Combining Muscle Stimulation with Elicitation of the Nociceptive Withdrawal Reflex in a Gait Controller to support Hemiparetic Gait

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MASTER THESIS - SPRING 2011
BIOMEDICAL ENGINEERING & INFORMATICS

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TITLE:

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PROJECT PERIOD:

Master Thesis, February 2011 - May 2011

PROJECT GROUP:

Medical Systems 1085a

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Copies: 6

Pages: 132

Appendices: 2

FINISHED: 31 May 2011

SYNOPSIS

Stroke patients often have a compromised gait pattern with kinematic deviations from normal walking, typically consisting of decreased hip-, knee-, and ankle dorsiflexion throughout the swing phase, and lack of stability in the paretic leg during the stance phase of gait.
The aim of this thesis was to design and develop a gait controller based on functional electrical stimulation to assist hemiparetic gait by combining muscle stimulation of quadriceps and solues in the stance phase with elicitation of the nociceptive withdrawal reflex (NWR) from the sole of the foot to initiate the swing phase. Experimental studies were carried out to investigate the modulation of the NWR during normal gait (n = 4 participants) and hemiparetic gait (n = 1). The results indicated that the kinematic hip-, knee-, and ankle responses were dependent on stimulation site on the sole of the foot and stimulation onset.
The modulatory effect of the NWR was utilised in the design of a sequence-based stimulation (SBS) controller to support hemiparetic gait. The performance of the SBS controller paradigm was tested (n = 1) against a simple paradigm composed of a fixed pattern of stimulation (FPS) controller. Overall, the SBS controller paradigm was superior in supporting the specific needs of the hemiparetic participant compared to the FPS paradigm.
The findings obtained in this thesis suggest that stroke patients may benefit from a stimulation paradigm where quadriceps and soleus are activated in the stance phase and the NWR elicited to initiate the swing phase during gait retraining.

PREFACE

This report is the master thesis of group 1085a of Biomedical Engineering and Informatics, Medical Systems, Department of Health Science and Technology, Aalborg University. The report was written in the period from February 1st to May 31st 2011.

The report is addressed to fellow students at the Department of Health Science and Technology, the project supervisors and others interested in the gait rehabilitation of stroke patients using Functional Electrical Therapy.

The report is written by:

Lotte Bjerre

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Reading Instructions

Structure of the master thesis

This report is organised in four parts as indicated in figure 1. Part I is a problem analysis that introduces specific terms in relation to the project and discusses earlier applications of Functional Electrical Stimulation (FES) used in rehabilitation of hemiparetic gait. This part ends with a system description and a problem specification.

The second part includes two experimental Case Studies carried out to investigate the kinematic responses obtained when muscle stimulation was combined with elicitation of the nociceptive withdrawal reflex during normal- (Case Study 1) and hemiparetic gait (Case Study 2).

Part III of the report deals with the design and implementation of the gait controller on the background of the results from the studies described in part II. This part ends with Case Study 3 aiming to test the gait controller on a hemiparetic participant.

The last part is the synthesis of the project, including a discussion, a conclusion, and at last some ideas for further development of the gait controller.

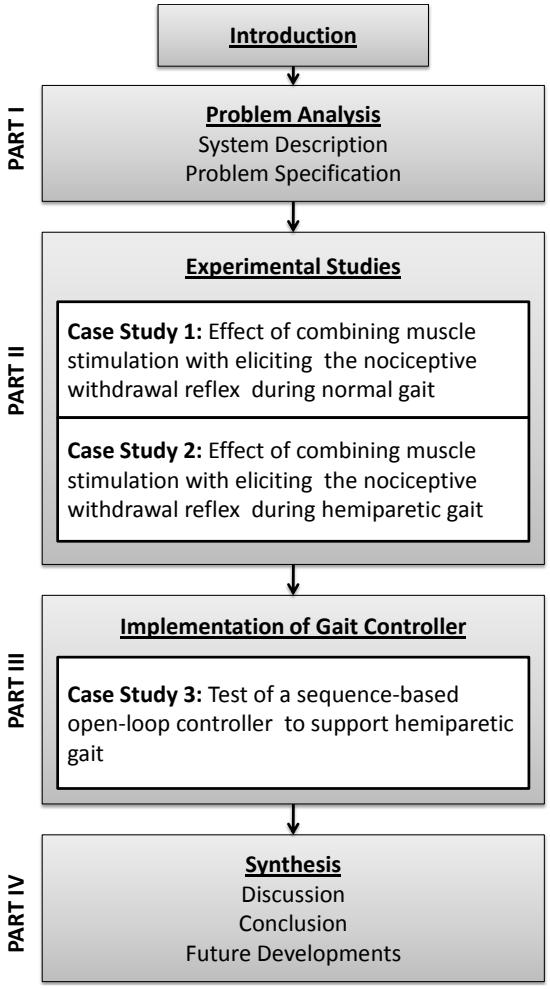


Figure 1: *Structure of the report.*

Citations are written in squared brackets, like [Sherrington, 1910]. Further information about the source can be found in the bibliography placed after part IV in the report. The entries in the bibliography are listed after alphabetical order according to the surname of the main author.

The report is supported by appendices and attachments, which can be found after the bibliography in the end of the report.

The documentation of the master thesis does also include a CD-ROM containing a copy of the report in pdf-format, the used references in pdf-format, data from Case Study 2, and a Matlab script for importing the lvm data files.

Abbreviations

ANOVA	Analysis of Variance
CTR0	Counter 0
CTR1	Counter 1
DAQ	Data Acquisition System
FES	Functional Electrical Stimulation
FET	Functional Electrical Therapy
FPS	Fixed pattern of stimulation
FSR	Force Sensitive Resistor
MIMO	Multiple Input Multiple Output
MRAC	Model Reference Adaptive Control
NWR	Nociceptive withdrawal reflex
QA	Quadriceps
R1	Stimulation site on the mid forefoot
R1R3	Combined stimulation of R1 and R3
R2	Stimulation site on the arch of the foot
R2R3	Combined stimulation of R2 and R3
R3	Stimulation site on the posterior aspect of the heel
SBS	Sequence-based stimulation
SISO	Single Input Single Output
SOL	Soleus

Contents

CHAPTER 1

INTRODUCTION

Stroke refers to the sudden loss of neurological functions caused by an interruption of the blood supply to areas of the brain. It is the third most common cause of death in developed countries, only surpassed by cardiovascular disease and cancer. Furthermore, stroke is the most common cause of chronic disability in these countries [Rosamond et al., 2007]. Every year, approximately 700,000 European citizens are affected by a stroke, and it is estimated that 3,500,000 people in the European Union live with the consequences of stroke [Sinkjaer and Popović, 2005]. In Denmark, the total number of people affected by stroke is estimated to 35,000 - 45,000 [Popović and Sinkjaer, 2003]. For more information about stroke in general, see appendix A.

Patients, who have suffered a cerebral stroke often have problems moving one or more of their limbs due to hemiparesis, usually on the side of the body opposite to the side of the brain lesion.
A stroke might affect the patient's ability to coordinate movements between limbs and perform relative simple functions necessary in daily living, such as walking, reaching, eating, and getting dressed by oneself. Thus, stroke is strongly correlated with a reduced quality of life. [Caplan, 2009]

Restoration of gait is important for the self-sufficiency and the quality of life for stroke patients. Before any type of rehabilitation is done, about 2/3 of all stroke patients have problems when walking [Pedersen and Olsen, 2007]. The typical gait kinematics of stroke patients deviate from normal walking in both the swing phase and the stance phase. Typical deviations in the swing phase include decreased flexions in both hip, knee, and ankle joints [Morre et al., 1993], whereas kinematic deviations in the stance phase are related to a lack of stability and balance of the affected leg [Moseley et al., 1993].

The rehabilitation of gait after stroke takes advantage of the capacity of the brain for recovery by focussing on improving practical skills in a real-life setting, such as walking. Functional Electrical Therapy (FET) is a rehabilitation method that makes use of this approach by combining patterned and timed electrical stimulation with task dependent exercise. The method has shown to carry potentials for promoting recovery of humans with paralysed extremities [Popović and Sinkjaer, 2003, Popović et al., 2003, Kojović et al., 2009].

Electrical stimulation can be applied as muscle stimulation that activates the motor nerves and thereby produces a contraction of the innervated muscles. This method has been used to support rehabilitation of gait for several years [Lyons et al., 2002], and the application of multi-channel stimulation that target several relevant muscles in the leg allows for support during both stance and swing phases of gait, e.g. [Stanic et al., 1978, Kojović et al., 2009]. The basic idea for stance phase support is to rectify the lack of stability in the affected leg by stimulating the extensor muscles of the knee that fixate the knee joint and stabilise the leg [Postans, 2004, Fuhr et al., 2008]. During late stance, the soleus muscle in the back of the lower leg might be stimulated to create further stability of the leg and to assist with push-off of the foot [Kojović et al., 2009]. The swing phase can be supported by e.g. stimulation of tibialis anterior to prevent drop foot [Kojović et al., 2009].

A disadvantage of electrical muscle stimulation is the reversed recruitment order of the motor units that gives rise to fatigue in the target muscles and often a loss of fine motor control, since the larger motor units are activated before the small ones [Baker et al., 2000] In addition, the limited number of stimulation channels limit the number of target muscles that can be activated with this approach. If surface electrodes are used, another drawback is that only superficially located muscles can be activated. Deeper muscles such as the main hip flexor (iliopsoas) is unsuitable for surface stimulation. These drawbacks led to the motivation for using reflex based FET, since the reflex loops in the spinal cord are usually intact in patients who have suffered a stroke, while the control of the motoric centre in the spinal cord from the brain is affected.

Eliciting the Nociceptive Withdrawal Reflex (NWR) results in natural activation of several muscles in the leg and produces a withdrawal of the limb from a potential harmful stimulus [Sherrington, 1910]. The execution of the NWR in the late stance phase of the gait cycle creates a powerful leg swing which might ease the patient's gait training. This approach has been used by Quintern et al. [2003] to initiate and support the swing phase by applying electrical stimulation to the peroneal nerve to activate the flexor reflex afferents during gait retraining.
The NWR can also be elicited by applying an electrical stimulus to the sole of the foot, which will make the patients withdraw their leg as if having stepped on something sharp. Studies in humans, where the NWR was elicited from the sole of the foot, indicate that the reflex response can be modulated, and that it is dependent on stimulation site [Andersen et al., 1999] and phase of the gait cycle at which the stimulation is presented [Spaich et al., 2004, 2006]. This modulatory property of the NWR can be utilised in the design of a gait controller since the desired reflex responses can then be tailored to the individual patient by altering the stimulation sequences. Recently, Emborg et al. [2011] came up with a closed-loop swing phase controller that exploited the differences in withdrawal strategies depending on stimulation site and onset of stimulation to support the production of the swing phase.

The aim of this project was to design and implement a gait controller to be used in stroke rehabilitation therapy. The controller should combine elicitation of the NWR to initiate the swing phase with muscle stimulation to give support and stability of the affected leg during the stance phase.

Part I

Problem Analysis

This part includes a description of normal gait and an analysis of the deviations from normal gait observed in hemiparetic patients. Furthermore, a historical note on the development of Functional Electrical Stimulation systems as gait support for hemiparetic patients is introduced. The part ends with a system description of the gait controller to be developed in this project.

Chapter 2

Human Gait

This chapter contains a brief description of human gait. The concepts of normal gait are important in the rehabilitation of patients with a pathological gait, since it provides the standard against which the gait of a patient can be judged. Pathological gait may result from a disorder in any part of the locomotor system, including the brain, the spinal cord, nerves, muscles, joints, and the skeleton. This report focusses only on the pathological gait of stroke patients.

2.1 Normal Gait

2.1.1 The gait cycle

For most people, walking is automatic and requires no thought. The subconscious mechanism of walking is meant to be part of the central pattern generator that is possibly responsible for the phase dependency of gait.
Gait describes the way of walking, and is composed of consecutive gait cycles. A gait cycle is defined as the period from the point where one foot has its first contact with the ground to the next point of initial ground contact with the same limb. The opposite foot goes through the exact same series of events, but displaced in time by half a cycle. [Vaughan et al., 1992, Whittle, 2007]
The gait cycle can be divided into two main phases: a stand phase and a swing phase. During the stance phase, the foot is in contact with the ground, whereas during the swing phase, the foot is lifted from the ground and the leg is moving forward to prepare the next ground contact, see figure 2.1.

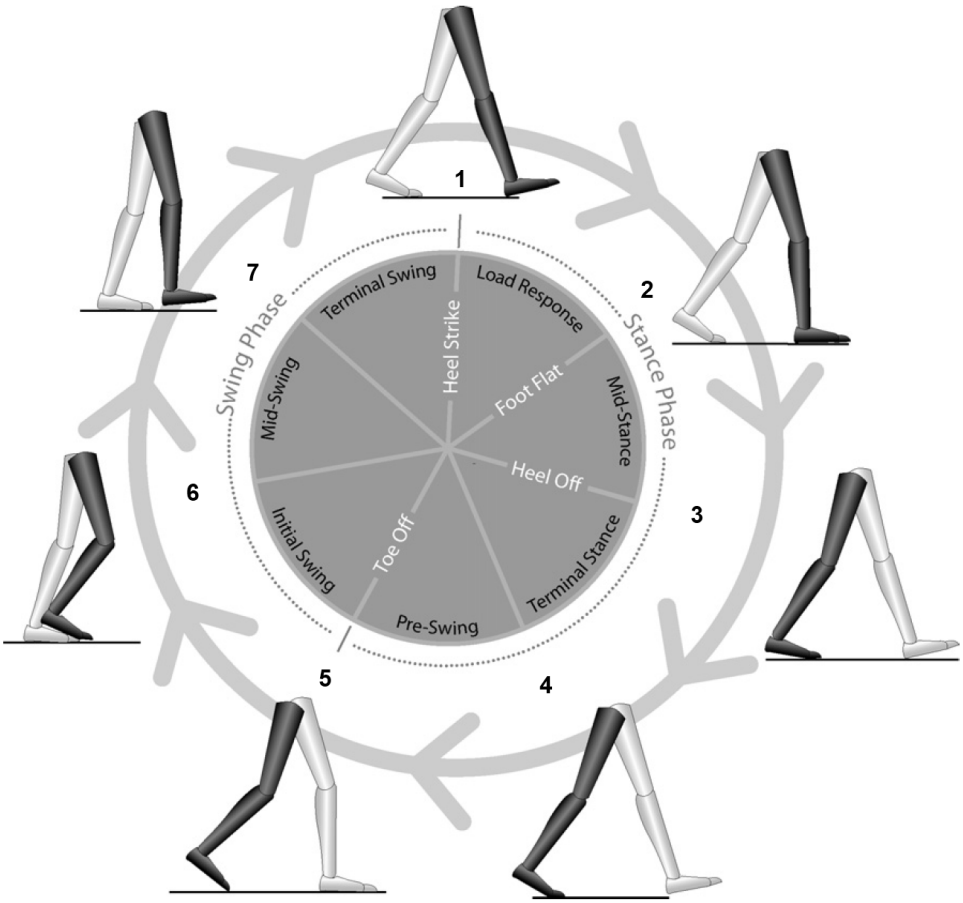


Figure 2.1: The gait cycle. *A schematic diagram indicating positions of the right leg (black) and left leg (grey) leg during a single cycle. From [Rueterbories et al., 2010], modified after [Whittle, 2007].*

As indicated in figure 2.1, the gait cycle can be divided into seven events, four during stance and three during swing [Whittle, 2007]:

1. **Initial contact (heel-strike)** initiates the gait cycle by creating the first contact of the foot to the ground.
2. **Opposite toe-off** represents the time when the opposite foot is lifted from the ground and the plantar surface of the standing foot touches the ground.
3. **Heel rise** is when the heel loses contact with the ground and the push-off is initiated by plantar flexion of the ankle.
4. **Opposite heel-strike** occurs when the opposite foot has its first contact with the ground.
5. **Toe-off** is the termination of the stance phase where the foot leaves the ground.
6. **Feet adjacent** represents the time, where the subject moves the swinging leg forward, and the standing and swinging leg are adjacent to each other.

7. **Tibia vertical** represents the event, where the tibia bone of the leg is in a vertical position. This is the last event in the swing phase just before the next initial contact to the ground.

The seven events subdivide the gait cycle into seven periods: [Whittle, 2007]

1. Loading response
2. Mid-stance
3. Terminal stance
4. Pre-swing
5. Initial swing
6. Mid-swing
7. Terminal swing

2.1.2 Gait cycle timing

The timings of heel-strike and toe-off for both feet divide the gait cycle into periods of double support (double limb stance) and single support (single limb stance). The first period of double support occurs between heel-strike of the right foot (1 in figure 2.1) and toe-off of the left (2 in figure 2.1). During the swing phase on the left side, only the right foot is on the ground, leading to the first period of single support, which ends with heel-strike of the left foot (2→4 in figure 2.1). There is then another period of double support (4→5 in figure 2.1), before toe-off of the right foot initiates the last single support phase of the gait cycle (5→1 in figure 2.1). The stance phase usually lasts about 60% of the gait cycle, the swing phase about 40%, and each period of double support around 10%. [Whittle, 2007] These percentages varies, however, with the speed of walking because the swing phase becomes proportionately longer and the stance phase and double support phases shorter as the walking speed increases [Murray, 1967].

2.1.3 Muscles activated during the gait cycle

To be able to create a system for stimulation of human muscles during gait, it is necessary to know which muscles are active during the different parts of the gait cycle. Figure 2.2 illustrates a typical activity diagram of the major muscle groups activated in healthy subjects during the gait cycle. It is not possible, however, to produce a precise diagram of the muscle activation during normal gait, since the same gait pattern may be achieved in a number of different ways and by activation of different muscle combinations at different time points. There might be inter-subject variability due to differences in anatomy, muscle strength, and walking speed between subjects. Furthermore, the usage of muscles may differ in the same person over time due to fatigue and changes in walking speed [Vaughan et al., 1992, Whittle, 2007].

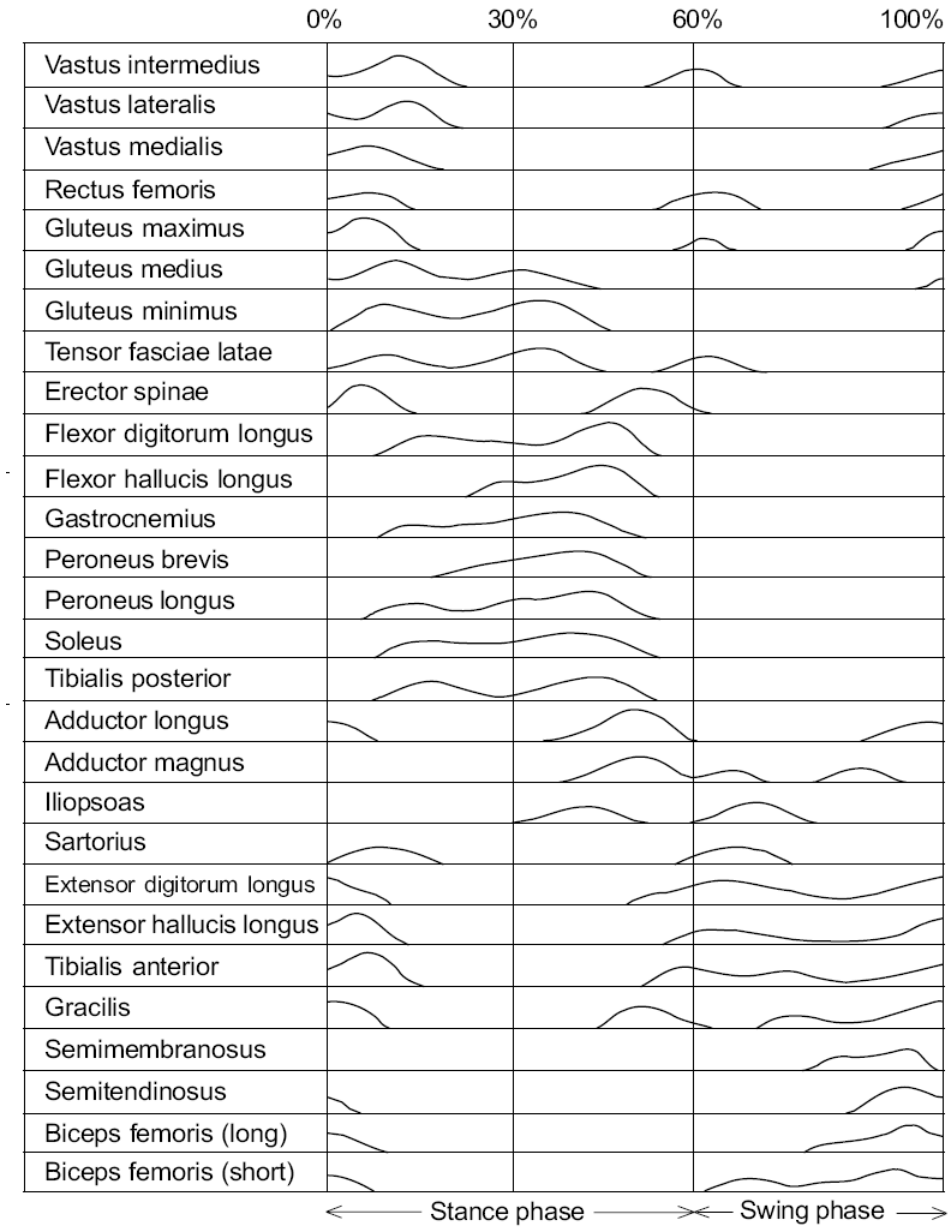


Figure 2.2: Typical muscle activity diagram for 28 of the major muscles in the lower limbs shown as a function of the gait cycle. *The muscle usage during gait may vary between subjects, and is also dependent of both fatigue and walking speed. The figure is made from EMG data during normal gait. [Vaughan et al., 1992].*

2.1.4 Kinematics during the gait cycle

Kinematics is the branch of classical mechanics that describes the motion of objects without consideration of the forces that cause the motion. Movement of the lower limbs in the sagittal plane can be described using goniometers attached on the hip, knee, and ankle joints [Vaughan et al., 1992, DeLisa, 1998]. Figure 2.3 illustrates an example of the changes in hip, knee, and ankle joint angles during a normal step in the sagittal plane.

Hip joint: The hip joint flexes and extends once during a single gait cycle. The hip reaches its flexion limit around the middle of the swing phase and is then kept flexed until heel-strike of the ipsilateral foot. The peak extension is reached before the termination of the stance phase, where the hip begins its flexion again to prepare for the next step.

Knee joint: The knee joint passes through two flexion and two extension peaks during a single gait cycle. It is approximately fully extended before initial ground contact, flexes during the loading response and first part of mid-stance, extends during the later part of mid-stance, then starts flexing again and reaching peak flexion during initial swing. Afterwards, it starts extending again prior to the next heel-strike.

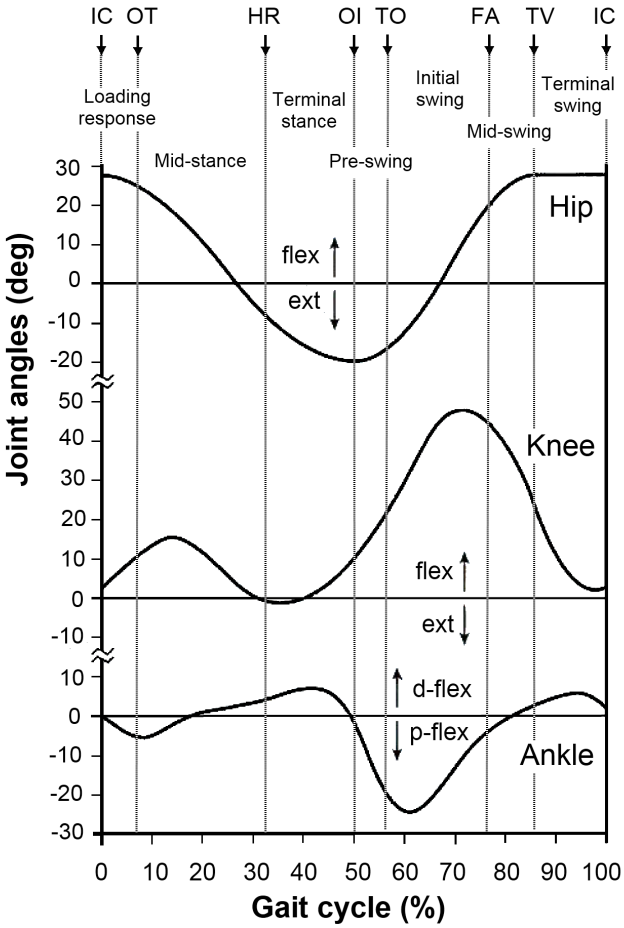


Figure 2.3: Sagittal plane joint angles during a single gait cycle of hip, knee, and ankle from a non-impaired subject. *Abbreviations: IC = initial contact; OT = opposite toe-off; HR = heel rise; OI = opposite initial contact; TO = toe-off; FA = feet adjacent; TV = tibia vertical. Modified from [Whittle, 2007].*

Ankle joint: After initial ground contact, the ankle joint plantarflexes to bring the forefoot down onto the ground. During mid-stance, the tibia moves forward over the foot and the ankle joint begins to dorsiflex. Before heel-strike of the contralateral foot, the ankle goes into plantarflexion until just after toe-off. During the swing phase, the ankle moves back into dorsiflexion until the forefoot has cleared the ground, after which the ankle is close to neutral position until next heel-strike. As the foot reaches the ground, the ankle angle changes from plantarflexion to dorsiflexion, and back to plantarflexion again just before next heel-strike of the foot. [Vaughan et al., 1992, Whittle, 2007]

2.2 Pathological gait of stroke patients

The distortion of gait following a stroke may manifest in a variety of ways depending on the individual injury (severity, location, extent of damage), the amount of time that has passed since the stroke, the amount of natural recovery achieved, and the rehabilitation interventions that have been implemented. A stroke often results in unilateral leg weakness due to diminished muscle strength and inappropriate timed or inappropriately graded muscle activity. After a few weeks, there may be further impairments such as spasticity, which also leads to a compromised gait pattern. [Olney and Richards, 1996]
Figure 2.4 summarises commonly observed kinematic deviations from normal gait in stroke patients.

Typical kinematic deviations observed in the stance phase include decreased peak hip extension in late stance, increased or decreased peak lateral pelvic displacement, increased or decreased knee extension in early or mid stance, and decreased plantarflexion at toe-off [Moseley et al., 1993].
Kinematic deviations observed in the swing phase include decreased peak hip flexion, decreased peak knee flexion, decreased knee extension for heel-strike and decreased ankle dorsiflexion throughout swing [Morre et al., 1993].

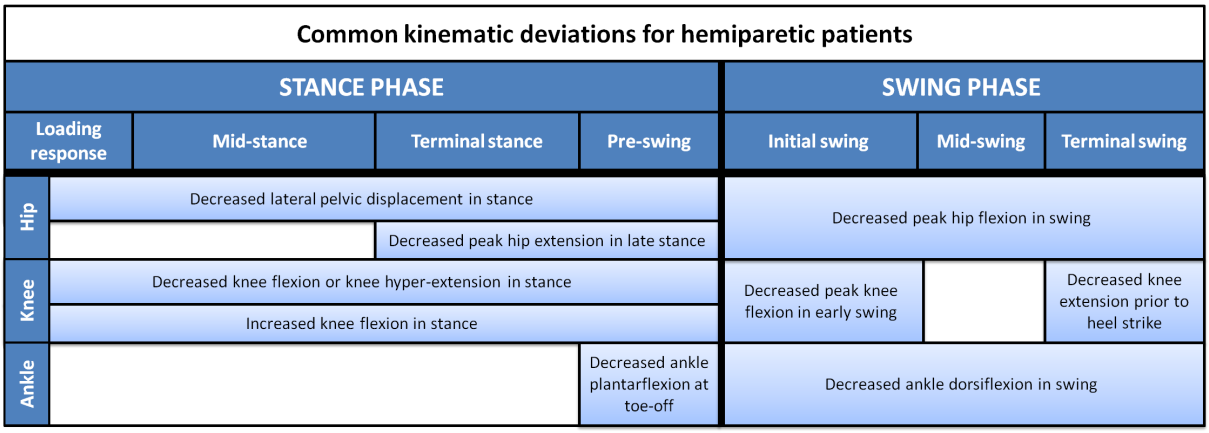


Figure 2.4: Schematic representation of commonly observed kinematic gait deviations in hemiparetic stroke patients. *The findings are based on studies by Moseley et al. [1993], Morre et al. [1993]; and Olney and Richards [1996].*

Compensatory movements

Individuals with hemiparesis compensate for their motor deficits by walking at a slower speed and having a slower cadence and shorter stride length compared with non-impaired control subjects. Stroke patients tend to spend more time in the double support phases of the gait cycle, where both feet are on the ground, and less time in stance phase of the affected limb. To compensate for the reduced knee flexion and the drop foot, some stroke patients tend to achieve ground clearance of the affected leg by hip circumduction and contralateral vaulting with excessive elevation of the pelvis to avoid toe drag. [Olney and Richards, 1996, DeLisa, 1998] These gait problems predispose the patients to secondary problems such as injuries from falls [Nyberg and Gustafson, 1995].

CHAPTER 3

REHABILITATION OF GAIT AFTER STROKE

Motor deficits due to stroke are typically characterised by different degrees of paralysis, usually present on the side of the body contralateral to the brain lesion. Today, medical treatment may help to prevent the major consequences of an ischaemic stroke if the patient is brought to hospital within few hours following the cerebrovascular accident. Unfortunately, not all stoke patients get to the hospital in time. In their case, rehabilitation is the primary goal to try to regain motor function and/or other functions after stroke.

The rehabilitation strategies make use of the ability of the brain to reorganise its neural pathways based on new experiences. This ability is termed plasticity and has been recognised as a part of the structural and physiological substrate for the recovery of function after an injury to the central nervous system. Corticomotor reorganisation might occur as a response to altered inputs to sensory cortex, as an adaption to the injury of the central or peripheral nervous system, or as a consequence of repeated and intense motor exercise [Sinkjaer and Popović, 2005]. The plasticity in the human brain is mostly evident in the early stage after stroke, i.e. during the first four weeks [Kwakkel et al., 2006]. Hence, it is important to initialise retraining and rehabilitation as soon as possible after the stroke has arisen.
This chapter discusses rehabilitation of gait in stroke patients with special focus on neural prostheses and Functional Electrical Stimulation (FES).

3.1 Physiotherapy-based Gait Training

The basic aim of conventional physiotherapy is to regain some of the physical functions lost as a consequence of stroke. The course of treatment is often individual for each patient because the functional loss, physical condition, and personal requirements differ between stroke patients. The typical conventional physiotherapy training involves physical fitness training composed of: a planned schedule of regular physical exercises performed to improve physical fitness, maintain cardiorespiratory fitness, and improve strength and muscular endurance. The training may also include some repetitive task training, where a motor sequence is performed repetitively within each training session in order to reach a clear functional

goal (e.g. being able to perform a particular movement). Specific gait retraining may involve the use of splints or orthoses, which are external, removable devices used to improve functional movement by supporting the affected leg or prevent over-stretching, etc. Other walking aids utilised in physiotherapy to increase balance and stability of the paretic leg while walking/standing are canes, crutches, and walking frames. To avoid stumbling while performing the gait retraining, the patient may be physically supported by the physiotherapist or another person, or eventually by a harness capable of supporting a percentage of the patient's body weight. In the last case, the patient is normally walking on a treadmill, where the harness is connected to the ceiling. [Popović and Sinkjaer, 2003, Langhorne et al., 2009]

3.2 Neural Prostheses and Functional Electrical Stimulation

Neural prostheses can be utilised in gait retraining. They are assistive systems aiming to replace or augment motor functions that are diminished or lost as a consequence of injury or disease in the nervous system. Generally, neural prostheses make use of FES to evoke involuntary muscle contractions and thereby overcome muscle weakness in the affected limb [Popović and Sinkjaer, 2003, Thrasher and Popović, 2008]. The aim of neural prostheses is either to be used as a temporary device during the early stages of recovery, or as a permanent assistance for the stroke survivors with chronic problems [Thrasher and Popović, 2008]. Several FES systems have been developed over the last years, and some of them have become commercialised and are, thus, available in clinical practise or for everyday use at home, e.g. ActiGait^{TM} [Burridge et al., 2007].

3.2.1 FES applications used in gait retraining

Patients suffering from stroke may recover a large amount of function by the natural neurologic recovery that occurs in the first months immediately after the stroke, but approximately 10-20% of the stroke survivors will suffer from long-term, hemiparetic drop foot [Burridge et al., 1997, Leane et al., 1998]. Drop foot involves an inability to dorsiflex the ankle joint during the swing phase of gait, loss of normal knee flexion, inability to initiate the "push-off" in the beginning of the swing phase, and spasticity of the calf muscle group [Lyons et al., 2002].

The first successful application of a transportable FES system utilised for drop foot correction was proposed by Liberson et al. [1961], who stimulated the peroneal nerve to prevent the drop foot and made use of a foot-switch to synchronise the application of electrical stimulation to the swing phase of gait. The simple system consisted of a power supply that could be worn by the patient in a belt, two stimulation electrodes, and a heel-switch (see figure 3.1). When the heel-switch (K) was open during the swing phase, a shunt resistor (S) was open-circuited and electrical stimulation delivered across the stimulation electrodes, E1 and E2. When the switch on the other hand was closed during the stance phase, the shunt resistor was connected across the output of the stimulator and no stimulation was delivered to the electrodes.

Since the pioneering work by Liberson et al. [1961], several similar applications were proposed. The first FES systems developed in the 1960's and 1970's were single-channel applications based on surface

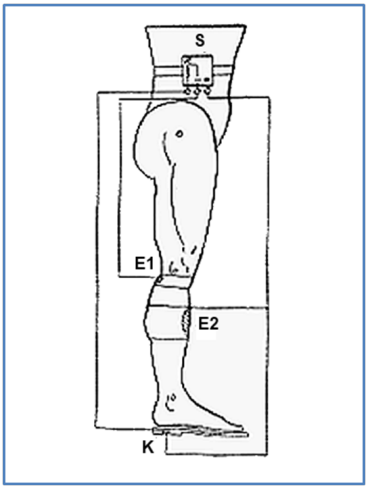


Figure 3.1: *The drop-foot stimulator approach proposed by Liberson et al. [1961].*

electrodes. During the 1980's and later on, the systems became more sophisticated as more stimulation channels were added with the purpose to stimulate several muscles controlling specific joints of the paretic leg during both stance- and swing phases of gait. The basic idea behind these stimulators was to stimulate the knee extensor muscles during the stance phase to stabilise the leg, and the common peroneal nerve during the swing phase to elicit the Nociceptive Withdrawal Reflex (NWR) and thereby prevent drop foot [Bajd et al., 1983, Graupe and Kohn, 1998, Postans, 2004, Fuhr et al., 2008].
Figure 3.2 shows a schematic overview of the four-channel system proposed by Fuhr et al. [2008], who built a control system for standing, walking, sitting down, and stair climbing based on common peroneal nerve stimulation to flex the knee and hip joints and to dorsiflex the ankle joint. Furthermore, the following muscles were stimulated: quadriceps to generate knee extension torques, gluteus to generate hip extension torques, and finally the hamstrings to generate flexion torques at the knee joint. The onset of stimulation to the different electrodes were triggered by a controller and relied on feedback from patient-mounted sensors monitoring joint angles in the lower leg, velocities, and ground reaction forces, and from cane-mounted finger switches that could be triggered manually by the patient.

The multichannel electrical stimulation opened the door to stimulate several muscles in different stimulation patterns to create a more fluent gait. However, most of these multichannel system suffered from several drawbacks, such as fast development of muscle fatigue due to continuous muscle stimulation, difficulties with donning and doffing of the system, and problems with tolerating the electrodes (which reduced the systems applicability to be used as a home-device).
Another drawback is the limited number of muscles that can be activated by the use of surface stimulation. Some of the deeply located muscles utilised in gait, e.g. the main hip flexor (iliopsoas) can not be activated by surface stimulation.
To account for some of these drawbacks, *implantable* neural prostheses based on intramuscular or implantable electrodes were proposed during the 1980's [Lyons et al., 2002]. Implantable stimulators for FES can be used for selective muscle or nerve stimulation. Originally, single channel devices were developed for the correction of drop foot and implanted in many hemiparetic patients with positive experience. One example of a commercially multi-channel drop foot stimulator is the implantable system called ActiGait™ from Neurodan A/S, Aalborg, Denmark [Burridge et al., 2007]. This system allows

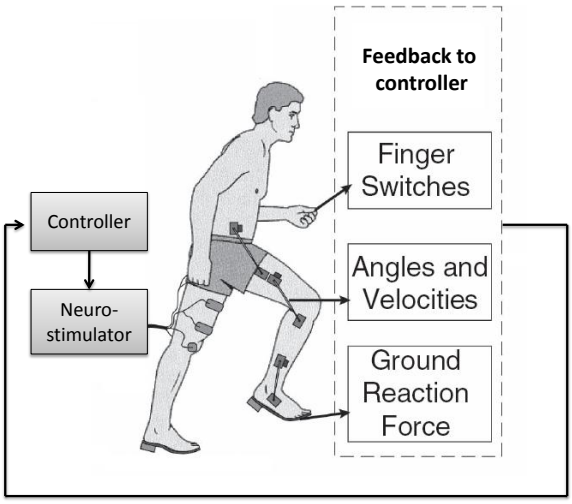


Figure 3.2: Schematic overview of the "WALK!" system proposed by Fuhr et al. [2008]. *The system is a four-channel, sensor-driven closed-loop controller used to restore gait in paraplegic patients. The figure is modified from Fuhr et al. [2008].*

independent adjustment of stimulation output from each of four channels via a single nerve cuff placed around the peroneal nerve (see figure 3.3). The system is composed of the implant, a control unit, and a heel-switch that is used for triggering each stimulation sequence. The nerve cuff is connected to a receiver positioned laterally on the thigh via a subcutaneous cable. The patient wears a control unit in a belt in which an antenna is positioned over the receiver. Electrical stimulation is activated by a radio frequency wireless signal from the foot-switch placed in the patient's shoe. [Burridge et al., 2007]

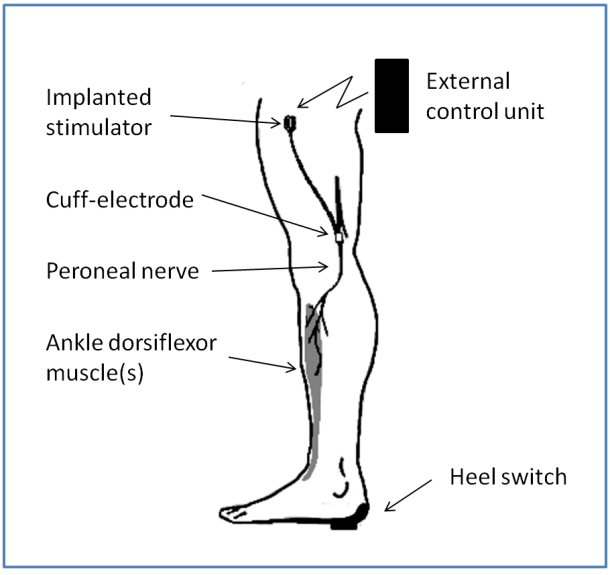


Figure 3.3: The ActiGait system. *The figure is modified from Burridge et al. [2007].*

3.2.2 A new FES approach based on elicitation of the NWR from the sole of the foot

As indicated in the text above, common peroneal nerve stimulation has been widely used to elicit the NWR and thereby lift the foot from the ground to initiate the swing phase. There are, however, some drawbacks of using peroneal nerve stimulation to evoke the reflex. First of all, there is a long latency of the mechanical reflex response making it difficult to determine the stimulation onset to time the reflex response to the gait cycle. Furthermore, peroneal nerve stimulation is subject to habituation, which reduces the mechanical responses over time.

As an alternative to common peroneal nerve stimulation to elicit the NWR, the reflex response can in stead be evoked by electrical stimulation delivered to the sole of the foot [Lee and Johnston, 1976, Decchi et al., 1997, Andersen et al., 1999]. Recent studies have indicated a modular organisation of the NWR resulting in different withdrawal strategies dependent on stimulation site at the sole of the foot [Andersen et al., 1999] and phase of the gait cycle at which the stimulation is delivered [Spaich et al., 2006] (a detailed description of the modulatory aspect of the NWR will be described in chapter 4). Thus, it is possible to tailor the desired response to the needs of the individual stroke patient. In addition, the effect of habituation can be decreased by changing stimulation pattern and not use the same site for stimulation every time. [Granat et al., 1993]
This approach was utilised in a closed-loop swing phase controller proposed by Emborg et al. [2011]. Their idea was to exploit the modular organisation of the NWR to implement a controller designed to choose the best stimulation parameters based on four electrode locations on the sole of the foot and three different stimulation onsets in late stance/early swing. Measures from goniometers at hip, knee, and ankle joints of the affected leg were fed back to the controller and used to select the best stimulation parameters to support the next step. The triggering of stimulation was controlled by Force Sensitive Resistors (FSRs) placed at the heel and big toe on the affected foot. Figure 3.4 shows a schematic drawing of the system.

The system proposed by Emborg et al. [2011] was not developed as a FES device for long term use, but was instead intended to function as a therapeutic tool that can be utilised in the rehabilitation of sub-acute stroke patients. The purpose of the system was to facilitate functional exercises and help the patient to achieve a lasting increase in gait function. This therapeutic approach is called Functional Electrical Therapy (FET) and is the scope of the next section.

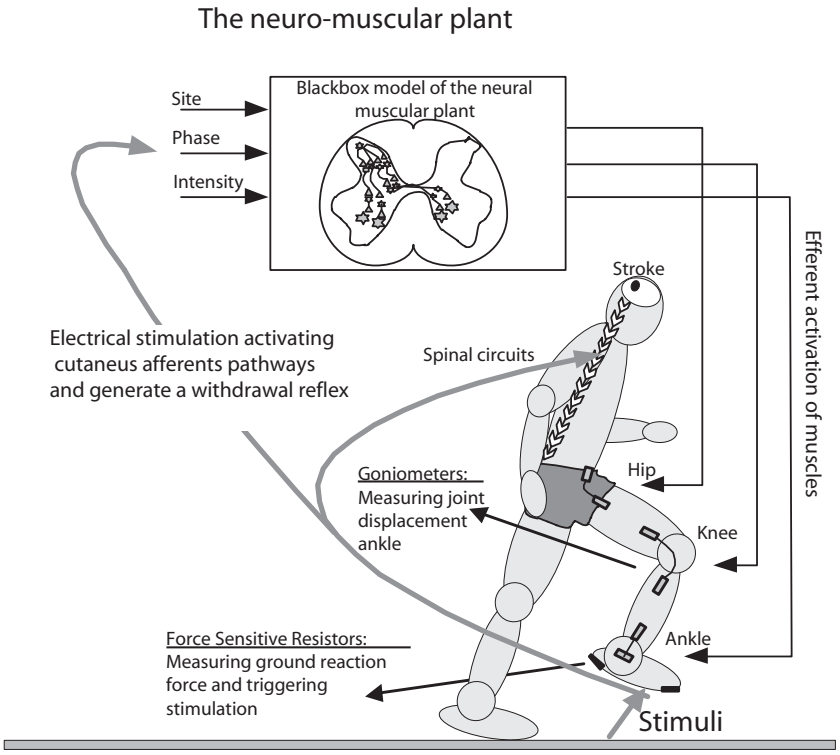


Figure 3.4: Schematic overview of the closed-loop control system proposed by Emborg et al. [2011]. *Electrical stimulation delivered to the sole of the foot evokes the NWR to withdraw the foot from the stimulus by activation of several muscles controlling hip, knee, and ankle joints dependent on the stimulation parameters. Goniometer output from hip, knee, and ankle is fed back to the controller in order to select the best stimulus parameters to support the coming step. Force sensitive resistors are used to trigger the stimulation.*

3.3 Functional Electrical Therapy

FET is a relative new therapeutic approach that combines FES with task-dependent voluntary exercise. The basic idea is that the stoke patient uses a neural prosthesis while performing intensive exercise in the sub-acute phase after stroke to facilitate functional motor control. The intention of FET is that the exercises result in an increase in function that outlasts the use of the prosthesis.
The background for FET is that many stroke patients using FES on a regular basis have experienced a significant carry-over effect in function that persisted when the FES device was no longer used [Rushton, 2003]. The carry-over effect of FET may be explained by the plasticity of the brain: it is possible that extensive use of the affected limb may produce a use-dependent cortical reorganisation that leads to regaining of motor control. [Popović and Sinkjaer, 2003]

The promoting effect of FET on walking has recently been demonstrated in acute stroke patients by Kojović et al. [2009]. They introduced a FET system based on a sensor-driven four-channel stimulator that stimulated four muscle groups (quadriceps, hamstrings, soleus, and tibialis anterior) in a particular pattern during walking. The system was tested in 13 acute stroke patients, who were assigned either to a FET group or to a CONTROL group. Both groups participated in a standard rehabilitation program and

45 minutes of gait training each day for 5 days and over the course of 4 weeks. The FET group received electrical stimulation via the FET system during walking, while the CONTROL group did not.

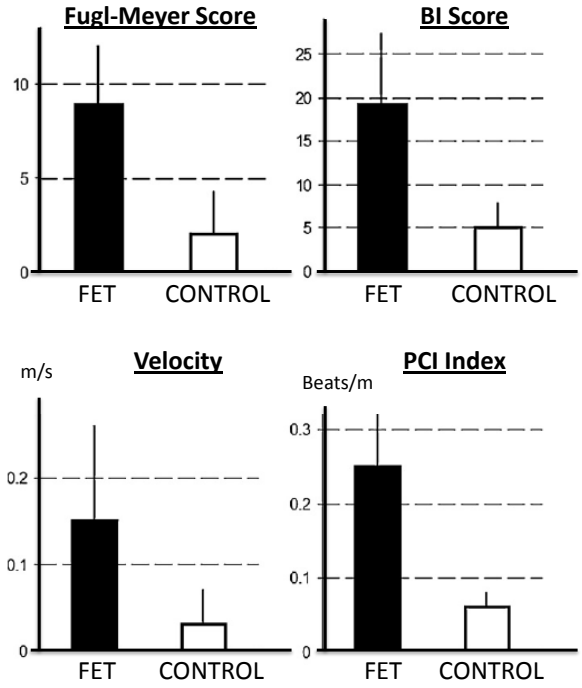


Figure 3.5: Outcome measures from the described FET study. *The bar plots show changes in Fugl-Meyer scores, Barthel Index (BI) scores, velocity of walking, and Physiological Cost Index (PCI) between the entry point and end point of treatment for both groups. Black bars indicate changes observed in the FET group and open bars indicate changes observed in the CONTROL group. Modified from [Kojović et al., 2009].*

Effect assessments of the rehabilitation program were performed in the beginning of therapy and after four weeks. The outcome measures were composed of the reduced Fugl-Meyer (FM) test for assessing the impairment of the lower extremities [Gladstone et al., 2002], Barthel Index (BI) that assesses functional abilities of the subject [Sulter et al., 1999], the mean walking velocity of the subjects, and finally the Physiological Cost Index (PCI), which is an indicator of the increased physical activity since it measures heart beats per meter of ambulation. The subjects in the two groups showed comparable baseline outcome measures in the beginning of the treatment, but after four weeks, there were significant changes of all scores between the FET and CONTROL group ($P < 0.05$, paired t-test) (Figure 3.5). Thus, four weeks of intensive FET was able to promote recovery and improve gait after stroke.

The intention of the gait controller to be developed in this project is also to be used in FET of hemiparetic patients.

CHAPTER 4

ELECTRICAL STIMULATION PARAMETERS

This chapter contains information about electrical stimulation parameters and considerations in relation to eliciting the NWR and applying muscle stimulation. The chapter ends with a description of methods for quantification of the responses to electrical stimulation. Choices of specific stimulation parameters for reflex- and muscle stimulation, plus choice of quantification method for use in this project will be discussed and outlined.

4.1 The Nociceptive Withdrawal Reflex

4.1.1 The basic mechanism

Withdrawal reflexes are rapid, automatic defence responses that seek to draw the limb away from potential damaging stimuli. It is a basic protective mechanism which exists in almost all living species, preserving homeostasis and avoiding tissue damage.

The NWR is a spinal reflex and it is elicited by a painful stimulus that reaches the skin, e.g. by stepping on a sharp object (see figure 4.1). The NWR is mediated via polysynaptic pathways within the spinal cord and activates motoneurons that supply different muscles. Thus, the stimulation will cause contraction of several muscles in a coordinated manner in order to produce a response that draws the affected skin area away from the source of the pain.

The NWR response is caused by the activation of spinal circuits and it persists after complete transection of the spinal cord [Sandrini et al., 2005]. Thus, the neural circuits responsible for the reflex response are entirely contained within the spinal cord although it can be modulated by control signals descending from higher centres in the brain.

Sherrington [1910] was the first scientist to study the NWR in detail. He termed it the "flexion reflex" and on the basis of studies in animals, he concluded that the withdrawal seen after electrical stimulation of the ipsilateral limb was a stereotypical flexion reflex response.

According to textbook literature on the flexor reflex concept, e.g. Despopoulos and Silbernagl [2003], the nociceptive input causes excitation of those motoneurons that innervate flexor muscles and inhibits those that innervate extensor muscles of the stimulated leg. This phenomenon is termed reciprocal inhibition, since antagonist muscles in the stimulated limb are stimulated in the opposite way. Another reported mechanism of the NWR is the crossed-extension mechanism, which serves to maintain postural balance after the nociceptive stimulation, because the opposite leg is stretched to support the body weight of the person, while the flexor reflex pulls the leg away from the stimulus (shown in figure 4.1). The cutaneous input from the stimulus activates the flexor muscles that contract and activate Ia afferents, which cross to the other side of the body within the spinal cord and inhibit the extensor muscles in the opposite leg. However, recent studies on the human NWR argue against this picture of a stereotyped, "sherringtonian" flexion reflex, since it has been shown that the reflex response is site-modulated [Andersen et al., 1999, Spaich et al., 2004]. Hence, these studies suggest a more refined behaviour of the NWR.

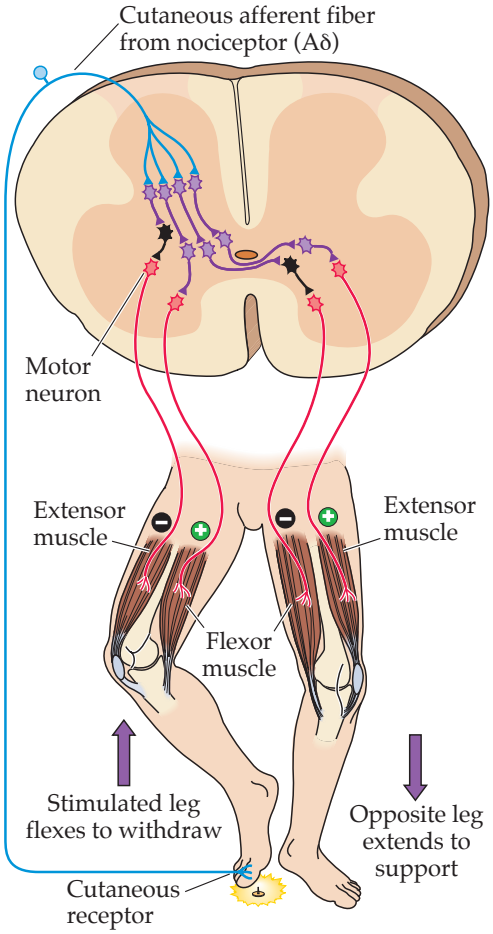


Figure 4.1: Schematic diagram of the NWR arc. *From [Purves and Augustine, 2004]*

4.1.2 Modulation of the NWR

The modulation of the NWR, and thereby the undermining of the classical flexor reflex concept, was shown from the middle of the nineteenth century. For instance, Grimby [1963] reported strongest tibialis

anterior responses when stimulating the medial and distal sole of the foot, and strongest gastrocnemius responses when stimulating the heel area of the foot. Since then, studies in both animals [Schouenborg and Kalliomäki, 1990, Schouenborg et al., 1992], and humans [Andersen et al., 1999, Sonnenborg et al., 2001] have reflected a modular organisation in the spinal reflex pathways, where each muscle or group of muscles have a cutaneous reflex receptive field from which a reflex can be evoked by a nociceptive stimulus. Thus, stimulation of a particular skin area will activate only the muscles needed for the biomechanically optimal withdrawal of the limb from the stimulus, and this exact withdrawal movement is dependent on the site of the stimulus.
The site modulation of the NWR has been studied by Andersen et al. [1999], Spaich et al. [2004, 2006], who found that electrical stimuli delivered to the distal stimulation sites on the sole of the foot evoked a distinct ankle dorsiflexion, while stimuli delivered to proximal sites evoked plantarflexion of the ankle joint.

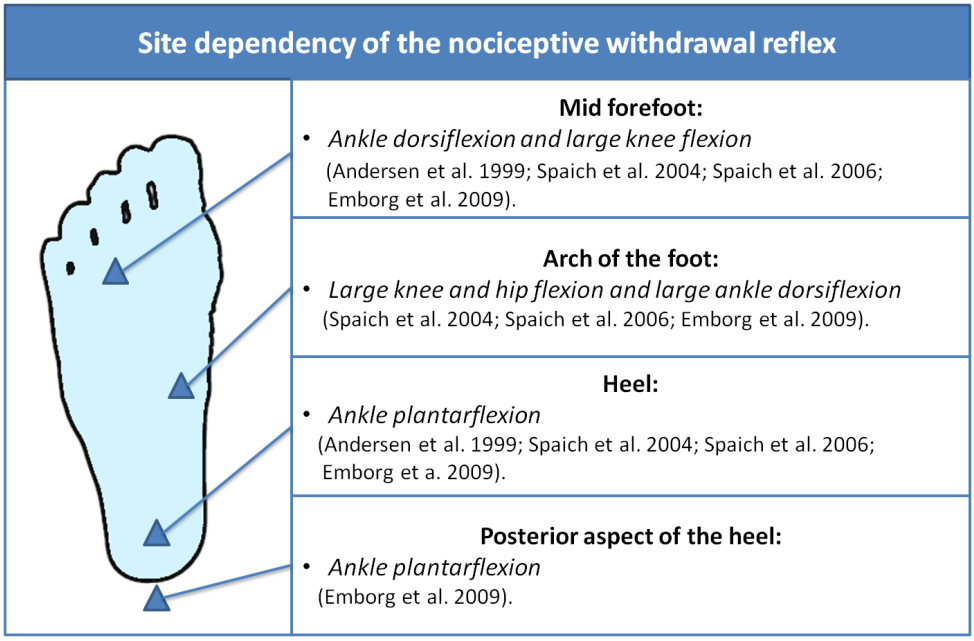


Figure 4.2: Site modulation of the NWR. *References are indicated in the figure.*

In addition to site modulation, studies on NWR modulation of the lower limb have shown that the intrinsic reflex response is also modulated by stimulation intensity [Kugelberg et al., 1960, Sonnenborg et al., 2001] and stimulation pulse frequency [Arendt-Nielsen et al., 2000]. Furthermore, reflex experiments during gait indicate that the reflex response is dependent on the phase of the gait cycle at which the electrical stimulus is delivered to the sole of the foot. In healthy individuals, stimulations near toe-off have primarily been accomplished by ankle dorsiflexion, whereas stimulations near heel-off have produced flexion of the knee and hip joints [Spaich et al., 2009, Emborg et al., 2009]. Hence, the withdrawal response elicited by painful electrical stimulation of the sole of the foot depends on several stimulation parameters. Figures 4.2 and 4.3 summarise the general findings on site- and phase modulation of the NWR.

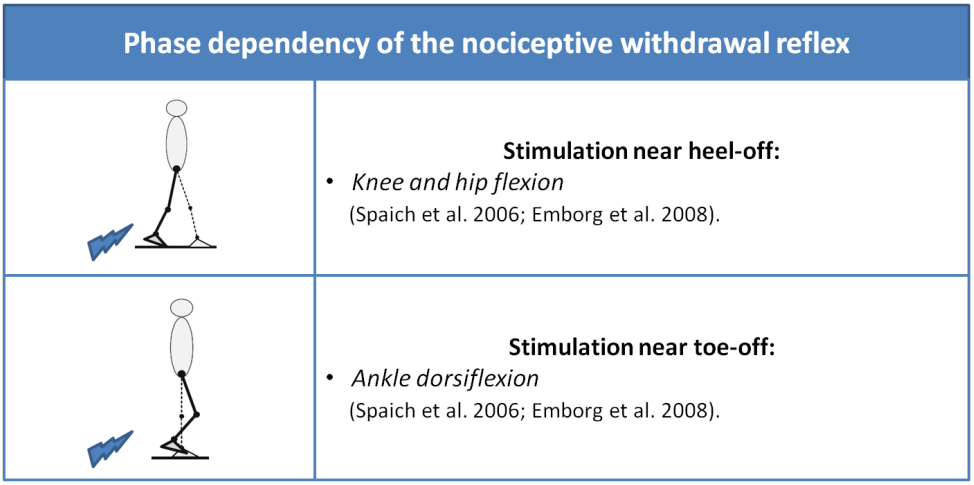


Figure 4.3: Phase modulation of the NWR. *References are indicated in the figure*

Stimulation parameters are, however, not the only parameters affecting the NWR response. The processing in the spinal cord integrates relevant afferent input, descending modulatory signals, and descending motor commands when determining the withdrawal strategy from the stimulus. Possible descending modulatory inputs might be determined on the background of the cognitive state of the subject. Inhibition of the NWR responses has for instance been reported during relaxation [Defrin et al., 2007], and attention to stimulation [Bjerre et al., 2011], whereas facilitation of the NWR responses has been reported when a warning signal was introduced prior to stimulation [Floeter et al., 1998] and during cognitive tasks that distracted the participant from the stimulation [Bjerre et al., 2011].

4.1.3 Elicitation of the NWR in experimental settings

Cutaneous stimulation such as mechanical, thermal, or electrical stimuli can be used to elicit the NWR. In most human studies, transcutaneous electrical stimulation is used to elicit the reflex, because it causes minimal tissue damage and because this method has a high level of reproducibility, obtained by activating the afferent nerves directly [Mørch et al., 2007].
Electrical stimulation is chosen as stimulation method in this project because stimulation parameters are easy to control through a computer program, and because the method is easier to apply during functional tasks, such as walking, than e.g. mechanical stimulation, especially taken into account that one of the goals of our experiments is to deliver stimulations at different sites and at different phases of the gait cycle.

4.1.4 Choice of stimulation parameters to elicit the NWR

Stimulation sites and electrode positions

To trigger a withdrawal of the foot, which is desired to initiate the swing phase of gait, electrical stimulation can be delivered to the sole of the foot through self-adhesive electrodes and with a common anode attached to the dorsum of the foot [Andersen et al., 1999, Emborg et al., 2009, Spaich et al., 2009].

This approach is also used in the present project, and three stimulation sites on the sole of the foot are chosen: the mid forefoot (R1), the arch of the foot (R2), and the posterior aspect of the heel (R3), see figure 4.4. The stimulation electrodes are attached to the defined sites on the sole of the foot to evoke different withdrawal strategies on the background of the findings from figure 4.2.

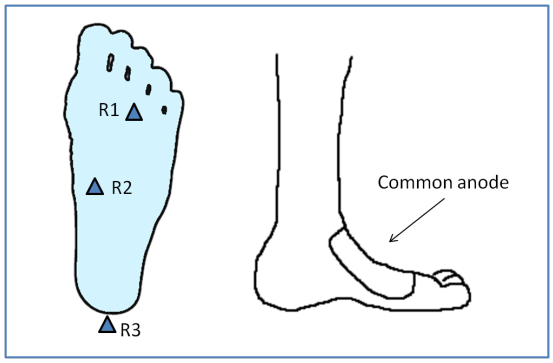


Figure 4.4: Electrode positions used in the this project to elicit the NWR.

Furthermore, it is decided to include dual channel stimulation, i.e. delivering of two electrical stimulations to two different sites on the sole of the foot during the same swing phase. Dual channel stimulations are included in order to elicit a train of two reflexes just after each other, and we hypothesise that this configuration will create a more controlled steering of the leg through the swing phase.
The first reflex should be elicited from either the forefoot or the arch of the foot, and the second reflex from the posterior aspect of the heel. It is hypothesised that the stimulation of the posterior aspect of the heel will create a forward propulsion of the foot, since the withdrawal away from the stimulus has this direction. Thus, the purpose of the first reflex is to lift the foot from the ground and create the appropriate hip and knee flexion, whereas the purpose of the next reflex is to maintain the hip and knee flexion, but also to "push" the foot forward in preparation of the next heel-strike. The proposed movement is illustrated in figure 4.5.

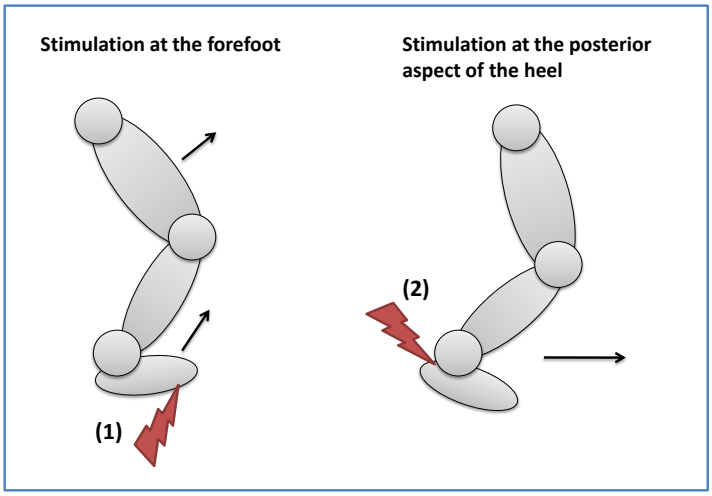


Figure 4.5: Proposed mechanical responses caused by dual channel stimulation to elicit the NWR. *The dual channel stimulation should be delivered to two different sites on the sole of the foot in late stance/early swing.*

Stimulation intensity

The stimulation intensity has previously been normalised to the pain threshold in several reflex studies, e.g. [Andersen et al., 1999, Emborg et al., 2009], to ensure equal afferent input to the different electrode sites and thereby allowing the comparison of the reflex responses across stimulation sites. This means that the stimulation intensity at each electrode site is determined as the pain threshold detected at each electrode site multiplied by a fixed factor common to all sites, e.g. 1.5. It has recently been indicated, however, that this method of normalising the stimulus intensities on the sole of the foot to a certain threshold found at each electrode site will not necessarily result in equal sensory perception when stimulation is applied. Bjerre et al. [2011] compared the stimulation intensities at detection thresholds determined at ten electrode positions on the sole of the foot with the stimulation intensities adjusted to give a uniform sensory input corresponding to 1.5 x reflex threshold at the arch of the foot. To find the latter intensities, the participants were presented to the stimulation in the arch of the foot associated to 1.5 x reflex threshold and then asked to adjust the intensities at the remaining positions individually until stimulation at all positions felt the same way. The multiplication factor between the detection threshold and the matched 1.5 x reflex threshold at the arch of the foot was not uniformly distributed over the sole of the foot, but showed higher values at the heel compared to the values in the arch and at the central pads of the forefoot.

Hence, to obtain equal afferent input to all stimulation sites, the stimulation intensities in the present project is adjusted individually to give the same sensory perception as an intensity resulting in a clear facilitatory reflex in the arch of the foot.

Stimulation profile

It has been shown that repetitive stimulation can be used to obtain larger mechanical responses than achieved with a single electrical stimulus, because repetitive stimulation exploits the temporal summation property of the reflex [Andersen et al., 1999].
It is decided to use a stimulation profile as follows: each stimulus should consist of a constant current pulse burst of five 1-ms pulses delivered at 200 Hz, and this stimulus burst repeated four times at a frequency of 15 Hz.
A similar profile has been used by e.g. Meinck et al. [1985], Decchi et al. [1997] and Emborg et al. [2009], and the profile seems appropriate to elicit the NWR during gait.

Stimulation onsets

In experimental settings, where the NWR is evoked from stimulation at the sole of the foot, there will be a latency period between the stimulation onset and the mechanical response from the stimulation. This latency may last up to 360 ms after the stimulation onset [Crenna and Frigo, 1984, Spaich et al., 2006].
In applications having the goal to facilitate the initiation of the swing phase during gait, this latency period must be considered in the timing of the stimulation onsets. The late stance and the early swing phases are the target intervals to deliver the electrical stimuli to initiate the swing of the paretic leg in an appropriate manner [Quintern et al., 2003]. In former studies by Emborg et al. [2009, 2011],

stimulations were delivered at three different onsets to investigate the phase-modulation of the NWR. The onsets were set between heel-off and toe-off to ensure that the kinematic reflex response would occur within the current step and not too early or too late in the gait cycle. The stimulation onsets were: **(1)** *Heel-off + 10% of the heel-off/toe-off interval*, **(2)** *Heel-off + 50% of the heel-off/toe-off interval*, **(3)** *Toe-off*.
It is decided to use similar stimulation onsets in the present project. The onsets are indicated in figure 4.6.

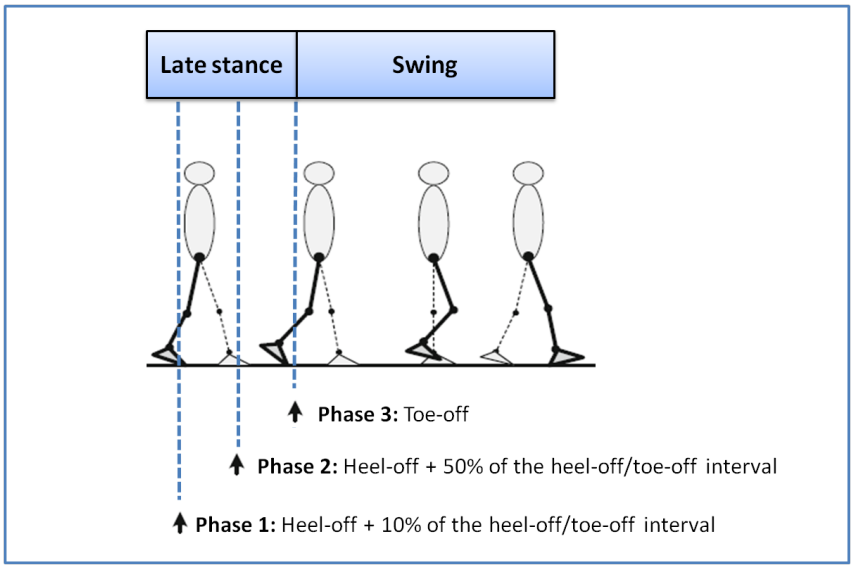


Figure 4.6: Stimulation onsets used in the present project to elicit the NWR during gait. *A similar onset approach has been used by [Emborg et al., 2009, 2011]. The figure is modified from [Emborg et al., 2009].*

Habituation of the NWR

The mechanical NWR response is subject to habituation, which means that the response gradually disappears if the same stimulation site is stimulated repetitively with the same stimulation intensity. Habituation is a drawback of using the NWR as a mechanism to initiate the swing phase, because it is difficult to rely on a reflex response that cannot be reproduced continuously when stimulation parameters are kept the same.
However, habituation of the reflex response can be minimised by changing the stimulation parameters. A study by Dimitrijević et al. [1972] has shown that habituation can be reduced by varying the stimulus intensities and the inter-stimulus intervals. Furthermore, Granat et al. [1993] has shown that multiplexing, i.e. varying the stimulation sites, can dishabituate the reflex response.

To avoid the effect of habituation in the present project, reflex stimuli are delivered at different locations on the sole of the foot, and at non-homogeneous inter-stimulus intervals.

4.2 Muscle Stimulation

4.2.1 The basic mechanism

Electrical muscle stimulation, also known as neuromuscular electrical stimulation, is the elicitation of muscle contractions using electric impulses. Electrical muscle stimulation is generally delivered through electrodes placed on the skin over the motor point of the muscle of interest. When electrical stimulation is applied to the skin via surface electrodes, motoneurons will be excited along with sensory fibres if the stimulation parameters meet or exceed their thresholds of excitation. In fact, sensory fibres will be activated before motor activation occurs, since they are located in the skin closest to the electrode. This is why the electrical stimulation can be felt before motor activation occurs.

Despite the fact that both adequate electrical stimulation and natural activation of a muscle results in its contraction, there are several differences between the two activation methods that need to be taken into account when designing a system using electrical muscle stimulation. These considerations are discussed in the following section.

4.2.2 Considerations when determining muscle stimulation parameters

Motor unit recruitment

During activities that are initiated by the central nervous system, small motoneurons with slow-fatiguing motor units are typically excited first. As more force is demanded, progressively larger and larger motor units are recruited [Hennemann et al., 1965]. When electrical stimulation is used to contract a muscle, the motoneurons activated first are generally those supplying the larger and more easy fatigueable motor units, since large fibres have a lower impedance than smaller fibres and therefore have a lower excitation threshold to externally applied currents. To excite the smaller motor units, capable of prolonged contractions without fatigue, the stimulation intensity must be increased, see figure 4.7. Thus, the phenomenon of the reversed recruitment order, when using electrical stimulation, causes muscle fatigue at a faster rate than with natural stimulation. Furthermore, the fine motor control of the innervated muscle is reduced during electrical stimulation, since primarily the smallest motor units are responsible for fine control [Baker et al., 2000, Despopoulos and Silbernagl, 2003, Rattay, 1990].

Synchronous versus asynchronous activation of motor units

In physiologic activity, the motoneurons of a muscle are recruited at different times and thereby excited asynchronously. This mechanism causes the muscle fibres to contract and relax at different times, allowing a smooth and continued contraction. The activation of muscles by electrical stimulation, however, results in an synchronous activation, since nerve fibres either fire an action potential or stay quiet as a response to stimulation. Because of this, stimulus frequencies must be higher than physiologic firing rates to obtain the same smooth contraction. Higher firing rates, however, contribute to more rapid muscle

fatigue. Thus, determining the stimulation frequency is a trade-off between the force level demanded and the development of muscle fatigue. [Baker et al., 2000, Rattay, 1990]

Effect of altering pulse duration and stimulation intensity

There is an inverse relationship between the pulse duration and the pulse amplitude of electrical muscle stimulation: The use of short duration stimulation pulses requires a high stimulation intensity to achieve excitation of the muscle fibres, and vice versa. Altering the stimulation intensity also alters the recruitment of muscle fibres as indicated in figure 4.7. Figure 4.7a illustrates a population of fibres excited by a current pulse of low intensity and a fixed duration. The excited fibres will be those closest to the stimulation electrode and, following the size ordering of excitability to electrical stimuli, those largest in diameter. If the intensity of stimulation is increased as shown in figure 4.7b, the stimulation will cause excitation of additional fibres, including both smaller fibres near the electrode and larger, deeper fibres. Thus, the recruitment of motoneurons by electrical stimulation is not strictly the inverse of voluntary recruitment, because smaller fibres closer to the electrode will also respond to increasing stimulus intensities. Increased recruitment can also be achieved by increasing the pulse duration of the stimulation. When additional motor units are recruited, the resultant motor response will cause more force.
Consequently, pulse duration of the muscle stimulation must be carefully matched with the stimulation intensity to achieve the desired motor response. [Rattay, 1990, Baker et al., 2000] Figure 4.8 demonstrates the variation of intensity and pulse duration required for excitation. Either stimulation intensity or pulse duration can be varied to control motor responses. On the given figure, a pulse duration of 400 μs enables the muscle force to be varied between threshold and maximal output by varying stimulation intensity within the interval 15-40 mA.

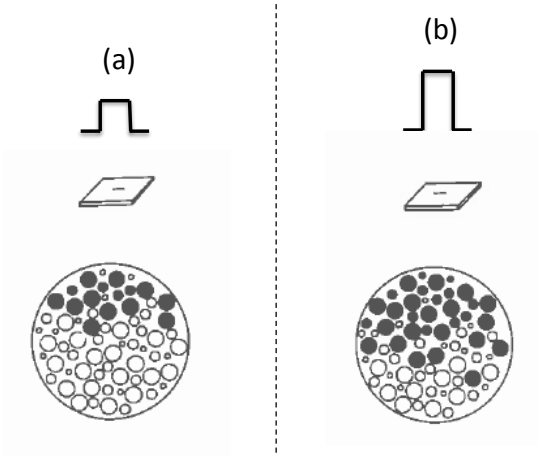


Figure 4.7: Recruitment order in a fibre when altering the electrical stimulation amplitude. *Figure (a) indicates that the largest fibres closest to the electrode will be excited at a certain stimulus intensity and pulse duration. If the intensity is then increased, while the pulse duration is kept constant, deeper large fibres and small fibres close to the electrode will be excited as well (b). Modified from Baker et al. [2000].*

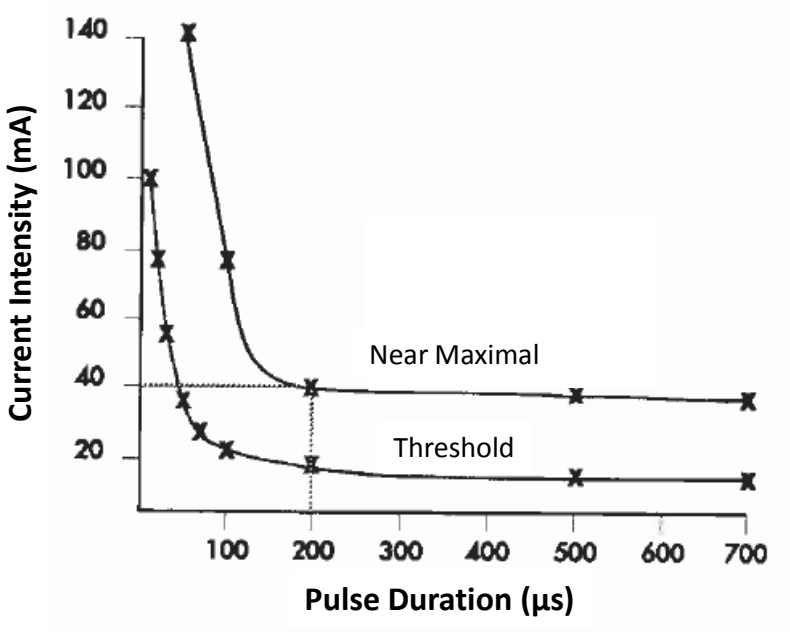


Figure 4.8: Variation of stimulation intensity and pulse duration necessary for excitation. *The figure indicates excitation at two levels: threshold for the largest and most excitable motoneurons, and the near maximal level corresponding to a motor response where even the smallest and least excitable motoneurons are activated. The figure is based on data from surface stimulation (35 Hz) of wrist extensor muscles [Baker et al., 2000].*

ON-OFF times of stimulation

The relationship between the amount of time the stimulation is turned on and the amount of time it is turned off is an important factor in the onset of muscle fatigue. This means that ON-OFF times can be used to reduce the problem of fatigue and thereby ensure that the clinical treatment with muscle stimulation can be maintained for a long enough period of time to achieve specific therapeutic goals.

ON:OFF ratios are calculated as the ratio between the ON- and OFF-time. Thus, a one second ON, three seconds OFF stimulation program would have an ON:OFF ratio of 1:3. The duration of the ON-time determines how long the motor response will be maintained, and the OFF-time determines the resting time before the next stimulation. By allowing the stimulated tissue to relax between each stimulation, the degree of fatigue can be decreased and the quality of the contraction during the ON-time is maintained over a longer period of time. Figure 4.9 illustrates the effect of varying the ON:OFF ratios on muscle fatigue. [Baker et al., 2000]

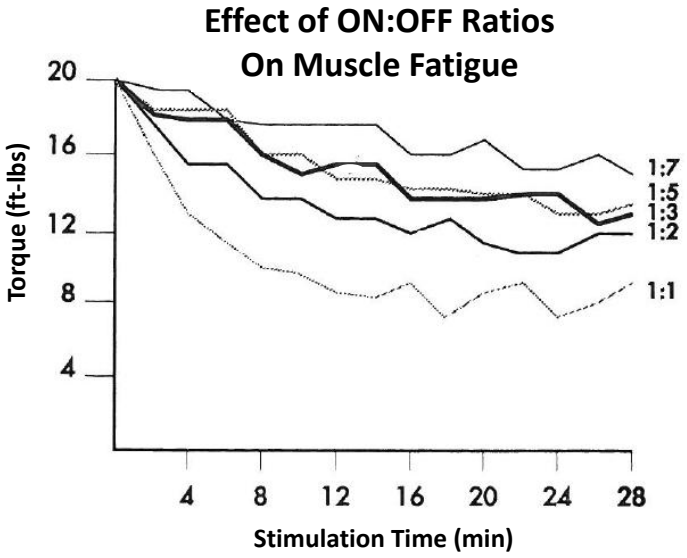


Figure 4.9: Effect of ON:OFF times on muscle fatigue. *The ON:OFF ratio has a great influence on the development of muscle fatigue. The figure is made on the basis of data from surface stimulation of quadriceps (300 μs pulses, 35 Hz) with a constant ON-time of four seconds, while the corresponding OFF-times were varied. [Baker et al., 2000]*

4.2.3 Muscle stimulation to support the stance phase of gait

Our gait controller should apply muscle stimulation in the stance phase of gait to support and stabilise the paretic leg. From figure 2.2 in chapter 2, it became evident that several muscles are activated during locomotion of non-impaired subjects. The figure contains data from 28 different muscles in the legs of which many are activated during the stance phase. It is not possible, however, to stimulate all of these muscles by electrical surface stimulation due to the deep location of some of the muscles and due to the limited number of stimulation channels. Table 4.1 summarises the main muscle function during gait of non-impaired subjects. Electrical stimulation of the quadriceps (QA) muscles has been utilised in several studies to extend the knee during hemiparetic gait and thereby provide a better weight bearing by the paretic leg, e.g. [Bajd et al., 1983, Bogataj et al., 1995, Kojović et al., 2009]. The soleus muscle (SOL) has also been stimulated in previous studies to provide further weight bearing during late stance and contribute to the push-off before the swing phase [Bogataj et al., 1995, Kojović et al., 2009]. Both QA and SOL are good candidates for muscle stimulation, since stroke patients often have problems maintaining balance during the stance phase of the paretic leg and obtaining push-off due to decreased plantarflexion at toe-off [Moseley et al., 1993].

Another candidate for muscle stimulation during the stance phase of hemiparetic gait is the gluteus maximus muscle in order to provide a increased hip extension [Bogataj et al., 1995, Fuhr et al., 2008]. However, Kojović et al. [2009] found in a recent study that stimulation of the gluteus muscles was impractical, since there was no significant functional benefit of the stimulation and the positioning of the electrodes was inconvenient for the participants.

Thus, the muscle stimulation in this project is decided to consist of two channels targeting the QA- and SOL muscles of the affected leg.

Muscles	**Gait cycle function**
Gastrocnemius and soleus	Midstance to heel-off
Gluteus maximus	Heel-strike to midstance
Gluteus medius and minimus	Heel-strike to toe-off
Hamstrings	Midswing to heel-strike
Iliopsoas and adductors	Toe-off to midswing
Quadriceps	Heel-strike to midstance
	Toe-off to midswing
Tibialis anterior and peroneals	Heel-strike to foot flat
	Toe-off to heel-strike

Table 4.1: Main muscle function for non-impaired ambulation. *From DeLisa [1998].*

4.2.4 Choice of muscle stimulation parameters

Stimulation sites and electrode positions

As indicated above, it is decided to achieve support of the paretic leg in the stance phase by applying electrical stimulation the QA- and SOL muscles.

Quadriceps femoris (QA) is the large extensor muscle of the thigh, and it is composed of the muscles rectus femoris, vastus lateralis, vastus medialis, and vastus intermedius, see figure 4.10A. QA can generate hip flexion as well as knee extension. If QA stimulation is used to stabilise the paretic leg during the stance phase of gait, only knee extension is desirable, because hip flexion will disturb the patient's balance when standing. When hip flexion is not desirable, stimulation of the rectus femoris should be avoided [Baker et al., 2000]. This can be achieved by placing the proximal electrode over the lateral muscle bulk of the thigh and the distal electrode medially, above the patella (figure 4.10B).

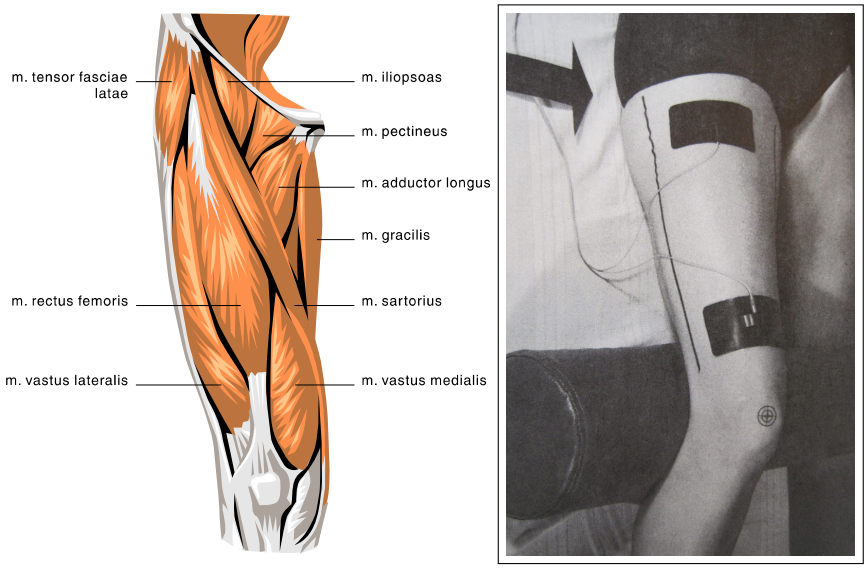


Figure 4.10: A) Muscles in the thigh, frontal view. *From [Open Clip Art Libary, 2011].*
B) Electrode placement for QA stimulation *[Baker et al., 2000].*

The soleus muscle (SOL) is part of the calf muscles placed in the back part of the lower leg, see figure 4.11A. The function of the calf muscles, including the soleus, is plantarflexion of the ankle joint. The calf muscles are vital in walking and running, and the soleus muscle specifically plays an important tole in maintaining standing posture and prevent the body from falling forward.
SOL can be stimulated by placing the negative electrode below the bulk of gastrocnemius and the positive electrode above the Achilles tendon (see figure 4.11B). The strength of the plantar flexion contraction which may be generated using this electrode configuration is generally adequate to stabilise the tibia in upright posture [Baker et al., 2000].

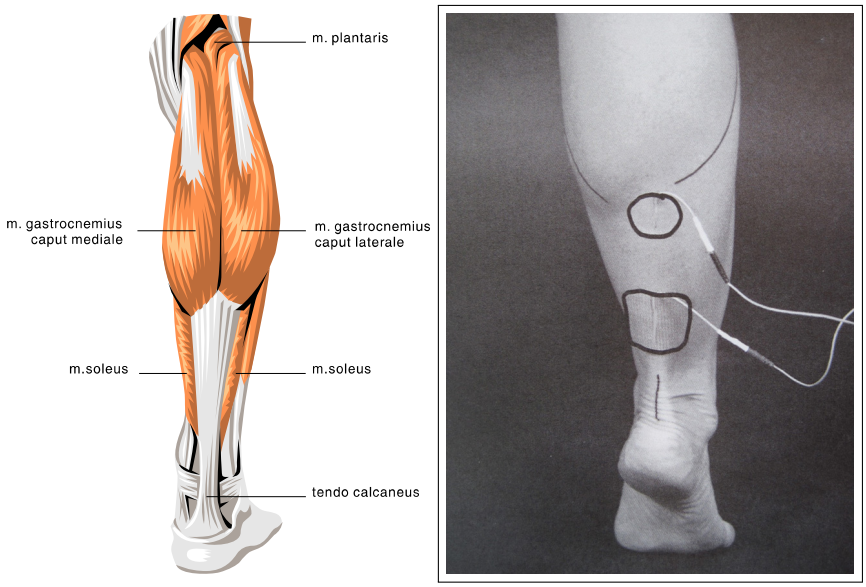


Figure 4.11: A) Muscles in the lower leg, posterior view. *From [Open Clip Art Libary, 2011].*
B) Electrode placement for SOL stimulation *[Baker et al., 2000].*

Stimulation intensity

The stimulation intensity or the current amplitude transferred to the skin is largely responsible for the strength of the sensory and motor responses evoked by the stimulation, since more and deeper neurons are activated at increased intensities.
In many experimental studies using FES to activate muscles, the stimulation intensity is the only stimulation parameter that is adjusted individually to the single participant in order to achieve the desired movement or contraction. Because sensory fibres are activated along with motor fibres, determining the intensity can be a trade-off between the desired motor response and the sensory tolerance of the participant. The goal is to find an intensity that results in an appropriate contraction, yet not too painful for the participant. [Baker et al., 2000]
In the present study, the stimulation intensity is determined by starting at low intensities and gradually turning up the current amplitude to familiarise the participant with the feeling of electrical stimulation. Visual inspection of the muscle contractions, palpation of the contracted muscles, and inspection of the evoked movements are used to determine the intensity to be used during the experiment.

Stimulation profile

The stimulation profile is composed of the stimulus pulse duration, stimulation frequency, and on-off times of stimulation (the latter aspect is discussed in the section about stimulation onsets).

In most clinical applications, the pulse duration is fixed at a certain level and the intensity is then determined by gradually increasing the current amplitude until a contraction that meets the determined criteria is reached. Stimulation with pulse durations between 200 and 400 μs has been shown to be within the comfort level of the user [Bowman and Baker, 1985] and efficient to provide a sensitive intensity control, see figure 4.8.
Stimulation frequency denotes the pulse repetition rate. A stimulation frequency capable of producing a fused tetanic contraction of the muscle is often desired in stimulation programs, since lower frequencies can result in a “tremorous” muscle contraction. A study about preference for pulse frequency, with surface stimulation of QA, showed that participants preferred higher stimulation intensities [McNeal et al., 1986]. However, frequency levels markedly higher than tetany threshold (usually around 50 Hz) result in faster development of muscle fatigue. [Baker et al., 2000]

It is decided to use a stimulation profile composed of 400 μs pulses delivered at 50 Hz with ramps lasting 1 ms (rising time and falling time). The stimulation profile is depicted in figure 4.12. A similar stimulation protocol was utilised in a recent study by Kojović et al. [2009], who also activated QA and SOL during the stance phase of hemiparetic gait.

Stimulation onsets

According to gait analysis of non-impaired participants, see figure 2.2 and table 4.1, the QA muscle is activated from the moment of heel-strike to mid-stance in order to keep the knee extended in the first part of the stance phase, and again from toe-off to mid-swing in order to extend the knee in preparation of the

next step. SOL is activated from mid-stance to heel-off. It is decided only to deliver muscle stimulation within the heel-on period of gait in order not to interfere with the elicitation of the NWR in the period from heel-off to toe-off. It is decided to stimulate QA in the first half of the heel-on period and SOL in the next part as indicated in figure 4.12. This configuration gives an ON-OFF ratio of approximately 1:5, which has been shown to be acceptable to avoid muscle fatigue over a 30 minute treatment period with short ON-times [Packman-Braun, 1988].

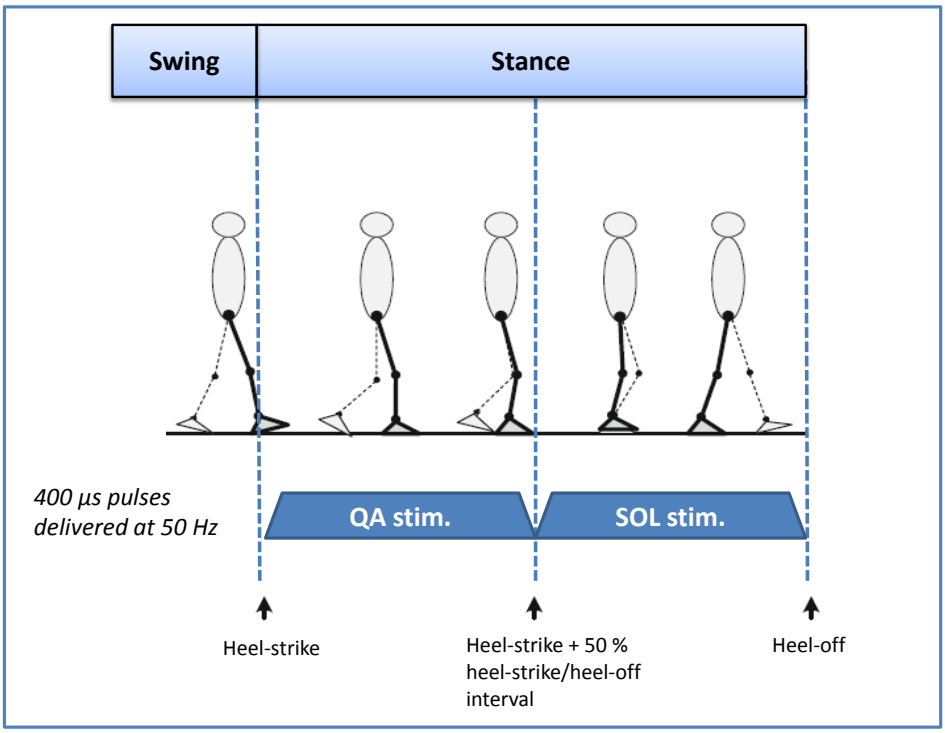


Figure 4.12: Stimulation onsets and durations for muscle stimulation used in the present project. *The muscle stimulation is delivered during the heel-on period of the paretic leg. QA is stimulated in the first half of the heel-on period to stabilise the knee joint by activating the knee extensors, while SOL is stimulated in the last half of the period to support the push-off prior to the swing phase.*

4.3 Quantification of the Response to Stimulation

To be able to investigate site- and phase modulation of the NWR and to investigate the effect of muscle stimulation on the gait we need a method to quantify the response to stimulation. Quantification has been done in several different ways in previous studies as described below.

4.3.1 EMG responses

Quantification of the NWR response by use of EMG recordings from selected muscles will often involve a description of the temporal characteristics of the response, and also an assessment of the "size" of the response. Thus, the EMG response from selected muscles can be utilised to quantify the NWR response. One method is to calculate the difference between the root mean square (RMS) of post- and pre-stimulation EMG [Andersen et al., 1995]. A drawback of using the EMG approach as a quantification method in a controller is that the recorded EMG signal often is the result of activity from the particular muscle plus eventually cross-talks from other muscles.
Regarding the muscle stimulation, it is not possible to record EMG from QA and SOL muscles during the stimulation period, because artefacts from the electrical stimulation will disturb the recordings.

4.3.2 Kinematic responses

Acquiring kinematic responses relates to the monitoring of the position of body segments over time. This can be done by mounting special markers on the joints of the participant and utilising 3D video motion analysis to record the position of the markers and thereby the kinematics during gait [Voigt and Sinkjaer, 2000]. The technique, however, is very time consuming and needs special and expensive equipment. This approach will therefore not be considered as a useful method to quantify the responses from our control system.
Other possibilities are the use of accelerometers or gyroscopes, which measure body-segment acceleration and angular displacement, respectively. Joint angles can be calculated and monitored from the output of both accelerometers and gyroscopes, but this requires additional signal processing [Rueterbories et al., 2010].
Finally, another method to monitor the relative position of the lower limbs is to use goniometers attached over the hip, knee, and ankle joints. A goniometer is a electro-mechanical device that span the joint to be measured with attachments to the proximal and distal limb segments. The goniometer provides an output voltage that is proportional to the angular change between the attachment surfaces, i.e. the angular change at the particular joint. The kinematic responses caused by the NWR and muscle stimulation can then be calculated as the relative change in hip, knee, and ankle joint angles between the goniogram from a stimulation step and the corresponding baseline goniogram from an unpertubated step. The output value is denoted the peak angle change and a positive value indicates an increased flexion in the particular joint as response to reflex stimulation compared with baseline [Spaich et al., 2009].
The use of goniometers do not require specific software or advanced signal processing to obtain the joint angles. Furthermore, they are quite easy to attach to the lateral side of the joints on the participants.

However, a drawback of goniometers is their relative poor accuracy and the fact that the output from the goniometers may drift over time caused by the body heat from the participant.

4.3.3 Choice of quantification method

On the background of the description of different quantification approaches above, it is decided to utilise the output from goniometers to quantify the NWR- and muscle stimulation responses.

CHAPTER 5

SYSTEM DESCRIPTION

The aim of this project is to design and implement a gait controller that combines the excitation of the NWR to initiate the swing phase, with muscle stimulation to give support and stability during the stance phase of hemiparetic gait. This chapter contains a system description of the gait controller and summarises the electrical stimulation parameters chosen to be used for eliciting the NWR and muscle stimulation in chapter 4.

Initiation of the swing phase by eliciting the NWR

It has previously been shown that the NWR response can be modulated by varying stimulation site and phase of the gait cycle at which the stimuli are delivered. Therefore, the basic idea behind the gait controller developed in this project is to make use of response modulation to be able to tailor the stimulation sequence so the best combination of site and phase is chosen to support the needs of the individual patient in the current step.

The NWR should be elicited via repetitive electrical stimulation delivered as a train of four bursts repeated at 15 Hz, each containing five 1-ms pulses delivered at 200 Hz. It should be possible to deliver single channel stimulation at three different electrode sites (mid forefoot (R1), arch of the foot (R2), and posterior aspect of the heel (R3)), and dual channel stimulation at two different site combinations (R1+R3 and R2+R3) as indicated on figure 5.1.
The stimulation should be initiated at one of three different onsets in the period from heel-strike to toe-off [Emborg et al., 2009, 2011], see figure 5.1.

Support and stability during the stance phase by use of muscle stimulation

Muscle stimulation should be delivered to QA during the first half of the heel-on period to activate knee extensors and thereby provide a stabilising support of the leg, and to SOL during the last half of the heel-on period to provide support and assist with push-off prior to the swing phase.

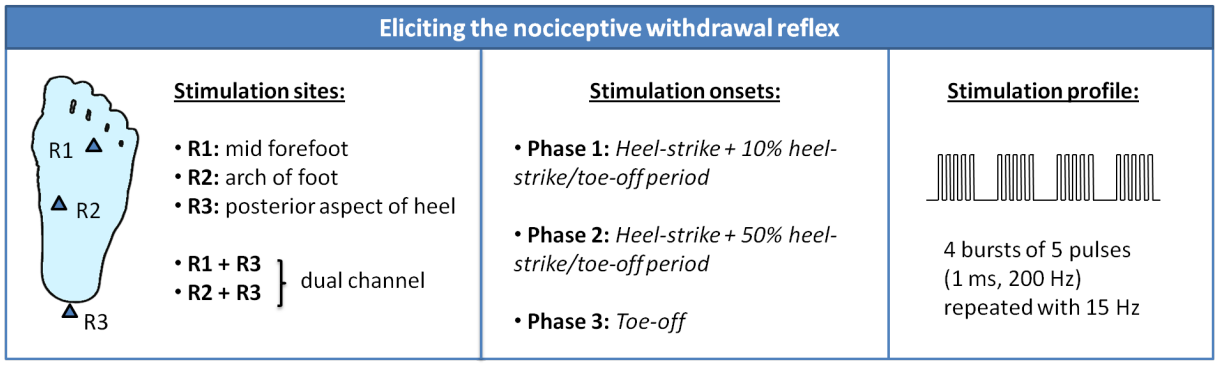


Figure 5.1: Stimulation profile, stimulation sites, and stimulation onsets to be utilised in the gait controller for eliciting the NWR to initiate the swing phase of hemiparetic gait.

The stimulation should consist of 400 μs pulses delivered at 50 Hz [Kojović et al., 2009] with ramps lasting 1 ms (rise- and fall-time). The parameters of the muscle stimulation are decided to be kept the same during the use of the gait controller (the same stimulation configuration should be used in each step). The stimulation parameters are summarised in figure 5.2.

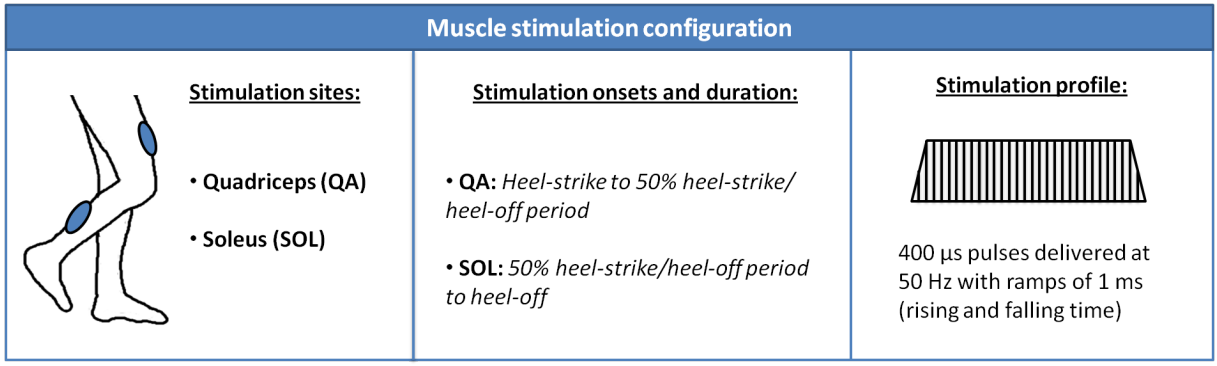


Figure 5.2: Stimulation profile, stimulation sites, and stimulation onsets to be utilised in the gait controller for muscle stimulation of QA and SOL to support and stabilise the paretic leg during the stance phase.

Gait controller

A schematic approach of the gait controller to be designed is illustrated in figure 5.3. The controller should manage the stimulator that delivers electrical stimulation to QA and SOL muscles, and to the stimulation sites at the sole of the foot. The aim of the controller is to choose the best stimulation sequences to support the gait of the specific user and to deliver the stimulations at specific time points in the gait cycle.

In order to investigate the kinematic responses obtained as a result of the electrical stimulations, joint angles from hip, knee, and ankle of the affected leg should be continuously monitored by use of goniometers.

The detection of gait events should be achieved by the use of FSRs placed on the heel and big toe of the user. The signals from these heel- and toe-switches should then be fed back to the controller and used to trigger the exact onsets of stimulation.

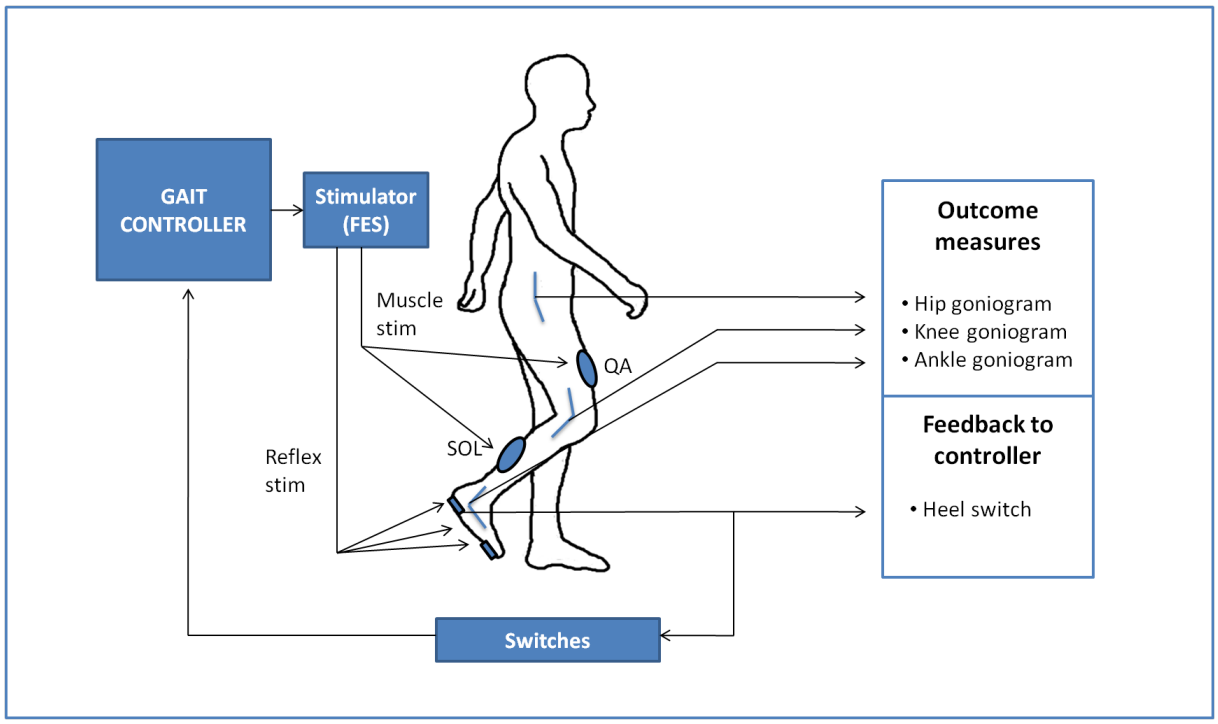


Figure 5.3: Schematic overview of the gait controller to be developed in this project. *The controller stimulates QA and SOL muscles during the stance phase, and elicits the NWR from the sole of the foot to initiate the swing phase. Signals from heel- and toe-switches are fed back to the controller and used to trigger the stimulation at the certain time intervals of the gait cycle. Goniograms from hip, knee, and ankle joints are used as output measures to investigate the evoked responses as a result of stimulation.*

Chapter 6

Problem Specification

The aim of this project is to design and implement a gait controller that combines the execution of the NWR to initiate the swing phase with muscle stimulation to give support and stability during the stance phase of gait. A control system like this has clinical relevance in the rehabilitation therapy of stroke patients.

To be able to design and implement the gait controller described in the System Description in chapter 5, two Case Studies on healthy- and hemiparetic participants, respectively, need to be conducted in order to model NWR responses and responses to muscle stimulation.

Based on the results from Case Study 1 and 2, the input-output relations for the gait controller is modelled, and the controller is designed and developed to assist the gait of a specific stroke patient.

The project can be divided into the following sub problems:

Experimental study on healthy participants (Case Study 1):

- Designing an experimental protocol for investigation of the kinematic responses achieved by combining muscle stimulation and elicitation of the NWR during gait in healthy participants.
- Designing a laboratory stimulation system in LabVIEW^{TM} to be able to deliver stimulation sequences and conduct the experiments.
- Conduction of the experiment on a number of healthy participants.
- Analysis of the acquired data.

Experimental study on a stroke patient (Case Study 2):

- Designing an experimental protocol for investigation of the kinematic responses achieved by combining muscle stimulation and elicitation of the NWR during gait in hemiparetic participants.
- Conduction of the experiment on one hemiparetic participant.

- Analysis of the acquired data.
- Understanding of the hemiparetic patient's gait deviations.

Design and development of the gait controller:

- Modelling the input-output relations of the controller on the background of the acquired data from Case Study 2.
- Implementation of the gait controller.

Test of the gait controller (Case Study 3)

- Test of the gait controller on the hemiparetic participant.

6.1 Problem Limitations

Due to the time constraints of the project period, the aim of this master thesis is not to produce a system ready for clinical use. The problem limitations of the project are listed below.

- The gait controller will only be designed to assist the gait of one single hemiparetic participant.
- The gait controller can only be used on a plain surface in a laboratory.

Part II

Experimental Studies

This part contains descriptions of Case Study 1 and Case Study 2. The Case Studies aim to investigate the effect of combining muscle stimulation in the stance phase with elicitation of the nociceptive withdrawal reflex to initiate the swing phase on kinematic responses obtained during normal- and hemiparetic gait.

CHAPTER 7

SPECIFICATION REQUIREMENTS FOR THE LABORATORY SYSTEM FOR STIMULATION

This chapter contains the specification requirements for the laboratory system that needs to be programmed to be able to deliver the electrical stimuli during the experiments. The specification requirements are made on the background of the System Description described in chapter 5 and the protocol used in the experimental studies (described in chapter 8). The laboratory system for stimulation is programmed in LabVIEW^{TM}. Information about the implementation of the program is described in appendix B.

Electrical stimulation:

- Muscle stimulation of QA and SOL during the heel-on period (two channels).
- Elicitation of the NWR to initiate the swing phase (three channels).
- Performing of dual channel reflex stimulation (delivering of two reflex stimulations to different site combinations during the same step).

Triggering of electrical stimulation:

- Possible computer-controlled triggering via signals from heel-switch.
- Possible manual controlled triggering via button in user interface (to be used in the beginning of the experiment to find detection thresholds and stimulation intensities for the individual stimulation sites).

Data collection:

- Ability to record a sequence of control steps and obtain output from FSR (toe-switch and heel-switch) to calculate stimulation onsets.
- Data collection from goniometers (hip, knee, and ankle). The obtained goniograms should be saved together with the stimulation profile.
- Saving of data in Matlab™ for offline analysis.

Graphical user interface:

- Calibration of goniometers.
- Possibility to determine stimulation profile (pulse length duration, number of bursts, frequency) for both NWR eliciting and muscle stimulation.
- Adjustment of stimulation intensity for each electrode position (possibility to set an individual stimulation intensity at each electrode site).
- Possibility to determine stimulation onsets in the gait cycle.
- Online view of goniograms, stimulation profile, and FSR output during the experiment.

Stimulation sequence:

- Randomisation of reflex stimulations (five site combinations, three phase combinations).
- Inter-stimulus intervals of 4-6 steps.

CHAPTER 8

CASE STUDY 1: EFFECT OF COMBINING MUSCLE STIMULATION WITH ELICITATION OF THE NOCICEPTIVE WITHDRAWAL REFLEX DURING NORMAL GAIT

8.1 Aim

To be able to design and develop a gait controller that supports the gait of stroke patients by combining muscle stimulation and elicitation of the NWR, we need to investigate the kinematic responses caused by this stimulation paradigm. Hence, the aim of this experimental study was to evaluate the kinematic responses in healthy participants obtained as a result of combining elicitation of the NWR in the late stance/early swing phase with muscle stimulation in the stance phase.

In addition, the experiment aimed to investigate the modulatory effect on the reflex responses when stimulations were delivered: to different sites on the sole of the foot, as single and dual channel stimulation, and at different phases prior to the swing phase.

We expect the findings to be in line with earlier reflex modulation studies which have shown largest knee and hip flexion responses following stimulation at heel-off, and largest ankle dorsiflexion following stimulation near toe-off of the ipsilateral leg [Emborg et al., 2009, Spaich et al., 2009]. Furthermore, we hypothesise the reflex responses during gait to depend on the stimulation site on the sole of the foot [Spaich et al., 2004, 2009].

The site- and phase specific responses might be useful in the design of the gait controller since we, by knowing the "stereotyped" reflex responses obtained from the different stimulation sequences, are able to tailor the responses to support the specific needs of a single stroke patient.

8.2 Methods and materials

Participants

The experiment was conducted on four healthy participants (1 female, mean age: 26 years, range 24-30 years). The participants did not have any neurological or present leg injuries. The study was approved by the local ethical committee (approval N-20090006), and all procedures were in accordance to the Declaration of Helsinki.

Electrical stimulation to elicit the NWR

The nociceptive withdrawal reflex (NWR) was elicited by transcutaneous electrical stimulation delivered to small areas on the sole of the foot by a computer-controlled constant current stimulator (Stimulator Neuromatic 2000 C, Disa, Skovlunde, Danmark). A similar approach has previously been used by Andersen et al. [1995, 1999], Spaich et al. [2004], Emborg et al. [2009]. Three stimulation electrodes (type 700, 20x15mm, Ambu A/S, Denmark) were mounted on the sole of the right foot in the following locations: (R1) the third metatarsophalangeal joint, (R2) the medial arch of the foot, and (R3) the posterior aspect of the calcaneus (see figure 8.1). The electrodes were attached to the skin after grinding off thick epidermal layers. A large common anode (model 895340, 7.5 x 10 cm, Pals, Axelgaard, Denmark) was placed on the dorsum of the foot to ensure that nociceptors were activated at the sole of the foot.

Each stimulus consisted of a constant current pulse burst of five 1-ms pulses delivered at 200 Hz, and this stimulus burst was repeated four times at a frequency of 15 Hz resulting in a total train duration of 221 ms [Emborg et al., 2009, Spaich et al., 2009]. Similar stimulation paradigms have been used in previous studies by Meinck et al. [1985], Decchi et al. [1997], Duysens et al. [1990].
The reason for using repetitive stimulation is that repetitive stimulation might be more effective than single stimulation to facilitate the stance-to-swing phase since it evokes larger kinematic responses than what could be achieved with a single stimulus Andersen et al. [2005].

Single and dual channel stimulation to evoke the NWR

The nociceptive withdrawal reflex was evoked by either single- or dual channel stimulation. Single channel stimulation consisted of the stimulus train described above delivered to one of the three stimulation sites on the sole of the foot: R1, R2, or R3. Dual channel stimulation consisted of the stimulus train delivered to either R1 or R2 followed by another train delivered to R3 with an inter-stimulus interval of 150 ms. The five different stimulation patterns are summarised in figure 8.1.
The reason for including dual channel stimulation was to create a more controlled swing phase, since we hypothesised that the first stimulus delivered to either the fore-foot (R1) or the arch (R2) would initiate the swing by lifting the foot from the ground and the next stimulus delivered to the posterior aspect of the heel (R3) would create a forward propulsion of the foot to support the step forward.

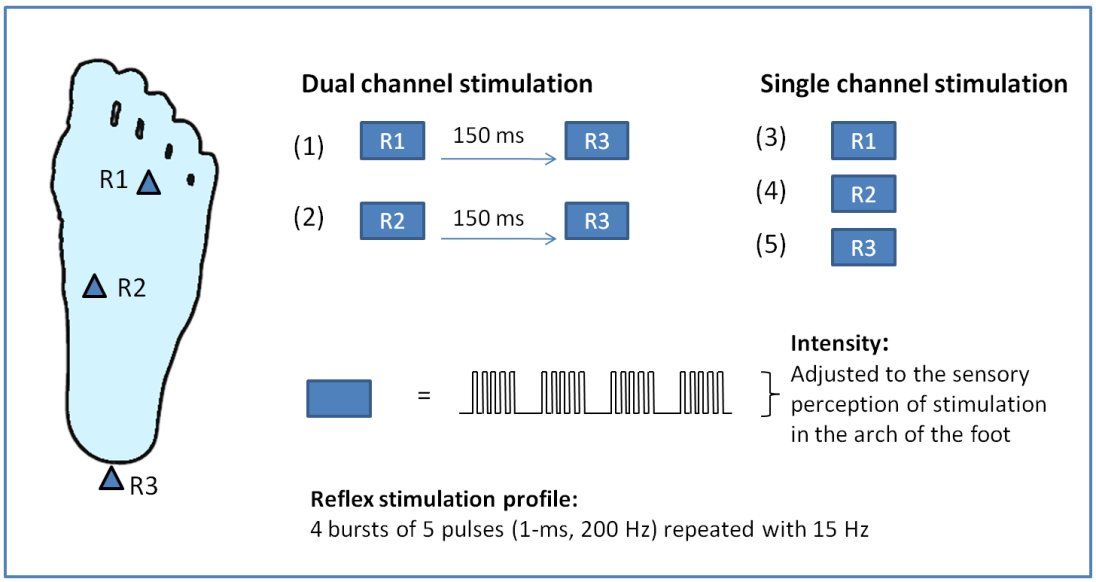


Figure 8.1: Stimulation profile for eliciting the nociceptive withdrawal reflex. *Stimulations were either delivered as dual- or single channel stimuli. Five different site combinations were used: two dual channel- and three single channel stimulations.*

Stimulation intensity to elicit the NWR

The stimulus intensity at each stimulation site was determined as a factor of the individual detection thresholds. The detection thresholds for the individual sites were determined using a staircase method, consisting of a sequence of single bursts of five stimuli with increasing and decreasing intensity. The detection threshold was defined as the stimulation intensity that was first felt by the participant. Once the detection thresholds were found, the stimulus intensity required to evoke the NWR was determined by adding steps of 10% of the stimulation intensity at detection threshold at the arch of the foot until a facilitatory reflex response, defined as an increment of the EMG activity of $>$ 100% in the interval 60-200 ms after stimulation compared with the prestimulus condition, was elicited in tibialis anterior in three successive trials [Spaich et al., 2009]. Then, the intensity at the two remaining stimulation sites were adjusted individually to obtain uniform sensory intensity across all stimulation sites. The arch of the foot was stimulated followed by a stimulation to one of the other sites, and the participant was asked to evaluate if the perception was identical or if the intensity of the latter had to be increased/decreased. To account for the effect of central temporal summation that has been shown to facilitate the human NWR response and perception of pain following repetitive stimulation [Arendt-Nielsen et al., 2000], a scale factor was multiplied to the intensities when a train of two reflexes were elicited (dual channel stimulation). The scale factor was adjusted until the train of two reflexes felt similar to stimulation at the arch. The intensity at the arch of the foot was repeatedly presented to the participant to avoid gradual drift in the perceived intensity. The entire procedure was conducted with the participant in sitting position with the foot hanging loose.

Electrical muscle stimulation

Monopolar two-channel stimulation was delivered via the same constant current stimulator as used to elicit the NWR. Stimulation was delivered to the following muscle groups: quadriceps (QA) and soleus (SOL) of the right leg. These target muscles were chosen in order to provide better weight acceptance, support, and weight bearing of the "paretic" leg during the stance phase [Kojović et al., 2009].
Two large electrodes (model 895340, 7.5 x 10 cm, Pals, Axelgaard, Denmark) were used for stimulation of QA. The proximal electrode was placed over the lateral muscle bulk of the thigh and the distal electrode medially, above the patella. The cathode (model 896230, 4 x 6.4 cm OVAL, Pals, Axelgaard, Denmark) for SOL stimulation was placed below the bulk of the gastrocsnemius muscle and the anode (model 895340, 7.5 x 10 cm, Pals, Axelgaard, Denmark) above the Achilles tendon, see figure 8.2. The electrode configuration for muscle stimulation was in accordance to recommendations from Baker et al. [2000]. Caution was taken in the positioning of the electrodes at appropriate places that led to sufficiently selective stimulation of the desired muscle groups.

The muscle stimulation consisted of 400 μs pulses delivered at 50 Hz [Kojović et al., 2009]. Trapezoidal shaped bursts of stimulation were utilised to produce smooth joint extensions based on findings from Bijak et al. [2005]. The slopes of the trapezoidal forms were 1 ms (both for rising- and falling time). The number of pulses delivered during each stimulation were adjusted according to the length of the stance phase of the individual participant (see description later).
The stimulation intensity was adjusted in the beginning of the experiment to be strong enough to produce an appropriate muscle contraction; yet, was still within the comfort level of the participant, i.e. 25 mA. Two seconds of stimulation delivered to QA should be able to create a contraction that fully extended the knee joint and felt supporting for the participant and two seconds of stimulation delivered to SOL should be able to plantarflex the ankle joint, when the foot was lifted from the ground. The intensities for muscle stimulation was determined with the participant in standing position.

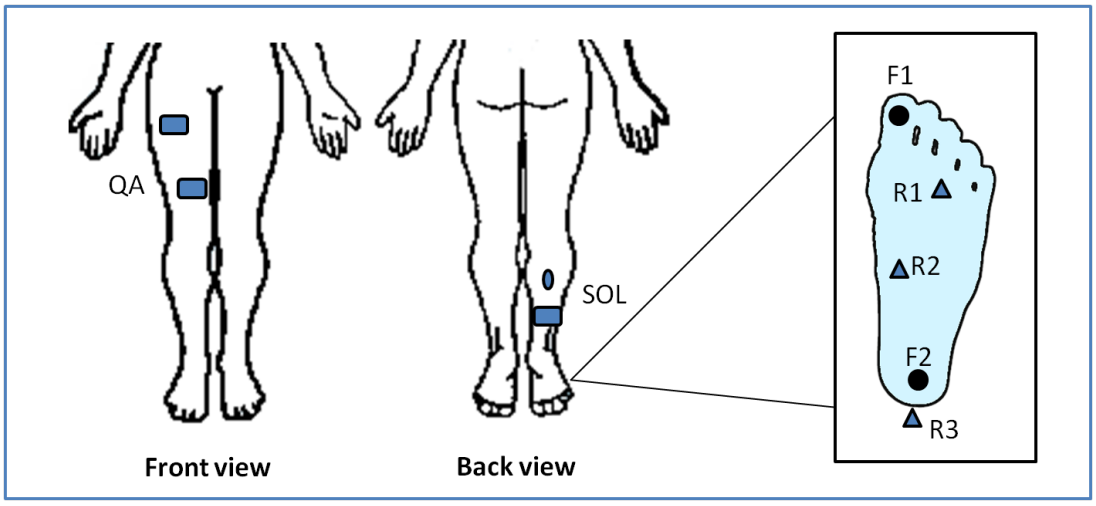


Figure 8.2: Electrode placements for muscle stimulation and elicitation of the NWR. *QA: quadriceps, SOL: soleus. R1, R2, and R3: stimulation electrodes on the sole of the foot. F1 and F2: force sensitive resistors used as toe- and heel-switch, respectively.*

Stimulation onsets

Two force sensitive resistors (FSR, LuSense, PS3, Standard 174) were firmly attached with tape to the heel and big toe of the right foot as indicated on figure 8.2. These FSRs functioned as a heel- and a toe switch, respectively, and were used to time the stimulation onsets. The output from the force sensors was a binary output being 1 when the heel or toe was on the ground and 0, when lifted from the ground.

SWING PHASE: To facilitate the initiation of the swing phase of hemiparetic gait by electrical stimulation, the target interval for stimulation is the late stance- and early swing phases [Quintern et al., 2003]. In this study, reflex stimulation was delivered at three different phases of the gait cycle between heel-off and toe-off: (Phase 1) *Heel-off + 10% of the heel-off/toe-off interval*, (Phase 2) *Heel-off + 50% of the heel-off/toe-off interval*, (Phase 3) *Toe-off*. Similar onsets have been used by Emborg et al. [2009]. The stimulation onsets are indicated on figure 8.3.

STANCE PHASE: Muscle stimulation was applied to QA in the time interval from *heel-strike* to *heel-strike + 50% of the heel-strike/heel-off interval*, and to SOL in the time interval from *heel-strike + 50% of the heel-strike/heel-off interval* to *heel-off* (see figure 8.3).

Outcome measures

The kinematic responses in the sagittal plane at the ankle, knee, and hip joints of the stimulated leg were recorded with three goniometers (type SG150 and SG110/A, Biometrics Ltd, Gwent, UK) mounted on the lateral side of the leg. The goniograms were sampled at 2 kHz, displayed, and stored on a computer for later analysis.

Experimental protocol

Stimulation electrodes, FSRs, and goniometers were mounted on the participant, and the stimulation intensities for both muscle stimulation and elicitation of the NWR were determined as described above.
A sequence of 10 unperturbed control steps were acquired and used for definition of the stimulation onsets as time delays after heel-off and heel-strike for eliciting the reflex and muscle stimulation, respectively. Afterwards, the signal from the heel-switch was used to trigger the computer-controlled stimulator. Stimuli were then delivered in a random sequence with respect to stimulation site and onset, where each combination of stimulation site (five possibilities: R1+R3, R2+R3, R1, R2, R3) and phase (three possibilities) was repeated five times, giving a total of 15 x 5 stimulation steps.
To prevent the effect of habituation, an inter-stimulus interval of 4-6 steps was used [Dimitrijević et al., 1972]. The randomisation of stimulation site should further prevent reflex habituation [Granat et al., 1993]. During the experiment, the participants walked on a treadmill with a constant velocity of 2.5 km/h in order to reduce inter-step variability between participants and over time. To further reduce the inter-step variability, the gait of the participants was paced by the auditory clue from a metronome [Spaich et al., 2009]. The participants were asked to set the pace of the auditory clue in the beginning of

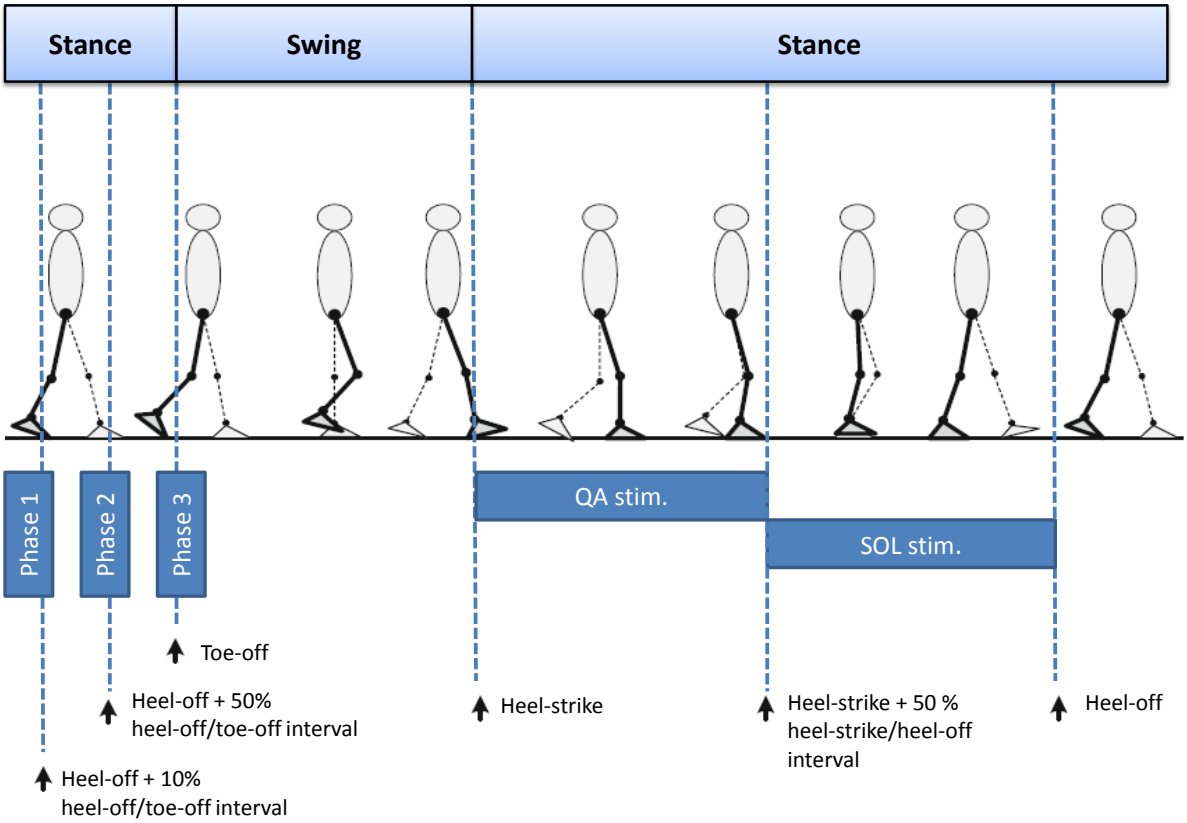


Figure 8.3: Stimulation onsets. *Dual- or single channel electrical stimulation was delivered to the sole of the foot at three different onsets (phases 1-3) between heel-off and toe-off. Muscle stimulation was applied to quadriceps (QA) in the time interval from heel-strike to heel-strike + 50% of the heel-strike/heel-off interval, and to soleus (SOL) in the time interval from heel-strike + 50% of the heel-strike/heel-off interval to heel-off.*

the experiment to a step frequency that resulted in a normal walking pattern at 2.5 km/h. The use of the metronome ensured that each participant produced strides of similar length throughout the experiment.

Data analysis

The goniograms containing a control step (the step immediately before stimulation) plus the response to stimulation were low-pass filtered (Butterworth, 25 Hz, sixth order, no phase lag). The kinematic response of the knee and hip joints as response to stimulation was then assessed as the peak angle change between the stimulated step and the corresponding control step in the heel-off period (Figure 8.6, first and second traces). The procedure for calculating the peak angle change is indicated on figure 8.4 for the knee joint. The moment of minimum knee flexion in the heel-off period for the baseline step is used as reference for both baseline peak angle and stimulation peak angle. In this way, we account for the eventual effect of the muscle stimulation on the kinematic reflex responses.
The response at the ankle joint was assessed as the peak angle change in two intervals due to the bipha-

sic nature of the ankle joint trajectory. These intervals were between heel-off and the moment of peak plantarflexion, and from this moment until heel-strike (figure 8.6, third trace). Same procedure as described above was used to calculate the peak angle changes. The peak angle changes were calculated for each sweep and then the five repetitions for each stimulation site and phase were averaged for each participant.

In order to investigate the effect of the muscle stimulation on the kinematic responses during the stance phase, the goniograms for the stimulation steps and the preceding baseline steps were averaged over the first half of the stand phase (corresponding to the on-time for QA stimulation) and second half of the stance phase (corresponding to the on-time for SOL stimulation). The relative difference in mean angle between stimulation step and baseline step was then calculated for the QA- and SOL stimulation interval, respectively (Figure 8.4). This analysis did not distinguish between the different reflex stimulations (site- and phase combinations), since the reflexes were evoked in the swing phases and did not have any effect on the response to stance phase muscle stimulation.

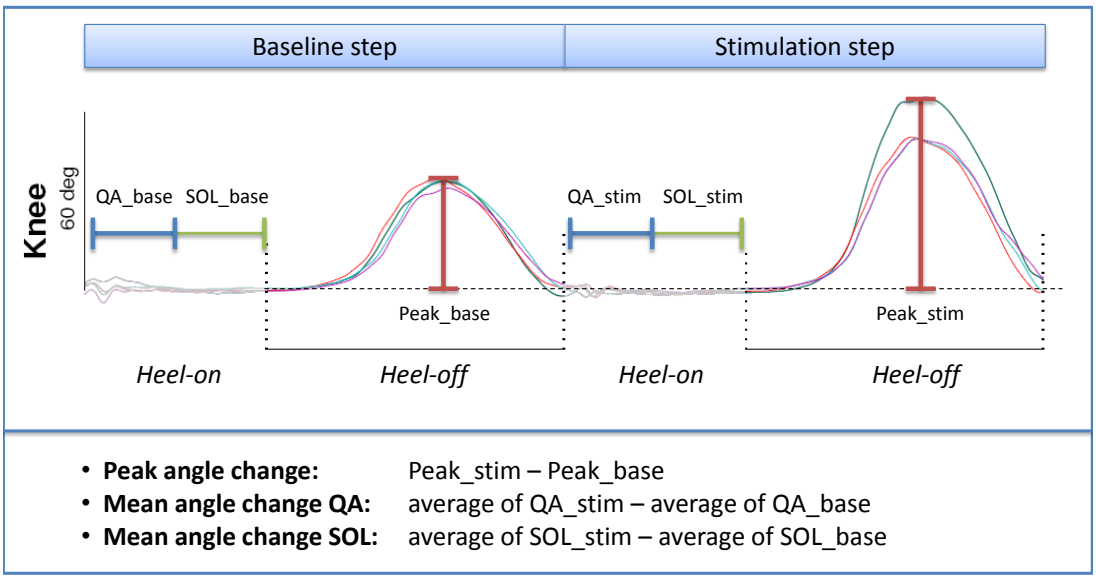


Figure 8.4: Procedure for calculating peak angle change and mean angle change. *The procedure is only shown for the knee joint, but a similar calculation method was used for hip-, dorsiflexion-, and plantarflexion peak angle changes. The goniograms shown in the figure are five stimulation repetitions obtained from one of the healthy participants (stimulation site: R2, phase: 1).*

Statistical analysis

One-way repeated measures ANOVA was used to analyse the effect of stimulation site (sole of the foot) on the detection threshold and the stimulation intensity used to evoke reflexes in the experiment.
Two-way repeated measures ANOVA was applied to analyse the effect of stimulation site on the sole of the foot and phase on the evoked responses in the swing phase of gait. Student-Newman-Keuls (SNK) test was used for post hoc pairwise comparisons.

To investigate the effect of muscle stimulation on the kinematic responses in the stance phase, one-sampled t-tests were used to investigate if QA- and SOL mean angle changes were significantly different from zero. $P < 0.05$ was considered as statistically significant. Results are presented as mean ($n = 4$) $\pm$ 1 standard error of the mean (SEM). The statistical tests were carried out despite the fact that only four participants were included in the study.

8.3 Results

Detection thresholds and stimulation intensities for the NWR

The mean detection thresholds at the sole of the foot, stimulation intensities used to evoke single channel stimulation NWRs, and scale factors used to evoke dual channel stimulation NWRs are presented in table 8.1. The smallest detection thresholds and stimulation intensities were detected at the arch of the foot (one-way repeated measures ANOVA, main effect, $P < 0.001$; SNK, $P < 0.05$, compared with the other two sites). The highest detection thresholds and stimulation intensities were detected at the mid forefoot (one-way repeated measures ANOVA, main effect, $P < 0.001$; SNK, $P < 0.05$, compared with all other sites). There was no significant differences in the scale factor multiplied to the stimulation intensities for dual channel reflex stimulation.
All participants described the sensation evoked by stimulation of the sole of the foot as sharp and pin-pricking. The stimulation did not evoke any sensation on the dorsum of the foot.

Stimulation site	Detection threshold (mA)	Stim. intensity (mA)	Scale factor
Mid forefoot (R1)	5.5 $\pm$ 0.5	23.8 $\pm$ 3.7	-
Arch of foot (R2)	2.5 $\pm$ 0.3 *	13.5 $\pm$ 2.9 *	-
Posterior aspect of heel (R3)	4.0 $\pm$ 0.4	18.8 $\pm$ 1.9	-
R1 + R3	-	-	0.8 $\pm$ 0.09
R2 + R3	-	-	0.9 $\pm$ 0.06

Table 8.1: Detection thresholds, stimulation intensities at the different stimulation sites, and scale factors for dual channel stimulations. *Values are expressed as mean $\pm$ 1 SEM ($n = 4$ participants). * denotes significantly smaller intensity (SNK, $P < 0.05$) compared to the other two sites.*

Stimulation intensities for muscle stimulation

The stimulation intensities used for muscle stimulation are presented in table 8.2. The stimulation was described as a prickling sensation by all participants.

Stimulation site	Stimulation intensity (mA)
Quadriceps (QA)	28.5 ± 1.2
Soleus (SOL)	25.8 ± 0.8

Table 8.2: Stimulation intensities used for muscle stimulation. *Values are expressed as mean ± 1 SEM (n = 4 participants).*

Baseline step

Figure 8.5 shows an average baseline step for each of the four healthy participants. The trajectory of the hip and knee joints were very similar for the four participants, which is in line with the literature [Winter, 1991] that human gait is highly stereotyped for healthy participants for the hip and knee joints. The trajectory of the ankle joint was more variable between participants, which can be explained by the fact that the ankle joint has more fine motor control than the two other more proximal joints.

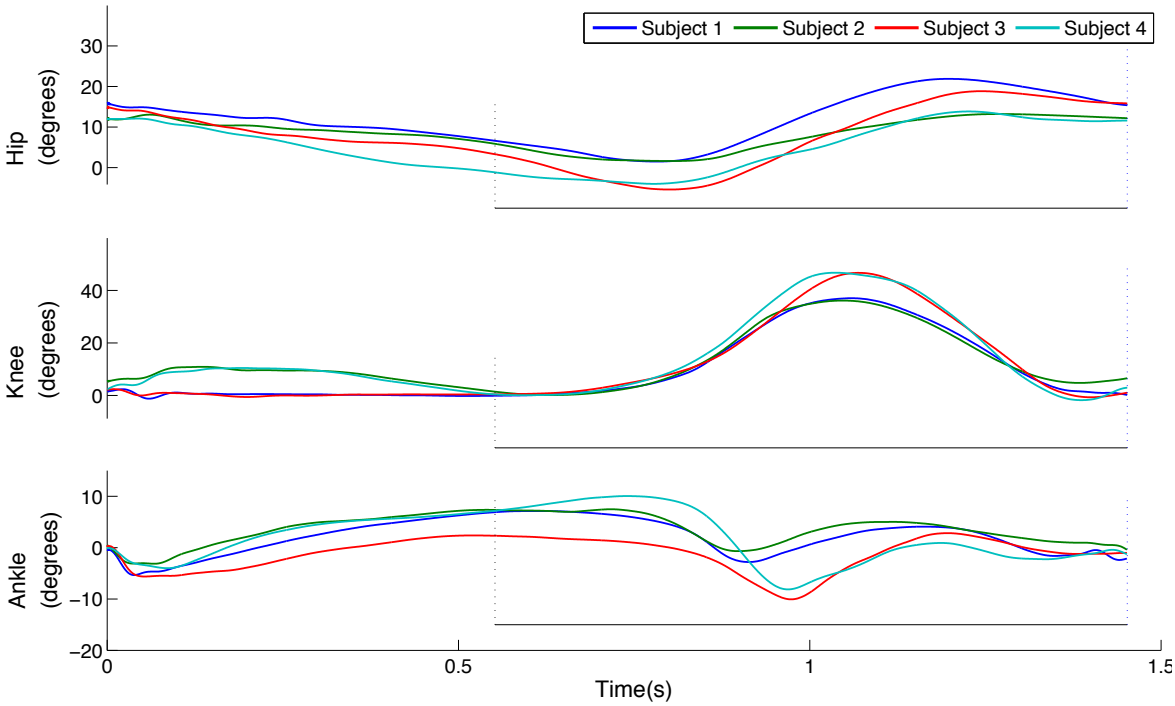


Figure 8.5: Mean baseline step from four healthy participants. *Five separate baseline steps were resampled to the same length and then averaged for each participant.*

Kinematic responses as a result of the combination of muscle stimulation and elicitation of the NWR

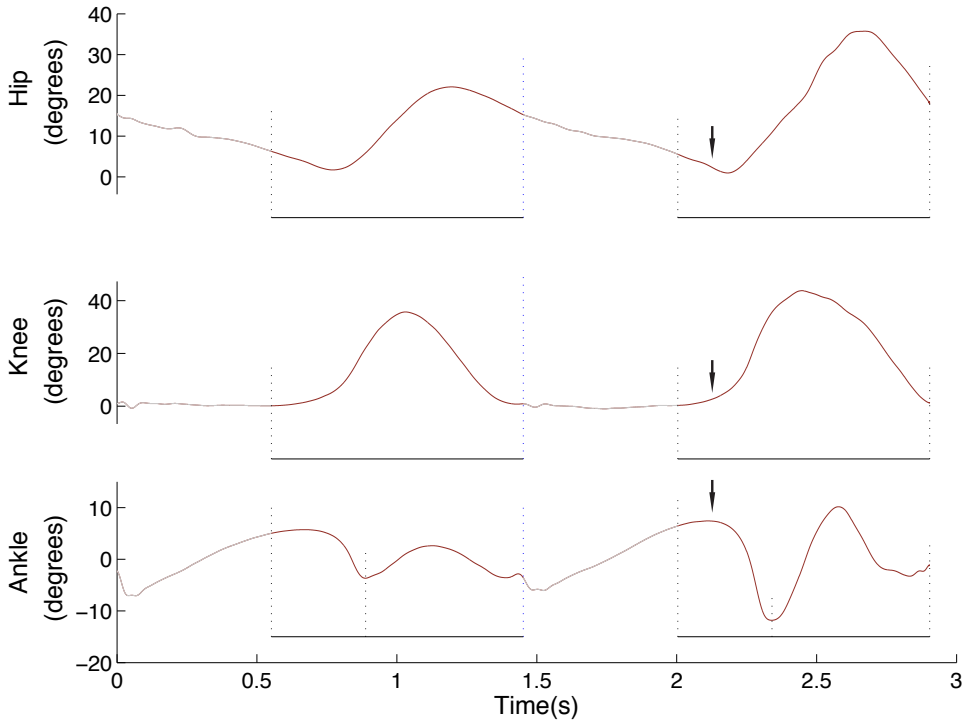


Figure 8.6: Hip, knee, and ankle goniograms corresponding to two consecutive steps of one single participant. *Stimulation was delivered at the mid forefoot (R1) in phase 2 (heel-off + 50% heel-off/toe-off interval = 212.5 ms ± 19.4 ms after heel-off) of the second step. The stimulation onset is indicated by vertical arrows in the top of the traces. The moments of heel-off are indicated in the bottom of each trace as black horizontal lines. The direction of ankle dorsiflexion, knee flexion, and hip flexion is upwards. The time windows in which the kinematic analyses are carried out, are outlined by vertical, dotted lines.*

Ankle joint

The ankle kinematic response in the first time interval (the period from heel-off and the moment of peak plantarflexion) was plantarflexion. There were no significant main effects of either phase or stimulation site on the kinematic responses, and no significant interaction effects (two-way repeated measures ANOVA) (Figure 8.7).

During the next time interval (the period from the moment of peak plantarflexion to heel-strike), the response to stimulation was ankle dorsiflexion. The response was modulated by phase (two-way repeated measures ANOVA, main effect, $P < 0.05$) and there was an interaction effect of site * phase (two-way repeated measures ANOVA, interaction, $P < 0.005$) (Figure 8.8).
At the mid forefoot (R1), the arch of the foot (R2), and when the forefoot was combined with the posterior aspect of the heel (R1R3), stimulation in phase 1 and 2 resulted in larger responses than in phase 3 (SNK, $P < 0.05$).

Within phase 1, stimulation at the posterior aspect of the heel (R3) resulted in less reduced dorsiflexion than stimulation at the mid forefoot (R1) and the arch of the foot (R2) (SNK, $P < 0{,}01$). Additionally, stimulation at the combined site of the arch of the foot and the posterior aspect of the heel (R2R3) caused larger dorsiflexion than stimulation at the mid forefoot (R1) and the arch of the foot (R2) (SNK, $P < 0.05$). Within phase 3 (at toe-off), stimulation at the mid forefoot resulted in more dorsiflexion than stimulation at the posterior aspect of the heel (R3) (SNK, $P < 0.05$).

Knee joint

At the knee joint, flexion was the typical reaction to stimulation. The degree of flexion depended on the stimulation site (two-way repeated measures ANOVA, main effect, $P < 0.01$), phase (two-way repeated measures ANOVA, main effect, $P < 0.005$), and site * phase (two-way repeated measures ANOVA, interaction, $P < 0.005$) (Figure 8.9).
Stimulation at the mid forefoot (R1) and the arch of the foot (R2) caused larger knee flexion in phase 1 compared to the other phases, and less knee flexion in phase 3 compared to the other phases (SNK, $P < 0.005$). Furthermore, stimulation at the combined site of R2R3 caused more knee flexion in phase 1 compared to phase 3 (SNK, $P < 0.05$).
Within phase 1 (near heel-off), stimulation at the arch of the foot (R2) and at the mid forefoot (R1) caused larger responses than stimulation at the posterior aspect of the heel (R3), arch of the foot and posterior aspect of the heel combined (R2R3), and the mid forefoot and posterior aspect of the heel combined (R1R3) (SNK, $P < 0.05$). In addition, the two combined stimulations (R1R3 and R2R3) caused larger responses than stimulation at the posterior aspect of the heel (R3) (SNK, $P < 0.05$).

Hip joint

At the hip joint, flexion was the typical response to stimulation. The size of the response was modulated by stimulation site (two-way repeated measures ANOVA, main effect of site, $P < 0.05$), see figure 8.10. There was a tendency that stimulation at the mid forefoot (R1) resulted in larger flexion than stimulation at the posterior of the heel (R3), but the post hoc test was unable to identify any significant differences in means among the stimulation sites. This could be explained by the fact that the p-value from the ANOVA was close to 0.05 (the determined level of significance), the small number of participants in the experiment ($n = 4$), or the fact that the normality test failed in the repeated measures ANOVA test.

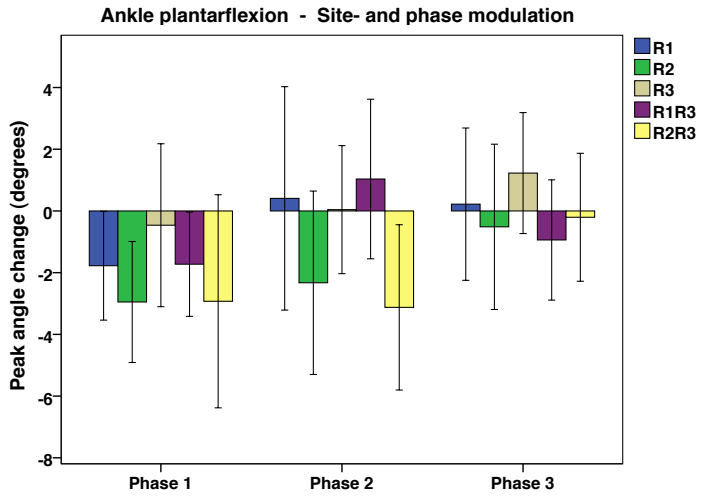


Figure 8.7: Kinematic ankle plantarflexion responses evoked by electrical stimulation delivered to five site combinations on the sole of the foot at three phases. *The negative values indicate a reduction in plantarflexion as a response to stimulation. Values represent mean ± 1 SEM (n = 4 participants). There were no significant main effect of either phase or stimulation site, and no interaction effects. Stimulation sites: R1: mid forefoot, R: arch of foot, R3: posterior aspect of heel, R1R3: R1 followed by R3, R2R3: R2 followed by R3.*

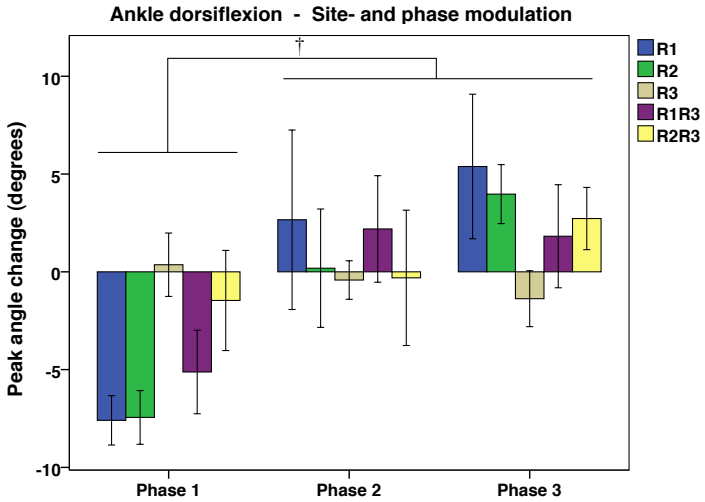


Figure 8.8: Kinematic ankle dorsiflexion responses evoked by electrical stimulation delivered to five site combinations on the sole of the foot at three phases. *The negative values indicate a reduction in dorsiflexion as a response to stimulation. Values represent mean ± 1 SEM. There was a main effect of phase and an interaction of site * phase. Stimulation sites: R1: mid forefoot, R2: arch of foot, R3: posterior aspect of heel, R1R3: R1 followed by R3, R2R3: R2 followed by R3. † indicates the main effect of phase.*

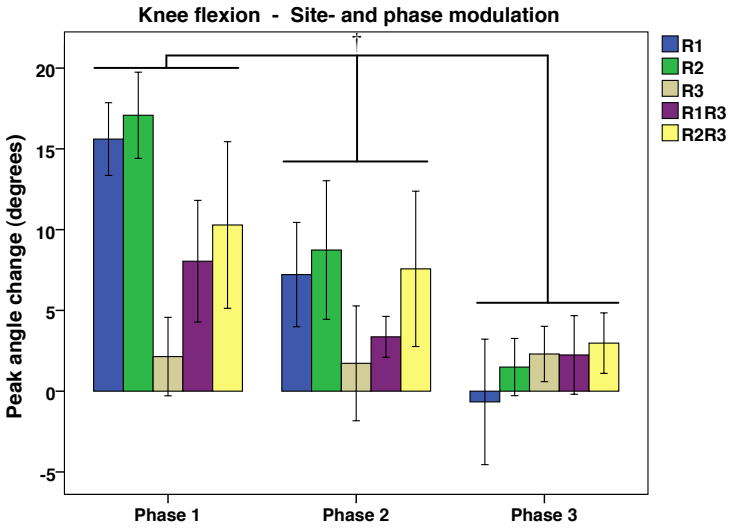


Figure 8.9: Kinematic knee flexion responses evoked by electrical stimulation delivered to five site combinations on the sole of the foot at three different phases. *Values represent mean ± 1 SEM. There was a main effect of both phase and stimulation site, and an interaction effect of site * phase. Stimulation sites: R1: mid forefoot, R2: arch of foot, R3: posterior aspect of the heel, R1R3: R1 followed by R3, R2R3: R2 followed by R3. † indicates the main effect of phase.*

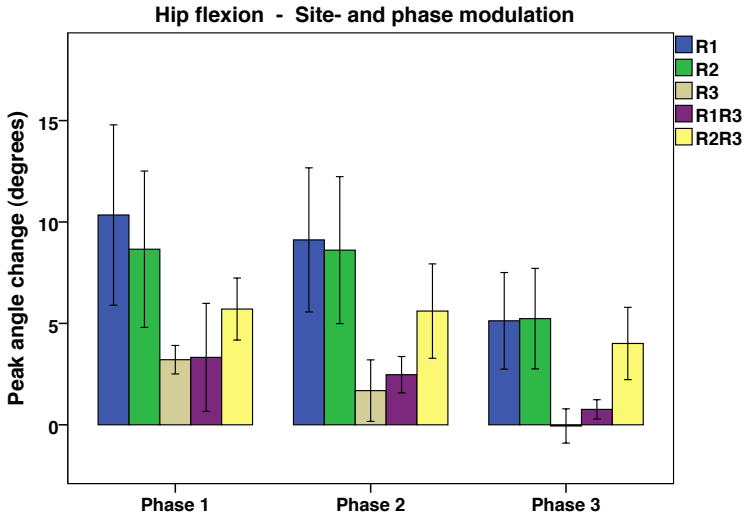


Figure 8.10: Kinematic hip flexion responses evoked by electrical stimulation delivered to five site combinations on the sole of the foot at three phases. *Values represent mean ± 1 SEM. Stimulation sites: R1: mid forefoot, R: arch of foot, R3: posterior of heel, R1R3: R1 followed by R3, R2R3: R2 followed by R3.*

Dual channel reflex stimulation

During the experiments, some of the participants reported that the last train in the dual channel stimulation arrived too late (especially when delivered in phase 3). They had almost their foot back on the ground when the reflex response came, which felt disturbing for their gait.

Effect of muscle stimulation on the kinematic responses in the stance phase

Figure 8.11 shows the means of five repetitions for four participants of the kinematic responses to muscle stimulation and NWR elicited from the arch of the foot in phase 1. The figure contains one baseline step followed by a stimulation step. The trajectories for hip, knee, and ankle joints were quite similar in the stance phase between baseline and stimulation steps, indicating that the kinematic responses to muscle stimulation were small as expected in healthy participants.

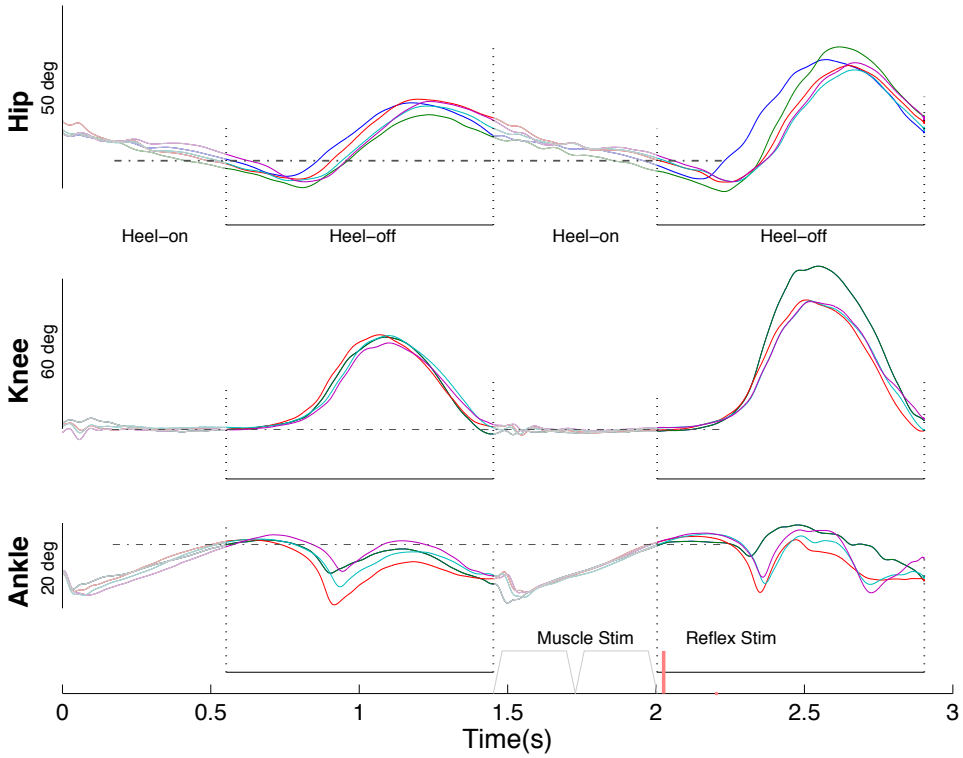


Figure 8.11: Hip, knee, and ankle goniograms corresponding to two consecutive steps of four participants. Muscle stimulation were delivered to QA and SOL in the stance phase of the second step and a NWR elicited at the arch of the foot in phase 1. *The stimulation profile and onsets are indicated in the last trace. The moments of heel-off are indicated in the bottom of each trace as black horizontal lines. The direction of ankle dorsiflexion, knee flexion, and hip flexion is upwards. The time windows in which the kinematic analyses are carried out, are outlined by vertical, dotted lines.*

The mean angle changes between the stimulation step and the baseline step for the QA- and SOL stimulation-on periods, respectively, are shown in figure 8.12. QA stimulation caused increased ankle

flexion and knee flexion in the QA stimulation-on interval compared to baseline ($P < 0.001$, one-sampled t-test). SOL stimulation caused increased ankle flexion, increased knee flexion, and decreased hip flexion in the SOL stimulation-on interval compared to baseline ($P < 0.001$, one-sampled t-test).

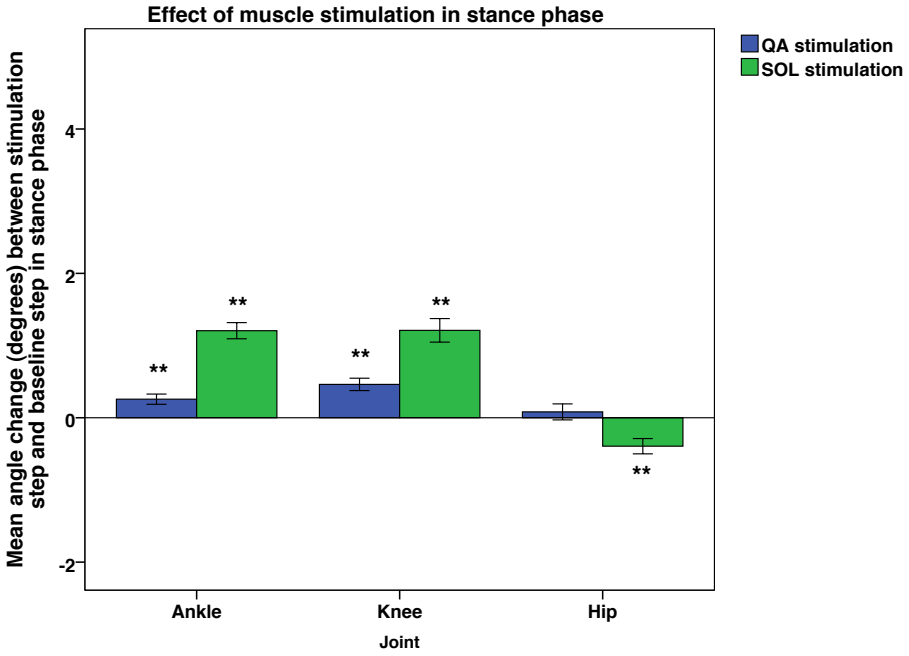


Figure 8.12: Effect of muscle stimulation on the kinematic responses in the stance phase. *Mean angle changes between stimulation and baseline were calculated over the first half of the heel-on period (corresponding to QA stimulation-on) and over the second half of the heel-on period (corresponding to SOL stimulation-on). Increased flexion is upwards.*

8.4 Subconclusion

Our study showed that the lower limb NWR was modulated by different site- and phase stimulations. The largest knee and hip flexion responses were observed following stimulation near heel-off (phase 1), whereas the largest dorsiflexion responses were observed at toe-off (phase 3). In general, single channel stimulation delivered to the distal sites of the foot (mid forefoot and arch of the foot) caused larger ankle dorsiflexion, knee- and hip flexion responses than stimulation delivered to the posterior aspect of the heel. There was no significant modulation in the ankle plantarflexion responses.

This reflex response modulation might have application in the rehabilitation of stroke patients, since the possibility of eliciting different responses may help to tailor the FES to the individual needs of each patient. By adding the use of muscle stimulation, it might be possible to support both stance- and swing phases of hemiparetic gait and thus, help the patient to achieve and relearn a more functional gait pattern. The next step is to conduct a similar experiment on a hemiparetic participant in order to investigate if the observed site- and phase modulations in healthy subjects are also present in hemiparetic subjects.

CHAPTER 9

CASE STUDY 2: EFFECT OF COMBINING MUSCLE STIMULATION WITH ELICITATION OF THE NOCICEPTIVE WITHDRAWAL REFLEX DURING HEMIPARETIC GAIT

9.1 Aim

The aim of this Case Study was to evaluate the kinematic responses obtained as a result of combining elicitation of the NWR in late stance/early swing phase with muscle stimulation in the stance phase during gait of a chronic hemiparetic participant.
As in the experiment on healthy participants, the modulatory effect on the reflex responses was investigated when stimulations were delivered to different sites on the sole of the foot, as single and dual channel stimulation, and at different phases prior to the swing phase.
A further purpose was to examine the gait deviations of the stroke participant in order to outline which specific corrections he needed to achieve a more functional gait. It is expected that the site- and phase specific kinematic reflex responses can be utilised in the development of the gait controller, which should allow a better control of the evoked movement compared to conventional therapy, and consequently, allow stroke patients to relearn a more functional gait.

9.2 Methods and Materials

Inclusion- and exclusion criteria

The inclusion criteria for participating in the experiment were: (1) at least six months after the cerebrovascular accident, (2) being able to walk continuously for at least 5 minutes on a treadmill with low speed, and to resume walking after a short period of rest, and (3) being able to communicate and give informed consent. The exclusion criteria were as follows: (1) severe medical condition (such as heart disease), (2) presence of wounds and/or local infections in the legs and feet, and (3) inability to understand instructions and make decisions.
The study was approved by the local ethical committee (approval N-20090006), and all procedures were in accordance to the Declaration of Helsinki.

Experimental setup and procedures

The setup for the experiment and the procedures were identical to the setup in Case Study 1 described in chapter 8, except for the following modifications: the hemiparetic participant was supported by a harness connected to the ceiling to avoid potential falling when walking on the treadmill at a constant velocity of 2 km/h. Furthermore, it was necessary to place the FSR functioning as toe-switch on the first metatarsophalangeal joint in order to avoid false-positive detections due to the participant's drop foot.
And finally, it was decided to use an interval of 100 ms instead of 150 ms between the trains in the combined reflex stimulations, since it was observed in Case Study 1 that the last stimulation train in the dual channel reflex stimulation was sometimes delivered too late in the swing phase.

9.3 Results

Participant

The experiment was conducted on one chronic hemiparetic participant (age: 52 years). For other details, see table 9.1.

Age (years)	Sex	Time since stroke (years)	Paretic side	CVA type	Helping aids used when walking
52	M	4.5	Left	Hemorrhage	None

Table 9.1: Demographic data from the stroke participant *CVA = Cerebrovascular accident.*

Detection thresholds and stimulation intensities for eliciting the NWR

Detection thresholds on the sole of the foot, stimulation intensities used to evoke single stimulation channel NWRs in the tibialis anterior muscle, and scale factors used to evoke dual stimulation channel

NWRs for the hemiparetic participant are presented in table 9.2. The smallest detection threshold and stimulation intensity were detected at the arch of the foot, and the highest stimulation intensity was associated with the mid forefoot as with the healthy participants. The hemiparetic participant described the sensation evoked by the electrical stimulation of the sole of the foot as sharp and pinpricking. The stimulation did not evoke any sensation on the dorsum of the foot.

Stim. site	**Healthy participants**			**Hemiparetic participant**		
	D-Th (mA)	Stim. int. (mA)	Scale factor	D-Th (mA)	Stim. int. (mA)	Scale factor
R1	5.5 ± 0.5	23.8 ± 3.7	-	6	16	-
R2	2.5 ± 0.3	13.5 ± 2.9	-	4	6	-
R3	4.0 ± 0.4	18.8 ± 1.9	-	6	13	-
R1+R3	-	-	0.8 ± 0.09	-	-	0.8
R2+R3	-	-	0.9 ± 0.06	-	-	1

Table 9.2: Detection thresholds, stimulation intensities at the different stimulation sites, and scale factors for dual channel stimulations for healthy participants and the hemiparetic participant. *Values for the healthy participants (n = 4) represent mean ± 1 SEM. Abbreviations: Stim. site = stimulation site, R1 = mid forefoot, R2 = arch of the foot, R3 = posterior aspect of the heel, D-Th = detection threshold, Stim. int. = stimulation intensity.*

Stimulation intensities for muscle stimulation

The stimulation intensities used for muscle stimulation of hemiparetic- and the healthy participants are presented in table 9.3. The stimulation was described by the stroke participant as prickling.

Stimulation site	**Healthy participants** Stimulation intensity (mA)	**Hemiparetic participant** Stimulation intensity (mA)
Quadriceps (QA)	28.5 ± 1.2	33
Soleus (SOL)	25.8 ± 0.8	20

Table 9.3: Stimulation intensities used for muscle stimulation for the healthy participants and the hemiparetic participant, respectively. *Values for the healthy participants (n = 4) represent mean ± 1 SEM.*

Baseline step

Figure 9.1 illustrates a comparison of an average baseline step from a healthy participant and that of the hemiparetic participant illustrating the typical gait deviations between normal and hemiparetic gait.

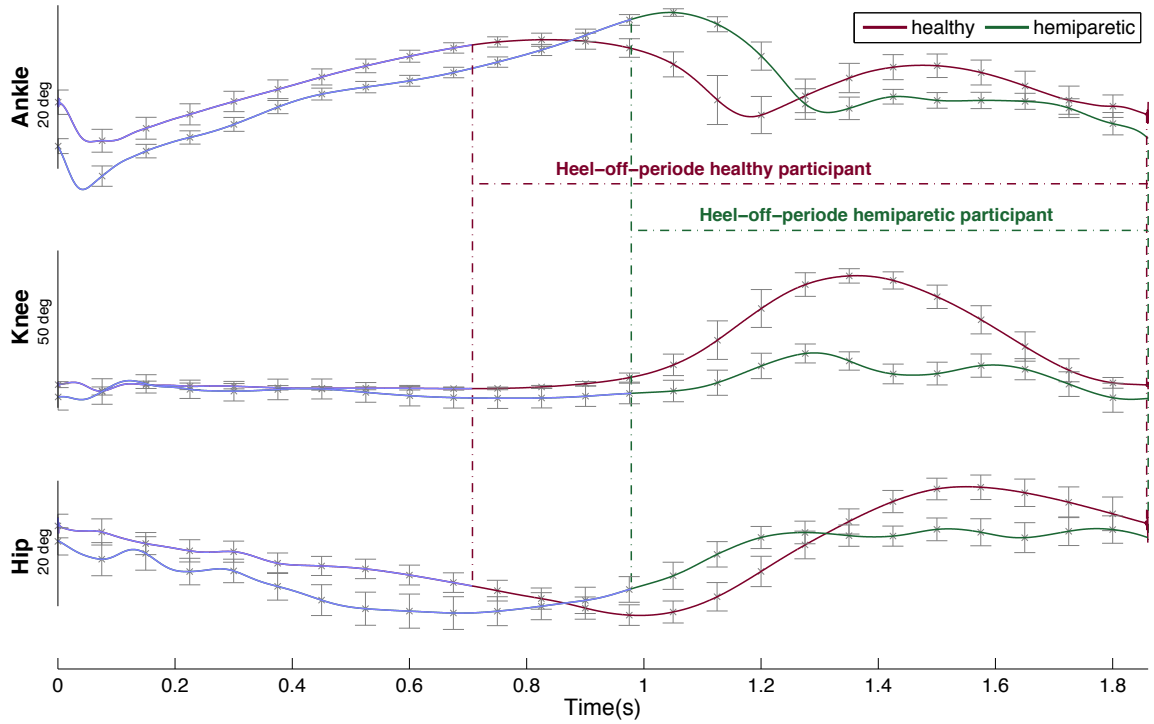


Figure 9.1: Average baseline step from the hemiparetic participant and from a representative healthy participant. *The shown goniograms are averaged over 90 baseline steps. Error-bars indicate ±1 standard deviation (SD). The goniograms have been resampled to the same length. Mean step duration for the hemiparetic participant was 1.86 ± 0.044 s at 2 km/h and for the healthy participant 1.45 ± 0.032 s at 2.5 km/h. The vertical, dotted lines indicate the beginning of the heel-off period for the healthy- and the hemiparetic participant, respectively.*

Hip joint: By inspecting figure 9.1, it is seen that the hip trajectory in the late swing phase of the hemiparetic participant had a smaller amplitude than the hip trajectory of the healthy participant indicating a decreased peak hip flexion.

Knee joint: The knee trajectories of the healthy participant and the hemiparetic participant were almost identical in the stance phase, but there was a large difference in the degree of knee flexion during the swing phase. The healthy participant had a clear point of maximum knee flexion at mid swing, whereas the hemiparetic participant had very reduced knee flexion throughout the swing phase.

Ankle joint: During the stance phase, the ankle trajectories were quite similar, starting with a plantarflexion at heel-on to bring the forefoot down to the ground and followed by a dorsiflexion as the lower leg is moved forward over the foot. In the swing phase, the two trajectories begin to differ: the ankle trajectory of the healthy participant is composed of plantarflexion at push-off followed by a dorsiflexion

to keep the foot lifted from the ground. The ankle joint of the hemiparetic participant, however, starts to plantarflex at approximately heel-off and this plantarflexion is only followed by a slight dorsiflexion in the mid swing, indicating the presence of drop foot.

The observed kinematic deviations corresponds to the typical description of the gait pattern of hemiparetic patients described in section 2.2.

Kinematic responses when the NWR was elicited in the swing phase and muscle stimulation was delivered during the stance phase

Figure 9.2 shows an example of the kinematic reactions as response to stimulation. The figure contains two consecutive steps from the hemiparetic participant; the first being a baseline step without stimulation and the next being a stimulation step with muscle stimulation applied to QA and SOL in the stance phase, and reflex stimulation delivered to the arch of the foot in phase 1.

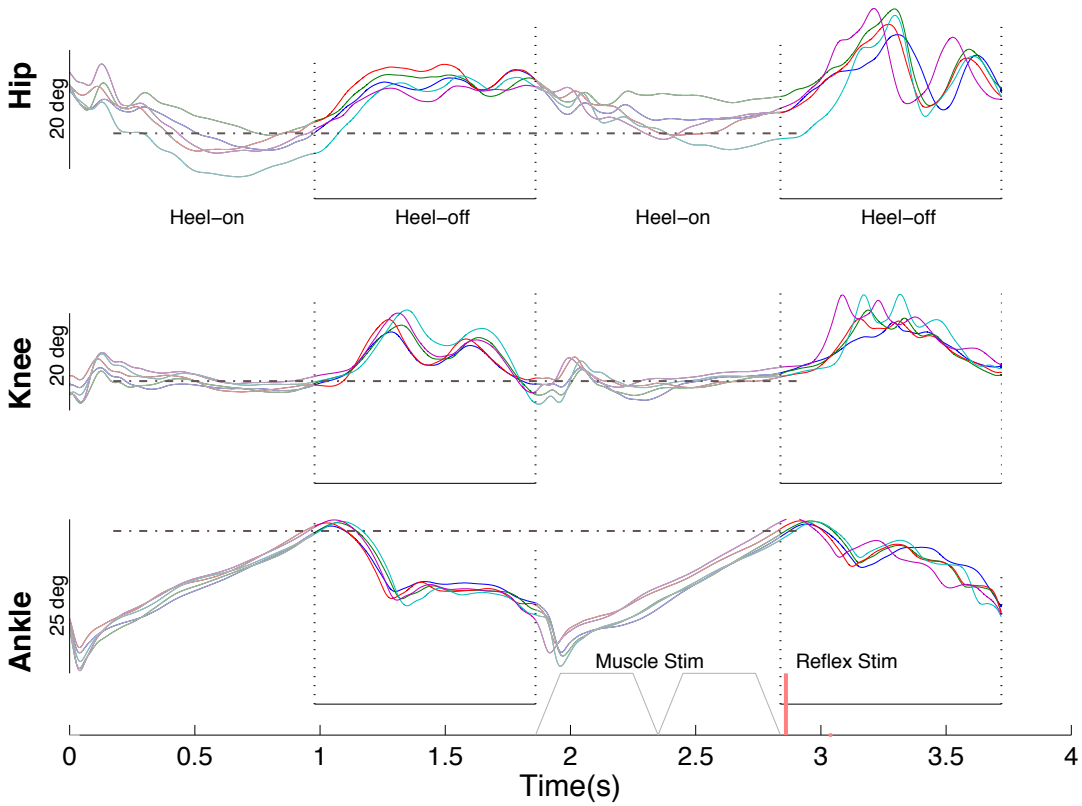


Figure 9.2: Hip, knee, and ankle kinematic recordings corresponding to a baseline step and a following stimulation step from the hemiparetic participant. *Muscle stimulation was delivered to QA and SOL during the stance phase and reflex stimulation was delivered at the arch of the foot (R2) in phase 1. The graph shows five repetitions of the same stimulation sequence. Stimulation onsets are shown in the lower trace. Moments of heel-off are indicated by horizontal lines below the traces. Direction of ankle dorsiflexion, knee flexion, and hip flexion is upwards.*

Ankle joint

The ankle kinematic response in the first time interval (the period from heel-off and the moment of peak plantarflexion) was plantarflexion. The degree of plantarflexion was modulated by stimulation site (two-way repeated measures ANOVA, main effect, $P < 0.005$) and phase ($P < 0.05$). Furthermore, there was an interaction effect of site * phase ($P < 0.001$) (Figure 9.3).
At the mid forefoot (R1), the arch of the foot (R2), and the combined sites of R2R3, stimulation delivered in phase 1 caused more plantarflexion reduction compared to phase 2 (SNK, $P < 0.05$). Furthermore, stimulation at the arch (R2) and the combined site of R2R3 resulted in more plantarflexion reduction in phase 1 compared to phase 3 (SNK, $P < 0.05$).
Within phase 1, stimulation at the posterior aspect of the heel (R3) caused less plantarflexion reduction compared to the combined site of R2R3, the arch (R2), and the mid forefoot (R1) (SNK, $P < 0.02$). In addition, R1R3 caused less plantarflexion reduction than R2R3 (SNK, $P < 0.02$). Within phase 2, stimulation at the mid forefoot (R1) caused less plantarflexion reduction than stimulation at R2R3, R1R3, and at the arch (R2) (SNK, $P < 0.05$).

During the next analysis period (the period from the moment of peak plantarflexion to heel-strike), the response to stimulation was ankle dorsiflexion. The degree of dorsiflexion depended on stimulation site (two-way repeated measures ANOVA, $P < 0.001$), but not phase ($P > 0.05$). There was an interaction effect of site * phase ($P < 0.005$) (Figure 9.4).
Stimulation at the arch (R2) of the foot caused more dorsiflexion in phase 3 compared to phase 1 (SNK, $P < 0.05$). Furthermore, stimulation at the combined site of R2R3 caused less dorsiflexion in phase 1 compared to the other phases (SNK, $P < 0.005$).
Within phase 2 and phase 3, stimulation delivered at the combined site of R2R3, the mid forefoot (R1), and the arch of the foot (R2) caused more dorsiflexion than when delivered at the other stimulation sites (SNK, $P < 0.01$).

Knee joint

Flexion of the knee was the typical response to stimulation. The degree of flexion depended on stimulation site and phase (two-way repeated measures ANOVA, main effect, both $P < 0.001$) (Figure 9.5). There were no significant interaction effects.
Stimulation at the mid forefoot (R1), the arch (R2), and the combined stimulation at the arch followed by the posterior aspect of the heel (R2R3) caused larger responses than stimulation at the posterior aspect of the heel (R3) and the combined stimulation of R1R3 (SNK, $P < 0.01$).
Stimulations delivered in phase 1 caused larger responses than stimulations delivered in phase 3 and 2 (SNK, $P < 0.005$). In addition, stimulations delivered in phase 2 caused larger responses than if delivered in phase 3 (SNK, $P < 0.05$).

Hip joint

At the hip joint, flexion was the typical response to stimulation. The degree of flexion was modulated by stimulation site and phase (two-way repeated measures ANOVA, main effect, both $P < 0.001$). Furthermore, the effect of the different stimulation sites depended on the phase in which the stimulation was delivered (two-way repeated measures ANOVA, interaction effect, $P < 0.001$) (Figure 9.6).
At the mid forefoot (R1), stimulation delivered in phase 3 resulted in smaller responses than when delivered in the other phases (SNK, $P < 0.005$). At the arch of the foot (R2), stimulations delivered in phase 1 caused larger responses than when delivered in phase 2 and 3 (SNK, $P < 0.001$). Within the combined stimulation site of R2R3, onsets in phase 1 caused larger hip flexion compared to onsets in phase 2 and 3 (SNK, $P < 0.001$). In addition, at stimulation site R2R3, onset in phase 2 resulted in larger responses than onset in phase 3 (SNK, $P < 0.05$).
Within phase 1, stimulation at the combined site of R2R3, the arch of the foot (R2), and the mid forefoot (R1) resulted in larger hip flexion responses than stimulation at the posterior aspect of the heel (R3) and the combined site of R1R3 (SNK, $P < 0.01$). Furthermore within phase 1, the combined stimulation of R1R3 caused larger responses than stimulation at the posterior aspect of the heel (R3) (SNK, $P < 0.05$).

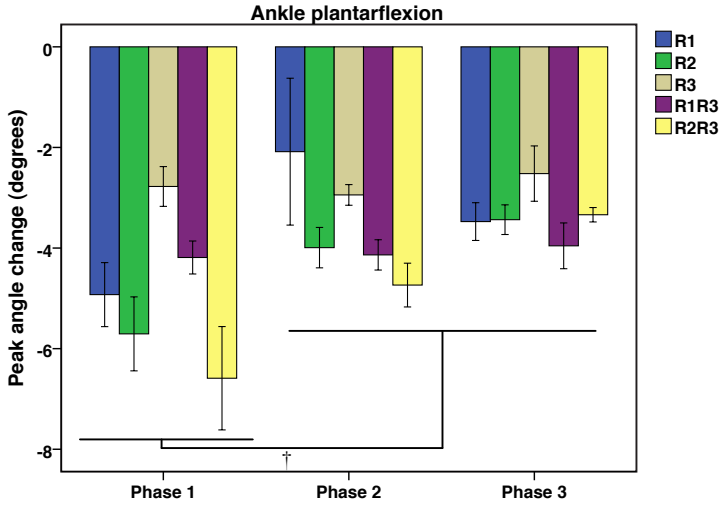


Figure 9.3: Kinematic ankle plantarflexion responses evoked by muscle stimulation applied in the stance phase and reflex stimulation delivered to five site combinations at the sole of the foot in three different phases. *The negative values indicate a reduction in plantarflexion as a response to stimulation. Values represent mean of the five sequence repetitions ± 1 SEM. There was a main effect of stimulation site and phase, and a significant interaction effect of site * phase. Stimulation sites: R1: mid forefoot, R2: arch of foot, R3: posterior of heel, R1R3: R1 followed by R3, R2R3: R2 followed by R3. † indicates main effect of phase*

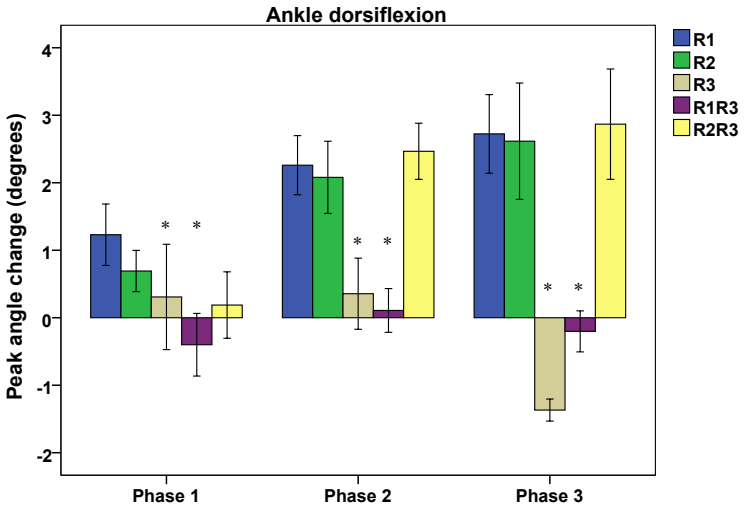


Figure 9.4: Kinematic ankle dorsiflexion responses evoked by muscle stimulation applied in the stance phase and reflex stimulation delivered to five site combinations at the sole of the foot in three different phases. *Values represent mean of the five sequence repetitions ± 1 SEM. There was a main effect of stimulation site and a significant interaction effect of site * phase. Stimulation sites: R1: mid forefoot, R2: arch of the foot, R3: posterior aspect of heel, R1R3: R1 followed by R3, R2R3: R2 followed by R3. ∗ indicates significant smaller responses compared to responses at the other sites.*

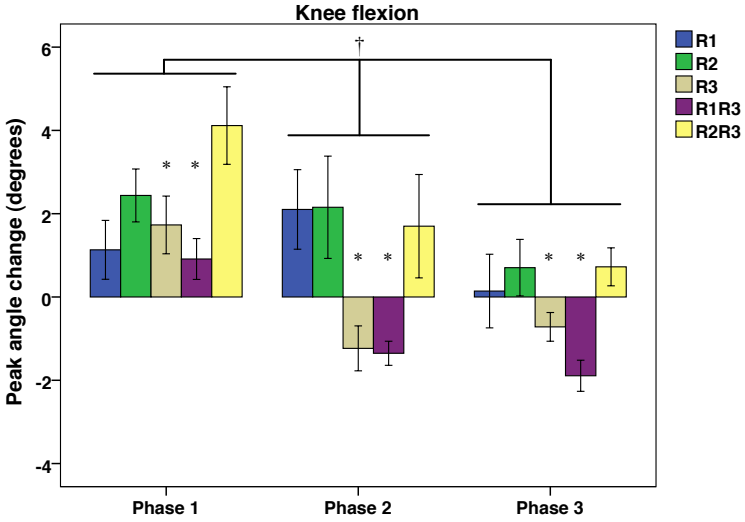


Figure 9.5: Kinematic knee flexion responses evoked by stance phase muscle stimulation and reflex stimulation delivered to five site combinations on the sole of the foot at three different phases. *Values represent mean of the five sequence repetitions ± 1 SEM. There was a main effect of both phase and stimulation site. Stimulation sites: R1: mid forefoot, R2: arch of the foot, R3: posterior aspect of heel, R1R3: R1 followed by R3, R2R3: R2 followed by R3. † indicates the main effect of phase. ∗ indicates significant smaller responses compared to the other sites.*

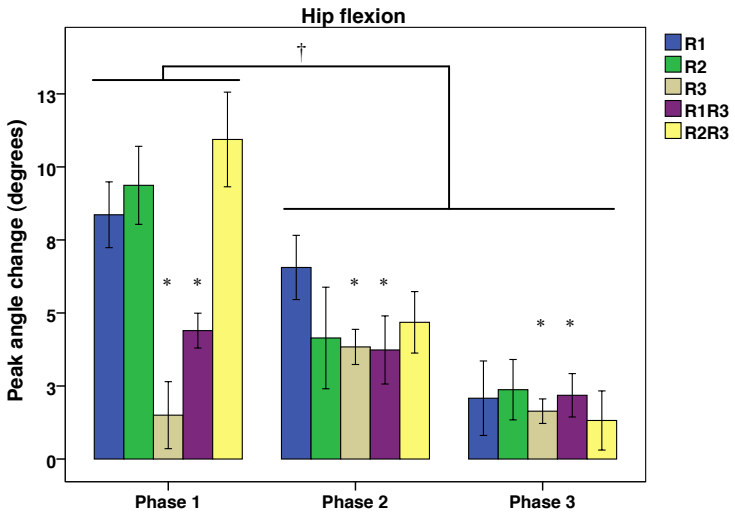


Figure 9.6: Kinematic hip flexion responses evoked by stance phase muscle stimulation and reflex stimulation delivered to five site combinations on the sole of the foot at three different phases. *Values represent mean of the five sequence repetitions ± 1 SEM. There was a main effect of both phase and stimulation site, and an interaction effect of site * phase. Stimulation sites: R1: mid forefoot, R2: arch of the foot, R3: posterior aspect of heel, R1R3: R1 followed by R3, R2R3: R2 followed by R3. † indicates the main effect of phase. ∗ indicates significant smaller responses compared to the other sites.*

Effect of muscle stimulation on the kinematic responses in the stance phase

Stimulation of QA and SOL resulted in modified kinematic recordings during the stance phase compared to baseline recordings, see example in figure 9.2. The horizontal dotted lines at the hip- and knee goniograms indicate that the mean starting point of the goniograms was not the same at the beginning of the baseline swing phase compared to the beginning of the stimulation step swing phase. This angle offset was created by the muscle stimulation, since the reflex stimulation responses were not evoked yet at this time point.

QA-stimulation resulted in decreased ankle flexion, decreased knee flexion, and increased hip flexion compared to baseline (no stimulation) (all $P < 0.001$, one-sample t-test). SOL-stimulation resulted in increased ankle flexion ($P < 0.05$, one-sample t-test), increased knee flexion, and increased hip flexion ($P < 0.001$, one-sample t-test) compared to baseline (Figure 9.7).

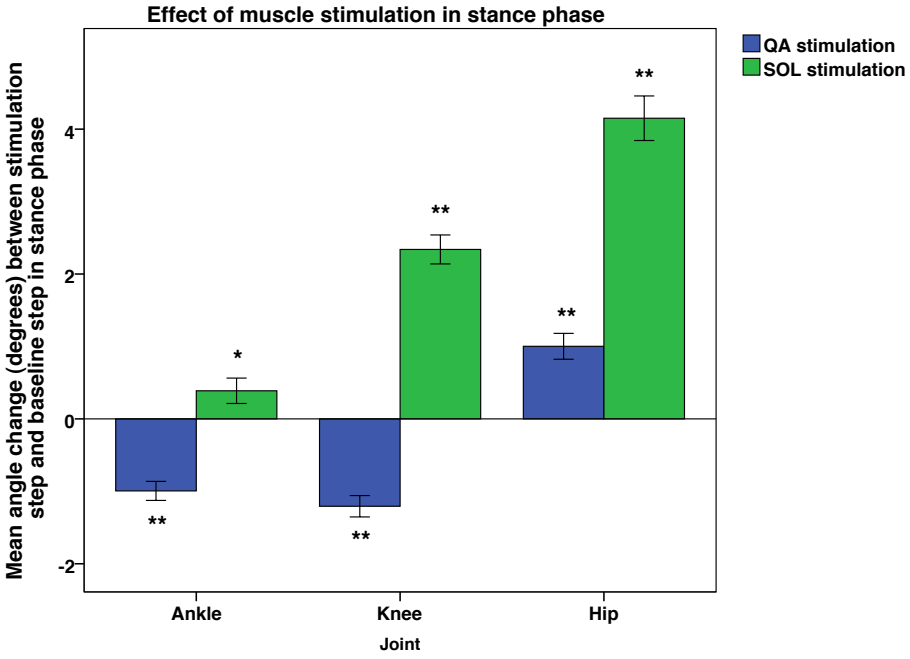


Figure 9.7: Effect of muscle stimulation to QA and SOL on the kinematic recordings during the stance phase. *The bars indicate mean angle changes between the QA- and SOL stimulation-on periods in stimulation steps and the corresponding periods in the baseline steps. Values represent mean of 75 sequence repetitions ± 1 SEM. * denotes significant different from baseline ($P < 0.05$) and ** denotes significant different from baseline ($P < 0.001$).*

9.4 Subconclusion

Case Study 2 investigated the effect of combining muscle stimulation in the stance phase of gait with elicitation of the NWR to initiate the swing phase in one hemiparetic participant.
The Case Study showed that the kinematic responses were modulated by stimulation site- and phase.

Stimulation delivered to the distal sites of the foot (R1 and R2) and to the combined site of R2R3 did generally cause more hip- and knee flexion, more reduction in ankle plantarflexion, and more ankle dorsiflexion than stimulation delivered to the other sites. Stimulations delivered near heel-off (phase 1) caused larger knee- and hip flexion, and a more pronounced reduction in ankle plantarflexion than stimulations delivered at toe-off (phase 3).

The QA muscle stimulation resulted in more extension of the knee joint and more flexion of the hip joint during the QA stimulation-on period compared to baseline stand phase, whereas the SOL stimulation caused a flexion increase in all joints during the SOL stimulation-on period, indicating that the muscle stimulation supported the push-off prior to the swing phase.

In conclusion, the modulation observed in Case Study 2 might have application in the rehabilitation of this hemiparetic patient, since the possibility of eliciting different responses may help to tailor the FES to the individual needs of the patient. By adding the use of muscle stimulation, it might be possible to support both stance- and swing phases of hemiparetic gait and thus, help the patient to achieve and relearn a more functional gait pattern. Part III of this report deals with the design and implementation of a gait controller that exploits the modulatory effect of the NWR and the support provided by the muscle stimulation to assist hemiparetic gait.

Part III

Implementation of the Gait Controller

This part deals with the gait controller; controller strategy, the specification requirements, and implementation of it. The part ends with Case Study 3 aiming to test the performance of the gait controller on a hemiparetic participant.

Chapter 10

Controller Strategy

The aim of this project was to design and implement a gait controller to be used for external control of gait for stroke patients. To be able to know exactly when and at which stimulation site to stimulate, different strategies for control and modelling of the plant can be utilised. Different controller approaches are discussed in this chapter.

The gait controller should be able to support the hemiparetic gait by combining muscle stimulation in the stance phase of gait with the elicitation of the NWR to initiate the swing phase. The control system to be developed is illustrated as a Multiple Input Multiple Output (MIMO) black box system in figure 10.1, where the plant is the stroke patient.

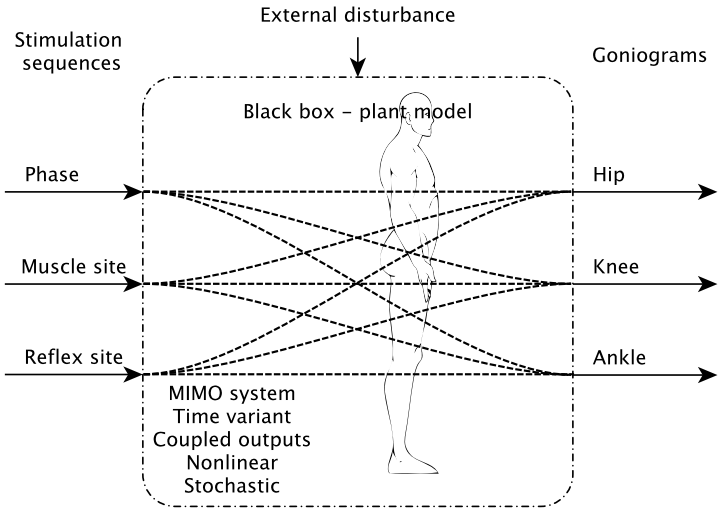


Figure 10.1: A black box representation of the control system. *The inputs are a set of stimulation parameters including phase in the gait cycle at which the NWR is elicited (three combinations), muscle stimulation site (two combinations), and reflex stimulation site (five combinations). The system is a Multiple Input Multiple Output (MIMO) system, and it is time variant, nonlinear, stochastic, and has coupled outputs.*

In Case Study 1 and 2, it was found that the reflex responses depended on stimulation site at the sole of the foot and phase in the gait cycle at which the stimulation was delivered. To make use of this property of the NWR in the gait controller, the input to the system is decided to consist of *reflex stimulation site* for eliciting the NWR and *phase* in the gait cycle at which the NWR is elicited. Furthermore, *muscle stimulation site* is included as input to the system. The inputs to the system are categorical, since the stimulation sites can not be interpolated.

The output from the system are continuous hip-, knee-, and ankle angles obtained from the goniometers. The outputs are coupled (see figure 10.1), since the joint angles depends on each other during the motion of gait, e.g. the posture of the hip joint affects the withdrawal of the knee joint. Furthermore, all inputs to the system may affect all outputs. The outputs are time variant, nonlinear and stochastic due to the nature of the NWR being influenced by descending commands, habituation, and voluntary contributions to the resulting movement. In addition, there are latencies in the system, because the reflex response to stimulation can be evoked in the time window 90-240 ms from stimulation onset [Spaich et al., 2006].

These characteristics of the system means that ordinary modelling tools such as Linear Time Invariant (LTI) tools and transfer functions can not be used. Thus, considering the above characteristics of the system, the modelling of the plant is a complex problem.

To control the output of the system (trajectories of hip, knee, and ankle joints), a controller can be applied to control the input parameters to the system. The strategy for designing and implementing the controller is important and depends on the type of system. In general there are two types of controllers: closed- and open-loop controllers. Depending on which type is chosen, the code-complexity of the controller, amount of training data, execution speed, and error reduction, may vary to great extent.

Closed-loop controllers

Closed-loop controllers, also called feedback controllers (see figure 10.2) have an ongoing knowledge of the effects of the disturbances to the plant. Sensors, such as joint-angle sensors or force sensors, are able to achieve this knowledge from the plant. The signals from the sensors are used to estimate the current state of the system, which is then fed back to the controller and used to choose the strategies for the next stimulation; hence, the term feedback controller.

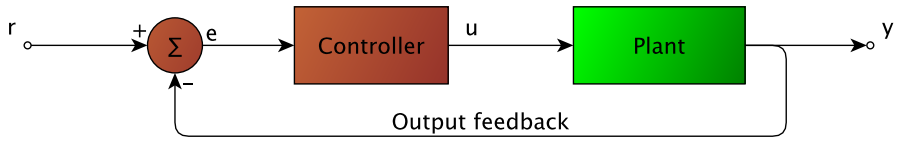


Figure 10.2: A schematic representation of a basic closed-loop controller. *The plant block corresponds to the black box seen in the figure 10.1. The closed-loop concept is explained in the text.*

Closed-loop controllers are error-driven, which means that the controller output (u) is based on the difference (error, e) between the reference trajectory (r) and the actual output (y). This error is used by the controller to determine which control signal to send back to the plant. How this control signal is determined, depends on the chosen controller strategy. Some controller strategies depend purely on the

post- and present values of the error, while other may also include a model of the plant to determine the error.
Closed-loop control systems are suitable for tasks, where the properties of the plant are constantly changing. [Åström and Wittenmarkt, 1995]

Open-loop controllers

Open-loop controllers are also called non-feedback controllers, because they do not use feedback from the plant to determine if the output has achieved the desired goal of the input to the plant, i.e. the system is not error-driven. This means that the control system is not observing the plant trajectories that it is controlling.
An open-loop controller delivers its command signals based on predefined sequences. In the case of a neural prosthesis, the command signals are pre-computed patterns of stimulation.

An open-loop controller cannot provide acceptable system behaviour in all situations, since the process to be controlled might have unknown or time-varying parameters, e.g. walking over uneven terrain, muscle spasms, or muscle fatigue. A possibility to provide a more robust control scheme to an open-loop controller is to trigger the onset of stimulation by sensors attached to the plant. In the case of a gait controller, the sensors might be composed of force sensors mounted under the sole of the feet, so that the stimulation onset can be adjusted to the actual gait pattern of the user. In this way, the controller is still based on pre-computed sequences, but the stimulation onsets are adjusted to the behaviour of the plant, if the user for instance changes walking speed or stops walking to take a break. [Popović and Sinkjaer, 2003, Sweeney et al., 2000, Åström and Wittenmarkt, 1995] A schematic overview of a sensor-based open-loop controller is depicted in figure 10.3.

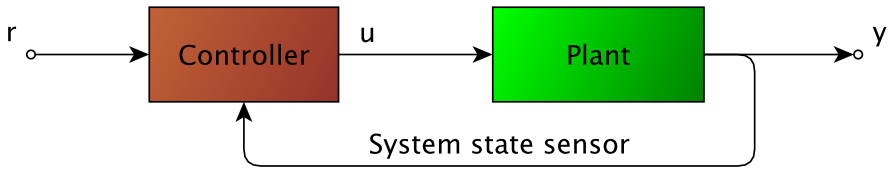


Figure 10.3: A schematic representation of a sensor-driven open-loop controller. *The plant block corresponds to the black box seen in the figure 10.1. The sensor-driven open-loop concept is explained in the text.*

When using the controller, the sensor is used to trigger the onset of a sequence (u) aiming to achieve the reference trajectory (r). The plant then responds with the actual output (y). In an ideal open-loop controller, (y) and (r) are similar.

10.1 Chosen controller strategy

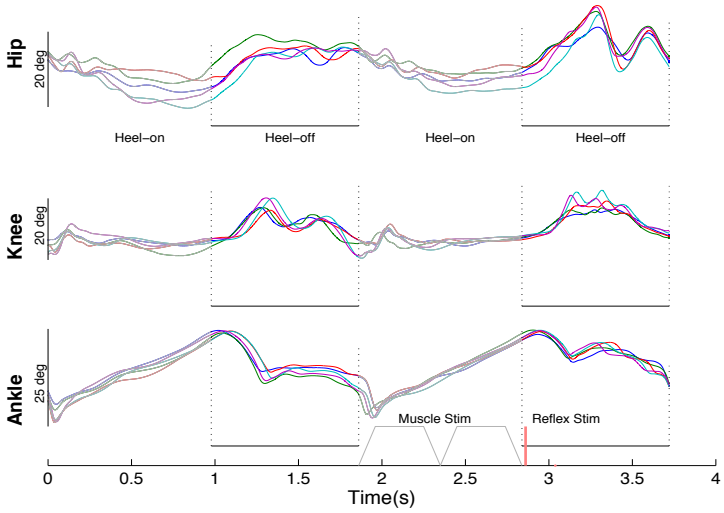
It has been decided to design and implement a sensor-driven open-loop gait controller. A closed-loop approach with feedback to the controller composed of goniometer output from hip, knee, and ankle joints could also have been applied, but the complexity of a system like this exceeds the scope of this

project. The goal is to investigate the kinematic responses obtained from the combination of muscle stimulation and elicitation of the NWR in order to rehabilitate the gait of stroke patients. This is usually done in a controlled environment for a limited amount of time, where the patient is walking on a treadmill or on a plain surface with minimal disturbances to affect the gait pattern. Thus, it is estimated that a sensor-driven open-loop gait controller provides sufficient control to test the intended protocols properly.

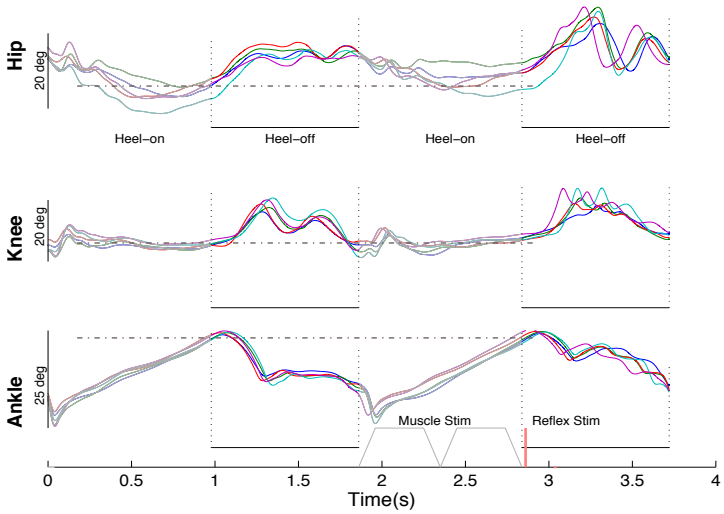
During the offline analysis of the data obtained in Case Study 2 from the hemiparetic participant, it became evident that the kinematic responses to stimulation were dependent on stimulation site on the sole of the foot and phase in the gait cycle at which the NWR was elicited.
The gait of the hemiparetic participant deviated from normal gait mainly because of decreased flexion in hip- and knee joints in the swing phase, increased plantarflexion after heel-off, and decreased dorsiflexion after toe-off (see baseline step comparison between the stroke patient and a healthy participant in figure 9.1, chapter 9). Thus, the target for the open-loop controller should be to rectify these deviations.
On the basis of the results from Case Study 2, three optimal stimulation sequences were chosen (figures 10.4a-c). These stimulation sequences fulfilled the needs of the specific hemiparetic participant by causing increased knee-, hip-, and ankle dorsiflexion and reduced ankle plantarflexion. Furthermore, the plant responses were quite similar when using these three stimulation sequences. The chosen stimulation sequences are:

- Mid forefoot (R1) stimulation delivered near heel-off (phase 1).
- Arch of the foot (R2) stimulation delivered near heel-off (phase 1).
- Combined site of arch and posterior aspect of the heel (R2R3) stimulation delivered near heel-off (phase 1).

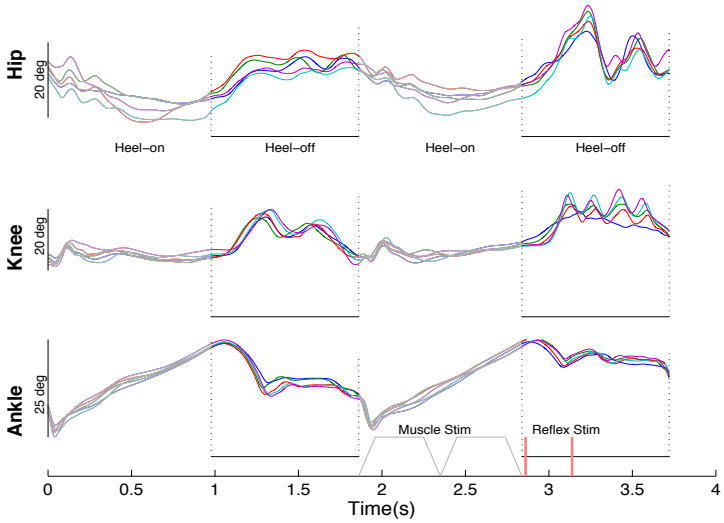
The order of the predefined stimulation sequences should be randomised in the gait controller to minimise the effect of reflex habituation compared to the case where only one type of stimulation sequence is used continuously. The onset of the stimulation sequences is controlled by a heel-switch, which provide the only feedback in the system. When the heel-switch sends a trigger to the gait controller, the controller executes one of the three stimulation sequences, hence the name: sequence-based stimulation (SBS) controller paradigm. Figure 10.5 shows a schematic overview of the gait controller to be developed.



(a): Stimulation sequence:R1, phase 1.



(b): Stimulation sequence:R2, phase 1.



(c): Stimulation sequence:R2R3, phase 1.

Figure 10.4: The three selected stimulation sequences utilised in the sequence-based stimulation controller. *The figures show the kinematic measures from two consecutive steps: a baseline step and a stimulation step.*

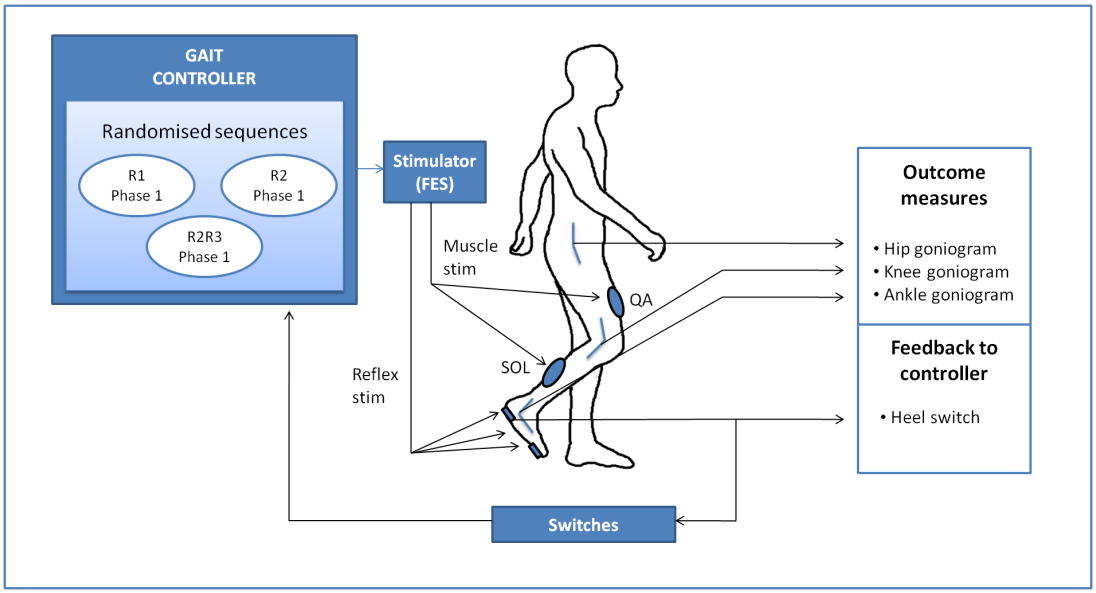


Figure 10.5: Schematic overview of the sequence-based open-loop controller developed in this project. *The controller output is randomised between three different stimulation sequences, which are known to support the gait of the specific hemiparetic patient by increasing hip- and knee flexion, increasing ankle dorsiflexion and reducing ankle plantarflexion. The timing of the QA and SOL muscle stimulation and the elicitation of the NWR is triggered by a heel-switch during the use of the controller. The toe-switch is only used in the calibration session before the actual use of the gait controller to determine the stimulation onsets as percentages of the heel-on- and heel-off/toe-off periods. Goniometers are used to monitor joint angles.*

CHAPTER 11

SPECIFICATION REQUIREMENTS FOR THE GAIT CONTROLLER

The requirements are created on the background of knowledge obtained in: Part I - “Problem Analysis” and the offline analysis of the data obtained in Case Study 1 and 2 in Part II - “Experimental Studies”. The gait controller is programmed in LabVIEW™, which provide both handy utilities and an easy way to implement interfaces.

Electrical stimulation:

- Muscle stimulation of QA in the first half of the heel-on period and SOL in the last part of the heel-on period.
- Random selection of one of three reflex stimulation sequences: (1) R1, phase 1, (2) R2, phase 1, (3) R2R3, phase 1.
- Every forth and fifth step during the use of the gait controller should be baseline steps without stimulation.

Triggering of electrical stimulation:

- The onset of the stimulation should be triggered via signals from a heel-switch.

Security:

- The interface should restrict the output of DAQ card if an event occurs, where it looses the connection to the PC and continues to output a signal.
- The operator of the system should be able to end the experiment at any time.

- The operator of the system should be able to monitor the data online during an experimental session to verify that the data is valid.

Data collection:

- The continuous goniometer data should be obtained and saved for offline analysis.
- Heel-switch signals should be obtained and saved to support the offline analysis.
- Toe-switch signals should be obtained for use in calibration of stimulation onsets before the use of the controller.

Graphical user interface:

- Online view of goniograms from hip, knee, and ankle joints, stimulation profile, and FSR output during the use of the gait controller.

CHAPTER 12

IMPLEMENTATION

Hardware setup

The controller uses the same physical setup as the laboratory stimulation system used during Case Study 1 and 2, see figure 12.1. The controller interface is programmed LabVIEW^{TM}8.6, and is the link between the system and the operator. The different modules of the system are mounted in a National Instruments BNC-2090 terminal board, which communicates with the control interface via a National Instruments PCI-6042E DAQ-card.

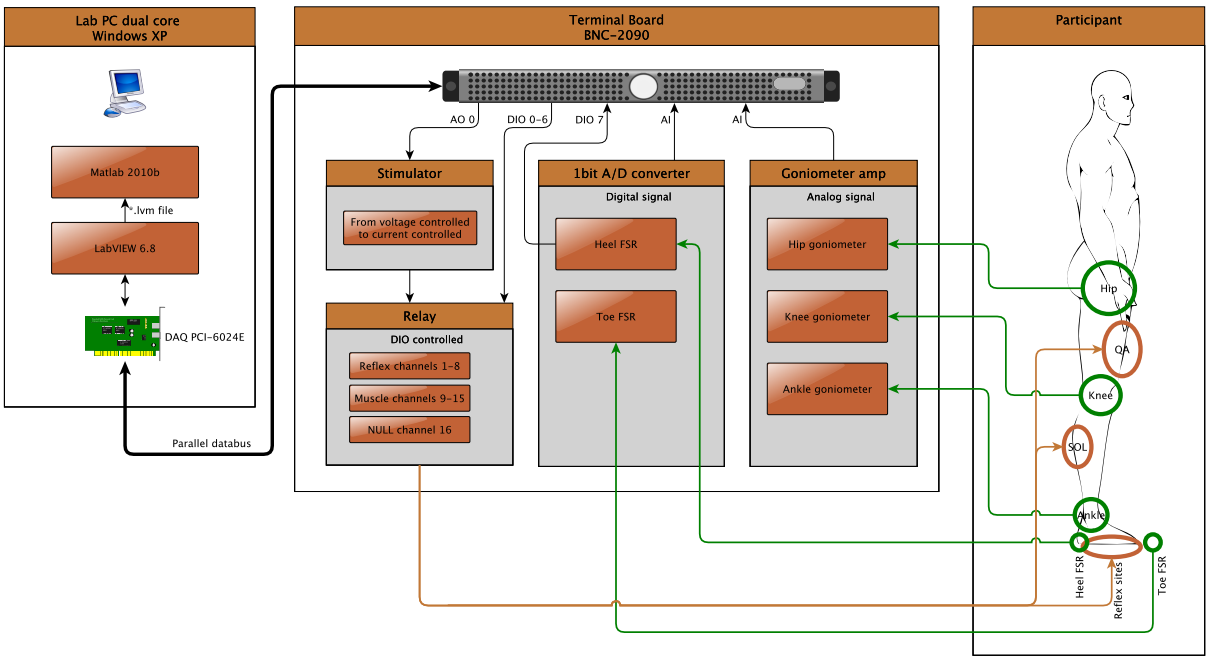


Figure 12.1: The setup and design of the control system.

The stimulator is controlled with the analogue output AO0, and is connected to the participant via a relay module. The relay makes it possible to select up to 15 different channels for delivering of electrical stimulation. The relay is controlled with the digital output DIO0-6 and activated when it receives a signal on counter 1 (CTR1). This is a security feature that will be explained further below in the text.
The first eight channels are available for reflex stimulation, the next seven are reserved for muscle stimulation, and the last channel is a NULL channel. To avoid unintentional stimulations, the last channel is selected by default when no stimulation is supposed to be delivered.

The foot-switches (heel- and toe-switch) are force sensitive resistors (FSRs), which are connected to a switch amplifier. The amplifier is calibrated so that it outputs a digital signal corresponding to the participant's heel-on/off and toe-on/off. The digital signal is sampled as an analogue signal, since the digital inputs are preoccupied for other uses, and it is easier to visualise. Furthermore, the heel-switch is digitally sampled, which is necessary for the controller to "sense" where in the gait cycle, the paretic leg is, and respond with a stimulation sequence when necessary.
The goniometers are connected via a filter- and an amplifier module, which have an output range from $-10V \rightarrow 10V$. The goniometers are calibrated first via the analogue offset knob at the amplifier and later in the control interface on the screen. On the amplifier, the hip goniometer is adjusted so that it outputs $0V$ when the goniometer angle is $180°$, and at the knee joint the amplifier should output around $8V$ when the goniometer angle is $180°$ in order to avoid clipping of the goniogram if the knee is overextended. At the ankle joint, the goniometer is calibrated so that it outputs $0V$ when the goniometer angle is $90°$.

Software interface and controller

Figure 12.2 depicts the sequence-based open-loop controller as it is implemented in the program. The controller is initialised by initialising the DAQ-card, test parameters: run time and stimulation intensity, and the three pre-defined stimulation sequences.
When the participant starts walking, and the data sampling is running, the program begins to wait for the heel-switch to initiate a new gait cycle. When the heel-switch is activated (at heel-strike), the controller executes a random sequence of the available sequences, unless the operator of the system has terminated the program. The continuous kinematic responses obtained from the goniometers attached to the participant are visualised on the screen and saved for offline analysis. When the next heel-strike arrives, another random stimulation sequence is executed and so on (unless it is a baseline step).

To prevent unintentional electrical stimulations, the opening of the relay and thereby the electrical stimulation is triggered by Counter 1 (CTR1) (see figure 12.3). Before the execution of a stimulation sequence is activated, the CTR1 is programmed to go high when it receives a rising edge from Counter 0 (CTR0), and it stays high for as long time as the window has been set to. This is a security measure and means that to execute the stimulation, the interface will only have to provide a single signal on CTR0 to execute. If the interface looses the connection to the DAQ-card, because the computer hangs or breaks down, the stimulation period is pre-programmed into the hardware and hence, it is independent of the operating system.
Data storage is executed independently and without interfering with the main controller program.

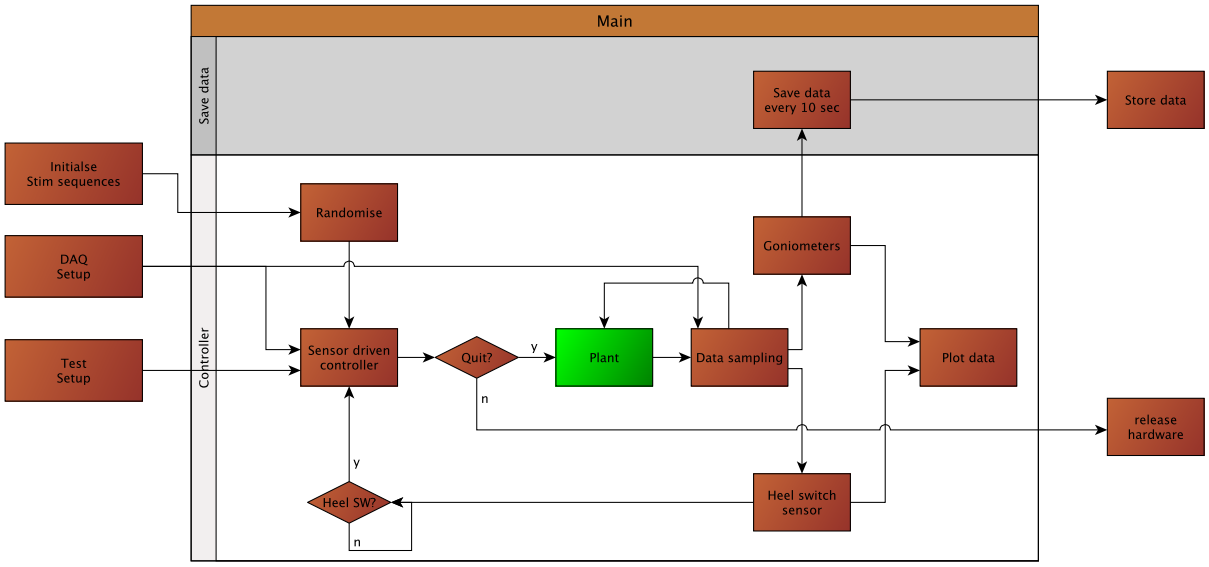


Figure 12.2: Flowchart of the implemented processes in the gait controller.

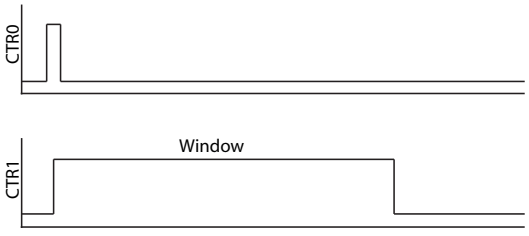


Figure 12.3: Control of the relay box. *Counter 1 controls the execution of the stimulation and the relay. Counter 0 is triggered by the interface and when activated, it makes the Counter 1 go high for a pre-determined period of time.*

CHAPTER 13

CASE STUDY 3: TEST OF SEQUENCE-BASED CONTROLLER TO SUPPORT HEMIPARETIC GAIT

13.1 Aim

The aim of this Case Study was to test the gait controller paradigm developed in this project (the design and implementation of the gait controller is described in chapter 10-12). The controller paradigm was tested against a simple controller paradigm, which was also based on elicitation of the NWR but without making use of its modulatory effect and without combining it with muscle stimulation in the stance phase of gait.
The gait pattern during the use of the controllers was evaluated based on measures of hip, knee, and ankle joint angles obtained from goniometers.

13.2 Method and Materials

Participant

The experiment was conducted on the chronic hemiparetic patient, who also participated in Case Study 2. Demographic details, plus inclusion- and exclusion criteria are described in chapter 9.
The study was approved by the local ethical committee (approval N-20090006), and all procedures were in accordance to the Declaration of Helsinki.

Electrical stimulation parameter setup

The method for evoking the NWR from the sole of the foot and applying muscle stimulation to QA and SOL muscles has been described in Case Study 1, chapter 8.

Gait controller paradigms

Sequence-based stimulation (SBS) controller

The SBS controller paradigm developed in this project was based on the findings from Case Study 2 showing that the NWR response was modulated during hemiparetic gait by stimulation site and phase of the gait cycle at which the reflex stimulation was delivered. On the basis of these results, we chose the three stimulation sequences causing the best gait support for the specific hemiparetic participant. The controller target was to give increased hip- and knee flexion throughout the swing phase, reduced ankle plantarflexion after heel-off, and increased ankle dorsiflexion after toe-off. The selected sequences were (1): R1, phase 1, (2): R2, phase 1, (3): R2R3, phase 1. The sequences were always composed of muscle stimulation of QA and SOL in the stance phase of gait and elicitation of the NWR to initiate the swing phase. The execution of the three different sequences was randomised to minimise the effect of habituation during the use of the controller. Stimulations onsets were triggered by a heel-switch.

Fixed pattern of stimulation (FPS) controller

The FPS controller paradigm was composed of a very simple control system, where electrical stimulations were always delivered to the mid forefoot at the time of heel-off. These parameters were based on findings from previous studies showing that stimulation at the mid forefoot resulted in large reflex responses causing knee flexion and ankle dorsiflexion [Spaich et al., 2004, 2006, Emborg et al., 2009], and stimulation at heel-off mainly caused hip- and knee flexion responses [Spaich et al., 2009]. Thus, according to the literature, these stimulation parameters would cause a good swing phase support for a hemiparetic participant. Muscle stimulation of QA and SOL was not included in the FPS controller. The reflex stimulation was triggered by a heel-switch.

Experimental protocol

Stimulation electrodes, FSRs, and goniometers were mounted on the participant, and the stimulation intensities for both muscle stimulation and elicitation of the NWR were determined as described in Case Study 1, chapter 8. To avoid false-negative toe-switch detections due to the patient's drop foot, the FSR used as toe-switch was placed on the first metatarsophalangeal joint in stead of the big toe. While the participant was walking on the treadmill, he was supported by a harness connected to the ceiling in order to prevent him from falling if the stimulations should make him stumble.

Before beginning the actual controller test, a sequence of 10 unperturbed control steps were acquired and used for definition of the stimulation onsets for the SBS controller paradigm. The signal from the

heel-switch was then used to trigger the computer-controlled stimulator.
The two different controller paradigms were tested with the participant walking on a treadmill with a constant velocity of 2 km/h (Figure 13.1). He walked 10 minutes with each of the controller paradigms and was instructed to request pauses whenever he needed it during the experiment to minimise the risk of fatigue. For both paradigms, every 4th and 5th step were baseline steps without any stimulation. The first controller paradigm to be tested was the SBS gait controller. We chose to test this controller paradigm before the simple FPS controller paradigm in case the participant could not finalise the experiment due to fatigue.

Data analysis

The goniograms were low-pass filtered (Butterworth, 25 Hz, sixth order, no phase lag). Only the second baseline step was used in the analysis to avoid a carry-over effect from the previous stimulation step. A moving average (MA) filter was applied to three baseline steps at a time in order to reduce the impact of possible non-stereotyped baselines steps on the analysis [Emborg et al., 2011]. The three stimulation steps between every two baseline steps were averaged and then peak angle changes were calculated between the averaged stimulation step and the following MA baseline step according to the same procedure as described in Case Study 1, chapter 8.

In addition to peak angle changes, the areas under the goniogram curves in the interval from heel-off to heel-strike were calculated, and the area change between stimulation steps and baseline steps was also used as a measure of controller performance. For the ankle joint, the area was calculated in two intervals to analyse the effect of both plantarflexion and dorsiflexion (plantarflexion: between heel-off and the moment of peak plantarflexion, and dorsiflexion: from this moment until heel-strike). The area changes were included in the analysis to investigate the temporal effects of the stimulations on the joint responses.

To analyse the overall performance of the two controller paradigms, the measures of peak angle changes and area changes, respectively, were summed and averaged for all joint reactions. This measure was denoted the overall performance score. Since the controller target was to reduce ankle plantarflexion after heel-off, the negative values from this measure were included as positive in the overall performance analysis.

Statistics

One-sample t-tests with 0 as the test value were used to analyse if the controller paradigms performed better than baseline (no stimulation) for the individual joint reactions.
T-tests were used to analyse the differences in peak angle change and area change for the single hip, knee, and ankle joint reactions, plus the overall performance score between the two controller paradigms.
$P < 0.05$ was considered as statistically significant. Error bars on the goniogram graphs indicate $\pm$ 1 standard deviation (SD), while the results on the bar plots are presented as mean of peak angle changes $\pm$ 1 standard error of the mean (SEM).

13.3 Results

Detection thresholds and stimulation intensities for the NWR

Detection thresholds on the sole of the foot, stimulation intensities used to evoke single stimulation channel NWRs, and scale factors used to evoke dual stimulation channel NWRs for the hemiparetic participant are presented in table 13.1.

Stimulation site	Detection threshold (mA)	Stimulation intensity (mA)	Scale factor
Mid forefoot (R1)	6	11	-
Arch of foot (R2)	4	11	-
Posterior of heel (R3)	3	10	-
R1 + R3	-	-	1
R2 + R3	-	-	1

Table 13.1: Detection thresholds, stimulation intensities at the different stimulation sites, and scale factors for dual stimulation channel stimulations.

Stimulation intensities for muscle stimulation

The stimulation intensities used for muscle stimulation of the hemiparetic participant are presented in table 13.2.

Stimulation site	Stimulation intensity (mA)
Quadriceps (QA)	33
Soleus (SOL)	23

Table 13.2: Stimulation intensities used for muscle stimulation.

Figure 13.1: Photos from the experiment. *A) Electrode position of R1 (mid forefoot) and R2 (arch of the foot). B) Electrode position of R3 (posterior aspect of the heel). C) The hemiparetic participant walking on a treadmill with support from the sequence-based stimulation (SBS) gait controller. Electrical stimulation was delivered to QA and SOL in the stance phase of his gait, while the NWR was elicited from the sole of the foot to initiate the swing phase.*

Overall performance of the two controller paradigms

Figure 13.2 shows hip, knee, and ankle goniograms of the mean baseline step followed by the mean stimulation step for the SBS- and the FPS controller paradigm, respectively.

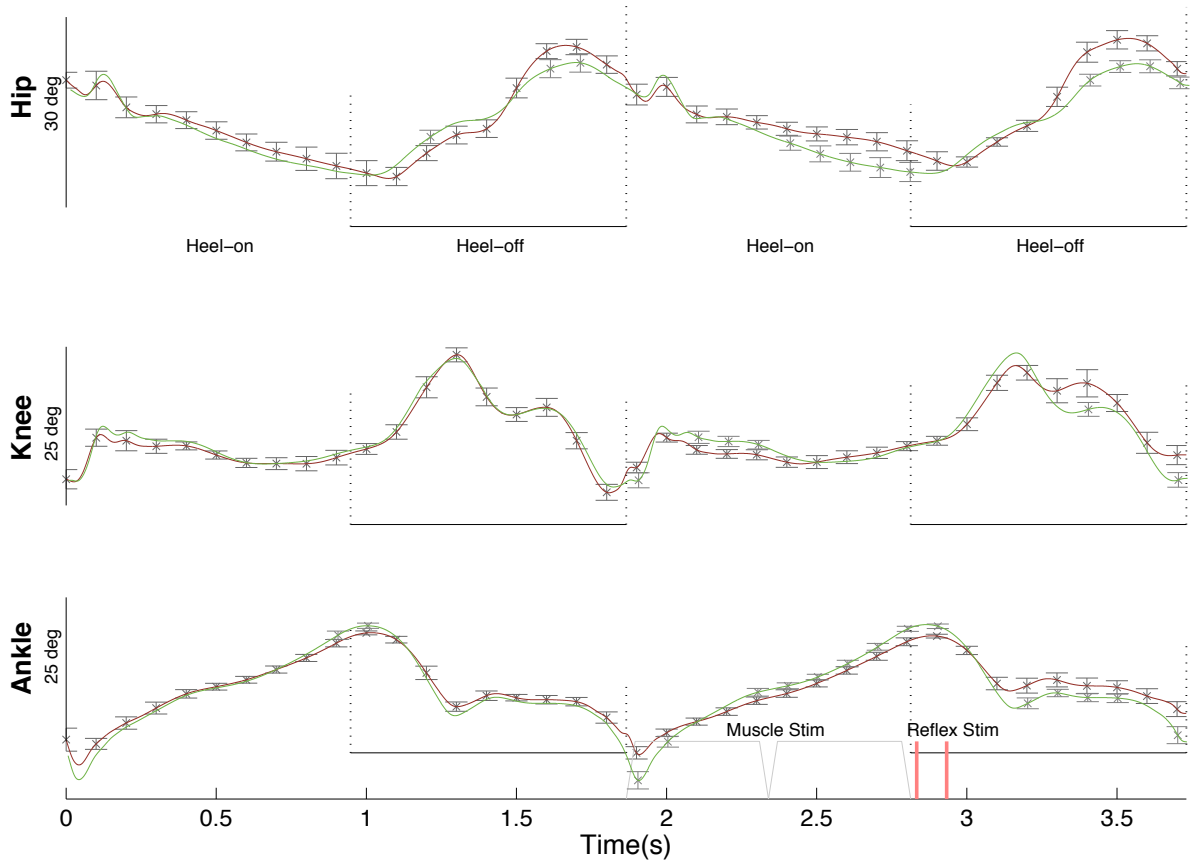


Figure 13.2: Mean responses from the two controller paradigms, when all three stimulation sequence responses are included from the SBS controller paradigm. *The figure shows the mean baseline step followed by the mean stimulation step from the SBS controller paradigm (red) and FPS controller paradigm (green), respectively. Error bars indicate ± 1 SD.*

Controller performances judged on the background of peak angle changes between stimulation steps and baseline steps

Overall, the SBS controller paradigm caused more hip peak flexion, more ankle dorsiflexion, and less peak knee flexion and ankle plantarflexion compared to baseline (all $P < 0.001$, one-sample t-tests), while the simple FPS controller paradigm caused more peak knee flexion, less peak ankle plantarflexion and dorsiflexion compared to baseline (all $P < 0.001$, one-sample t-tests).

The SBS controller paradigm was superior in providing hip and ankle support judged by significantly increased peak hip- and ankle dorsiflexion and reduced peak ankle plantarflexion compared to the FPS controller paradigm (all $P < 0.001$, t-tests). The FPS controller paradigm was superior in providing knee support judged by increased knee peak flexion compared to the SBS controller paradigm ($P < 0.001$, t-test)(Figure 13.3A).
According to the overall performance score, the SBS controller was superior in supporting the needs of the hemiparetic participant compared to the FPS controller paradigm ($P < 0.01$, t-test)(Figure 13.3B).

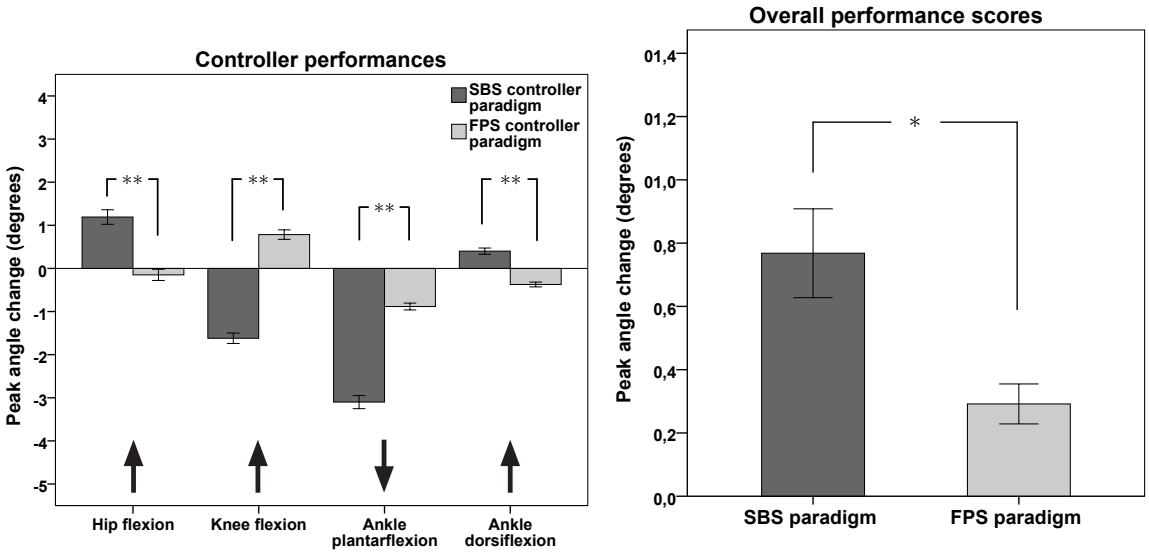


Figure 13.3: Controller performances and performance scores based on measures of peak angle changes between stimulation steps and baseline steps for the two controller paradigms. *A) Peak angle changes for the individual joint reactions. The arrows in the bottom of the figure indicate the target of the controllers, where increased flexion is upwards. B) Controller performance scores for the two controller paradigms. The bars represent mean of the summed peak angle changes for all joints ± 1 SEM. * and ** denote significant difference ($P < 0.05$ and $P < 0.001$, respectively) in peak angle change between the SBS- and the FPS controller paradigms.*

Controller performances judged on the background of area changes between stimulation steps and baseline steps

Overall, the SBS controller paradigm caused more hip- and knee flexion, and more ankle dorsiflexion compared to baseline (all $P < 0.001$, one-sample t-tests), while the simple FPS controller paradigm caused a reduction in plantarflexion and an increase in ankle dorsiflexion compared to baseline (all $P < 0.001$, one-sample t-tests).
The SBS controller paradigm was superior in providing increased hip-, knee-, and ankle dorsiflexion compared to the FPS controller paradigm (all $P < 0.001$, t-tests)(Figure 13.4A).
According to the overall performance score, the SBS controller was superior in supporting the needs of the hemiparetic participant compared to the FPS controller paradigm ($P < 0.001$, t-test)(Figure 13.4B).

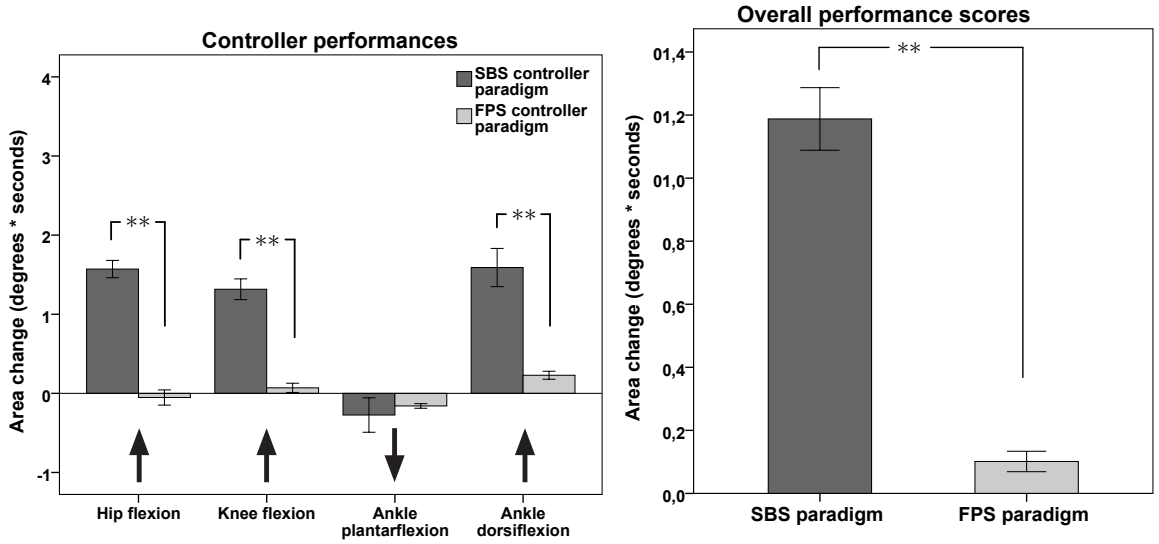


Figure 13.4: Controller performances and performance scores based on measures of area changes between stimulation steps and baseline steps for the two controller paradigms. *A) Area changes for the individual joint reactions. The arrows in the bottom of the figure indicate the target of the controllers, where increased flexion is upwards. B) Controller performance scores for the two controller paradigms. The bars represent mean of the summed area changes for all joints ± 1 SEM. * and ** denote significant difference ($P < 0.05$ and $P < 0.001$, respectively) in area change between the SBS- and the FPS controller paradigms.*

13.4 Subconclusion

Case Study 3 examined the performance of two gait controller paradigms to support the gait of a hemiparetic participant. Both controller paradigms were built on the basis of a sensor-based open-loop controller; the sequence-based stimulation (SBS) paradigm included muscle stimulation of QA and SOL in

the stance phase and execution of the NWR to initiate the swing phase. The NWR was elicited by one out of three stimulation sequences in randomised order during the use of the controller.
The fixed pattern of stimulation (FPS) controller paradigm included elicitation of the NWR to initiate the swing phase, and only the same stimulation sequence was used throughout the use of the controller.

The performances of the controller paradigms were judged on the basis of peak angle changes and area changes between stimulation steps and baseline steps. Peak angle changes examined the peak effects on the kinematic responses as a result of the stimulation, whereas the area changes examined the temporal effects on the kinematic responses as result of the stimulation.

Based on measures of peak angle changes, the SBS controller paradigm was superior in providing increased hip flexion, reduced plantarflexion, and increased dorsiflexion, whereas the FPS was superior in providing increased knee flexion.
Based on measures of area changes between stimulation steps and baseline steps, the SBS controller paradigm was superior in providing both increased hip- and knee flexion, reduced ankle plantarflexion, and increased dorsiflexion. Thus, overall the SBS controller paradigm proved better in supporting the gait needs of that specific hemiparetic participant.

Part IV

Synthesis

The part synthesises the findings and observations obtained in relation to this project by gathering the threads in a discussion of the three Case Studies and a conclusion. The part ends with a description of ideas for further development of the gait controller.

Chapter 14

Discussion

The aim of this project was to design and implement a gait controller that combines muscle stimulation to stabilise the paretic leg during the stance phase with elicitation of the NWR to initiate the swing phase of hemiparetic gait.
The project includes three Case Studies: two of them investigating the kinematic responses obtained when muscle stimulation is combined with elicitation of the NWR at different stimulation sites on the sole of the foot and at different phases in the gait cycle of normal gait and hemiparetic gait, respectively. The third Case Study aimed to test the performance of the gait controller designed on the background of the results from Case Study 1 and 2. The findings from the three Case Studies and general methodological issues and thoughts about the studies and work done in relation to the project are discussed in this chapter.

Case Study 1 and 2: Modulation of the NWR in Healthy- and Hemiparetic Participants

Case Study 1 and 2 showed that the NWR evoked by repetitive electrical stimulation at the sole of the foot was site- and phase modulated during both normal- and hemiparetic gait. Stimulation delivered near heel-off (phase 1) resulted in the most enhanced hip- and knee flexion, whereas stimulation at toe-off (phase 3) produced the most enhanced ankle dorsiflexion. Stimulation at distal sites (mid forefoot and arch of the foot) resulted in the largest knee- and hip flexion, whereas stimulation at the posterior aspect of the heel was associated with only a small increase in knee- and hip flexion. The modulatory effects observed in this study are in line with previous NWR modulation studies in healthy participants [Emborg et al., 2009, Spaich et al., 2009] and in stroke patients [Spaich et al., 2006] using similar stimulation protocols to elicit the NWR during gait, but without applying muscle stimulation in the stance phase.
We did only include four healthy participants in Case Study 1 and only one hemiparetic participant was included in Case Study 2, which mean that the power of the statistical tests performed on the obtained

data was quite low. It is therefore possible that the inclusion of more participants in both studies would have caused more valid results.

Site modulation of the NWR in the swing phase

The results indicated a site-modulation of the responses in the hip- and knee joints, where the highest degree of flexion was found after stimulation of the mid forefoot and the arch of the foot compared to stimulation at the posterior aspect of the heel. This is in line with the hypothesis that the painful stimulation creates a withdrawal of the foot away from the stimulus. Stimulation at the distal sites caused a withdrawal of the foot from the ground by flexion in hip- and knee, while stimulation at the posterior aspect of the heel caused only a slight flexion in these joints most likely because the primary movement was that the leg was pushed forward.

Phase modulation of the NWR in the swing phase

The stimulation protocols used in Case Study 1 and 2 showed phase modulated responses during both normal- and hemiparetic gait. The general picture was as follows: Stimulation at toe-off resulted in minimal reduction in plantarflexion, maximal increase in dorsiflexion, and minimal increase in knee- and hip flexion. The pattern was almost reversed when stimulation was delivered near heel-off, where there was a maximum reduction in ankle plantarflexion and ankle dorsiflexion, and a maximum increase in knee- and hip flexion. This phase-dependent pattern suggests a change in strategy dependent on the phase of the gait cycle: knee- and hip flexion is needed near heel-off to produce the push-off, whereas dorsiflexion of the ankle joint is not that important at push-off.
At toe-off, the push-off is already near its end, so dorsiflexion of the ankle joint is useful to keep the foot cleared from the ground, while enhanced flexion in knee and hip joints is not the most energy effective solution.
Phase-modulated withdrawal reflexes have previously been observed as a result of stimulation of the sural nerve during pedaling and locomotion [Andersen et al., 1995, Crenna and Frigo, 1984].

Effect of dual channel reflex stimulation

The purpose of the dual channel reflex stimulation was to achieve a more refined kinematic response with a higher degree of control, where the first stimulation delivered to one of the distal sites of the foot would lift it from the ground and the next stimulation delivered to the posterior aspect of the heel would create a forward propulsion of the foot to prepare for the step forward.
For the healthy participants, single channel stimulation of either the mid forefoot (R1) or arch of the foot (R2) typically caused additional hip- and knee flexion than when the stimulation site was combined with the site at the posterior aspect of the heel (R3); thus, the degree of flexion was decreased by the second stimulation in the dual channel stimulation train. Some of the healthy participants did also report that the dual channel stimulation felt very disturbing on their gait pattern because it felt like their foot was "braked" in the middle of its normal trajectory and instead forced downwards.

For the hemiparetic participant, however, the dual channel stimulation, especially the combination of arch followed by posterior aspect of heel (R2R3), caused more or similar degrees of reduced plantarflexion, and increased knee- and hip flexion as when single stimulations were delivered to the mid forefoot (R1) or the arch of the foot (R2). Opposite the healthy participants, the hemiparetic participant reported that the dual channel stimulation actually supported his forward propulsion of the paretic leg during his gait, which was in line with our observations during his gait.
The distortion of the normal gait in opposition to the support of the hemiparetic gait is most likely explained by the differences in voluntary control between healthy participants and the stroke patient. It is possible that the healthy participants counteracted the reflex responses caused by the dual channel stimulation because the responses felt disturbing on their normal walking pattern, whereas the paretic leg of the hemiparetic participant was more easily controlled by the electrical stimulation.

A drawback observed with the dual channel stimulation was that the reflex response to the second stimulation was often elicited too close to heel-strike, especially when the stimulation was delivered in phase 3 (at toe-off). This caused two of the healthy participants to nearly stumble during Case Study 1. The interval between the two stimulations was 150 ms to allow the first reflex response to be initiated before the next one would start. The interval was reduced to 100 ms in Case Study 2 on the hemiparetic participant to allow a better support, but the last reflex response seemed still to be evoked too late in the swing phase in phase 3.
A more optimal solution could be to utilise an interval of 50 ms or even skip the interval and let the two trains follow directly after each other. Another solution to shorten the duration of the dual channel stimulation is to modulate the stimulation trains, so they consist of two bursts in stead of four when dual channel stimulation is delivered. This means that two bursts would be delivered to the first site followed by two bursts delivered to the next site. In this way, the dual- and the single channel reflex stimulations would have the same duration.

Effect of muscle stimulation during the stance phase

The aim of stimulating QA was to extend the knee joint in the first part of the stand phase. According to mean angle changes between stimulation and baseline heel-on periods, this was not achieved in the healthy participants, but only in the hemiparetic participant. This finding can be explained by the fact that the participants counteracted the muscle stimulation in order to keep control over their QA muscle group during walking.
The aim of stimulating SOL was to provide support for the push-off prior to the swing phase. According to mean angle changes, this was achieved in both groups, but in a greater extent in the stroke patient. The results indicate that it is difficult to evaluate the supporting effect of muscle stimulation in healthy participants, since they are already able to control their muscles during gait. After the experiments, all participants expressed that the muscle stimulation felt supporting for their leg during the stance phase, and two of them (including the hemiparetic participant) did also indicate that the SOL stimulation helped them to produce a more pronounced push-off prior to the swing phase.
Muscle stimulation has been a standard solution to support the stand phase of hemiparetic gait in several previous studies, e.g. Fuhr et al. [2008], Kojović et al. [2009].

Case Study 3: Controller Performances

The SBS controller paradigm included both muscle stimulation as stand phase support and elicitation of the NWR as swing phase support, whereas the FPS paradigm only included elicitation of the NWR to support the swing phase. Overall, the SBS controller paradigm proved better than the FPS controller paradigm in reaching the controller targets of increased hip- and knee flexion throughout the swing phase, reduced ankle plantarflexion after heel-off, and increased ankle dorsiflexion after toe-off.
Based on measures of peak angle changes between stimulation steps and baseline steps, the simple FPS controller paradigm performed better in providing increased knee peak flexion compared to the SBS paradigm, whereas the SBS paradigm caused better knee support than the FPS paradigm based on measures of angle changes.
These results indicate that both peak- and temporal effects need to be taken into account when analysing the performance of the gait controller paradigms. Stimulation with the FPS controller caused a larger peak angle change than stimulation with the SBS paradigm, but the temporal effects of the SBS paradigm lasted for a longer period of time for the knee joint, since the area under the goniogram curve in the heel-off period was larger for the SBS paradigm compared to the FPS paradigm.

Choice of stimulation sequences to include in the SBS controller paradigm

The stimulation sequences implemented in the SBS gait controller paradigm were selected on the background of the results from Case Study 2. The sequences giving the largest peak kinematic responses during the swing phase were selected in order to provide the best support for the specific hemiparetic participant. When inspecting the results from Case Study 2 and 3, it is clear that the peak angle changes as result of stimulation were several degrees larger for the three selected sequences in Case Study 2 than in Case Study 3. This can mainly be explained from the fact that the stimulation intensities were lower at the mid forefoot (R1) and at the posterior aspect of the heel (R3) in Case Study 3 compared to Case Study 2, since the participant could not tolerate higher intensities when he was told that the stimulations would be delivered over a period of 10 minutes in order to test the controller performances. Furthermore, small variations in electrode positions on the sole of the foot and differences in skin impedance could have caused the same stimulation protocol to yield smaller kinematic responses during Case Study 3 compared to Case Study 2. Altering the stimulation intensity generally causes a scaling in magnitude of the reflex response, so it seems reasonable that the use of higher stimulation intensities would have caused similar results just with more pronounced reflex magnitudes. However, the stimulation intensity can also be too high, which will cause perturbation of the gait in stead of support.

Methodological Issues

Statistical power

Case Study 1 included four participants, while Case Study 2 and 3 only included one participant. The statistical power of the performed statistical tests are therefore quite low. Inclusion of more participants in all studies would have resulted in higher statistical power and, thus, more valid results.

Calibration of stimulation onsets

The triggering of both muscle- and reflex stimulation was controlled in real-time by the heel-switch, but the time durations from e.g. heel-off to the onsets of reflex stimulations in the three different phases were determined on the basis of 10 baseline steps obtained in the beginning of the experiment. The onsets for phase 1, 2, and 3 were determined as different percentages of the time duration from heel-off until toe-off. When the stimulation onsets were once determined, they were kept the same during the experiment regardless of possible changes in the walking speed and walking pattern of the participant. It is obvious that changes in walking speed would cause the stimulations to be delivered at inappropriate time points, e.g. too late or too early in the gait cycle. To ensure that the walking speed was kept the same throughout the experiment, the participants walked on a treadmill with a constant velocity of 2.5 km/h. Furthermore, the sound from a metronome was used to ensure that the participants kept the same cadence during the experiment.

In the design of a gait controller, it is important to account for possible changes in walking speed of the user when designing the triggering of stimulation. Stimulation delivered at inappropriate time points (e.g. a stimulation delivered to the sole of the foot after heel-strike) to a hemiparetic patient may cause him/her to stumble and fall. Therefore, it is necessary to update the baseline step of the user continuously in order to adjust the stimulation onsets to the present walking pattern of the user [Emborg et al., 2011].

Equal afferent input to stimulation electrodes on the sole of the foot

To study the site modulation of the NWR, it is essential to have an equal afferent input at each stimulation site. To reduce the effect of skin thickness, a constant current electrical stimulator was used, and grinding-off the areas on the sole of the foot with thick epidermis was performed prior to electrode attachment. Furthermore, the stimulus intensity at each stimulation electrode was adjusted to give the same sensory perception as a determined reference at the arch of the foot (stimulation site R2). Calibrating the stimulation intensities using this approach seems appropriate to ensure equal afferent input across stimulation sites when using single channel stimulation. However, it was very difficult for the participants to compare the sensory perception when stimulating the arch of the foot with the perception caused by dual channel stimulation, i.e. when two sites were stimulated just after each other. We instructed the participants to adjust the scale factor multiplied to the two intensities in the reflex stimulation train, so that the dual channel stimulation felt as painful as the single channel stimulation to the arch of the foot. The dual channel stimulation consisted of a total of eight bursts, whereas the single channel stimulation

consisted of only four bursts. It is possible that a pulse train of four bursts, where the first two bursts are delivered to one stimulation site and the two last bursts to another site might have resulted in a more equal input to the stimulation electrodes, because the number of pulses then would have been equal between single- and dual channel stimulation.

Determination of muscle stimulation intensity

When determining the intensity level for the muscle stimulation of QA and SOL, no clear criterion was used. The determination was in stead based on a subjective decision after assessing the contraction of the muscle by visual inspection and discussion of the perception of the stimulation with the participants. To implement a criterion for the determination of muscle stimulation intensity, e.g. a Kin-Com dynamometer could be used to obtain force measurements during stimulation. If a particular force level was set as criterion for each muscle, the stimulation intensity could be determined as the lowest intensity necessary to exceed this force level, when applied to the muscle.

The reflex responses might be biased by the "warning cue" of the muscle stimulation preceding the painful stimulation at the sole of the foot

The stimulation protocol used in Case Study 1 and 2 consisted of a stimulation step followed by a number of baseline steps without stimulation before the next stimulation step (inter-stimulus interval of 4-6 steps). The stimulation step was composed of muscle stimulation during the stance phase followed by stimulation of the sole of the foot to elicit the NWR, i.e. the evoked reflexes were always preceded by muscle stimulation. This protocol could have biased the kinematic responses, since the participants were warned about the unpleasant and sometimes painful reflex stimulation. They knew that the painful stimulation at the sole of the foot would follow right after the muscle stimulation, so they would keep their foot lifted from the ground a little longer than during a normal step in order to prepare for the kinematic distortion that the reflex response would cause on their gait. This unconscious behaviour of the participants became evident when we analysed some stimulation steps where the muscle stimulation was not followed by reflex stimulation. These steps showed a clear increase in dorsiflexion at the ankle joint during the swing phase, but the kinematic response was present approximately 350 ms after the end of the SOL stimulation delivered during late stance, which indicates that the response is most likely not a result of the stimulation but caused by descending control from the brain. This behaviour might only be present in the healthy participants, since the hemiparetic participant has reduced voluntary control of his paretic leg.
It is hard to judge the effect of the "warning cue" of muscle stimulation on the kinematic responses obtained in Case Study 1, and we cannot rule out that the responses might be biased. However, our results are in line with previous reflex studies [Emborg et al., 2009, Spaich et al., 2009] using a similar stimulation protocol to elicit the NWR (without applying muscle stimulation in the stance phase), so it is assumed that the observed responses are produced by a site- and phase dependant modulation of the NWR circuits.

The gait controller was tested on a chronic stroke patient despite the fact that the control system is intended to be used in the rehabilitation of sub-acute stroke patients

The controller paradigms were tested on a chronic stroke patient, who had already learnt to walk again after his stroke using compensatory movements, e.g. hip circumduction to compensate for the decreased knee flexion through the swing phase. He had already practised a non-functional gait pattern for a long period of time, and hence, it is difficult to "teach" him a more functional gait pattern by use of electrical stimulation.
To be able to design a gait controller to be used in the rehabilitation of sub-acute stroke patients, which is the aim of Functional Electrical Therapy (FET), it is necessary to analyse the NWR modulation and contribution of muscle stimulation in the sub-acute phase after stroke.

Chapter 15

Conclusion

The basic idea behind this project was to make use of functional electrical stimulation to assist hemiparetic gait. The aim was to design and implement a gait controller that combines muscle stimulation to stabilise the paretic leg during the stance phase with elicitation of the NWR to support and initiate the swing phase of hemiparetic gait.

The experimental content of this report was composed of three Case Studies; two of them dealing with basic research on the modulation of the NWR during normal and hemiparetic gait, and a third dealing with test of the developed gait controller to support hemiparetic gait.

The objective of Case Study 1 and 2 was to investigate the sensitivity of the kinematic responses obtained when combining muscle stimulation with elicitation of the NWR from different locations on the sole of the foot at different onsets in late stance/early swing phase of normal gait (n = 4 participants) and hemiparetic gait (n = 1), respectively.

Surface muscle stimulation was delivered to quadriceps (QA) in the interval from *heel-on to 50% of the heel-on/heel-off interval* to stabilise the leg by extending the knee joint, and to the soleus (SOL) muscle in the last half of the heel-on period to provide further support of the paretic leg and assist with push-off prior to the swing phase. Muscle stimulation was composed of 400μ-pulses delivered at 50 Hz with ramps of 1 ms (both rising time and falling time).
The NWR was evoked by cutaneous electrical stimulation of five stimulation sites on the sole of the foot: three single channel reflex stimulations (R1: mid forefoot, R2: arch of the foot, R3: posterior aspect of the heel) and two dual channel reflex stimulations (R1R3: R1 followed by R3, R2R3: R2 followed by R3). The reflex stimulations were delivered at three different time onsets between heel-off and toe-off of the paretic leg: phase 1: *heel-off + 10% of the heel-off/toe-off interval*, phase 2: *heel-off + 50% of the heel-off/toe-off interval*, and phase 3: *toe-off*. The electrical stimulation used to evoke the NWR was composed of a train of four bursts delivered at 15 Hz, each burst consisting of 1-ms pulses delivered at 200 Hz.

To set up the stimulation parameters, control the execution of electrical stimulation at certain onsets during the gait cycle, and control the recording of data from the experiments, a laboratory system was

programmed in LabVIEW^{TM}. The system enabled execution of muscle stimulation from two channels and execution of reflex stimulation from three channels. The triggering of the stimulation was controlled by force sensitive resistors (FSRs) used as a toe- and a heel-switch. Kinematic data obtained from goniometers attached to hip, knee, and ankle joints was recorded continuously and saved for offline analysis.

The results from Case Study 1 and 2 showed that both healthy and hemiparetic participants presented site- and phase modulations of the kinematic responses evoked by the combination of muscle stimulation and elicitation of the NWR. Generally, largest knee- and hip flexion responses, and largest reduction in ankle plantarflexion responses were observed following stimulation in phase 1 near heel-off, while largest ankle dorsiflexion was observed following stimulation in phase 3 at toe-off of the ipsilateral leg. Stimulation at distal sites of the foot caused large hip- and knee flexion responses, while stimulation at the posterior aspect of the heel provided increased ankle plantarflexion for the healthy participant and minimum reduction in plantarflexion for the hemiparetic participant.
Both muscle stimulation and dual channel reflex stimulation had the largest impact on the responses obtained from the hemiparetic participant indicating that his kinematic movements were easier to manipulate with electrical stimulation due to his decreased voluntary control of the leg muscles. For the hemiparetic participant, QA stimulation caused increased extension of the knee- and ankle joints, and increased flexion of the hip joint during the QA stimulation period. On the other hand, SOL stimulation caused increased flexion in hip- and knee joints during the SOL stimulation period indicating a facilitation of foot push-off.

On the background of the results from Case Study 2 on the hemiparetic participant, a sequence-based stimulation (SBS) controller paradigm was designed and implemented. Three stimulation sequences were selected, which caused the best kinematic responses to support the gait of this specific hemiparetic participant. The selected stimulation sequences were composed of reflex stimulation to R1, R2, and R2R3, all delivered in phase 1. When combined with muscle stimulation of QA and SOL in the stance phase, these sequences caused marked increased hip- and knee flexion, reduced ankle plantarflexion, and increased ankle dorsiflexion compared to baseline.
In addition to the SBS controller paradigm, a simple fixed pattern of stimulation (FPS) controller paradigm was implemented. The FPS paradigm included elicitation of the NWR from the mid forefoot (R1) at heel-off without including muscle stimulation in the stance phase. Both controller paradigms were implemented as sensor-based open-loop controllers triggered by signals from a heel-switch.

Case Study 3 tested the performance of the SBS controller paradigm against the simple FPS paradigm. The controller paradigm was tested on one chronic hemiparetic participant in a single session. The participant walked with each of the two controller paradigms for 10 minutes, and the performance of each controller paradigm was judged on the basis of peak angle changes and area changes between stimulation steps and baseline steps. Peak angle changes examined the peak effects on the kinematic responses as a result of the stimulation, whereas the area changes examined the temporal effects on the kinematic responses as result of the stimulation.
Overall, the SBS controller paradigm was superior in providing gait support for the hemiparetic participant compared to the FPS paradigm ($P < 0.01$ based on measures of peak angle changes between stimulation steps and baseline steps, and $P < 0.001$ based on measures of area changes between stimulation steps and baseline steps).

In conclusion, the findings obtained in relation to this master thesis suggest that hemiparetic patients may benefit from being exposed to the SBS controller paradigm, where QA- and SOL muscles are activated in the stance phase and the NWR elicited to initiate the swing phase. The stimulation paradigm is intended to be used in Functional Electrical Therapy (FET) of patients in the sub-acute phase after stroke. The purpose is that this gait training will facilitate the rehabilitation of gait by supporting the existing voluntary effort to establish a faster recovery and a more functional gait pattern compared to conventional therapy.

CHAPTER 16

FUTURE DEVELOPMENTS

Our system is only applicable in a laboratory setting, which limits the clinical usability of the system. The aspects listed below are possible future developments that would improve the system and its performance. These aspects needs to be taken into account before our gait controller can be used as a tool in clinical practise in the rehabilitation of stroke patients.

The gait controller should be adaptive to the individual stroke patient

The gait controller is developed specific to one stroke patient, which means that it is designed to take care of his special needs during gait. Therefore, it would probably not be as helpful to assist other stroke patients, since the needs for walking assistance is very individual after stroke. If the gait controller should be utilised as a clinical rehabilitation tool, it is important that it is adaptive to the single user. In order to develop an adaptive controller, a more detailed analysis of stroke patients' gait and responses to stimulation needs to be gained.

Incorporation of the possibility to vary the stimulation intensity during the use of the controller

With the gait controller developed in this project, the stimulation intensity is determined in the beginning of the experiment and kept the same throughout the use of the controller. It could, however, be useful to implement a variable stimulation intensity into the controller to be able to change the magnitude of the reflex response. This implementation could be beneficial if the reflex responses starts to habituate over time, since it has been shown that varying the stimulation intensity might prevent the habituation of the NWR [Dimitrijević et al., 1972].

Implementation of a better method to detect gait events

During the Case Studies carried out in relation to this project, it became evident that the use of force sensitive resistors (FSRs) as heel-switch and toe-switch to detect the gait events was not as robust and suitable as expected. The sensors were used as force based binary switches, and even with healthy participants having a normal gait pattern, it was difficult to mount the sensors at appropriate locations on the sole of the foot and determine a proper on/off threshold for the sensors without causing problems with false-positive and false-negative heel- and toe contacts. With the hemiparetic participant it was even harder to position the sensor, since he suffered from drop-foot and often had initial contact with his forefoot instead of the heel. It is vital for a gait controller to adequately detect the gait events to be able to deliver the stimulations on the right time instants in the gait cycle. If stimulations are not timed to the gait events, the response to the stimulation may cause the user to loose balance and fall.
Accelerometers may replace FSRs for the detection of gait events. The use of accelerometers requires additional signal processing to make the detection happen in real-time, which is required in a gait controller to be able to time the triggering of the next stimulation.

Minimisation of donning/doffing

If the gait controller has to be used in clinical practise, another important aspect is the time it takes to fixate the sensors, electrodes etc. (donning) and also the time it takes to dismount the sensors of the controller (doffing). The time of donning and doffing should be as minimal as possible in order to ensure that the time set aside for each stroke patient in a rehabilitation session is mainly spent on walking retraining with the gait controller and not on fixation and dismounting of the control system.

Implementation of more output channels

With the gait controller approach developed in this project, it was only possible to use one stimulation channel at a time, i.e. overlap between stimulations from different channels was not possible. If the controller should be further developed, it could be practical to implement more than one output channel. In this way, the muscle stimulation could overlap the elicitation of the NWR, or the muscle stimulation of QA could overlap that of SOL, which would possible cause a more functional gait pattern.

References

Åström, K. J. and Wittenmarkt, B. *Adaptive Control*. Addison-Wesley, 2nd edition, 1995. ISBN 0-201-55866-1.

Andersen, O. K.; Jensen, L. M.; Brennum, J.; and Arendt-Nielsen, L. Modulation of the human nociceptive reflex by cyclic movements. *European journal of applied physiology and occupational physiology*, 70(4): 311–21, January 1995.

Andersen, O. K.; Sonnenborg, F. A.; and Arendt-Nielsen, L. Modular organization of human leg withdrawal reflexes elicited by electrical stimulation of the foot sole. *Muscle & Nerve*, 22:1520–1530, 1999.

Andersen, O. K.; Spaich, E. G.; and Madeleine, P. Gradual enlargement of human withdrawal reflex receptive fields following repetitive painful stimulation. *Brain Research*, 1042:194–204, 2005.

Arendt-Nielsen, L.; Sonnenborg, F. A.; and Andersen, O. K. Facilitation of the withdrawal reflex by repeated transcutaneous electrical stimulation: An experimental study on central integration in humans. *European journal of pain*, 81:165–173, 2000. doi: 10.1016/j.ejpain.2004.02.009.

Bajd, T.; Kralj, A. R.; Turk, R.; Benko, H.; and Sega, J. The use of a four-channel electrical stimulator as an ambulatory aid for paraplegic patients. *Phys Ther*, 63:1116–1120, 1983.

Baker, L. L.; Wederich, C. L.; McNeal, D. R.; Newsam, C. J.; and Waters, R. L. *NeuroMuscular Electrical Stimulation - A Practical Guide*. Los Amigos Research & Education Institute, Inc. Rancho Los Amigos National Rehabilitation Center, Downey, California, USA, 4ed edition, 2000. ISBN 0-9676335-0-8.

Bijak, M.; Rakos, M.; Hofer, C.; Mayr, W.; Strohhofer, M.; Raschka, D.; and Kern, H. Stimulation parameter optimization for FES supported standing up and walking in SCI patients. *Artificial organs*, 29(3): 220–3, March 2005. doi: 10.1111/j.1525-1594.2005.29039.x.

Bjerre, L.; Andersen, A. T.; Hagelskjær, M. T.; Ge, N.; Mørch, C. D.; and Andersen, O. K. Dynamic tuning of human withdrawal reflex receptive fields during cognitive attention and distraction tasks. *European journal of pain (London, England)*, March 2011. doi: 10.1016/j.ejpain.2011.01.015.

Bogataj, U.; Gros, N.; Kljajić, M.; Aćimović, R.; and Malezic, M. The rehabilitation of gait in patients with hemiplegia: a comparison between conventional therapy and multichannel functional electrical stimulation therapy. *Physical therapy*, 75(6):490–502, June 1995.

Bowman, B. R. and Baker, L. L. Effects of waveform parameters on comfort during transcutaneous neuromuscular electrical stimulation. *Annals of Biomedical Engineering*, 13(1):59–74, 1985. doi: 10.1007/BF02371250.

Burridge, J. H.; Taylor, P.; Hagan, S.; and Swain, I. Experience of clinical use of the Odstock Dropped Foot Stimulator. *Artificial Organs*, 21(3):254–260, 1997. doi: 10.1111/j.1525-1594.1997.tb04662.x.

Burridge, J. H.; Haugland, M.; Larsen, B.; Pickering, R. M.; Svaneborg, N.; Iversen, H. K.; Christensen, P. B.; Haase, J.; Brennum, J.; and Sinkjaer, T. Phase II trial to evaluate the ActiGait implanted drop-foot stimulator in established hemiplegia. *Journal of rehabilitation medicine : official journal of the UEMS European Board of Physical and Rehabilitation Medicine*, 39(3):212–8, April 2007. doi: 10.2340/16501977-0039.

Caplan, L. R. *Caplan's Stroke: A Clinical Approach*. Saunders Elsevier, 4th ed edition, 2009. ISBN 978-1-4160-4721-6.

Cheeran, B.; Cohen, L.; and Dobkin, B. H. The future of restorative neurosciences in stroke: driving the translational research pipeline from basic science to rehabilitation of people after stroke. *Neurorehabil Neural Repair*, 23(2):97–107, 2009. doi: 10.1177/1545968308326636.

Crenna, P. and Frigo, C. Evidence of phase-dependent nociceptive reflexes during locomotion in man. *Experimental Neurology*, 85:336–345, 1984.

Decchi, B.; Zalaffi, A.; Spidalieri, R.; Arrigucci, U.; Di Troia, A. M.; and Rossi, A. Spinal reflex pattern to foot nociceptive stimulation in standing humans. *Electroencephalography and Clinical Neurophysiology/-Electromyography and Motor Control*, 105(6):484–489, 1997. doi: 10.1016/S0924-980X(97)00048-9.

Defrin, R.; Peleg, S.; Weingarden, H.; Heruti, R.; and Urca, G. Differential effect of supraspinal modulation on the nociceptive withdrawal reflex and pain sensation. *Clinical Neurophysiology*, 118(2):427–437, 2007. doi: 10.1016/j.clinph.2006.10.015.

DeLisa, J. A. *Gait Analysis in the Science of Rehabilitation*. Department of Veterans Affairs, 1998.

Despopoulos, A. and Silbernagl, S. *Color Atlas of Physiology*. Thieme, 5ed edition, 2003. ISBN 3-13-545005-8.

Dimitrijević, M. R.; Faganel, J.; Gregorić, M.; Nathan, P. W.; and Trontelj, J. K. Habituation: effects of regular and stochastic stimulation. *Journal of neurology, neurosurgery, and psychiatry*, 35(2):234–42, April 1972.

Duysens, J.; Tax, A. A. M.; Nawijn, S.; Berger, W.; Prokop, T.; and Altenmüller, E. Gating of sensation and evoked potentials following foot stimulation during human gait. *Experimental Brain Research*, 105(3):423–431, February 1990. doi: 10.1007/BF00233042.

Emborg, J.; Spaich, E. G.; and Andersen, O. K. Withdrawal reflexes examined during human gait by ground reaction forces: site and gait phase dependency. *Medical & biological engineering & computing*, 47(1):29–39, January 2009. doi: 10.1007/s11517-008-0396-x.

Emborg, J.; Matjačić, Z.; Bendtsen, J. D.; Spaich, E. G.; Cikajlo, I.; Goljar, N.; and Andersen, O. K. Design and test of a novel closed-loop system that exploits the nociceptive withdrawal reflex for swing-phase

support of the hemiparetic gait. *IEEE transactions on bio-medical engineering*, 58(4):960–70, April 2011. doi: 10.1109/TBME.2010.2096507.

Floeter, M. K.; Gerloff, C.; Kouri, J.; and Hallett, M. Cutaneous withdrawal reflexes of the upper extremity. *Muscle & nerve*, 21(5):591–8, May 1998.

Fuhr, T.; Quintern, J.; Riener, R.; and Schmidt, G. Walking with WALK! A cooperative, patient-driven neuroprosthetic system. *IEEE engineering in medicine and biology magazine : the quarterly magazine of the Engineering in Medicine & Biology Society*, 27(1):38–48, 2008. doi: 10.1109/MEMB.2007.911408.

Gladstone, D. J.; Danells, C. J.; and Black, S. E. The Fugl-Meyer assessment of motor recovery after stroke: a critical review of its measurement properties. *Neurorehabil Neural Repair*, 16(3):232–240, 2002. doi: 10.1177/154596802401105171.

Granat, M.; Heller, B.; Nicol, D.; Baxendale, R.; and Andrews, B. Improving limb flexion in FES gait using the flexion withdrawal response for the spinal cord injured person. *Journal of Biomedical Engineering*, 15(1):51–56, 1993.

Graupe, D. and Kohn, K. H. Functional neuromuscular stimulator for short-distance ambulation by certain thoracic-level spinal-cord-injured paraplegics. *Surg Neurol*, 50:202–207, 1998.

Grimby, L. Normal plantar response: integration of flexor and extensor reflex components. *Journal of neurology, neurosurgery, and psychiatry*, 26(1):39–50, November 1963.

Hennemann, E.; Somjem, G.; and Carpenter, D. O. Functional significance of cell size in spinal motoneurons. *Journal of Neurophysiol*, 28(3):560–580, 1965.

Kojović, J.; Djurić-Jovicić, M.; Dosen, S.; Popović, M. B.; and Popović, D. B. Sensor-driven four-channel stimulation of paretic leg: functional electrical walking therapy. *Journal of neuroscience methods*, 181 (1):100–5, June 2009. doi: 10.1016/j.jneumeth.2009.04.005.

Kugelberg, E.; Eklund, K.; and Grimby, L. An electromyographic study of the nociceptive reflexes of the lower limb. Mechanism of the plantar responses. *Brain : a journal of neurology*, 83:394–410, September 1960.

Kwakkel, G.; Kollen, B.; and Twisk, J. Impact of time on improvement of outcome after stroke. *Stroke; a journal of cerebral circulation*, 37(9):2348–53, September 2006. doi: 10.1161/01.STR.0000238594.91938.1e.

Langhorne, P.; Coupar, F.; and Pollock, A. Motor recovery after stroke: a systematic review. *Lancet neurology*, 8(8):741–54, August 2009. doi: 10.1016/S1474-4422(09)70150-4.

Leane, G. E.; Lyons, G. M.; and Lyons, D. J. The incidence of drop foot following stroke in the St. Camillus' Hospital catchment area within the Mid-Western Health Board. *Ir. J. Med. Sc*, 167(4):275, 1998.

Lee, K.H. and Johnston, R. Electrically induced flexion reflex in gait training of hemiplegic patients: induction of the reflex. *Arch Phys Med Rehabil*, 57:311–314, 1976.

Liberson, W. T.; Holmquest, H. J.; Scot, D.; and Dow, M. Functional electrotherapy: stimulation of the peroneal nerve synchronized with the swing phase of the gait of hemiplegic patients. *Arch Phys Med Rehabil*, 42:101–105, 1961.

Lyons, G. M.; Sinkjaer, T.; Burridge, J. H.; and Wilcox, D. J. A review of portable FES-based neural orthoses for the correction of drop foot. *IEEE transactions on neural systems and rehabilitation engineering : a publication of the IEEE Engineering in Medicine and Biology Society*, 10(4):260–79, December 2002. doi: 10.1109/TNSRE.2002.806832.

McNeal, D. R.; Baker, L. L.; McCaffrey, S.; and Lopez, N. Subject preference for pulse frequency with cutaneous stimulation of the quadriceps. *Proc Rehabil Eng Soc North Am*, 9:273–275, 1986.

Meinck, H. M.; Kuster, S.; Benecke, R.; and Conrad, B. The flexor reflex: influence of stimulus parameters on the reflex response. *Electroencephalography and Clinical Neurophysiology*, 61(4):287–298, 1985. doi: 10.1016/0013-4694(85)91095-8.

Mørch, C. D.; Andersen, O. K.; Graven-Nielsen, T.; and Arendt-Nielsen, L. Nociceptive withdrawal reflexes evoked by uniform-temperature laser heat stimulation of large skin areas in humans. *Journal of neuroscience methods*, 160(1):85–92, February 2007. doi: 10.1016/j.jneumeth.2006.08.014.

Morre, S.; Schurr, K.; Wales, A.; Moseley, A.; and Herbert, R. Observation and analysis of hemiplegic gait: swing phase. *Australian Physiotherapy*, 39(4):271–278, 1993.

Moseley, A.; Wales, A.; Herbert, R.; Schurr, K.; and Morre, S. Observation and analysis of hemiplegic gait: stance phase. *Australian Physiotherapy*, 39(4):259–267, 1993.

Murray, M P. Gait as a total pattern of movement. *American Journal of Physical Medicine*, 46(1):290–333, 1967.

Nyberg, L. and Gustafson, Y. Patient falls in stroke rehabilitation. A challenge to rehabilitation strategies. *Stroke*, 26(5):838–842, 1995.

Olney, S. J. and Richards, C. Hemiparetic gait following stroke, part 1: characteritics. *Gait & Posture*, 4 (2):136–148, 1996. doi: 10.1016/0966-6362(96)01063-6.

Open Clip Art Libary, . Anatomy Image collection, 2011. URL http://openclipart.citizen-web.com/.

Packman-Braun, R. Relationship between functional electrical stimulation duty cycle and fatigue in wrist extensor muscles of patients with hemiparesis. *Physical Therapy*, 68(1):51–56, 1988.

Pedersen, P. M. and Olsen, T. S. Rehabilitering af patienter med apopleksi. *Ugeskrift for Læger*, 169(40): 3398–3400, 2007.

Popović, D. B. and Sinkjaer, T. *Control of Movement for the Physically Disabled*. Center for Sensory-Motor-Interaction, Department of Health Science and Technology, Aalborg University, 9220 Aalborg, Denmark, 2003. ISBN 87-90562-10-0.

Popović, M. B.; Popović, D. B.; Sinkjaer, T.; Stefanovic, A.; and Schwirtlich, L. Clinical evaluation of Functional Electrical Therapy in acute hemiplegic subjects. *Journal of rehabilitation research and development*, 40(5):443–53, 2003.

Postans, N. Functional Electric Stimulation to Augment Partial Weight- Bearing Supported Treadmill Training for Patients With Acute Incomplete Spinal Cord Injury: A Pilot Study. *Archives of Physical Medicine and Rehabilitation*, 85(4):604–610, April 2004. doi: 10.1016/j.apmr.2003.08.083.

Purves, D. and Augustine, G. J. *Neuroscience*. Sinauer Associates, 3 edition, 2004.

Quintern, J.; Krewer, C.; Husemann, B.; Hartmann, E.; Heller, S.; Müller, F.; and Koenig, E. *Controlled clinical study of stimulation of flexor reflex afferents for gait rehabilitation in patiens with hemiplegia*, pages 240–246. St. Kliment Ohridski University Press, Sofia, 2003.

Rattay, F. *Electrical Nerve Stimulation - Theory, Experiments, and Applications*. Springer-Verlag, New York, 1990.

Rosamond, W.; Flegal, K.; and Friday, G. Heart disease and stroke statistics-2007 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*, 115:e69–e171, 2007. doi: 10.1161/CIRCULATIONAHA.106.179918.

Rueterbories, J.; Spaich, E. G.; Larsen, B.; and Andersen, O. K. Methods for gait event detection and analysis in ambulatory systems. *Medical engineering & physics*, 32(6):545–552, April 2010. doi: 10.1016/j.medengphy.2010.03.007.

Rushton, D. Functional Electrical Stimulation and rehabilitation—an hypothesis. *Medical Engineering & Physics*, 25(1):75–78, January 2003. doi: 10.1016/S1350-4533(02)00040-1.

Sandrini, G.; Serrao, M.; Romaniello, A.; Cruccu, G.; and Willer, J. C. The lower limb flexion reflex in humans. *Progress in neurobiology*, 77(6):353–95, December 2005. doi: 10.1016/j.pneurobio.2005.11.003.

Schouenborg, J. and Kalliomäki, J. Functional organization of the nociceptive withdrawal reflexes. I. Activation of hindlimb muscles in the rat. *Experimental Brain Research*, 83:67–78, 1990.

Schouenborg, J.; Holmberg, H.; and Weng, H. Functional organization of the nociceptive withdrawal reflexes. II . Changes of excitability and receptive fields after spinalization in the rat. *Experimental Brain Research*, 90:469–478, 1992.

Sherrington, C. S. Flexion-reflex of the limb, crossed extension-reflex, and reflex stepping and standing. *The Journal of physiology*, 40(1-2):28–121, April 1910.

Sinkjaer, T. and Popović, D. B. Trends in the Rehabilitation of Hemiplegic Subjects. *Journal of Autonomic Control*, 15:1–10, 2005.

Sonnenborg, F. A.; Andersen, O. K.; Arendt-Nielsen, L.; and Treede, R-D. Withdrawal reflex organisation to electrical stimulation of the dorsal foot in humans. *Experimental Brain Research*, 136(3):303–312, January 2001. doi: 10.1007/s002210000587.

Spaich, E. G.; Arendt-Nielsen, L.; and Andersen, O. K. Modulation of lower limb withdrawal reflexes during gait: a topographical study. *Journal of neurophysiology*, 91(1):258–66, January 2004. doi: 10.1152/jn.00360.2003.

Spaich, E. G.; Hinge, H. H.; Arendt-Nielsen, L.; and Andersen, O. K. Modulation of the withdrawal reflex during hemiplegic gait: effect of stimulation site and gait phase. *Clinical neurophysiology : official journal of the International Federation of Clinical Neurophysiology*, 117(11):2482–95, November 2006. doi: 10.1016/j.clinph.2006.07.139.

Spaich, E. G.; Emborg, J.; Collet, T.; Arendt-Nielsen, L.; and Andersen, O. K. Withdrawal reflex responses evoked by repetitive painful stimulation delivered on the sole of the foot during late stance: site, phase, and frequency modulation. *Experimental brain research*, 194(3):359–68, April 2009. doi: 10.1007/s00221-009-1705-9.

Stanic, U.; Acimović-Janezic, R.; Gros, N.; Trnkoczy, A.; Bajd, T.; and Kljajić, M. Multichannel electrical stimulation for correction of hemiplegic gait. Methodology and preliminary results. *Scandinavian journal of rehabilitation medicine*, 10(2):75–92, January 1978.

Sulter, G.; Steen, C.; and Jacques, D. K. Use of the Bartel Index and Modified Rankin Scale in acute stroke trials. *Stroke*, 30(8):1538–1541, 1999.

Sweeney, P. C.; Lyons, G. M.; and Veltink, P. H. Finite state control of functional electrical stimulation for the rehabilitation of gait. *Medical and Biological Engineering and Computing*, 38(2):121–126, 2000.

Thrasher, T. A. and Popović, M. R. Functional electrical stimulation of walking: function, exercise and rehabilitation. *Annales de réadaptation et de médecine physique : revue scientifique de la Société française de rééducation fonctionnelle de réadaptation et de médecine physique*, 51(6):452–60, July 2008. doi: 10.1016/j.annrmp.2008.05.006.

Vaughan, C .L.; Davis, B. L.; and O'Connor, J. C. *Dynamics of Human Gait*. Kiboho Publishers, Cape Town, South Africa, 2nd editio edition, 1992. ISBN 0-620-23558-6.

Voigt, M. and Sinkjaer, T. Kinematic and kinetic analysis of the walking pattern in hemiplegic patients with foot-drop using a peroneal nerve stimulator. *Clinical Biomechanics*, 15(5):340–351, 2000. doi: 10.1016/S0268-0033(99)00082-0.

Whittle, M. W. *Gait Analysis - an introduction*. Butterworth Heinemann Elsevier, 4ed edition, 2007. ISBN 9 780 7506 8883 3.

Winter, D. A. *Biomechanics and Motor Control of Human Gait: Normal, Elderly and Pathological*. University of Waterloo Press, second edi edition, 1991. ISBN 0-88898-105-8.

Part V

Appendix

Additional information that supports the report.

APPENDIX A

STROKE

This chapter gives a short description of the effects and causes of stroke. The chapter is not an extensive examination of stroke, but is rather meant as a support when reading the rest of the report. The chapter is primarily written on the background of the text book by Caplan [2009].

Magnitude of the Stroke Threat

Stroke is the third most common cause of death in developed countries, behind cardiovascular disease and cancer. It is the most common cause of chronic disablement in many developed countries and is a severe disease in Denmark, where approximately 12,000 people get a stroke every year [Popović and Sinkjaer, 2003]. 20% of stroke patients die within the first month and half of these survivors will experience injury of a permanent character and require assistance to do everyday functions for the rest of their lives. It is estimated that 35,000 - 45,000 people in Denmark live with consequences of stroke. Survivors of stroke are often unable to return to work or to assume their former effectiveness as spouses, parents, and friends, which can have far-reaching economic consequences as well as a strong psychosocial influence on the patients. [Cheeran et al., 2009].

Effects of Stroke

Stroke or apoplexia are the common terms for the clinical syndromes appearing when blood flow to part of the brain is cut off due to cerebral thrombosis or cerebral hemorrhage. The brain is a metabolically active organ and uses approximately a quarter of the body's energy supply to function properly. The essential nutrients, glucose, and oxygen are carried to the brain by the blood, which makes it very important that the cerebral blood flow is maintained at a steady level to allow the brain to function properly. Cerebral blood flow is normally around 50 mL for each 100 g of brain tissue per minute, depending on the level of neuronal activity. When blood flow to a region of the brain is reduced, survival of the at-

risk tissue depends on the intensity and duration of the ischemia and the availability of collateral blood flow. At cerebral blood flow levels of 20 mL/100 g brain tissue per minute, animal experiments have shown that electroencephalographic (EEG) activity becomes affected, and at levels below 10 mL/100 g per minute cell membranes and functions become severely affected by the ischemia. Neurons can only survive for few minutes at cerebral blood flow below 5 mL/100 g brain tissue per minute. Neuronal death as a consequence of markedly reduced blood stream might result in a rapid loss of brain functions.

The effects of a stroke depend primarily on the location of the obstruction and the extent of brain tissue affected. Strokes may affect many functions ranging from e.g. paresis in one side of the body, vision problems, memory loss, alterations in behaviour, and/or speech problems. As this project deals with regaining motor functions after stroke the paresis of the body will be the only consequence of stroke explained in further details here.

Hemiparesis

Approximately 80 % of patients with stroke experience a significant reduction in motor functions due to hemiparesis (paresis in one side of the body). The side of the body opposite the hemispheric location of the stroke is the side affected with loss of function. The paresis can affect the patient's ability to coordinate movement between limbs which affects everyday functions like gait, balance, grip function, eating and getting dressed by oneself. Stroke is strongly correlated with reduced life quality. The level of disability following the stroke ranges from mild to severe and, similarly, the impact on daily living activities can be minimal to significant.

Classification of Strokes

Stroke is broadly classified into brain ischemia and brain hemorrhage. Ischemic strokes account for 80-85 % of strokes and are mainly caused by thrombotic or thromboembolic arterial occlusion. A thrombosis refers to the obstruction of blood flow due to a localised occlusive process within one or more blood vessels, and embolism refers to the condition where material formed elsewhere within the vascular system lodges in an artery and blocks the blood flow. Brain hemorrhages account for the remaining 15-20 % of strokes and are caused by a leakage of blood from ruptured vessels into the brain tissue. The causes of the two types of strokes are depicted in figure A.1.

Besides the cause of the condition, stroke is also classified on the background of its location in the brain: Subcortical stroke, cortical stroke, hemispheric stroke, cerebellar stroke, or brainstem stroke.

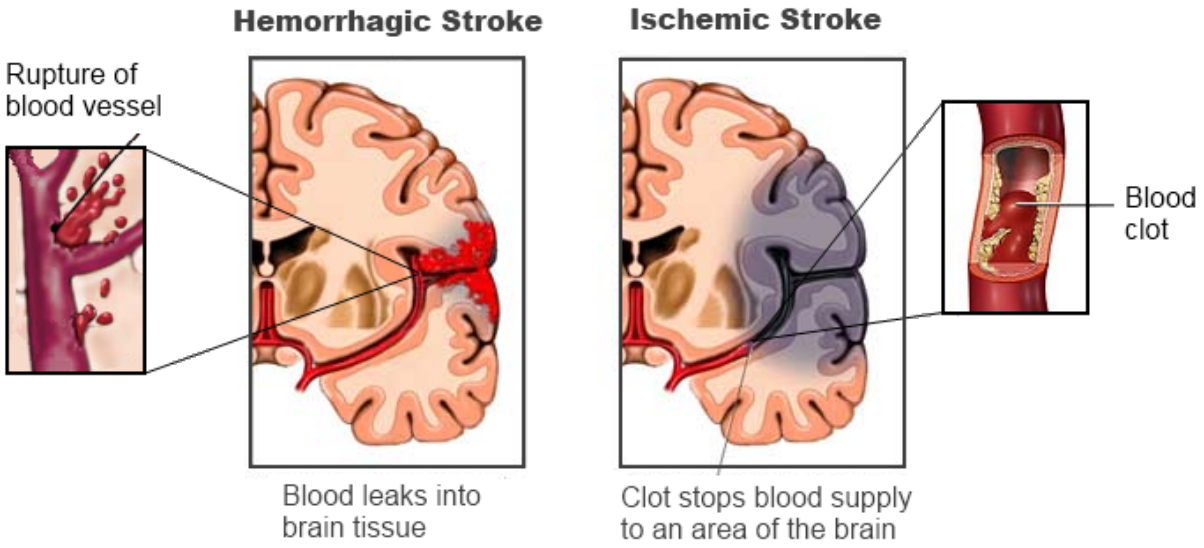


Figure A.1: Classification of stroke

Strokes can be classified into brain hemorrhage (bleeding from blood vessel into brain tissue) and brain ischemia (occlusion of blood vessel).

Recovery After Stroke

Rehabilitation is an important part of the treatment post-stroke as it has been shown that the brain is able to relearn motor functions [Popović and Sinkjaer, 2003]. Rehabilitation focuses on recovery and adaption to the loss of neurologic function.
Recovery of neurological functions after stroke is complex and depends on many factors. Some of these factors relate to the severity and location of the stroke mechanism, whereas others relate to individual factors such as age, personality, support from family and friends, and medical comorbidities. Patients with brain hemorrhage recover at a different rate and extent than patients with thromboses in the same location. In many patients, ischemia might be transient, meaning that portions of the ischemic zone can return to normal without leaving any permanent damage to the brain.

Studies of motor recovery after strokes that involve the primary motor cortex have shown that some brain structures on the same hemisphere as the lesion begin to take on new functions as a consequence of the hemiparesis. The ability of the brain to "rewire" connections and sparing of primary motor cortex to other brain regions is known as plasticity.

APPENDIX B

DESIGN AND IMPLEMENTATION OF A LABORATORY SYSTEM FOR STIMULATION AND DATA ACQUISITION

To carry out the protocol described in Case Study 1, chapter 8, a program was developed in LabVIEW™ to manage the execution of stimulation sequences and collect the data generated. The laboratory system is programmed on the background of the specification requirements described in chapter 7.

Objective

The flowchart diagram in figure B.1 describes the overall structure of how the interface is put together. The execution flow of the developed interface (figure B.3) is divided into three steps starting with initialisation of variables used in the program, then proceeding to the main function of the program, before shutting down gracefully. When the overall structure was defined, the specification requirement from chapter 7 was used to construct the different sub-functions of the program.
After the initialisation of the Protocol, Current step, and Hardware variables, the program is in the main part. This part is further divided into three ways of running functions: by events, always running, or by notifications.
Events are generated when the user interacts with the interface, e.g. by clicking a button, selecting a text or pointing at a graph. These events are generally used to control the main functions of the program, so when the user interacts with the system, the program responds accordingly.
Functions that have to execute, regardless of and without interference of the user, are created in their own loops. Hence, they will run in parallel with the rest of the code and not stop because some of the code is waiting for the user or finishing a heavy resource demanding code. The data acquisition and the stimulation functions use this method to execute the protocol and obtain the data continuously.
The last way is by notifications. A notification is useful when the program has to do some heavy compu-

tational code without affecting the calling code. An example is saving the data. Every once in a while, the data has to be saved to a file and doing so takes some time. To avoid stopping the data acquisition, a notification is used to send the data to another part of the code which will take care of saving the data. When the experiment is done and the user closes the interface, it is checked whether the data is saved. When it is, the loaded hardware is cleared and the running functions are stopped before the interface terminates.

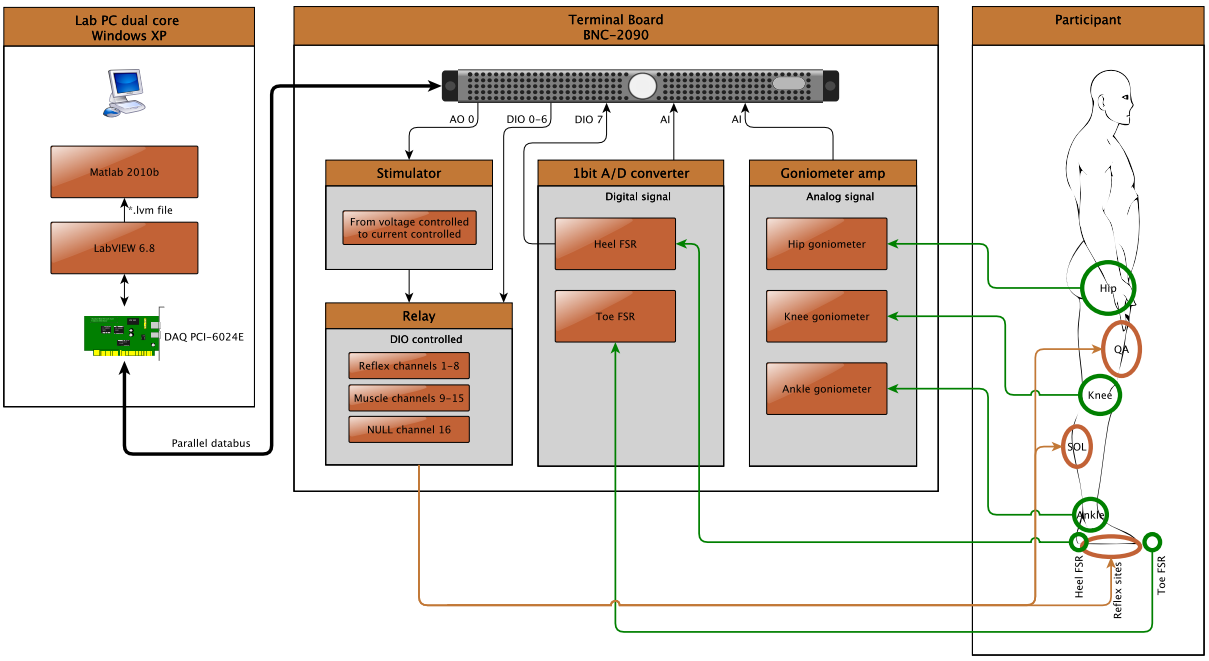


Figure B.1: *The design of the system*

Hardware setup

The system uses a NI-DAQ PCI-6024E and a terminal board BNC-2090 as its central components. The computer runs Windows^{TM}XP with LabVIEW^{TM} which is communicating through a NI-DAQ PCI-6024E daq card with the different hardware components mounted in a BNC-2090 Terminal Board. The components are designed and created at Aalborg University.

The goniometer used in the setup are connected to an amplifier, which contains a primitive three options low-pass filter, an input range/scale switch, and an adjustable offset knob. The filter is set to 100 Hz and the actual filtering is then done digitally during the offline analysis. The range switch is set to $\pm 75^{\circ}$ since it is not expected that the joints reaches above a range of 150°. The offset is adjusted to obtain the best use of the 150° range available: hip $= 0V$, knee $= -8V$ and ankle $= 0V$, when the participant is in standing position.

The heel- and toe-switches are composed of two FSRs connected to a 1-bit Analog-to-Digital converter (A/D converter) with an adjustable threshold. The threshold is calibrated before each experiment.

To control the stimulation, a constant current stimulator is used to convert the controlled voltage output from the daq card to the controlled current needed in the experiment. The current output from the stimulator ranges between 0-100 mA, linearly correlated with the input ranging between 0-10 V. The output

from the stimulator is connected to a relay module, which controls which electrode is the destination for the present stimulation train. To switch between the outputs, the daq card flashes a series of digital numbers on the digital ports 1-6 [DIO0-6] that are recognised by a microchip in the relay module and in turn switched to the desired output channel. Although a channel has been selected, it is not opened yet; to open a channel, the Counter 1 on the daq card has to go high.

Functions

The developed laboratory system contains several functions created to satisfy the requirements specified in chapter 7. Below are the most important functions described.

Generating the protocol When generating the protocol, the program uses the data entered to the interface by the user and the data generated during calibration. The protocol consist of four or five baseline steps between each stimulation step. The phase and stimulation site of the sequences are randomised and do only occur once during a session, resulting in a session length of 75-90 steps. Each index of the protocol array corresponds to one step cycle and consists of four sub protocols: two muscle trains and two reflex trains. When the protocol array is generated, the calibration data are locked to that session, which means that the user is not able to change the protocol during a session. If some of the values need to be changed, the user has to stop the experiment and generate a new protocol. This is done in order to avoid that the user changes the experiment conditions, which will make it harder to analyse the data afterwards.

Calibration Before the beginning of the experiment, the user needs to do some hardware- and participant calibration. The goniometers need to be calibrated so they output the correct joint angles, and this is done before every experiment to avoid changes in the output due to prolonged storage. The calibration is done by measuring the voltage generated when the goniometers span 0° and 60°. Afterwards, a linear regression is used to convert the voltage output to an angle measure.
For each participant, the user has to calibrate the reflex stimulation intensity for each stimulation site. An appropriate reflex is found at the arch of the foot and the other sites are then adjusted so the sensation of the stimulation is equal across the sites. For sequences containing two stimulation sites, a multiplication factor is used to scale the two individual sites down to an intensity, which matches the sensation obtained at the arch of the foot. Furthermore, the step cycle timings are measured in order to determine the duration of the muscle stimulation and the onsets of the reflex stimulation. This is done by asking the participant to walk a pre-specified number of steps, where the timings of the heel-switch and toe-switch are collected. Afterwards, the heel-on/heel-off and heel-off/toe-off periods are calculated.

Running the experiment When the user pushes the run-button on the interface, the program initialises the hardware and starts the experiment. The program runs the data acquisition independent from rest of the functions in the program, measuring the goniometer values, the stimulation sequence, and the heel-switch. This is important to avoid breaks or slowdowns occurring because of a resource heavy code.

When the participant starts walking, the heel-switch is also sampled digitally via the DIO7, which is used to detect the beginning of a new gait cycle. By sampling the heel-switch digitally, LabVIEW™ offers better functions for controlling the code execution flow contrary to use analog values. When a heel-strike is detected, the first muscle stimulation train is delivered to QA, unless it is a baseline step, and the three subsequent trains (one muscle stimulation to SOL and two reflex stimulation trains) follow automatically with delays specified in the protocol.

As a security precaution, the program utilises the two counters available on the daq-card (see figure B.2) to execute the stimulation and control the relay. When a heel-strike is detected on DIO7, the function generates a signal on Counter 0 (CR0) that in turn activates Counter 1 (CTR1), which will stay high as long as it has been programmed to, i.e. the time it takes to execute the stimulation train. By executing it this way, the stimulation is almost independent of the operating system, because the beginning and end of the train is programmed into the daq card. So, if the system hangs or the interface breaks down, and thus is not able to communicate with daq card, the stimulation does not continue.

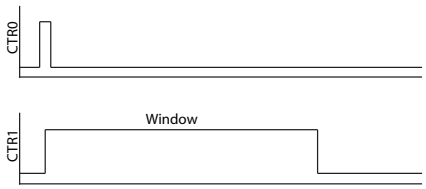


Figure B.2: Control of the relay box. *Counter 1 controls the execution of the stimulation and the relay. Counter 0 is triggered by the interface and when activated, it makes the Counter 1 go high for a predetermined period of time.*

Every ten seconds, the recorded data is saved to a file in another section of the program. This will help free up system resources and prevent the loss of data if something breaks down. Along with the measured data, some meta data is also stored: participant ID, measurement number, the protocol, and relevant channel names. These data are saved in a "*.lvm"-file, which can be imported into Matlab™ as a struct with a mat-script. The raw data output from LabVIEW™ can be seen on figure B.4 plotted in Matlab™.

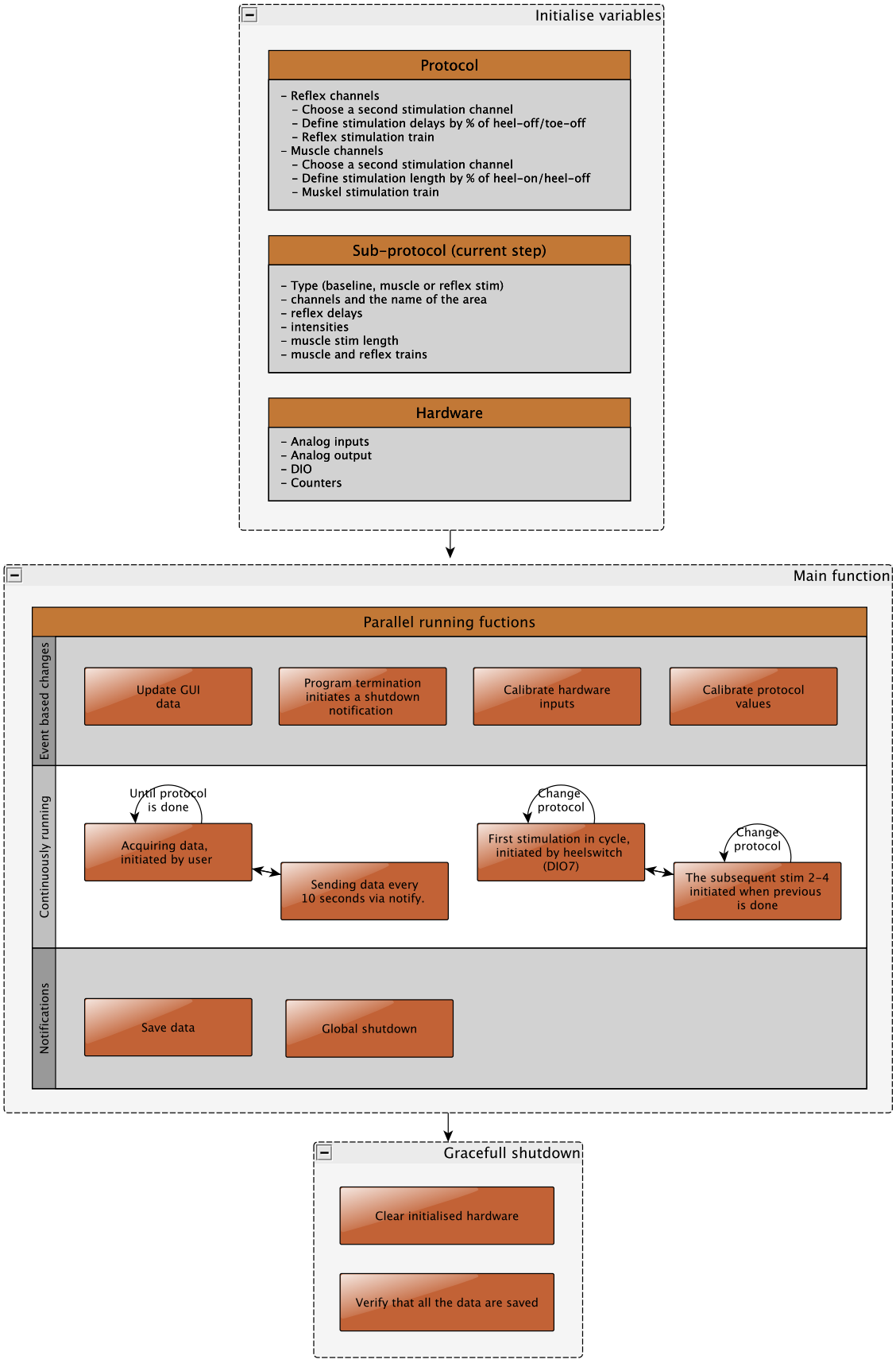


Figure B.3: *The overall layout of the program divided into three parts: The initialisation of the used variables, the main function of the program, and exiting a graceful shutdown.*

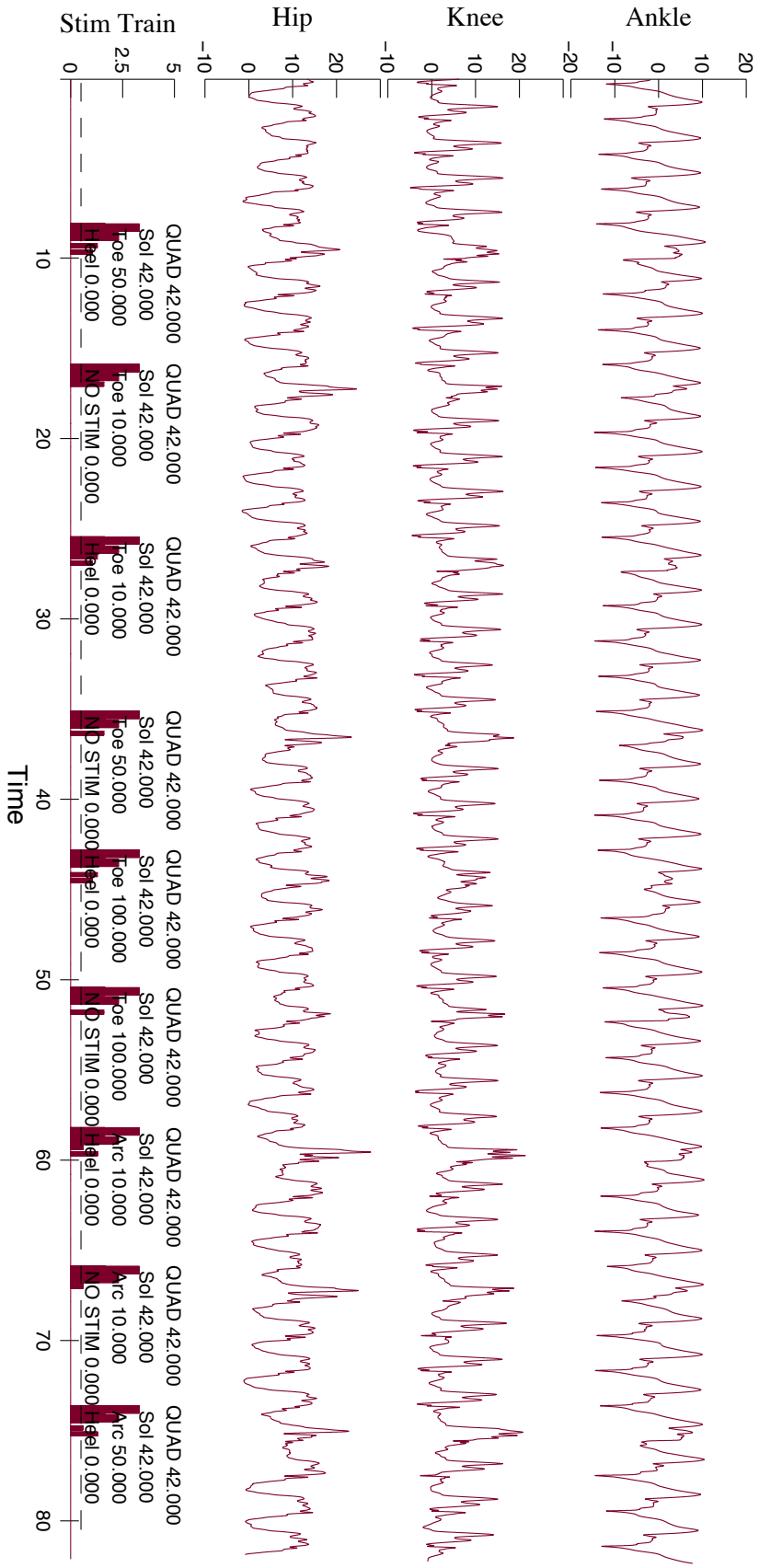


Figure B.4: *The output from LabVIEW plotted in Matlab. The black lines in the forth plot indicate the heel-on period from the heel-switch.*