceps brachii ('triceps') which primarily effects the flexion and extension movements respectively. These muscles were chosen because they are simpler to implement an NMES model on – they can be specifically stimulated to produce only one motion (i.e. stimulation of biceps produces elbow flexion only), and they are not biarticular. While wrist movements could contribute more to functional tasks such as grasping, elbow movements are necessary to place the wrist in a suitable position. The model could then be extended for other joints in future.

4.5.1 Determining Mass and Inertial Properties of the Upper Limb

NMES on the muscles produce a moment at the joint, causing the limb to move. In order to predict the resulting motion of the limb, it is necessary to know the mass and inertial properties of the limb. Perhaps the most extensive study on the mass and

centres of mass of various body parts can be credited to Zatsiorsky [Zatsiorsky 1983], who performed cadaveric experiments to determine these parameters. As there is no other way to determine the exact centre of mass or radius of gyration of each living person's body segment, Zatsiorsky's findings shall be used.

The mass of each body part can be predicted as follows:

$$m_{forearm} = 0.165 + 0.0139 \times m_{body} \pm 0.102 \quad (4.1a)$$

$$m_{hand} = 0.109 + 0.0046 \times m_{body} \pm 0.060 \quad (4.1b)$$

where $m_{forearm}$ and m_{hand} are the mass of the forearm and hand respectively, and m_{body} being the total body mass. Mass is measured in kilograms (kg).

The lengths of the forearm and hand can be measured directly, and the locations of the centres of mass can be predicted as follows:

$$r_{forearm} = 0.4274 \times L_{forearm} \quad (4.2a)$$

$$r_{hand} = 0.3691 \times L_{hand} \quad (4.2b)$$

These parameters are illustrated in Figure 4.6.

Figure 4.6 – Centres of mass and radii of gyration of each segment of the forearm

With the above estimations and the assumption that the two body segments are point masses at their respective centres of mass, the mass moment of inertia, J , about the elbow joint can be calculated:

$$J = m_{forearm} \times r_{forearm}^2 + m_{hand} \times (r_{hand} + L_{forearm})^2 \quad (4.3)$$

For the sample healthy subject, the physical properties are shown in Table 4.1.

Table 4.1 – Physical properties of a sample healthy subject

body mass (actual)	77.80 kg
$m_{forearm}$ (estimated)	1.25 kg
$L_{forearm}$ (actual)	0.250 m
$r_{forearm}$ (estimated)	0.107 m
m_{hand} (estimated)	0.47 kg
L_{hand} (actual)	0.200 m
r_{hand} (estimated)	0.074 m
Inertia about elbow	0.0636 kg.m ²

4.5.2 Muscle Activation Characteristics

As briefly mentioned in Section 2.1, the depolarization of a nerve by an action potential is quickly followed by a re-polarization by the membrane charge pumps. Therefore, in order to generate an artificial action potential, depolarization of sufficient intensity must occur faster than the re-polarization process; failing which, no action potential is generated and obviously no muscle contraction takes place [Keller 2001]. This explains the threshold level, which is unique to each individual and to each muscle. The threshold level is the minimum level of stimulation that just produces a muscle response.

Any stimulation above the threshold level can be said to be linearly proportionate to the amount of force produced, *ceteris paribus*, until it reaches the saturation level. At the saturation level, any extra stimulation does not excite any more muscle fibres. Correspondingly, no extra force is produced.

The relationship between stimulation intensity and muscle activation level is exemplified in Figure 4.7. This relationship can be approximated as either piecewise linear, or as an *arctan*-function. Both methods agree with the threshold and saturation characteristics and provide good approximations, but the piecewise linear approximation is preferred for its simplicity.

Figure 4.7 – The recruitment curve relates stimulation intensity with activation level. There exists threshold and saturation levels, which can be approximated by an *arctan*-function (dotted) or piecewise linear function (solid).

The activation level, normalized between 0 (no force) and 1 (maximum force) can be expressed as follows:

$$\text{Activation Level, } Act = \begin{cases} 0 & \text{For } PW < Thres \\ \frac{(PW - Thres)}{(Sat - Thres)} & \text{For } Thres < PW < Sat \\ 1 & \text{For } PW > Sat \end{cases} \quad (4.3)$$

where PW is the pulse width of the stimulation current.

To determine the threshold (*thres*) and saturation (*sat*) levels, the arm was placed on a smooth horizontal surface, i.e. table top. The arm was bent 90° at the elbow, and restrained with Velcro straps such that the stimulation would produce an isometric muscle contraction. The wrist was attached perpendicularly to a force sensor (*Mecmesin Advanced Force Gauge*), which fed the data to the computer. Stimulation pulse width was ramped up linearly, from 0 – 372μs within a duration of 6.4s. The

experiment setup is shown in Figure 4.8 and a sample graph of the amount of force produced against the stimulation pulse width is shown in Figure 4.9.

Figure 4.9 – Graph of activation level against stimulation pulse width. Threshold (*thres*) and saturation (*sat*) values were optimized to reduce RMS error between the fitted line (solid) and recorded values (red dots). Amplitude and frequency were kept constant during this experiment, at 20 mA and 25 Hz respectively.

Figure 4.6 above shows a good fit between the experimental data and the fitted piecewise-linear function, with an RMS error of only 3.1%. This measurement is repeated once for each muscle and the threshold and saturation values are averaged across both runs.

4.5.3 Muscle Force and Power Characteristics

Muscle contraction is caused by the actin and myosin filaments pulling against each other. The myosin heads attach themselves to the actin filaments and undergo an angular deformation, thus pulling the actin filament. They then detach themselves and extend themselves to the original position where they attach to the actin again to repeat the process until they reach the ends of the actin filaments which are called the Z-discs. More detailed anatomical information can be found in [Silbernagel 1991].

Moment-Angle Relationship

The amount of force that a muscle can produce is related to the number of myosin-actin attachments. The latter is dependent on the amount of overlap between the actin and myosin filaments, which is also related to how stretched the muscle is. When a muscle is stretched, there is less overlap, hence fewer number of myosin-actin attachments and less force produced. Conversely, when a muscle is almost fully contracted, the myosin filaments have reached the ends of the actin filaments and are unable to pull any further. The length of the muscle is directly related to the joint angle. As the muscle contracts and joint angle changes, the moment arm also changes. The moment arm can be estimated using high-order polynomial functions of joint angle, but is not useful in this model. In this dissertation, muscle output is expressed in terms of moment about the joint instead of muscle force, because it is the resultant moment that causes movement about the joint. There is therefore little value in expressing moment in terms of either of these variables per se. This justifies why a combined, normalized moment-angle relationship shall be used.

Figure 4.10 illustrates the moment produced at the elbow joint by contraction of the biceps and the moment-angle relationship is expressed in Equation 4.4.

Figure 4.10 – Moment produced by muscle contraction. As muscle force, F , and moment arm, r , vary, the resultant moment, M , also varies. The moment-angle relationship is expressed in Equation 4.4.

The moment-angle relationship is an adaptation of Hatze's force-length relationship [Hatze 1981], in angular form:

$$f_a = \exp \left[- \left(\frac{\theta - K_1}{K_2} \right)^2 \right] \quad (4.4)$$

where f_a is the moment-angle factor that ranges from 0 to 1, the subscript a denotes that this factor is due to joint angle. K_1 and K_2 are constants to be determined experimentally for each person. K_1 corresponds to the joint angle that produces the peak force and K_2 reflects the spread around the maximum. Figure 4.11 illustrates this relationship.

Figure 4.11 – Moment-Angle Relationship

Parameters K_1 and K_2 were determined by stimulating the arm to produce isometric muscle contractions at various joint angles spanning the full range of motion. The setup was similar to that shown in Figure 4.8 for finding threshold and saturation values. The curve was fitted by minimising the RMS error. Figure 4.12 shows two sample graphs for determining K_1 and K_2 for the biceps and triceps respectively. Stimulation parameters were 20 mA, 25 Hz, and 250 μ s.

Parameters K_1 and K_2 define the moment-angle relationship of the elbow joint. Among the factors that affect moment-angle relationship are the amount of overlap between muscle fibers, which affects the force produced, and the stretching of the muscles and surrounding tissue. The resistance felt during passive limb movement is called stiffness, and Pisano [Pisano 2000] describes it as the change in force developed by the muscle in response to a change in length. These factors are independent of stimulation pulse width.

The moment produced is directly related to the stimulation pulse width, but that should not affect the values of K_1 and K_2 since the moment-angle relationship is normalized.

Figure 4.12 – Experimental graphs of isometric muscle contraction at various angles, normalized to the maximum force produced.

From the data of isometric force at various angles, the maximum isometric moment, M_{max} , is the corresponding maximum force multiplied by the length of the forearm, $L_{forearm}$:

$$M_{max} = F_{max} \times L_{forearm} \quad [\text{Nm}] \quad (4.5)$$

Moment-Velocity Relationship

As mentioned earlier, the myosin heads attach/detach themselves to/from the actin filaments during muscle contraction. There is a limit to how fast they are able to do this, and how much force can be produced. Perhaps it could be intuitively put that power, which equals *force* $\times$ *velocity*, is limited. In addition, viscous forces also reduce the amount of force produced by the muscle. Zajac described a force-velocity relation [Zajac 1989]. However, since a moment-velocity relationship is more useful for this model, a linear approximation [Riener 2000, Ferrarin 2001] of Zajac's equation would be more appropriate. The moment-velocity relationship is shown in Equation 4.6.

$$\begin{aligned} f_v &= 1 - \left(\frac{1}{v_m} r \right) \frac{d\theta}{dt} \\ &= 1 - K_3 \dot{\theta} \end{aligned} \quad (4.6)$$

where f_v is the moment-velocity factor, the subscript v denotes that this factor is due to joint velocity, v_m is the maximum contraction velocity, l is the muscle length, $\dot{\theta}$ is the angular velocity of the joint, r is the moment arm of the muscle, and K_3 is a constant representing $\left(\frac{1}{v_m} r\right)$. Values of K_3 are highly sensitive to assumptions of these values. Since it is impossible to determine exactly what these values are, K_3 shall be assumed to be subject-independent [Reiner 2000]. The maximum contraction velocity, v_m , can be estimated from the percentage of slow muscle fibres and the optimal muscle length. It has been proposed that the maximum contraction velocity can be calculated as follows [Winters 1990]:

$$v_m \approx (8 - 6 \times P_{slow}) \times l_{opt} \quad (4.7)$$

With values of $P_{slow} \approx 40\%$ and $l_{opt} \approx 10$ cm, v_m can be found to be 0.56, and with $r \approx 4$ cm, K_3 is estimated to be 0.07 s/rad.

4.5.4 Active Muscle Moment

The four muscle characteristics described thus far (muscle activation level, moment-angle characteristic, moment-velocity relationship, and maximum isometric moment) come together to form the active muscle moment:

$$M_{active} = Act \times f_a \times f_v \times M_{max} \text{ [Nm]} \quad (4.8)$$

This is the active moment that the muscle produces at particular stimulation intensity. From Equations 4.4 to 4.8, the active moment is dependent on i) Stimulation intensity, ii) Threshold and saturation levels, iii) Joint angle, and iv) Joint angular velocity. This, however, is not the resultant moment that acts on the limb as the resultant moment also depends on passive characteristics.

4.5.5 Passive Characteristics of the Muscles and Joints

The passive moment arises from elasticity and viscosity of the agonist-antagonist musculotendon units at each joint when no active muscle activation is involved.

These forces are attributed to the connective tissues such as the muscle fibre membranes, musculotendon sheath, ligaments and the fluids within the tissue. Of interest in this dissertation is the combined passive joint property, hence the individual properties shall not be determined.

Passive Viscous Characteristics

The passive pendulum test [Ferrarin 1996] is often used to determine damping characteristics of the limbs. In this test adopted for the upper limb, the subject is asked to lie face down and hang his/her forearm over the edge of the bench. The forearm is then displaced by a small distance and allowed to swing freely until the damping forces bring the forearm to a halt. Joint angle is recorded throughout the swinging motion.

The viscous damping coefficient, V , can be calculated as follows:

$$V = 2J\zeta\omega_n \quad (4.9)$$

where J represents the inertia, ζ is the damping ratio and ω_n is the undamped natural frequency. The damping ratio can be calculated using the log-decrement method:

$$\zeta = \frac{\ln\left(\frac{\alpha_n}{\alpha_{n+1}}\right)}{\sqrt{4\pi^2 + \left[\ln\left(\frac{\alpha_n}{\alpha_{n+1}}\right)\right]^2}} \quad (4.10)$$

where α_n and α_{n+1} are two successive amplitudes of the oscillation.

The damped natural frequency, ω_d , can be observed from the graph of joint angle vs. time, and can be used to calculate the natural frequency, ω_n :

$$\omega_n = \frac{\omega_d}{\sqrt{1 - \zeta^2}} \quad (4.11)$$

As viscous moments always act against the impending motion, the passive moment due to viscosity can be found as follows:

$$M_{pas,v} = -V\dot{\theta} \quad (4.12)$$

Figure 4.13 presents a sample graph and illustrates how these parameters are determined.

Figure 4.13 – Graph of joint angle vs. time, of the freely-swinging forearm.

With the values shown in Figure 4.10 and inertia, J , of 0.0636 kg.m^2 as found earlier, the viscous coefficient, V , was found to be 0.0554 Nms/rad ; this value agrees with Hill's model of a lightly damped system.

Passive Elastic Characteristics

For most of the joint's operating range, elasticity is minimal. Elasticity only plays a significant role when muscles are stretched beyond their optimal lengths [Garner 2003], or when surrounding tissue are compressed or stretched. This phenomenon is

also shown in studies by Stein [Stein 1996], Riener [Riener 1999], and Ferrarin [Ferrarin 2001] on the lower limb.

The passive elastic moment is found by performing quasi-static pull tests of the forearm. In the quasi-static movement, joint angular velocity was kept below 5 degrees/second (0.0873 rad/s) to reduce any viscous forces. In order to measure moment as accurately as possible, care was taken to position the force sensor perpendicular to the forearm. The pull test was done in two parts: one for flexion, and one for extension. The setup is shown in Figure 4.14.

Figure 4.14 – Experiment setup to determine passive elastic forces; (a) flexion and (b) extension.

For the flexion part, the elbow is moved from approximately 90° to full flexion which is typically about 120°. For the extension part, the elbow is moved from 90° to full extension, and may include a few degrees of hyper-extension. Joint angle is taken to be zero degrees at full extension and increases with elbow flexion. Moment that causes flexion is positive.

From Figure 4.11a, under quasi-static conditions, the equilibrium equation is:

$$\begin{aligned}(F \times L_1) + M_{pas,e} &= (mg \times R) \sin \theta \\ M_{pas,e} &= (mg \times R) \sin \theta - (F \times L_1)\end{aligned}\quad (4.13)$$

From Figure 4.11b, under quasi-static conditions, the equilibrium equation is:

$$\begin{aligned}M_{pas,e} - (mg \times R) \cos \theta &= (F \times L_1) \\ M_{pas,e} &= (F \times L_1) + (mg \times R) \cos \theta\end{aligned}\quad (4.14)$$

where $M_{pas,e}$ is the passive moment due to elasticity, F is the force exerted perpendicular to the forearm, g is the acceleration due to gravity, θ is the joint angle, L_1 is the length of the forearm and R is the radius of gyration of the forearm.

Together, Equations 4.12 and 4.13 enable the passive moment to be estimated over the whole range of joint angles. Passive moment can be approximated as a double-exponential function of joint angle [Edrich 2000], of which a modified equation is shown in Equation 4.14:

$$\begin{aligned}M_{pas,e}(\theta) &\approx \exp(c_1 + c_2\theta) - \exp(c_3 + c_4\theta) + c_5 \\ M_{pas,e}(\theta) &\approx \exp(c_1) \bullet \exp(c_2\theta) - \exp(c_3) \bullet \exp(c_4\theta) + c_5 \\ M_{pas,e}(\theta) &\approx A \exp(B\theta) - C \exp(D\theta) + E\end{aligned}\quad (4.15)$$

where A , B , C , D , and E are shape parameters found by using a least-squares method. The Levenberg-Marquardt algorithm from MATLAB was used to find these parameters. Figure 4.15 shows a sample graph of how passive moment varies with joint angle. In this sample, $A = 0.8609$, $B = -0.1590$, $C = 3.04\text{E-}12$, $D = 0.2151$, and $E = 0$.

Figure 4.15 – Passive moment as a function of elbow angle; note that passive moment is negligible for most of the operating range from 20-100 degrees.

4.5.6 Predicting Joint Motion from Stimulation Pulse Width

With a pair of agonist-antagonist muscles controlling one degree of freedom of the elbow joint, an inherent redundancy exists. With co-contractions of the muscles, the resultant torque is due to the difference in force produced by the two muscles. For this model, it is assumed that the antagonist muscle is relaxed, and that the torque is produced from single-muscle activation.

With the above information, the output from muscle stimulation can be predicted [Ferrarin 2001]. Newton's 2nd law, in the angular form is:

$$\sum M = J\ddot{\theta} \quad (4.16)$$

The components of total moment in a gravity-eliminated plane, are:

$$\sum M = M_{active} + M_{pas,e} + M_{pas,v} \quad (4.17)$$

Substituting the various moments, the equation of motion becomes:

$$\left(\frac{PW - Thres}{Sat - Thres} \right) \left\{ \exp \left[- \left(\frac{\theta - K_1}{K_2} \right)^2 \right] \right\} \left(1 + K_3 \dot{\theta} \right) (M_{max}) - V \dot{\theta} + [A \exp(B\theta) - C \exp(D\theta) + E] = J \ddot{\theta} \quad (4.18)$$

The motion of the limb (in terms of θ , $\dot{\theta}$, and $\ddot{\theta}$) can then be predicted from stimulation pulse width, PW . The inverse of this model can be found by rearranging the above equation:

$$PW = \frac{\left\{ J \ddot{\theta} - [A \exp(B\theta) + C \exp(D\theta) + E] + [V \dot{\theta}] (Sat - Thres) \right\}}{\left\{ \exp \left[- \left(\frac{\theta - K_1}{K_2} \right)^2 \right] \right\} [1 + K_3 \dot{\theta}] (M_{MAX})} + Thres \quad (4.19)$$

In a gravity eliminated plane, deceleration of the limb can only be achieved by viscous forces and activation of the antagonistic muscle (i.e. activation of triceps for elbow flexion movements, and activation of biceps for elbow extension movements). As flexion and extension movements of the elbow require contraction from the biceps and triceps respectively, the model has two inputs. The schematic diagram of the model is shown in Figure 4.16.

Figure 4.16 – A schematic diagram of the model developed. NMES intensity to the biceps and triceps are the two inputs, while elbow angle is the single output. This model is an extension of Ferrarin's [Ferrarin 2001] model to include two muscles.

Based on the inverse model, the stimulation pulse widths required to perform a certain desired motion can be determined. The muscles are then stimulated accordingly, and output in the form of joint angle can be recorded. Figure 4.17 shows the block diagram of the open-loop control method used here, where θ_r and θ_a are the reference and actual elbow angles respectively.

Figure 4.17 – Block diagram of the open-loop control method. Based on the reference trajectory, θ_r , the required pulse width is found using the inverse model and the muscle is stimulated accordingly to produce elbow movement, measured by θ_a .

4.5.7 Desired Arm Motion

The objective is to move the arm through a predefined range in a smooth manner comfortable for the subject. This entails specifying the duration of movement and using a jerk-free motion profile. The following sinusoidal profile was used:

$$\theta = Y \sin \omega(t - \tau) + C \quad (4.19a)$$

where Y is the desired angular deflection of the arm and τ is equal to half of the desired duration. For example, if the desired arm movement is either flexion or extension between 20° and 60° , in a time of 1 second, the motion of the arm would be as shown in Figure 4.18.

Figure 4.18 – Ideal motion profile for extension (red line) and flexion (blue line) for a smooth movement of the arm

4.6 Model Validation

The model was implemented using MATLAB and Simulink. Simulation results show that, in order to achieve the motion described in Figure 4.18, only the agonist muscle needs to be stimulated to produce a resultant moment about the elbow joint, while viscous forces will damp the motion and bring the arm to a stop. Figure 4.19 (a) and (b) show the amount of active torque required to flex and extend the arm respectively, through a range of 40 degrees in a time of 1 second.

To measure the muscle activation during elbow flexion and extension, the arm was placed on an arm rest that was supported by a hinge and allowed to swing freely in the horizontal plane. The subject was asked to relax completely, and apart from making one voluntary flexion or extension, make no other movements. Electromyogram (EMG) electrodes were placed over the belly of the biceps and triceps, and EMG was acquired through the *Biopac MP150* and *EMG100C* systems at a rate of 2000 Hz and amplified 500x. The RMS value was then normalized to show activation level. The EMG recordings are shown in Figure 4.20 (a) and (b) respectively.

The EMG recorded during actual elbow movement suggests activity from only the agonist muscle, i.e. only the biceps show EMG activity during flexion, and only the triceps during extension. The movement of the arm is decelerated by passive viscous forces of the joint and surrounding tissue.

The model was then implemented and evaluated on two healthy subjects. Section 4.6.1 documents the results from the first subject and Section 4.6.2 documents the results from the second subject.

Figure 4.19 (a) – Simulation: active torque (red line) produced by the biceps from NMES and the resulting elbow movement (blue line) from 20° to 60° and elbow velocity (green line).

Figure 4.19 (b) – Simulation: active torque (red line) produced by the triceps from NMES and the resulting elbow movement (blue line) from 60° to 20° and elbow velocity (green line).

Figure 4.20 (a) – Biceps activation produces elbow flexion, as shown by EMG recordings over the biceps (blue line) and triceps (red line). Passive viscous forces then act to decelerate the movement.

Figure 4.20 (b) – Triceps activation produces elbow extension, as shown by EMG recordings over the biceps (blue line) and triceps (red line). Passive viscous forces then act to decelerate the movement.

4.6.1 Evaluation of NMES Model in the First Subject

The first subject is a 28-year-old healthy male subject. To recap, Table 4.2 lists the various parameters involved, as well as subject-specific values. Stimulation amplitude and frequency were kept constant at 20 mA and 25 Hz respectively, while pulse width was modulated in a sinusoidal pattern between threshold level and a level as determined by the inverse model.

The subject's resting elbow angle was used as the initial value in the simulation. The desired final angle was chosen arbitrarily such that the model was evaluated for elbow motion ranging from about 20° to 50°. For example, in Figure 4.21(a), the elbow was initially at rest at an angle of 15°, and the desired final angle was arbitrarily chosen to be 60°, thus giving the elbow flexion movement of 45°. The same process was repeated for elbow extension movements.

The resulting flexion and extension movements in terms of joint angle, are compared against the simulated trajectory in Figures 4.21 to 4.25. Parts (a) and (b) of each figure are for flexion and extension movements respectively.

Table 4.2 – Summary of all parameters for Subject 1

Parameters	Subject-Specific Values	
Weight	78 kg	
Length of Forearm	27 cm	
Length of Hand	20 cm	
<u>Muscle Recruitment Parameters</u>	<u>Biceps</u>	<u>Triceps</u>
<i>Thres</i> : threshold pulse width	120 μ s	100 μ s
<i>Sat</i> : saturation pulse width (at constant 20 mA and 25 Hz stimulation)	263 μ s	178 μ s
<u>Moment-Angle Parameters</u>		
K_1 : related to angle of maximum torque	55°	45°
K_2 : related to spread	49°	54°
M_{max} : maximum isometric moment	8.1 Nm	5.1 Nm
<u>Moment-Velocity Parameters</u>		
K_3 : combined coefficient for velocity effects	0.07 s/rad	0.07 s/rad
<u>Passive Characteristics</u>		
V : viscous damping coefficient	1.09 Nms/rad	
A, B, C, D, E : shape factors for passive elastic moment	0.8609, -0.1590, 3.04E-12, 0.2151, and 0 respectively	
<u>Arm Parameters</u>		
J : inertia	0.0554 kg.m ²

Figure 4.21 (a) – Trial #1 (elbow flexion): comparison between measured and simulated elbow angle trajectory based on identified model with sinusoidal pulse width modulation. Target angle = 60°.

Figure 4.21 (b) – Trial #1 (elbow extension): comparison between measured and simulated elbow angle trajectory based on identified model with sinusoidal pulse width modulation. Target angle = 20°.

Figure 4.22 (a) – Trial #2 (elbow flexion): comparison between measured and simulated elbow angle trajectory based on identified model with sinusoidal pulse width modulation. Target angle = 60°.

Figure 4.22 (b) – Trial #2 (elbow extension): comparison between measured and simulated elbow angle trajectory based on identified model with sinusoidal pulse width modulation. Target angle = 20°.

Figure 4.23 (a) – Trial #3 (elbow flexion): comparison between measured and simulated elbow angle trajectory based on identified model with sinusoidal pulse width modulation. Target angle = 90°.

Figure 4.23 (b) – Trial #3 (elbow extension): comparison between measured and simulated elbow angle trajectory based on identified model with sinusoidal pulse width modulation. Target angle = 45°.

Figure 4.24 (a) – Trial #4 (elbow flexion): comparison between measured and simulated elbow angle trajectory based on identified model with sinusoidal pulse width modulation. Target angle = 90°.

Figure 4.24 (b) – Trial #4 (elbow extension): comparison between measured and simulated elbow angle trajectory based on identified model with sinusoidal pulse width modulation. Target angle = 45°.

Figure 4.25 (a) – Trial #5 (elbow flexion): comparison between measured and simulated elbow angle trajectory based on identified model with sinusoidal pulse width modulation. Target angle = 80°.

Figure 4.25 (b) – Trial #5 (elbow extension): comparison between measured and simulated elbow angle trajectory based on identified model with sinusoidal pulse width modulation. Target angle = 60°.

RMS error was computed starting from the time the stimulation started until the time the arm came to rest at the final angle. The ideal range is the difference between the initial angle and the target angle, and the deviation is the difference between the measured angle when the arm came to rest and the target angle. The results are shown in Table 4.3 below.

Table 4.3 – Results of model validation for Subject 1

Trial No.	1	2	3	4	5
Elbow Flexion					
Initial Angle (°)	15	21	42	51	58
Target Angle (°)	60	60	90	90	80
Measured Final Angle (°)	71	61	88	95	77
Deviation from Target (°)	11	1	2	5	3
RMS Error (°)	5.8	3.9	2.3	4.3	1.3
Maximum Error (°)	10.6	6.9	3.2	7.2	2.7
RMS Error as % of range	12.9%	10.0%	4.8%	11.0%	5.9%
Deviation as % of Expected Range	24.4%	2.6%	4.2%	12.8%	13.6%
Elbow Extension					
Initial Angle (°)	69	61	88	94	77
Target Angle (°)	20	20	45	45	60
Measured Final Angle (°)	17	19	51	49	57
Deviation from Target (°)	3	1	6	4	3
RMS Error (°)	2.7	3.7	2.8	6.6	3.1
Maximum Error (°)	5.2	6.7	6.1	11.2	5.0
RMS Error as % of range	5.5%	9.0%	6.5%	13.5%	18.2%
Deviation as % of Expected Range	6.1%	2.4%	14.0%	8.2%	17.6%

Of particular interest is the deviation of arm position from the target angle. Based on the above 10 movements (flexion and extension for each trial), the average deviation was found to be 3.9°, or 10.6% of the intended range of motion. If the flexion movement from Trial #1 were excluded because of exceptionally high deviation, the average deviation would be only 3.1°, or 9.1% of intended range of motion.

4.6.2 Evaluation of NMES Model in the Second Subject

The same procedures were performed on a second subject, a 27-year-old healthy male. Table 4.4 lists his subject-specific values. Stimulation amplitude and frequency were also kept constant at 20 mA and 25 Hz respectively, while pulse width was modulated in a sinusoidal pattern between threshold level and a level as determined by the inverse model.

The initial value used in the simulation was the subject's elbow angle just prior to the NMES stimulation, while the target angle was varied in order to test the model for different arm positions and movement ranges. The resulting flexion and extension movements in terms of joint angle, are compared against the simulated trajectory in Figures 4.26 to 4.30. Parts (a) and (b) of each figure are for flexion and extension movements respectively.

Table 4.4 – Summary of all parameters for Subject 2

Parameters	Subject-Specific Values	
Weight	82 kg	
Length of Forearm	29 cm	
Length of Hand	22 cm	
<u>Muscle Recruitment Parameters</u>	<u>Biceps</u>	<u>Triceps</u>
<i>Thres</i> : threshold pulse width	223 μ s	183 μ s
<i>Sat</i> : saturation pulse width (at constant 20 mA and 25 Hz stimulation)	316 μ s	315 μ s
<u>Moment-Angle Parameters</u>		
K_1 : related to angle of maximum torque	81°	91°
K_2 : related to spread	84°	79°
M_{max} : maximum isometric moment	5.4 Nm	5.0 Nm
<u>Moment-Velocity Parameters</u>		
K_3 : combined coefficient for velocity effects	0.07 s/rad	0.07 s/rad
<u>Passive Characteristics</u>		
V : viscous damping coefficient	1.021 Nms/rad	
A, B, C, D, E : shape factors for passive elastic moment	-1.96E-7, 0.1055, 15.39, -0.0432, and 0 respectively	
<u>Arm Parameters</u>		
J : inertia	0.0675 kg.m ²

Figure 4.26 (a) – Trial #1 (elbow flexion): comparison between measured and simulated elbow angle trajectory based on identified model with sinusoidal pulse width modulation. Target angle = 80°.

Figure 4.26 (b) – Trial #1 (elbow extension): comparison between measured and simulated elbow angle trajectory based on identified model with sinusoidal pulse width modulation. Target angle = 20°.

Figure 4.27 (a) – Trial #2 (elbow flexion): comparison between measured and simulated elbow angle trajectory based on identified model with sinusoidal pulse width modulation. Target angle = 60°.

Figure 4.27 (b) – Trial #2 (elbow extension): comparison between measured and simulated elbow angle trajectory based on identified model with sinusoidal pulse width modulation. Target angle = 30°.

Figure 4.28 (a) – Trial #3 (elbow flexion): comparison between measured and simulated elbow angle trajectory based on identified model with sinusoidal pulse width modulation. Target angle = 100° .

Figure 4.28 (b) – Trial #3 (elbow extension): comparison between measured and simulated elbow angle trajectory based on identified model with sinusoidal pulse width modulation. Target angle = 40° .

Figure 4.29 (a) – Trial #4 (elbow flexion): comparison between measured and simulated elbow angle trajectory based on identified model with sinusoidal pulse width modulation. Target angle = 110° .

Figure 4.29 (b) – Trial #4 (elbow extension): comparison between measured and simulated elbow angle trajectory based on identified model with sinusoidal pulse width modulation. Target angle = 60° .

Figure 4.30 (a) – Trial #5 (elbow flexion): comparison between measured and simulated elbow angle trajectory based on identified model with sinusoidal pulse width modulation. Target angle = 100°.

Figure 4.30 (b) – Trial #5 (elbow extension): comparison between measured and simulated elbow angle trajectory based on identified model with sinusoidal pulse width modulation. Target angle = 80°.

Table 4.5 – Results of model validation for Subject 2

Trial No.	1	2	3	4	5
Elbow Flexion					
Initial Angle (°)	25	29	42	59	78
Target Angle (°)	80	60	100	110	100
Measured Final Angle (°)	84	63	110	109	103
Deviation from Target (°)	4	3	10	1	3
RMS Error (°)	7.7	9.9	13.5	7.7	7.3
Maximum Error (°)	14.9	17.7	24.0	15.6	13.4
RMS Error as % of range	14.0%	31.9%	23.3%	15.1%	33.2%
Deviation as % of Expected Range	7.3%	9.7%	17.2%	2.0%	13.6%
Elbow Extension					
Initial Angle (°)	84	64	110	109	103
Target Angle (°)	20	30	40	60	80
Measured Final Angle (°)	27	33	42	51	84
Deviation from Target (°)	7	3	2	9	4
RMS Error (°)	4.7	5.7	7.3	8.3	2.4
Maximum Error (°)	8.7	11.6	15.9	14.2	4.3
RMS Error as % of range	7.3%	16.8%	10.4%	16.9%	10.4%
Deviation as % of Expected Range	10.9%	8.8%	2.9%	18.4%	17.4%

For the second subject, the average deviation of the arm from the target angle was 4.6°, or 10.8% of the intended range of motion. This error was larger than for the first subject (3.9° and 10.6% respectively). From the graphs above, it can be observed that actual flexion movements tended to exceed the predicted value, while extension movements tended to fall short of the predicted value. For flexion movements, this could be because the threshold level used in simulation was higher than the actual threshold level (recall from Section 4.5.2 that the threshold and saturation levels are averaged across two trials), which resulted in a higher torque and hence greater range of motion. For extension movements, the saturation level could have been underestimated, resulting in a lower torque towards the tail end of the motion, indicated by the measured angle first leading the simulated angle at the onset of movement, then lagging the simulated angle towards the end of the movement.

Nevertheless, the average angular deviation (across 10 trials for each of the two subjects) of less than 5° is hardly noticeable, and even healthy subjects would be hard-pressed to discern the difference. Thus, the results suggest that this simple model provides a reasonable prediction of actual arm movement.

4.7 Limitations and Sources of Errors in This Model

This model enables a specific amount of electrical stimulation to be delivered in order to produce a certain movement, under given constraints such as the arm being in a gravity-eliminated plane and used for short durations. However, when NMES is used for extended periods, muscle fatigue becomes significant. This model does not adapt to such time-varying aspects of the muscle. Instead, the parameter K_3 and inertia J , can be tweaked manually such that a higher amount of electrical stimulation and a lower inertia compensates for the reduced movement, due to weaker muscle forces after fatigue. As this model uses an open-loop control method with fixed parameters, it is highly susceptible to changes in internal physiological characteristics and unable to adapt to the constantly changing dynamics of the muscle.

This model uses a single-muscle contraction to determine the net torque and hence movement about the elbow joint. In many movements, co-contraction of the agonist and antagonist muscles are required in order to perform dexterous and controlled movements. There are, however, infinitely many ways to produce a certain amount of net torque, if both muscles are contracted simultaneously. This model thus focuses on the net torque produced by one muscle to predict the resulting movement. One benefit arising from this simplification is that fatigue does not set in as fast, since there is no co-contraction of the muscles.

Although spastic conditions are a common occurrence in stroke patients, this model cannot account for these conditions because the torque produced by muscle contractures are difficult, if not impossible, to predict, and the resulting movement of the limb is thus impossible to model. This model is thus beneficial only for stroke patients with spasticity of less than 3 on the Modified Ashworth Scale.

Given the highly non-linear and indeterministic characteristics of the musculo-skeletal system and the estimations used, various sources of error are inevitable. Firstly, the elbow is not a perfect hinge. Hence it is neither possible to ensure that the entire motion occurs in a gravity-eliminated plane, nor is it possible to measure the exact angle of tilt as the axis of rotation cannot be identified. Nonetheless, the effects of gravity are minimal when the arm is placed in a horizontal plane.

Measurement errors also arise from the *Biopac TSD130B* goniometer, which has an accuracy of $\pm 2^\circ$ and repeatability of $\pm 1^\circ$.

Another error is the movement of electrodes over the muscles, which is a common drawback of using external electrodes. During flexion and extension, the skin may slide over the muscles, thus changing the position of the electrodes relative to the muscle and affecting the amount of stimulation sent to the muscle.

There is also a time delay from the time that the electrical pulses are sent to the nerves to the time that the muscle contracts. This time delay was not included in the model.

Due to the nature of muscle, with the larger, fatigue-prone muscle fibres being recruited before the smooth and fatigue-resistant ones, the onset of fatigue is faster with NMES than when muscles are normally activated. Fatigue may have already set in by the time the model was evaluated.

4.8 Future Work

Ethics approval has been sought from Tan Tock Seng Hospital's Institutional Review Board to evaluate the performance of this model on stroke patients. However, due to the outbreak of the H1N1 Influenza A pandemic, all non-essential clinical trials were suspended until further notice, thus delaying trials with stroke patients. Thus, this model was first evaluated in a healthy subject. Results are not expected to differ significantly when used on post-acute stroke patients, as muscle atrophy is unlikely to be significant within the short time span of the post-acute phase.

Chapter 5 – Clinical Trials: Acute Stroke Patients' Use of BCI-NMES

The BCI-NMES neuroprosthesis was evaluated with post-acute stroke patients at the Tan Tock Seng Hospital, Department of Rehabilitation Medicine. This clinical trial was approved by the hospital's Institutional Review Board.

5.1 Introduction to Stroke Patients' Use of BCI

Although the prospect of direct brain control of the paretic limb opens up many options for rehabilitative or assistive applications, using a BCI is not easy. Both man and machine must undergo a certain amount of training in order to use it, and high levels of concentration must be maintained during its use. Thus, when using a BCI neuroprosthesis in stroke, one question that has surfaced is if stroke patients are able to produce a sufficient change in EEG that can be used as a control signal, and whether this would be repeatable.

The aim of this study is to evaluate whether acute stroke patients (less than 3 months after stroke onset) are able to control a BCI. The output of the BCI system triggered neuromuscular electrical stimulation (NMES) on the wrist extensors. The wrist, instead of the elbow, was targeted for NMES stimulation because wrist extension has always been a perennial problem for stroke patients, and it would be motivating, for hemiplegic stroke patients, to see their paretic wrist move again.

The NMES model described earlier had to be built for the relatively simpler elbow joint because the relative position of the NMES electrodes are fixed with respect to the biceps and triceps, making the resulting muscle contraction more predictable. The stimulation of wrist flexors and extensors, however, is dependent on wrist supination and pronation as well, since the skin will roll over different muscles when the wrist rotates, and the electrode placement with respect to the muscles would change. With the knowledge contributed by this report, on how the muscles behave under electrical

stimulation, future work could examine how muscle output changes when electrode positions shift, and perhaps that could be applied to stimulation of the wrist extensors.

NMES has been shown to facilitate post-stroke upper limb recovery [Thrasher 2008, Shin 2008, Chae 2008]. Wrist and finger extensions are also essential pre-requisites for useful hand function. As most motor recovery occurs within 6 months of stroke onset, interventions to facilitate recovery, including BCI-based therapy, should ideally occur during this time frame. However, there have been very few studies examining the use of BCI in patients less than 6 months post stroke onset, therefore little is known about their ability to operate a BCI-NMES neuroprosthesis. In a study by Buch *et al* [Buch 2008], it was demonstrated that 6 out of 8 chronic stroke patients with hand plegia were able to learn to operate a binary magnetoencephalography (MEG)-based BCI after 13-22 sessions where they could voluntarily open and close a prosthesis attached to their paralysed hand. In another study, 5 chronic (>6 months) stroke patients with severe upper limb paresis managed to regulate their EEG to gain control of a binary BCI after 9 training sessions [Daly 2008b]. Although many ideas have sprung up for the use of BCI-mediated stroke rehabilitation, it has not been demonstrated that acute stroke patients are able to use an EEG-based BCI; this clinical trial fills that gap.

5.2 Methods

5.2.1 Subjects

This is a pilot study of patients with a first clinical stroke admitted to a rehabilitation centre. Patients recruited for this study met the following inclusion criteria:

- Age 21-80 years
- Diagnosis of stroke as confirmed on CT and/or MRI brain scan
- Within 3 months of stroke onset
- Medical Research Council (MRC) power grading of <4 for the hemiplegic upper extremity
- Ability to understand simple instructions and learn

The exclusion criteria were:

- History of seizures or epilepsy
- History of neurosurgical operations
- Presence of significant cognitive and/or language deficits which prevents ability to follow study protocol. Cognitive deficits were defined as a score of 8 or less on the Abbreviated Mental Test [Hodkinson 1972]
- Presence of contractures of significant spasticity (defined as Modified Ashworth Scale of 3 or higher) of the hemiplegic wrist and fingers
- Presence of a pacemaker

Informed consent was sought from all patients, and the study was approved by the Institutional Review Board of Tan Tock Seng Hospital.

5.2.2 Protocol

Prior to the training sessions to use the BCI, the patient's EEG was recorded and analyzed offline to determine the optimum frequency band that exhibited the most significant change during movement or motor imagery. By identifying the optimum band and movement, the BCI was focused on the most significant changes in order to shorten training time.

EEG from positions C3 and C4, located directly over the sensorimotor cortex, was recorded while the patient was cued to perform 4 actions:

- i Left hand grasp
- ii Right hand grasp
- iii Left foot tapping
- iv Right foot tapping

In this screening phase, EEG was recorded during both hand and foot movements to observe the attenuation during each movement. When subjects were training to use the BCI, they instructed to use motor imagery of the affected hand only.

On-screen instructions were used as cues for subjects to perform each movement. When they were not supposed to be moving, they faced a blank, black screen and were told to rest during that period. Each movement was carried out for 45 seconds at a rate of 1 repetition every 2 seconds (0.5 Hz). Rest periods were interspersed

between each movement, but the rest time was not conveyed to the patients to avoid anticipation. The whole sequence lasted for exactly 5 minutes.

In order to minimize contamination of EEG signals with electromyographic (EMG) artefacts, patients were asked to minimize fidgeting. They were instructed not to move their eyes, eyebrows or ears, or clench their teeth during the training. EMG artefacts which are of higher frequency and amplitude, are undesirable in EEG analysis. Whenever EMG artefacts were observed, that segment of the training was ignored. Recordings contaminated with multiple EMG artefacts were discarded and the recording was repeated. EMG artefacts are easily spotted in EMG recordings as they are of much higher amplitude, shown in a sample recording in Figure 5.1.

Figure 5.1 – EEG recordings contaminated with EMG artefacts (circled in red)

Subjects who were unable to move their paretic hand were instructed to use motor imagery of the same movement, since actual and imagined movements produce similar EEG patterns. Figure 5.2 shows one of the patients training to use the BCI system.

Figure 5.2 – A post-acute stroke patient with a paretic right wrist using the BCI to trigger NMES on the wrist extensor muscles.

The recorded EEG was then analyzed offline, as described earlier in Chapter 3. EEG graphs of the effects of each type of motor imagery (similar to Figure 3.4) were then shown to the subjects to keep them well informed of trial procedures as well as convince them that their brain waves are changing with motor imagery.

Each subject was given up to 5 sessions to learn to operate the BCI successfully. BCI training for each subject was conducted on alternate days, excluding weekends. The first session started on a Monday, with the fifth session ending the following Wednesday. Training was conducted in the afternoons. Success was defined as the ability to perform 6 consecutive L/R cursor movements in a pre-determined sequence. The odds of six consecutive correct cursor movements happening entirely by chance is less than 2%, therefore we were reasonably certain that the subject was controlling the cursor. As a high level of concentration was needed to elicit the necessary changes in EEG, each session generally lasted no longer than 1 hour because of the onset of mental fatigue which diminished the effectiveness of training. The BCI-FES training was considered completed if the subject could use BCI to trigger NMES of the wrist/finger extensors once. Alternatively, it is also considered completed if he/she was still unable to do so after 5 training sessions.

Once the subject was able to operate the BCI, NMES was introduced. The paretic arm was placed such that the wrist could flex/extend in a gravity-eliminated plane and the forearm was midway between supination and pronation.

The direction of cursor movement corresponded to the direction of desired hand movement. For example, if the subject wanted to extend his/her paretic left wrist, he/she would then use motor imagery of his/her left limb to move the cursor to the left, thus triggering NMES to the wrist extensors. The subject rests his/her hand on the table top, with the palm in a vertical plane, such that wrist extension movements are performed in a gravity-eliminated plane. This position is illustrated in Figure 5.3

Figure 5.3 – For patients with a paretic left limb, motor imagery of left limb movement moves the cursor to the left. When the left target is hit, NMES is applied to the wrist extensors on the left hand. The mirror image of the above setup is used for patients with a paretic right hand.

5.3 Results

This study recruited 9 stroke patients who met the above inclusion and exclusion criteria. There were 7 male and 2 female patients, with a mean age of 58.2 ± 9.3 years. The demographic and clinical characteristics of the patients are shown in Table 5.1. The subjects were studied at a mean of 31.4 days post-stroke (range 8 – 66 days). The motor power of wrist extension (MRC score) was less than grade 3 in all but 1 subject. 3 subjects had complete plegia of the affected upper extremity (Subjects 5, 7, 8), i.e. with an MRC score of 0. As for the site of stroke, 2 patients had a stroke that was located predominantly cortically, 5 of them had a stroke in the subcortical region, and another 2 had a brainstem stroke.

Table 5.1 – Demographic and clinical characteristic of subjects (n=9)

Patient No.	Age / Sex	Days After Stroke	Nature of Stroke	Location of Stroke	Affected Hand	Wrist Extensor MRC Score	Completed BCI Training?	Managed to use BCI?
1	61/M	56	Infarct	Pons	Left	2	Yes	No
2	54/M	66	Infarct	Frontoparietal lobe	Left	3	Yes	Yes
3	48/M	12	Haemorrhage	Basal ganglia	Left	4	Yes	Yes
4	64/M	10	Infarct	Corona radiata	Left	1	No	No
5	73/M	34	Infarct	Corona radiata & lentiform nucleus	Left	0	Yes	Yes
6	48/F	12	Infarct	Pons	Left	4	No	No
7	69/F	26	Infarct	Corona radiata & lentiform nucleus	Right	0	Yes	No
8	56/M	8	Infarct	Frontoparietal lobe & corona radiata	Left	0	No	No
9	51/M	59	Infarct	Lentiform nucleus & corona radiata	Right	2	Yes	Yes

3 subjects did not complete BCI training for the following reasons: One of them decided to withdraw from the study after 1 session (Subject 4), as he was concerned that BCI training may affect his health. Another was discharged home prematurely after one session and chose not to continue (Subject 6). The last subject could not participate in BCI training because of short attention span and left-sided neglect (Subject 8).

Of the remaining 6 subjects, 4 of them (Subjects 2, 3, 5 and 9) were successful in controlling the BCI. The pie chart in Figure 5.3 shows the proportion of stroke patients who could/could not use the BCI, as well as those who dropped out. Subject 2 had a cortical stroke while the other 3 had subcortical strokes. All 4 subjects took only 2 sessions (each session consisting of 45 minutes of training time) to learn to operate the BCI successfully to activate NMES of the wrist and finger extensors. The sensitivity of the BCI and speed of the ball (cursor) falling were customized for every individual. On average, it took about 42 seconds to trigger NMES once. Table 5.2 lists the times taken by each of the 4 successful subjects to trigger NMES once. Improved response time can probably materialize, given further training.

Figure 5.4 – Proportion of stroke patients who could/could not use the BCI and those who dropped out

Table 5.2 – Time taken for each of the 4 successful subjects to trigger NMES

Subject No.	Time Taken (s)
2	64
3	32
5	48
9	24
Average	42

Of the two subjects who could not use the BCI after 5 sessions of training, one (subject 7) did not elicit a sufficient change in EEG that could be used to control the BCI. While the other patient (subject 1) had a noticeable change in EEG, he was unable to regulate it in order to control the BCI. Apart from Subject 4 who was concerned that BCI training may affect his health, no adverse events were reported for the other 8 subjects.

The following graphs in Figures 5.5(a-i) are for individual patients. They show how μ -rhythm EEG varies with time over C3 and C4 (which are located above the motor cortex) during resting (black line), hand grasping (blue line), and foot tapping (green line).

Patient #1 (did not manage to use BCI)

Figure 5.5 (a) – Comparison of EEG power for Patient #1

Although Patient 1 did show a significant attenuation of the μ -rhythm during motor imagery, he was unable to repeat it consistently in order to use the BCI.

Patient #2 (managed to use BCI)

Figure 5.5 (b) – Comparison of EEG power for Patient #2

Patient #3 (managed to use BCI)

Figure 5.5 (c) – Comparison of EEG power for Patient #3

Patient #4 (did not manage to use BCI)

Figure 5.5 (d) – Comparison of EEG power for Patient #4

Patient #5 (managed to use BCI)

Figure 5.5 (e) – Comparison of EEG power for Patient #5

Patient #6 (did not manage to use BCI)

Figure 5.5 (f) – Comparison of EEG power for Patient #6

Patient #7 (did not manage to use BCI)

Figure 5.5 (g) – Comparison of EEG power for Patient #7

Patient #8 (did not manage to use BCI)

Figure 5.5 (h) – Comparison of EEG power for Patient #8

Patient 8 had a very short attention span. He could not keep still even for a brief moment for the recording of EEG. His frequent fidgeting resulted in numerous EMG artefacts.

Patient #9 (managed to use BCI)

Figure 5.5 (i) – Comparison of EEG power for Patient #9

For Subjects 1, 3 and 6, the attenuation of μ -rhythm on the side of the lesion was more pronounced than that on the healthy side, with a clearer separation of EEG power between resting and movement states. Figure 5.5 shows box plots of EEG power during resting, hand and foot movements at locations C3 and C4 for the 3 patients, where the medians, lower and upper quartiles, and ranges are indicated. The data shown was for one trial over a period of 25 seconds during which the respective actions were performed.

Patient #1

Patient #3

Patient #6

Figure 5.6 – Patients No. 1, 3 and 6 showed greater attenuation of the μ -rhythm on the side of the lesion (C4) as compared to the healthy side (C3). They were right-handed and suffered a stroke on the right hemisphere of the brain (C4), which resulted in paresis of the left limbs.

5.4 Discussion

In this study, we ask the question of whether patients with acute to subacute stroke could control a BCI to activate NMES of the wrist/finger extensors. The reason for choosing NMES of the wrist/finger extensors was because NMES has been demonstrated in previous studies to facilitate upper limb recovery in stroke [Chae 2008, Buch 2008, Daly 2008b] and active wrist/finger extension are pre-requisites for useful hand function. The findings of this study indicate that movement intention as characterized by the attenuation of μ -rhythm EEG is detectable in 4 out of 9 subjects (44.4%) at an average of 31.4 days after stroke onset, and that this signal is repeatable and can be used by the subjects to operate a BCI to trigger NMES on the paretic wrist.

Encouraging is the finding where the 4 subjects successfully managed to learn and use the BCI with only 2 sessions of training. It has been estimated that about 1 in 5 persons are 'BCI illiterate' because their motor-related μ -rhythms do not show sufficient variation to be used as a control signal [Nijholt 2008]. As the sample size of this study was small, no conclusion could be made on the rate of BCI literacy among post-acute stroke patients. As a result, neither are we able to comment on meaningful differences in clinical or stroke characteristics between those who succeeded and those who did not.

Another observation is that the attenuation of EEG power on the contralateral hemisphere was more pronounced when the subjects 1, 3 and 6 were trying to move their paretic hand, as compared to moving their healthy limb. The author conjectures that this could be due to the subjects needing to concentrate and focus harder in order to move the paretic hand, as opposed to movement of the healthy hand which is easier, and thus does not warrant as much concentration.

In the 2 subjects (Subject 1 and 7) who were unsuccessful in controlling the BCI after 5 sessions, 1 (Subject 1) was unable to do so despite exhibiting a clear attenuation of EEG during limb movement, while the other (Subject 7) showed no change in EEG during limb movement. Whether more training sessions would have improved outcome is uncertain. The finding that Subject 8, who was unable to participate fully in BCI training because of short attention span despite a normal Abbreviated Mental

Test score, suggests that more detailed cognitive screening is necessary when recruiting subjects for future BCI studies.

As the objective of this study is to use a BCI to trigger NMES of the paretic limb, the control signal must be non-invasive and based on movement intention. The most suitable phenomenon is thus the attenuation of the μ -rhythm, which can be recorded by either magnetoencephalography (MEG) or EEG. While Buch *et al* has proven the feasibility of using an MEG-based BCI for chronic stroke patients [Buch 2008], our findings show that despite the poorer spatial resolution, EEG recorded over the motor cortex in acute and subacute stroke patients can also be used to control a BCI. As Buch pointed out, the use of EEG rather than MEG allows the system to be portable and is also less costly; these are desirable traits if such a neuroprosthesis to be used in rehabilitation centres and even in homes.

The use of EEG is not without its drawbacks. Preparation time of about ten to fifteen minutes for matching impedances between the electrodes and scalp, takes up a sizeable portion of the duration of BCI use and invariably contributes to fatigue. As such, perhaps the best part of the subject's attention span is wasted. The use of impedance matching gel also requires subjects to wash their hair after each session - not an easy task without a caregiver to assist them. The screening method used here narrowed the frequency band to focus only on the frequencies with the greatest changes that can enable post-acute stroke patients to learn to use a BCI in as little as two sessions. Wolpaw [Wolpaw 2000a] found that most EEG-based BCI users (with or without disabilities) developed substantial control within 5 half-hour sessions (2.5 hours), and our findings with post-acute stroke patients are in line with this finding.

Although no adverse side effects such as headaches or giddiness were reported, it was evident that patients were fatigued after approximately 45-60 minutes of using the BCI.

While the results of this study are encouraging, the following study limitations and caveats need to be highlighted. Firstly, the average time taken to trigger one BCI-activated NMES was 42 seconds which is probably longer than that achieved by

conventional NMES. The timing can be adjusted for each individual, and can also be further optimized. There is however, a trade-off between a fast response time and false-positive errors.

Secondly, subjects were required to activate NMES only once in this study. However, for rehabilitation exercises to be effective, it should be repeated continuously for 30-45 minutes for multiple sessions, typically 3 times a week for 6 weeks. It remains to be seen whether this is possible in this group of stroke patients.

There is also the question of whether BCI-activated NMES offers any additional benefits as compared to conventional NMES, or conventional rehabilitation. We hypothesize that it does, as most conventional NMES very much involves a passive process with little patient engagement. BCI-activated NMES on the other hand, is an active and engaging process that requires patients to think about moving the paretic hand, and since it involves mental imagery, it has been shown to augment functional outcome in stroke [Sharma 2006, Müller 2007]. The efficacy of BCI-NMES in reorganizing neural pathways and promoting neural plasticity could not be proven, but will be the focus of a future multi-centre study with the developed BCI-NMES neuroprosthesis.

In summary, our results demonstrate that patients within 3 months of a stroke can learn to control a BCI and use it to activate NMES of the wrist/finger extensors. As outlined above, the results presented in this dissertation show that it is thus feasible to carry out further studies to evaluate the efficacy of such a rehabilitation method.

Chapter 6 – Conclusion

6.1 Conclusion

The intention to move is detected by an electroencephalogram (EEG)-based brain computer interface (BCI), and movement is then artificially induced by neuromuscular electrical stimulation (NMES). Together, the BCI and NMES subsystems form a neuroprosthesis that enables users with paretic upper limbs to move their elbow joints. This dissertation describes its development, and presents results from the first ever clinical trial on post-acute stroke patients' use of a BCI.

Chapter 1 discusses the physiological processes behind voluntary motor function and how a tragically located lesion in the brain renders one paralysed. It then presents various efforts to repair the central nervous system, which unfortunately does not heal by itself, followed by Man's current understanding of how neural rehabilitation takes place. Latest trends in robot-assisted therapy, interventions using neuromuscular electrical stimulation (NMES), the premise of repetitive and intense exercise of the paretic limb for improved rehabilitation are presented next, followed by current opinions on how neuroprostheses offer a promising approach to neural rehabilitation. The basis for a brain-computer interface (BCI) triggered neuromuscular electrical stimulation is then put forward, with the problem statements, objectives and cope of this dissertation being defined.

Chapter 2 describes the parts of the human anatomy which interact with the BCI-NMES neuroprosthesis. It starts with the neuromuscular system and the pathologies that cause paralysis, followed by the underlying mechanisms for neural rehabilitation.

Chapter 3 provides details of the electroencephalogram (EEG)-based BCI that can decipher motor intent from the attenuation of μ -rhythm EEG during motor imagery. It then presents a method to identify specific frequency bands by decomposing the EEG signal using the Bandlimited Multiple Fourier Linear Combiner (BMFLC) and observing the frequencies that show the largest changes. By narrowing the frequency band, a more sensitive signal can be obtained to operate the BCI. EEG amplitudes

from 6 electrodes over the motor cortex then form a control vector which controls the horizontal movement of a ball (on a graphical user interface) as it drops into a 'basket', which then triggers NMES of the respective muscle.

Chapter 4 focuses on NMES and presents a muscle model that predicts elbow movement due to a certain amount of electrical stimulation. The integration of the BCI and NMES sub-systems to enable paralysed stroke patients to 'think to move' is then described. This phenomenological physiological model for artificial activation of the muscles through NMES is an extension of Ferrarin's model [Ferrarin 2001] for the knee, and it involves the stimulation of the agonist-antagonist muscle pair (biceps and triceps) of the elbow. Active muscle activation characteristics, passive musculo-tendon characteristics, and physical properties of the arm are estimated to build a model, such that a specific arm movement can be achieved using NMES. The model was evaluated in two healthy subjects and is found to provide a reasonable prediction of elbow movements when stimulated by NMES. The average angular deviations for elbow movements were 3.9° and 4.6° for the two subjects respectively – small enough such that even healthy subjects would find it difficult to notice the difference in elbow angle.

Chapter 5 presents the first ever study on post-acute stroke patients' use of an EEG-based BCI. The rationale for performing the clinical trial is explained. Trial methods, protocols, and results are then presented, followed by a discussion on the findings. These results show that 4 out of 6 post-acute stroke subjects who completed the study were able to use the mu-rhythm EEG-based BCI to activate NMES on their paretic wrists. The results demonstrate that it is feasible for post-acute stroke patients to use a mu-rhythm EEG-based BCI, and paves the way for future studies on whether this technique could enhance rehabilitation outcomes.

Lastly, this chapter summarizes the key contributions of this dissertation. It also suggests future efforts directed toward the realization of a BCI-NMES neuroprosthesis that could possibly one day enable paralysed persons to move their paretic limbs again.

This dissertation puts forward the idea of how paralysed users can control the movement of one upper limb joint using an EEG-based BCI coupled with a muscle model for NMES movement. This approach differs from Pfurtscheller's BCI-FES system [Pfurtscheller 2003] as it focuses on performing a controlled, arbitrary movement in order to position the hand, rather than using the BCI to switch FES on or off completely. Functionality, however, is compromised at this stage, and future work to extend the capabilities of BCI-NMES must be undertaken. Despite this, a large population of disabled persons could still benefit even if a few mere motor activities are reinstated. This is because almost all functional tasks can be achieved with compensatory movements of other joints. Furthermore, consideration must also be given to the potential for neuroplasticity or other therapeutic effects to occur during BCI-NMES usage. The concept of the BCI-NMES neuroprosthesis was demonstrated in stroke patients, and even though neural plasticity could not be proven at this stage, it will be the focus of future multi-centre study with the developed BCI-NMES neuroprosthesis.

6.2 Contributions

The key contributions of this dissertation work are:

- 1) Design and implementation of a BCI-NMES neuroprosthesis that can enable people with upper limb paralysis to perform specific movements of their elbow joints.
- 2) Proposal and implementation of a muscle model of the upper limb for artificial activation by NMES. The muscles (biceps & triceps) that flex and extend the elbow were modelled to predict arm movement for a given stimulation by NMES. Results from two healthy subjects showed that this model provided reasonable accuracy.
- 3) Through clinical trials, the feasibility of post-acute stroke patients using an EEG-based BCI to trigger NMES was established. Encouraging results show that a significant change in μ -rhythm EEG could be detected in 4 out of 6 post-acute stroke patients who completed the training. These 4 patients were able to regulate their EEG and operate the BCI to trigger NMES on their paretic arm. This is the first ever study on EEG-based BCI usage in post-acute stroke patients, thus paving the way for future

studies on how such a neuroprosthesis can facilitate neurorehabilitation during the post-acute phase of stroke.

6.3 Future Work

The BCI-NMES neuroprosthesis is still far from realizing the vision of performing complex processes of the nervous system to enable paralysed users to regain functional movement of their paretic arm. More engineering effort is required to improve the capabilities of both the BCI and NMES subsystems. At the same time, a better understanding of neurological process of voluntary motor function is also needed.

For BCI-NMES mediated rehabilitation, further questions have to be answered. For instance, what level of exercise intensity is achievable, and what is optimum? What protocols are suitable for promoting neural plasticity? Many challenges still lie ahead, such as the short duration in which subjects can use a BCI and NMES due to a limited attention span and fatigue, compared to conventional therapy where it is common for each session to last more than two hours. Furthermore, the time-varying characteristics of the muscle model must also be addressed before BCI-NMES mediated therapy can be evaluated in large-scale clinical trials.

Although this dissertation focuses on stroke patients' use of a BCI and NMES, the concept of an alternate neural pathway between the brain and peripheral parts of the body can also be applied to users paralysed by spinal cord injury and multiple sclerosis. For these users, the 'robotic crutch' can serve as a purely assistive device, while for stroke patients whose primary goal is improved neural rehabilitation, the therapeutic effects of BCI-NMES mediated rehabilitation are of greater importance.

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