Real time closed loop functional electrical stimulation system for use in upper extremity motor rehabilitation

Rune Skødt Poulsen Rasmus Stengaard Sørensen Master thesis Biomedical Engineering Aalborg University



Title:

Real time closed loop functional electrical stimulation system for use in upper extremity motor rehabilitation.

Theme:

Master's thesis

Project period:

10th semester, Spring 2012 February 1st - June 4th

Project group:

Group 1071

Members:

Rune Skødt Poulsen

Rasmus Stengaard Sørensen

Supervisors:

Ole Kæseler Andersen John Hansen

No. printed Copies: 5

No. of Pages: 83

Finished: January 4th

Abstract:

Introduction: The aim of the present study was to develop a real time closed loop functional electrical therapy system for use in upper extremity motor rehabilitation. System requirements were specified based on principles extracted from the motor rehabilitative techniques constraint induced movement therapy and functional electrical therapy.

Methods: A solution strategy was established with basis in relevant background information. The solution strategy was implemented in MATLAB using i.a. a Microsoft kinect camera and an electrical stimulator. The depth data from the kinect camera was used to detect a cup and the user's hand. Electrical stimulation was applied to the user's forearm to assist in gripping the cup. The stimulation was adjusted based on the interaction between the cup and user's hand. If the level of assistive stimulation was insufficient to reliably lift the cup, the intensity could be increased by sliding the hand closer to the top of the surface of the cup.

Results: The system was tested on five healthy subjects and one unilateral motor impaired subject. The system usability, optimal electrode placement, stimulation intensity and stimulation regulation were qualitatively evaluated on all subjects. System performance was evaluated through technical tests.

Conclusion: The motor impaired subject was considered to have improved grip control and steadier manipulation of the cup when assistive stimulation was applied compared to without stimulation. Due to rapid muscle fatigue in the motor impaired subject, no data about the subject task performance was recorded. The system provides a basis for further development.

The contents of this report is freely accessible, however publication (with source references) is only allowed upon agreement with the authors.

Resume

Introduktion: Formålet med dette studie var at udvikle et real tid lukket sløjfe funktionelt elektrisk terapi system til anvendelse i øvre ekstremitet motor rehabilitering. Systemkravet blev specificeret baseret på principper uddraget fra motor rehabilitations teknikkerne constraint induced movement therapy og funktionel elektrisk terapi.

Metode: En løsningstrategi blev etableret med udgangspunkt i relevant baggrunds information. Løsningsstrategien blev implementeret i MATLAB ved hjælp af bl.a. et Microsoft Kinect kamera og en elektrisk stimulator. Dybdedata fra Kinect kameraet blev anvendt til at detektere en kop og brugerens hånd. Elektrisk stimulering blev tilført brugerens underarm til at assistere med at gribe om koppen. Stimulering blev løbende justeret baseret på interaktion mellem koppen og brugerens hånd. Hvis intensiteten af stimulering var utilstrækkelig til at assistere med at løfte koppen, kan stimuleringsintensiteten øges ved at løfte hånden mod toppen af koppen.

Resultat: Systemet blev testet på fem raske personer og en unilateral funktionsnedsat person. Systemets brugervenlighed, optimal elektrode placering, stimulations intensitet og stimulations regulering blev kvalitativt evalueret på alle personer. Systemets ydeevne blev evalueret gennem tekniske tests.

Konklusion: Den funktionsnedsatte person blev anset for at få bedre grebs kontrol og mere stabil håndtering af koppen når den assisterende stimulering blev anvendt i forhold til uden stimulering. På grund af tidlig muskeltræthed hos den funktionsnedsatte person, blev der ikke optaget data af personens ydeevne, under anvendelse af systemet. System danner et godt udgangspunkt for den videre udvikling.

Preface

This report was composed by group 1071 as part of the 10th semester at the Master education Biomedical Engineering and Informatics at Aalborg University. The project was conducted and written from February 1st 2012 to June 4th 2013.

The conducted work had focus on developing a real time closed loop functional electrical therapy system for use in upper extremity motor rehabilitation.

References to publications are written according to Chicago style and the bibliography is located at the end of the project. The author's surname and publication year are noted in squared brackets e.g. [Baker 2003]. Publications with two authors e.g. [Wolpert and Flanagan 2009] and publications with more than two authors e.g. [Taub et al. 1998]. In-text references are written as e.g. Nudo and Milliken [1996]

References to figures are written as e.g. "Figure 3.3" where the first number refers to the chapter and the second refers to the sequence in which the figure occurs in the given chapter. Abbreviations are written in a parenthesis when presented the first time. Abbreviations is not written in the introduction section.

We would like to thank the staff at Træningsenheden Øst and Vest i Aalborg, together with the residents we got the chance to meet and observe during their rehabilitation training. A special thanks to the resident we tested our rehabilitation system on.

Contents

1	Introduction		9
	1.1	Introduction	9
2	Background		13
	2.1	Constraint induced movement therapy	13
	2.2	Electrical stimulation	18
	2.3	Biomechanical sensors	27
	2.4	Aim	29
3	System development		
	3.1	System requirements	31
	3.2	Solution strategy	34
4	Implementation		
	4.1	Equipment	41
	4.2	Main function	43
	4.3	Motivational feature	56
	4.4	Calibration tool	57
5	System test		59
	5.1	Overall system test	59
	5.2	Individual component system test	61
6	Discussion 6		65
	6.1	General system discussion	65
	6.2	Individual system discussion	67
	6.3	Future perspectives	72
	6.4	Summary	73
7	Appendix		75
	7.1	Electrical stimulator	75
	7.2	National Instruments USB-6229 BNC	76
Bil	Bibliography		

Introduction

1.1 Introduction

Stroke is a global health problem. In Denmark the annual incidence of first time stroke is 10.000-15.000 [Sundhedsstyrelsen 2011]. 20 % of the stroke patients do not survive the first month, and only half is still alive after four years [for hjerneskade 2007]. A correlation between stroke incidence and age have been documented in countries across the world [Truelsen et al. 2006, Donnan et al. 2008] and since the European population is getting older, it will most likely results in an increase in the annual stroke incidence rate. Together with a decrease in the mortality rate of stroke patients, this could cause an increased burden on the health care system [Truelsen et al. 2006, for hjerneskade 2007].

Stroke occurs when normal blood flow in the brain is interrupted, either by a blockage of a blood vessel (ischemic stroke) or a hemorrhage, where a blood vessel ruptures and bleeds into the brain (hemorrhagic stroke). The brain cells high demand for oxygen and nutrients cannot be sustained in the affected brain area, and the brain cells start to die, causing permanent damage to the neural tissue in the brain. The consequences of stroke vary and are related to what brain area is affected. Stroke often leads to severe motor impairment or disability in one or more limbs, but can also cause visual, speech and cognitive impairments [Donnan et al. 2008]. Since the right-brain hemisphere controls the motor function of the left side of the body and the left-brain hemisphere controls the motor function of the right side of the body, stroke primarily affect the motor function on one side of the body. Damage in the left-brain hemisphere will thus primarily cause motor impairment on the right side. It is common to divide the body into the more affected side and the less affected side. The degree of motor impairment is called hemiplegia and hemiparesis, which is the paralysis and weakening of one side of the body respectably [Kandel et al. 2000]. Of the stroke survivors 75 % are left with motor impairments [Shi et al. 2011].

Stroke survivors that experience physiological impairment as a consequence of the stroke incident will also experience some degree of neurological and functional motor recovery in the first six months post stroke, being most significant during the first month. Regenerative processes in the brain such as formation of new neurons, glia and synapses and axonal sprouting are some of the factors that lead to recovery of some of the lost function [Wieloch and Nikolich 2006, Jørgensen et al. 1995, Duncan et al. 1994]. Post stroke rehabilitation programs strive to increase the gains in motor function beyond that of the spontaneous recovery [Schaechter et al. 2002].

Much of our knowledge, about the effect of a cortical injury and the structural and functional alteration occurring in the brain post injury, originate from animal studies [Nudo 1999; 2007]. A primate study by Nudo and Milliken [1996] induced a confined ischemic infarct in the motor cortex controlling a small part of a hand, and observed the monkeys spontaneous recovery after the injury. The movement lost by the infarct did not reappear in the cortex surrounding the infarct, and the surrounding hand territory that was not directly affected by the infarct lost cortical territory. In the study, the primates did not receive training of the affected hand, and loss of hand territory could be due to the hand not being used.

A following study by Nudo et al. [1996] induced the same cortical injury as in Nudo and Milliken [1996] and then subsequently trained the monkeys affected hand. The monkeys regained their pre-injury performance level after three to four weeks of training, picking up food from wells of different sizes. The hand territory surrounding the injury was not reduced but instead occupied adjacent brain areas, previously representing the shoulder and elbow. This suggests that training the affected hand produced reorganization in the motor cortex and might be an important element in motor recovery. However, further studies by Nudo and coworkers on primates and rodents, demonstrated that repetitive training tasks already mastered did not cause any significant changes in the motor cortex of the animals, whereas training a task not previously acquired did induce cortical changes. Thus, repetitive motor activity alone does not induce cortical reorganization, the motor learning process is also an important factor in producing plastic changes in the motor cortex [Kleim et al. 1998, Plautz et al. 2000].

Conventional post stroke rehabilitation in humans often involves immediate application of physical therapy. Physical therapy promotes mobility among motor impaired patients by performing different physical activities. These activities are often based on specific function tasks that are related to performing activities of daily living [Latham et al. 2005]. Where most stroke survivors have regained the ability to walk six months after stroke onset [Jorgensen et al. 1995], between 30 % and 60 % are left with persistent motor impairment of their upper extremity, even after rehabilitation training [van der Lee et al. 1999, Shi et al. 2011]. The inability for stroke survivors to manipulate objects with the more effected upper extremity cause severe limitations in performing daily activities and self care [Brennan et al. 2011]. This results in a demand for an effective stroke rehabilitation program to enhance upper extremity motor function.

Rehabilitation of upper extremity function is generally considered to be more difficult to rehabilitate than lower extremity [Shi et al. 2011]. One explanation for this is that the stroke survivors often avoid using the more affected upper extremity, leading to what is known as learned nonuse. This is an issue since re-learning a motor movement requires repetitive practice of that particular movement, where feedback from each attempts are used to correct and improve the next attempt. A continued nonuse of a severely impaired extremity acts only to further decrease the usability of the extremity [Taub et al. 1998, Freeman et al. 2012].

Constraint induced movement therapy (CIMT) is a promising technique that was proposed in 1993 to address the learned nonuse phenomenon. CIMT involves constraining the functioning limb with a strap, forcing the patient to use the more affected extremity, and train the more affected limb for many hours each day in a two to three week period [Taub et al. 1993]. CIMT differs from conventional physical rehabilitation therapy in its intensity and duration [Taub et al. 2006]. CIMT produces cortical reorganization and functional motor gain, but the

link between the changes in brain structure and function have yet not been fully discovered [Wittenberg and Schaechter 2009].

One of the inclusion criteria for stroke patients to participate in CIMT, is that they need to possess a minimum of residual motor capacity [Taub et al. 1999]. The patients with very low residual motor function will experience improvement in the shoulder and elbow from participation in CIMT, but since they have little to non-finger function there is no basis to train the hand. Since most activities performed by the upper extremity involves the hand, the functional gain experienced will only transfer very little into real life situations [Taub et al. 2002].

The low functioning stroke patients, who will not gain much from participating in a CIMT program, can be assisted with electrical stimulation in performing functional tasks with the hand and arm. Stimulating specific muscles in the forearm and hand, of the more affected arm, allow the motor impaired patient to incorporate the hand in movements not previously possible. Beside the directly production of limb function the application of electrical stimulation has a therapeutic effect that lasts when the stimulation stops. Applying electrical stimulation to excitable tissue is not a new technique but have recently gained increasing attention in its application in rehabilitation settings [Sheffler and Chae 2007, Rosewilliam et al. 2012, de Kroon et al. 2005, Baker 2000].

It is the purpose of this project to investigate the characteristic features of CIMT and electrical stimulation as a therapeutic treatment and extract the properties that shows evidence for improved motor gain. Furthermore, the current availability of biomechanical sensors is investigated. Using a sensor that can provide measurement of movements, it is our aim to combine the key properties of CIMT and electrical stimulation into a rehabilitation system for upper extremity impairment stroke patients.

Background

2.1 Constraint induced movement therapy

Constraint induced movement therapy (CIMT) is a family of movement rehabilitation techniques for stroke patients. In its original form, the therapy involves constraining movements of the less affected arm with a sling for 90 % of waking hours, while doing intensive repetitive training with the more affected arm, six to seven hours a day, during a two to three week period. The inclusion criteria for stroke patients to participate in CIMT are that they do not have excessive spasticity, are highly motivated, have minimal cognitive dysfunctions and have good enough balance to safely walk around while wearing the arm restraint [Taub et al. 1999, Taub and Morris 2001].

CIMT primarily consists of repetitive task practice supplemented with shaping principles. Shaping is the approach to do motor tasks in small progressive steps, allowing the patients to experience successful gains even with just small amounts of motor improvement. During shaping training, the therapist provide feedback focusing on the positive elements of the subjects performance. The idea is to keep the participant motivated, since the participants cooperation and motivation is important elements for a positive rehabilitation outcome [Morris and Taub 2001, Taub and Morris 2001, Taub and Uswatte 2006].

The concept of CIMT originates from research on monkeys. The studies showed that when one of a monkeys forelimb was deafferented, the monkey stopped using that limb. With one deafferented forelimb, the monkey learned to operate with its three remaining functional limbs. Even though the monkey over time would regain some motor function in the deafferented forelimb (spontaneous recovery), the monkey was positively reinforced in its three limb use. Since attempts to use the deafferented forelimb resulted in punishing the monkey by falling and dropping food, the monkey learned not to use that limb, a phenomenon termed "learned nonuse". Taub and coworkers discovered that by restricting the movement of the intact forelimb over a period of several days, the monkey started to use the affected forelimb again. The previous useless limb could thereby be converted back into a functional one again [Taub and Morris 2001, Brogårdh 2006]. This mechanism of learned nonuse is thought to apply in humans too, where cortical injury have led to motor impairments.[Taub et al. 1999]

In stroke rehabilitation studies, it is common to divide the stroke patients into different subgroups in regards to the stroke onset. In rehabilitation research it is relevant in what stage the stroke patients are in, since the recovery rate is not the same across the stages and could bias the results if the patients are mixed across the groups [Jørgensen et al. 1995, Duncan et al. 1994, Schaechter et al. 2002]. de Kroon et al. [2005] define the acute stage after a stroke to be within one month post stroke, the subacute stage to be between one and six months post stroke and the chronic stage is more than six months post stroke. The definition often varies from study to study, however the general assumption is that the majority of recovery occurs in the acute phase, in the subacute phase recovery occurs at a lesser rate than the acute and in the chronic phase the recovery is halted. CIMT have primarily and with success, been applied to the chronic stroke population [Taub et al. 2006].

The benefits from CIMT have also been documented in a study by Wolf et al. [2006] on 222 stroke patients, who had the stroke incidence within the last three to nine months prior to the study. A study by Dromerick et al. [2009] indicated however, that too much intensive training too early after the stroke incidence is not beneficial to the patients. A patient group that performed three hours of daily CIMT training, five days per week for two consecutive weeks, had lower motor improvement measured 90 days after treatment start, compared to groups who performed just two hours of CIMT or two hours of traditional therapy a day. The three hour CIMT did not cause lesion enlargement, but might cause a negative effect due to fatigue or injury due to overtraining interfering with the motor re-learning processes. A total of 52 acute stroke patients participated in the study, who had the stroke 9.65 \pm 4.5 days prior to study start.

2.1.1 CIMT effect on motor rehabilitation

To examine the effect of CIMT several methods are used. The therapists can evaluate the patients with a large range of simple functional tests to examine the degree of change in motor function, but these test cannot really tell anything about what and where the properties leading to the change in motor function have occurred [Taub et al. 1994; 2006, Shi et al. 2011, Schaechter et al. 2002]. More technically advanced methods can be used to answer that question. Transcranial magnetic stimulation (TMS) can for instance provide information about the functional status of the entire motor system by measuring the motor evoked potentials initiated by the TMS. Functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) can measure the changes in blood flow and provide information about activity in cortical and subcortical regions during motor tasks, before and after the treatment and detect possible changes. Magnetic resonance imaging (MRI) can provide information of the brain's gray and white matter structure [Wittenberg and Schaechter 2009].

Functional gains in the upper extremity after CIMT have been reported in more than 120 CIMT studies [Taub et al. 2006]. At two year follow up measurements, the motor function gained from the standard therapy (6h/d) is almost fully retained in the higher functional patient whereas lesser functional patients approximately lose 20 % of their gains after one year and even more after a two year period [Taub et al. 2002, Sterr et al. 2002]. The documented effects are believed to be caused by two linked but independent mechanisms, overcoming the learned nonuse, and through use dependent cortical reorganisation [Wolf et al. 2002]. The learned nonuse can be overcome by restraining the less affected limb, thereby forcing the patients to use the more affected arm, along with applied shaping or repetitive task practice [Wolf et al. 2002].

CIMT studies have shown a cortical reorganization following rehabilitation in stroke survivors who showed functional motor gain. In this reorganization, there is evidence that the brain

area adjacent to the infarction adapted to the function of the stroke-affected extremity, thereby restoring some of the lost function [Liepert et al. 2000; 1998]. Liepert et al. [2000] found that the brain area innervating the stroke-affected extremity not only increased in size but also its center of gravity of the area shifted after rehabilitation. In motor learning theory it is hypothesized that this cortical reorganization is dependent on functioning feedback and feedforward mechanisms [August et al. 2006, Freeman et al. 2012, de Kroon et al. 2005]. In these mechanisms, both afferent and efferent signals play a role in motor control and in motor learning. For these mechanisms to work properly it is therefore required that the subjects receive sensory feedback and also exert voluntary effort during their rehabilitation [Wolpert and Flanagan 2009b].

A TMS study by Liepert et al. [1998] on six chronic stroke patients showed that the cortical motor maps of the abductor pollicis brevis (APB) muscle in both hemispheres changes after a stroke incident, and that the motor maps can be altered back to a more normal shape through 14 days of CIMT, see figure 2.1. At the baseline measurement, the motor map of the APB muscle in the more affected hemisphere was significantly smaller than the motor map of the APB muscle area in the unaffected hemisphere. After the intervention, the motor map where it was possible to elicit a response in the APB muscle using TMS, was significantly enlarged and the motor map of the less affected hemisphere was decreased. Studies by Liepert et al. [2000], Park et al. [2004], Ro et al. [2006], Sawaki et al. [2008] all showed similar results.

Functional MRI studies have reported that gains in motor function, after CIMT, in some stroke patients are accompanied by an increased activity in the contralateral brain hemisphere. Whereas the same and other studies show the opposite in other stroke patients, that increased activity is found in the ipsilesional hemisphere [Wittenberg et al. 2003, Schaechter et al. 2002, Johansen-Berg et al. 2002, Wittenberg and Schaechter 2009]. Park et al. [2004], Wittenberg and Schaechter [2009] states that further and larger studies have to be conducted to investigate the relation between motor gain and change in brain function and structure and explore the underlying mechanisms of cortical reorganization in the brain of stroke patients participation in a CIMT protocol.

2.1.2 CIMT limitations

Even though the effect of CIMT are promising, the acceptance of the therapy among patients and therapists is not overwhelming. In a questionnaire study by Page et al. [2002] 68 % of the asked patients were not willing to participate in a CIMT treatment. Their biggest concerns were the daily amount of time the less affected arm have to be restrained, the number of days the therapy lasted and the number of hours having to train each day. Therapists had concerns about the patients not fully adhering to the therapy program and the patients safety. Therapists also stated that rehabilitation facilities may not have the resources needed to provide CIMT. The results were based on 208 stroke patients and 85 physical and occupational therapists [Page et al. 2002]. Trying to solve the patients concerns with the therapy, modified versions of CIMT were derived, both shortening the training sessions and the amount of time the patient was asked to wear the constraint [Shi et al. 2011].

A study by Sterr et al. [2002] on 15 chronic hemiparetic patients showed that a three hour CIMT training schedule significantly improved motor function but that it was less effective than a



Figure 2.1. Pre and post CIMT motor maps of the abductor pollicus brevis muscle measured by TMS and MEP. The data is from the CIMT subject with the largest change in motor map ratio, in the study by Wittenberg et al. [2003]. The contour plots are the relative MEP of the muscle. The (0.0) coordinate is scalp vertex, the x axis is the medial-lateral axis. The affected hemisphere is the left hemisphere and the negative x coordinates. The y axis is the anterior-posterior axis, anterior being the positive values of y. The figure is redrawn from [Wittenberg et al. 2003].

six hour schedule. Both the three and six hour training protocols were performed five times a week for a period of two weeks. The only difference between the protocols was the amount of hours spend training[Sterr et al. 2002]. Stroke patients might be more prone to be willing to participate and stick to the treatment protocol, but at the cost of a less effective treatment.

Studies by Dromerick et al. [2009], Ro et al. [2006] evaluating CIMT against traditional therapy in the acute stage of stroke, found that both treatment methods were equally effective at inducing motor improvement. In both studies the acute stroke patients trained for two hours a day for five days a week for two weeks. In the study by Dromerick et al. [2009] the patients wore the restraint for six hours a day, and in the study by Ro et al. [2006] the restraint were worn for 90% of waking hours. The same trend is showing when applying six hours/day of traditional therapy or six hours/day of CIMT for ten straight days in chronic patients. This suggest that it is more the frequency and delivery of the treatment than it is the specific treatment method itself that is the important factor to produce motor gains [Taub et al. 1998].

A meta-analyse by Corbetta et al. [2010] on 18 randomised controlled trials and quasi randomised controlled trials CIMT, states that the majority of the CIMT studies were imprecise

and underpowered (too few subjects and too many methological errors) and conclude that the overall benefit from the therapy is close to the null effect, and that larger randomised controlled trials must be conducted to sort out the uncertainties. A systematic review by Hakkennes and Keating [2005] on 14 randomised controlled trials, states the CIMT might improve upper limb function, but larger studies are required before the real effect can be evaluated.

2.1.3 Summary of CIMT properties

- Restrainment of the less affected arm leads to massed repetitive training with the more affected arm, which acts as a technique to overcome learned nonuse and produce motor gains.
- The application of shaping principles allows the patients to re-learn movements step by step, and experience motor gain even with just small improvements.
- Patients with severe motor impairments are likely to gain very little function from CIMT that can be transferred into real life situations.

2.2 Electrical stimulation

Stroke patients not eligible for CIMT can effectively use electrical stimulation techniques to assist functional use of the limb and or prevent muscle atrophy by facilitating voluntary movement [Takka et al. 2011].

Electrical current applied to a motor nerve or the muscle itself, can get the involved muscle to contract. This external control of muscle contraction can be applied on paralyzed or paretic muscles to assist function in neurologically impaired people or as a tool in motor control rehabilitation [Peckham and Knutson 2005]. Most work involving muscle contraction with electrical stimulation, focus on activating nerve fibres rather than muscle fibres. Eliciting a nerve fibre to fire requires less intensity and pulse duration than that of muscle fibres. The threshold for eliciting a nerve fibre to fire is 100 to 1.000 times less than the threshold for muscle fibre activation [Sheffler and Chae 2007]. When activating a denervated muscle with electrical stimulation, the stimulus may cause injury to the cells closest to the electrodes before current applied to the tissue is strong enough to activate the most distant muscle fibres in the muscle [Horch and Dhillon 2002].

Motor neurons are not recruited in the same manner during voluntary and electrical stimulated contractions. When a peripheral nerve is electrically stimulated, the large diameter nerve fibres are recruited before the small diameter nerve fibres. This is opposite to the natural recruitment of motor neurons, from initially firing of small diameter motor neurons followed by larger motor neurons, when the force requirements in the muscle are increased [Peckham and Knutson 2005, Kandel et al. 2000, Baker 2000].

When muscle contractions are evoked using electrical stimulation and the muscle contractions are coordinated in such a manner that it provides function, it is termed functional electrical stimulation (FES). FES systems have been developed which can help impaired individuals in activities of daily living, by restoring function in the upper extremity, lower extremity, bladder, bowel and respiratory system. FES is an aid for continuous use. The therapeutic element of electrical stimulation is termed functional electrical therapy (FET). FET is used to improve tissue health and to induce physiological changes that remain after the stimulation is no longer applied [Peckham and Knutson 2005, Wei et al. 2011, Takka et al. 2011, Rushton 2003].

FET can be used as a treatment for impaired hand function that integrates intensive voluntary exercise assisted with electrical stimulation to complete the desired function/movement. FET may thereby provide hemiparetic patients with the ability to grasp, a function some cannot achieve by themselves. In upper extremity FET studies several different motor activities are used while applying stimulation, such as using a toothbrush, combing hair, using a fork, picking up a VHS tape, drinking from a 0.3 l can or a 0.33 l bottle, writing with a pen, using the telephone, pouring from a juice box, eating finger food or dragging a 500 g weight for a distance on a table [Popovic et al. 2003; 2004, Takka et al. 2011].

There exists no uniform guidelines regarding the duration and frequency of treatment sessions or the overall length of the treatment [Schuhfried et al. 2012], but FET training sessions are typically done in duration of 30 to 45 min, one to two times daily, for five to seven days a week for two to six consecutive weeks. In some FET studies, FET are supplemented with conventional therapy [Takka et al. 2011, Popovic et al. 2006, Rosewilliam et al. 2012].

FET have been applied in acute, subacute and chronic motor impaired stroke patients with positive results on hand function and condition [leung Chan et al. 2009, Takka et al. 2011, de Kroon et al. 2005, leung Chan et al. 2009, Popovic et al. 2004; 2003].

The electrical stimulation activating the paralyzed or paratic muscle(s) can be controlled and triggered in different manners, such as stimulation programmed to mimic prehension, cyclic controlled, EMG-triggered and other forms of triggers [de Kroon and IJzerman 2008, Sheffler and Chae 2007]. Neural hand prostheses are programmed to mimic prehension by opening and closing the hand in an orderly fashion [Sheffler and Chae 2007]. In cyclic controlled stimulation, the stimulation is pre-programmed, for instance five seconds with stimulation followed by five seconds with no stimulation continuously in a set period of time. Cyclic controlled stimulation is often not used in performing functional tasks [Baker 2000]. EMGtriggered stimulation requires the user to perform an activation of a specific muscle in the more affected upper extremity. If the muscle activation exceeds a set threshold, the muscle is assisted by the electrical stimulation. EMG-triggered stimulation is not suited to be used on all stroke patients since not all can produce sufficient muscle activation in the muscle [Chae et al. 2008]. A review by de Kroon et al. [2005] conducted on 19 clinical trials, concluded that EMG-triggered stimulation and other trigger techniques, requiring cognitive effort to exceed a set threshold, might be more effective in producing upper extremity motor recovery in stroke patients, that non-triggered stimulation activation.

A FET study by Popovic et al. [2004] combined electrical stimulation with intensive voluntary movement of the upper extremity in 41 hemiplegic subjects. The stroke incidence had occurred more than two weeks and less than three months prior to the start of the study, all subjects had some residual wrist and finger function. Nineteen patients participated in FET during their acute phase of hemiplegia and 22 patients participated in FET during their chronic phase. The daily FET training sessions were 30 min long and continued for three weeks. The study showed that the patients in the acute phase of hemiplegia experienced a high amount of arm and hand rehabilitation (near to normal use), whereas the gain in the chronic hemiplegia patients were measurable, yet not significant. The conclusions was that FET greatly promotes the recovery of the paretic arm if applied during the acute phase of post stroke hemiplegia, and that three weeks of FET treatment applied in chronic patients was not sufficient to promote significant recovery [Popovic et al. 2004].

A FET study by Popovic et al. [2003] divided 28 acute hemiplegic patients into lower functioning groups and higher functioning groups. The stroke incidence had occurred in average 7 ± 2 weeks prior to the start of the study. The patients were randomly separated into FET or controls groups. Every day for three consecutive weeks, the FET groups received conventional therapy and 30 min exercise with the paretic arm while being assisted with a neural prosthesis. The patients in the control groups also received conventional physiotherapy and 30 min of exercise with the paretic arm, performing the same tasks as the FET groups, but without the neural prosthesis, every day for three consecutive weeks. The subjects were evaluated at the start of the study after 3, 6, 13, and 26 weeks of study start.

Both the FET and control groups showed an increase in recovery and functionality of the paretic arm, see figure 2.2, but the gains in the FET groups were much greater compared with the control groups. The lower functioning groups patients showed less improvement than the higher functioning groups in both the FET and control groups [Popovic et al. 2003].



Figure 2.2. The bars show the average number of successful trials performed by 28 acute hemiplegic subjects using their more affected upper extremity during 2 min sessions, in 11 different tasks, at the start of the treatment and at 3, 6, 16 and 26 weeks after treatment start. (a) is the results from the higher functioning groups and (b) is the results from the lower functioning groups. The horizontal bars on top of bars are the standard deviations. The dashed lines are the trend lines. The figure is redrawn from Popovic et al. [2003].

2.2.1 Electrical stimulation effect on motor rehabilitation

The positive effect of using FET compared to conventional treatment only, is poorly understood, but both cortical and spinal mechanisms is thought to play a role [Smith et al. 2003, Rushton 2003].

Learning a new motor skill, requires repetitive movements of the particular movement and significant cognitive effort to execute and have shown to produce task specific cortical reorganization. If repetitive movement, of a specific task, facilitates motor re-learning, it is possible that repetitive movement mediated by electrical stimulation also facilitates motor re-learning [Sheffler and Chae 2007].

A functional magnetic resonance imaging (fMRI) study by Han et al. [2003] showed that electrical stimulation applied to a peripheral muscles seemed to have a direct effect on the contralateral somatosensory cortex and bilateral supplementary motor areas. A fMRI study by Smith et al. [2003] showed in addition that there existed a dose-responsive relationship between electrical stimulation to the lower extremity and brain activation, in specific brain areas. An increase in stimulation intensity to the peripheral muscle increased the blood flow in the brain. Smith et al. [2003] states that it is not the activating pathway but the cortical activation itself that is believed to be the important element in regard to brain rehabilitation. These studies could suggest that repetitive movement training mediated by electrical stimulation has the potential to facilitate motor re-learning via cortical mechanisms [Sheffler and Chae 2007].

It is hypothesised that electrical stimulation may facilitate motor re-learning at the spinal level [Rushton 2003]. Electrical stimulation activates nerve fibres both orthodromically and antidromically, where the orthodromically impulses travel to the muscle and the antidromically impulses travel to the anterior horn at the spinal cord. If the corticospinal-anterior horn cell synapse is a Hebb-type modifiable synapse (the synapse is strengthened by the coincidence of presynaptic and postsynaptic activities) and that the synapse can be modified by electrical stimulation, then electrically induced impulses coincident with voluntary effort arriving through the pyramidal tract, could help to produce restorative synaptic alterations at the anterior horn cell level. The neural activity in the pyramidal tract is greatly reduced following a brain injury and failure to restore the activity leads to a weakening of the synapse. Rushton [2003] suggests that electrical stimulation-mediated antidromic impulses provide a means to strengthen the synapse and also predict that electrical stimulation together with simultaneous voluntary effort could be a way to facilitate motor re-learning [Rushton 2003, Sheffler and Chae 2007].

As mentioned in section 2.1.1 it is hypothesized that this cortical reorganization is dependent on functioning feedback and feedforward mechanisms [August et al. 2006, Freeman et al. 2012, de Kroon et al. 2005]. In these mechanisms both afferent and efferent signals play a important part in motor control and motor learning. For these mechanisms to work properly it is required that the subjects receive sensory feedback and also exert cognitive effort during the rehabilitation training [Wolpert and Flanagan 2009b]. This correlate with the findings in de Kroon et al. [2005] that voluntary triggered stimulation might be more effective in producing upper extremity motor recovery in stroke patients than non-triggered stimulation activation. FET can provide the afferent feedback needed in the motor learning process in motor impairment stroke patients. If FET is timed with cognitive effort to produce the specific movement the FET is evoking then both components for the motor learning process are present [de Kroon et al. 2005, Popovic et al. 2004].

In the study by Popovic et al. [2004] where a larger recovery was found in acute subjects compared to the chronic subjects, it is suggested that the larger recovery in the acute subjects, could be due to the greater degree of plasticity in the central nervous system (spontaneous recovery) in the first months post stroke, and that synchronizing FET with the spontaneous recovery promote upper extremity rehabilitation.

In addition electrically stimulating muscle tissue increases the blood flow to the muscle (bringing nutrients to the muscle and surrounding tissue) and thereby prevent loss of muscle mass (atrophy) or even rebuild the muscle tissue. And the ability to use the more affected hand, with the assistance of electrical stimulation, contributes to increased motivation to exercise [Sheffler and Chae 2007, Popovic et al. 2004].

2.2.2 Stimulation setup and parameters

To produce electrical activation of neuromuscular tissue, a minimum of two electrodes are required. It is possible to use many different waveforms to excite neural tissue through the electrodes, but pulsed currents are very common when using electrical stimulation in a therapeutic setting. Pulsed currents can be monophasic (the current is only flowing in one direction) or biphasic (the current is flowing both in positive and negative direction), see figure 2.3. Monophasic waveforms have the disadvantage that it can alter the charge in the tissue under the electrodes and cause skin irritation and burns. The current only flowing in one direction, will produce unequal charge distribution. This unequal charge distribution in the tissue can be reduced by using the biphasic waveform since both electrodes acts as a cathode in some part of the waveform.

Biphasic waveforms can be symmetric or asymmetric. In the asymmetric configuration, (figure 2.3 b) only one direction usually allows for exciting the tissue underlying the electrodes. The opposite current direction is longer in duration and have lower amplitude and can restore the ionic balance without exciting the tissue. The asymmetric biphasic waveform can be balanced, where an equal amount of current flows in both direction, or unbalanced. Balanced currents are best to maintain neutral charge in the tissue. The symmetric biphasic waveform (figure 2.3 c) have equal magnitude and duration in both directions, and is very effective in reducing unequal charge distributions [Peckham and Knutson 2005, Meadows 1991].



Figure 2.3. Common shapes of pulsed currents. (a) Monophasic waveform with current (ions) flowing in only one direction. (b) Asymmetric balanced biphasic waveform with current (ions) flowing in both direction. The waveform only recruit excitable tissue in one direction. (c) Symmetric biphasic waveform, both the positive and negative part of the pulse are equally effective in recruiting excitable tissue. The figure is modified and redrawn from Baker [2000].

The electrical stimulation waveform delivered through the electrodes to neuromuscular tissue, is usually characterized by three parameters: frequency, pulse duration and amplitude. The strength of a muscle contraction is coordinated by changing these three parameters [Peckham and Knutson 2005].

To produce a smooth muscle contraction the stimulation have to be above a certain threshold frequency, if the frequency is too low the response is a series of muscle twitches. Up to a maximum, an increase in frequency produce a stronger contraction. A smooth muscle contraction produced voluntary or by electrical stimulation may look similar, but the stimulated contraction is metabolically more expensive and fatiguing. A smooth voluntarily contraction discharges the neurons asynchronously with an individual neural discharge rate of 5-25 per second. The asynchronously firing of the neurons allow the motor units discharge to sum up and produce a smooth muscle contraction at low discharge frequencies. Electrical stimulation activate the larger neurons close to the stimulation electrodes synchronously, and have a reduced availability to the neurons in the motor neuron pool compared to voluntary contraction. Increasing the intensity to activate the needed neurons to produce the contraction often produce discomfort to the receiver, so to produce the smooth contraction, the firing rate can be increased. Frequencies greater than 30 to 40 Hz have shown to produce rapid muscular fatigue due to a decrease in neurotransmitter release. The higher the stimulation frequency the faster the muscle fatigue. It is common to use frequencies between 25 and 50 Hz to produce smooth steady contraction in electrical stimulation systems [Baker 2000, Peckham and Knutson 2005].

The nerve fibres primarily activated during electrical stimulation are the ones innervating the rapid firing and fast-fatiguing muscle fibres. Fast muscle fibres rely on a well-developed glycolytic system, and a faster firing rate than normal will cause reduced contraction capability since the muscle fibres need for energy cant be sustained [Baker 2000, Peckham and Knutson 2005].

The pulse duration and intensity affects the number of activated motor units in the muscles. An increase in pulse duration and/or amplitude will increases the electric charge applied to the tissue and produce a larger electric field activating more motor units. An increase in activated motor units will increase the force produced by the contraction (spatial summation) [Peckham and Knutson 2005].

Figure 2.4 show the relationship between amplitude and pulse duration, and how varying one or the other or both control the motor responses in wrist extensors muscles, at a stimulation frequency of 35 Hz. The "Threshold" line is the threshold for the most excitable motor neuron, and the "Near Maximal" line is where the least excitable motor neuron is activated. If the pulse duration is set to 200 μ s the grading of the muscle force will be achieved by changing the amplitude of the stimulation between 15 and 40 mA, and if the amplitude is set to 40 mA, pulse duration from 40 to 200 μ s will control the entire muscle activation from Threshold to Near Maximal [Baker 2000].



Figure 2.4. The figure illustrates the relationship between current amplitude and pulse duration, during activation of motor neurons in wrist extensors muscles at a stimulation frequency of 35 Hz. The Threshold line indicates the threshold for the most excitable motor neuron, and the Near Maximal line indicates where the least excitable motor neuron is activated. The figure is redrawn from [Baker 2000]

When all the stimulation parameters are set, another element relevant to muscle fatigue, is the overall duration of applied stimulation and the in between stimulation breaks. An electrical stimulation study by Packman-Braun [1988] investigated the relationship between the ratio of stimulus on-time to off-time and muscle fatigue, on wrist extensor muscles of 18 patients with hemiparesis, during isometric contractions. The stimulation waveform characteristics were a biphasic square (asymmetrical balanced) waveform at 36 Hz with a pulse duration of 300 μ s and an amplitude of 40 mA. The stimulation intensity had a 2 seconds ramp up time and stayed at peak intensity for 5 seconds. The time off between the stimulus were 5, 15, or 25 seconds giving on/off cycle ratios of 1:1, 1:3, or 1:5 respectively. The study showed that if force needed to

be maintained throughout the treatment session, the on/off cycle ratio influenced the duration of the treatment session. If the force were to be sustained at >50 % of initial force output, the on/off cycle ratio of 1:5 could be performed in sessions of >30 minutes, 1:3 ratio in 11-20 minute sessions, and the 1:1 ratio in 1-10 minute sessions. The shorter the rest period with respect to the stimulation time, the faster the muscle fatigue [Packman-Braun 1988]. Evidence indicates that the actual duration of the stimulation is at least as important as the on/off ratio, but all in all the stimulation on and off durations, should be based on the individual patients fatigue rate and treatment program [Baker 2000].

To minimize user discomfort, motor units can be recruited gradually instead of all abruptly at once. This can be done by ramp up the intensity, or increasing the pulse duration during a rise time. A ramp down period can also be applied at the end of a stimulation, and is used to return the stimulated limb/muscle to a resting position in a controlled way [Baker 2000].

2.2.3 Grasping estimation

When designing a FET system that can assist stroke patients with prehension durings tasks, characteristics of the grip can be used to adjust the level of assistance. For instance the level of assistance can be based on the amount of force they are exerting on the object.

Many stroke survivors do however not only suffer from prehension weakness, but also show difficulties in opening the hand to grasp around or release objects. It is therefore often important also to assist the users with finger extension, allowing them to grasp around and release an object. FET studies by Popovic et al. [2003; 2004], de Castro and Jr [2000], Popovic et al. [2006] all use the stimulation sequence of first opening the hand to allow the hand to grasp an object, close the hand to allow object manipulation and finally open the hand to release the object. They used three to eight channels of electrical stimulation to produce and control the muscle contractions.

Most FET systems do not incorporate real-time modifications to the stimulation pattern [Sheffler and Chae 2007]. When muscles start to fatigue, more assistance is required to ensure that the objects do not slip out of the users grasp. Automatic intensity regulation using biomechanical sensors could be a solution to this problem.

A study by Chen et al. [2007] incorporated force and slip sensors in an electrical stimulation grasping system to regulate the stimulation intensity when the slip sensor detected a slip. The subjects in the study received electrical stimulation to the palm and forearm. The force sensor was located on the inner side of the thumb whereas the slip sensor was too big to be placed on the hand and was installed elsewhere in the experimental setup. The system worked as intended, but the system design is not very simple. The slip sensor could not be placed on the hand and sensors in general requires good contact to the objects to provide the desired information.

A simpler way to detect slip, not requiring implanted electrodes and sensors or mounting additional sensors on the users hand, forearm and the objects to be manipulated, would be desired.

2.2.4 Summary of FET properties

- FET can allow severely motor impaired stroke patients to perform motor functions not possible without the assistance of electrical stimulation.
- Repetitive training with the assistance of electrical stimulation is thought to facilitate motor re-learning.
- Exerting voluntary effort to produce a movement that is timed with assistance of electrical stimulation, is believed to be an important factor in motor learning process.

2.3 Biomechanical sensors

Several different sensors exist that can be used to measure biomechanics of the human body. The purpose of these sensors is usually to quantify the movements of the human body for analysis. This section explores some of the various sensors that previously have been used to quantify hand movements and/or object interaction during grasping. The requirement for the sensors used in the project is described in the system requirement section 3.1 and the choice of sensor is elaborated in the solution strategy section 3.2.

2.3.1 Electromyography

Electromygraphy (EMG) measures the voltage differences that happen during muscle contractions. This can either be measured using electrodes placed on the surface of the skin (surface EMG) or by placing electrodes directly inside the muscle (intramuscular EMG). EMG systems provide a direct measure of muscle activity and by placing electrodes on specific muscles of interest, it is possible to determine if certain movements are being performed. EMG can be used to distinguish between several different hand movements, and can provide information on the intent of the user [Cheron et al. 1996, Ito et al. 2008]. The user must however have a certain degree of motor control in order for the electrodes to reliably detect muscle activity.

2.3.2 Image sensors

Image sensors, such as most cameras, record light to quantify observed colours. Techniques have been developed that allows the use of cameras to quantify movements, referred to as motion capture. The purpose of motion capture systems is to translate real world movements into discrete three-dimensional cartesian coordinates. Having a three dimensional representation allows the use of various analysis methods on the objects of interest. These analyses can for instance be used to determine limb position, movements and interaction with objects. Optical motion capture systems requires the use of several specialized cameras that all record from different angles, as well as placing markers on the limbs or objects of interest. These markers reflect light emitted from the cameras and by adjusting camera threshold, it is possible to only record the light emitted from the markers [Guerra-Filho 2005]. Motion capture systems has previously been used to accurately determine hand and finger movements as well as evaluating hand rehabilitation by measuring range of motion [Mitobe et al. 2010, Li et al. 2012]. Motion capture system can however not provide information regarding forces in the interaction with objects.

2.3.3 Depth sensors

Depth sensors are cameras that use light to quantify distance. One of the first depth sensors was the Microsoft Kinect camera that acts as a motion sensing input device and was originally created as a peripheral for the Microsoft Xbox 360 console. The kinect consists of an infrared projector that projects a grid of infrared dots on the objects in front of it. An infrared camera installed in the kinect, can capture the grid of infrared dots created by the projector. The kinect is calibrated to know where each of the projected dots appear when projected against a flat surface, at a set distance. If objects are located closer or further away from the calibrated distance, the infrared dots will be pushed and shifted out of its original grid. It is thereby

possible for the kinect to calculate the displacement of the dots in relation to the calibrated infrared dot grid to create a depth image [Khoshelham and Elberink 2012, Borenstein 2012]

The kinect also features a normal colour camera, with a resolution of 640 by 480 pixels. Both the colour and dept data are captured at a rate of 30 frames per second. The colour camera can be used separately or be lined up with depth information from the infrared camera, making it possible to alter the colour image based on its depth, and to colour the 3D images created from the depth information [Borenstein 2012]. An array of four microphones is installed inside the kinect casing, making it possible for the device to detect sound, and in some instances even locate the sound source. A motor located in the plastic base enables the Kinect to tilt the cameras and speakers, in the range of about 30 degrees [Borenstein 2012].

The kinect can besides being used with the Xbox 360 also be plugged into other devices, with its USB connection. This opportunity spawned a massive interest among computer enthusiasts to be able to connect the kinect with a computer, and retrieve data from the kinect. When the kinect was first launched in 2010, the drivers allowing the kinect to communicate with a computer were not released along with it. It was first later, as a response to the big interest, that PrimeSence released their software for working with the kinect [Borenstein 2012]. This allowed the Kinects technology to be used for other purposes than original intended by Microsoft, as a gaming peripheral.

The depth accuracy and resolution are affected by the sensor, system setup and the surface the infrared dots are projected against [Khoshelham and Elberink 2012]. Sensor errors are mainly related to poor calibration, and can be corrected by recalibrating the sensors. System setup errors are mainly related to the lighting condition. Strong lighting influences the measurements of the infrared dots displacement. Depending on the specific kinect device, its operation range is between 0.5 m to 5.0 m and the further away the objects are placed from the sensor, the less precise the depth measurements become. This is visualized in figure 2.5 where the minimum distance the camera can distinguish between (point spacing) is shown as a function of distance from the camera.

Smooth and shiny surfaces can get overexposed and affect the measurement of the dots displacement and results in gaps in the image [Khoshelham and Elberink 2012].

2.3.4 Transducers

Transducers, such as pressure sensors or accelerometers, convert one form of energy into voltage, thereby allowing quantification of the input. Pressure sensors could be integrated into the object to be manipulated with, to gain information on when and how the interaction with the object is performed, as used by Chen et al. [2007] to maintain grasping force. Accelerometers could be used to detect movement of limbs or objects, as used by Seitz et al. [2011] to measure arm and finger movement activity of hemiparetic patients following a stroke incident.



Figure 2.5. Resolution of the kinect camera as a function of distance. The minimum distance the camera can distinguish between is represented by the point spacing. When an object is close, the point spacing is low, resulting in a high resolution. At a distance of 1 meter, the point spacing is thus about 0.3 cm, whereas the point spacing is almost 7 cm at 5 meters distance. The depth conversion equation used was estimated by Magnenat [2010].

2.4 Aim

The primary aim of this study was to produce a real time closed loop functional electrical therapy system for use in upper extremity motor rehabilitation. The system should incorporate elements from both constrained induced movement therapy and functional electrical therapy rehabilitation techniques, since both techniques have properties that show evidence for improved motor gain motor in motor impaired stroke patients. The system should be simple in design and operation, with the goal to increase user acceptance. Motivational elements should be introduced to ensure patient adherences to the rehabilitation training.

System development

The current section describes the development of a system that can fulfill the requirements described in section 2.4 by translating the overall aim of the system into more specific requirements. A solution strategy is then created based on the requirements. Finally the solution strategy is fully realised through implementation.

3.1 System requirements

As described above, the general aim of the system is to assist the user in performing a simple movement task, using the more affected upper extremity, utilizing electrical stimulation if needed. In the following the main aim is divided into sub requirements.

- a) Sensor: When developing a system that could achieve the aim in this project, a highly advanced system could be created that would have very precise and accurate performance if relying on several different sensors, e.g. pressure and accelerator sensors could provide a lot useful information. But this would also have the drawback of increasing the system complexity, which can limit the user-friendliness of the system (e.g. active portable system requires batteries). For instance, an EMG based trigger would be a reasonable solution to initiate the electrical stimulation. But adding an EMG-trigger would result in additional electrodes applied on the subjects arm and require additional hardware, resulting in a system with increased complexity. It is therefore a requirement that the amount of sensors used in the system is as few as possible, to simplify the system design and usage.
- b) Task: A suitable task should be chosen. The task should be simple to explain and execute. The task should involve the user gripping an object with the more affected hand. It should be possible to break the task into sub-tasks incorporate shaping principles from CIMT. If the user do not have the capacity to perform the entire task the sub-tasks can with advantage be trained individually, as done with success in CIMT [Morris and Taub 2001, Taub and Morris 2001, Taub and Uswatte 2006]. The task should be a task that can be transferred into the users daily activities, such as gripping and manipulation a drinking cup.
- **c) Stimulation:** The system should incorporate electrical stimulation to assist the user with prehension. Previous FET prehension studies uses stimulation parameters in

the frequency range of 20-70 Hz, with 40-50 Hz as the most common settings. Pulse durations between 200-300 μ s and a stimulation amplitude between 8-50 mA [Popovic et al. 2004; 2003, Rosewilliam et al. 2012, Popovic et al. 2006, de Castro and Jr 2000]. The pulse duration and amplitude values match well with the information provided in section about the 2.2.2 relationship between stimulation amplitude and pulse duration. Frequencies greater than 30 to 40 Hz have shown to produce rapid muscular fatigue, for which reason 40-50 Hz might be too high [Baker 2000].

In FET prehension studies by [Popovic et al. 2006, de Castro and Jr 2000, Popovic et al. 2003; 2004] the stimulation electrodes are placed on the forearm to assist grip function, most commonly activating the following muscles: Flexor digitorum profundus, flexor digitorum superficialis, flexor pollicis longus, Abductor Pollicis Brevis opponens pollicis.

- d) Finger extension assistance: As mentioned in section 2.2.3 stroke patients do not just have difficulties closing the hand and grasping objects, but also to open the hand and release objects. However, the system should only assist the user with electrical stimulation during grasping and not also in opening the hand. The goal behind the idea is to increase user acceptance by simplifying the system and solve the problem by other means, than by applying electrical stimulation to the extensor muscles in the hand and forearm.
- e) Assistive stimulation: Electrical stimulation should only be applied when the user is exhibiting intention toward manipulating the task object. As mentioned in section 2.2.1 that cognitive intent coupled with afferent feedback (produced from electrical activating the muscles) are important elements in motor control and motor learning. It is therefore a requirement, that electrical stimulation is only applied when the user is not only in contact with the cup, but also trying to grasp around the cup. Furthermore, the system should for safety and comfort reasons be able to stop stimulation if the user drops the cup (i.e. grip is lost), if the cup is moved out of the task area or if the task is not completed within a specific time limit.
- f) Stimulation intensity regulation: The system should automatically regulate the intensity of stimulation according to the user requirement. Stroke patients have various degrees of motor control impairment, resulting in a need of different degrees of assistance. This requirement is also highlighted through muscle fatiguing during the course of training, or the possible improvement of motor control over time in which case the need for assistance may decrease or disappear. Varying degrees of assistance can be achieved by increasing or decreasing the intensity of the applied electrical stimulation. The intensity regulation should happen automatically and should be regulated throughout every task repetition, so that the assistance is adapted for every repetition.
- **g**) **Simplicity and user-friendliness:** A key aspect of the system is that it is possible to be operated and used without specialized personnel assisting the user. It is therefore a requirement that the system is as simple as possible, which also might help achieving a better acceptance of the system among the big population of elderly stroke patients [Zampolini et al. 2008, Brennan et al. 2011]. Making the system subtle by operating in the background and limiting the need for user interaction, is also a way to convince and encourage the more sceptical patients. This can be achieved by limiting the amount of

hardware and by incorporating intuitive instructions to the user during exercises. Setting up the system for each training session should also be made as easy and quick as possible. Placing the electrodes in the correct position can prove quite difficult for people without the necessary training.

- **h) Motivation:** It takes a lot of time and effort to rehabilitate an upper extremity impaired by a stroke incident. To ensure that the patients train with high intensity, throughout each training session, the patient needs to be motivated [Taub et al. 2002].
- i) **Patient safety:** The system should prioritize patient safety. Always when applying electrical stimulation on human subjects, several safety measures have to be upheld. If sufficient current is allowed to flow through the body, severe damage can occur [Enderle et al. 2005].

3.2 Solution strategy

In this section, the solution strategies for complying with the specified requirements are briefly described. The enumerations of items in this section correspond to the enumerations in the requirement section. The applied solution and how it works is expanded in the implementation section.

a) Sensor: The general aim of the project describes the need for a system that is able to continuously recognize the users hand as well as the object to be manipulated. Based on the interaction on the hand and the object, electrical stimulation should be applied. Recognition of objects can be done through the use of an normal camera. These devices are cheap and the data is easy to access. Pictures from a normal camera only provide colour (RGB) information, which limits the possibility to quantify the interaction between the users hand and the object. The data from a RGB camera would essentially only be able to provide us information of the hand and object interaction in two dimensions. Thus any movement directly towards or away from the camera would be difficult to quantify. Using a depth camera however, such as the kinect camera, the pictures provide information of the distance to each pixel in the picture. A depth map essentially provides both the two dimensional shape information that the RGB camera provides (without colour), but also adds the depth information, resulting in a partial 3D model of the objects. The result is only partial because a single camera cannot detect the object from all sides, without taking several pictures of the object from different angles. As a depth camera seems to be able to provide all the information needed, we want to design the system using a Kinect camera as the only sensor. Furthermore, the Kinect camera also contains a RGB camera, so without increasing hardware requirements, colour pictures can also be utilized in the system design.



Figure 3.1. Visual representation of the Kinect camera recording depth data from a hand gripping a cup. To the right is the data from the camera visualized. Dark shades of gray represent distances close to the camera, whereas lighter shades of gray represent distances further from the camera. Black pixels represent distances the camera was unable to detect due to shadowing.

b) Task: The chosen task involves lifting a cup from a table surface and moving the cup from a start location to a finish location. Completion is reached when the cup is placed on the table surface at the finish location. Ideal task execution involves grasping the cup, lifting the cup from the table surface, moving the cup to the finish location and placing the cup down at the table surface within the finish area. The task can be broken down into subtasks to incorporate shaping principles, and trained individually. The movement task is chosen on basis of similar activities that are used in both CIMT and FET studies and because it is a typical movement that has a functional value.



Figure 3.2. The task which the system is designed for. 1) the cup is lifted from its starting position. 2) the cup is moved across the table while lifted. 3) the cup is placed on the table in the finishing position.

c) Stimulation: Stimulation electrodes were to be placed on the users more affected forearm to assist in grip function. The muscle chosen to stimulate were the flexor pollicis longus, flexor digitorum superficialis and flexor digitorum profundus, this match well with the muscles used in other FET perhension studies [Popovic et al. 2003; 2004, de Castro and Jr 2000, Popovic et al. 2006]. The electrode placement is illustrated on figure 3.3.

The stimulation waveform parameters is chosen to be a squared and monophasic waveform with a pulse width of 200 μ s and pulse amplitude from 10 to 45 mA, see figure 3.4. These parameter values are the values found to be most commonly used in FET studies and the values also match well with the information given in section 2.2.2 about amplitude and pulse duration. The stimulation frequency is set to 30 Hz, this value is lower than in most FET studies, but is chosen with the intention to reduce the muscle fatigue rate [Baker 2000] Due to hardware limitation the waveform had to be monophasic, a biphasic waveform might have been prefer due to its ability to maintain neutral charge in the stimulated tissue.



Figure 3.3. Illustration of the stimulation electrode placement on the forearm. The small round electrode is the active electrode whereas the big rectangular electrode is the return electrode.



Figure 3.4. Visual presentation of the chosen electrical stimulation waveform. a) the shape of a single stimulation pulse, lasting 200 μ s. b) a 30 Hz stimulation pulse train for a 0.3 second duration.

- d) Finger extension assistance: A cone shaped cup turned upside down allow the user, with hand opening difficulties, to slide the hand from the narrow part of the cup down to the wide part of the cup, and also slide the hand off the cup again. By doing so, no additional stimulation to the extensor muscles in the hand and forearm is needed to open the hand or releasing the cup.
- e) Assistive stimulation: Electrical stimulation is initiated when the user's hand is gripping the cup, and contact between the hand and the cup is detected by the kinect camera. Stimulation should however not be applied when only a part of the hand is touching the cup, i.e. one finger. This problem can be solved by creating a program that is able to identify and separate the cup and the user's hand. When the hand is in contact with the cup, the program can measure the distance between the two furthest points of the hand that is in contact with the cup (intersection between the two objects). Only if this distance is above a certain threshold, i.e. the minimum distance required to normally grab a cup, should stimulation be applied, see figure 3.5.

However by using the distance threshold between two points, it is still possible to grip the cup using only two finger tips, which might not be desirable. This could be solved by
also setting a threshold for the number of points (pixels) of the hand that is found to be in contact with the cup (pixels intersecting both object and hand). Another way could be to analyse the shape of the object, consisting of the intersecting pixels, and only apply stimulation if the object resembles the shape of the outer rim of the cup at a particular length.

Stimulation is only applied as long as the hand is continuously gripping the cup. If for instance the cup is dropped, no grip between cup and hand is detected and the stimulation should be terminated. A maximum stimulation duration and breaks in between trials should be implemented to reduce muscle fatigue in the stimulated muscle.



Figure 3.5. The figure illustrates when the system is set to stimulate. a) The hand is in good contract with the cup, the furthest connections points between the hand and the cup exceeds the set threshold and stimulation can be applied. In b) and c) the connection between the hand and the cup do not exceed the threshold distance, and no stimulation will be applied before a better connection between the hand and the cup has been achieved. The threshold distance can be set according to the radius of the cup.

f) Stimulation intensity regulation: Stimulation is initially applied when the hand is gripping and in contact with the lower base of the cup. While the cup is still placed on the table, the intensity can be regulated as a function of the distance between the hand and the top of the cup. When stimulation is initially applied the distance between the hand and the top of the cup is largest and the intensity applied is the lowest (i.e. the starting intensity). If the hand moves upward without the cup moving upward, this could be considered a sign that the user is trying to lift the cup, but the gripping force is insufficient. Intensity should then be increased to provide further assist in lifting the cup. Maximum intensity should be delivered when the distance between the hand and the top of the cup is close to zero, i.e. the hand is gripping around the top of the cup.

The stimulation intensity is also regulated in the same manner when the cup is lifted from the table and traveling through the air. If the grip force is not sufficient to sustain a firm cup grip for the entire duration of the task, the cup will slip out of the user's hand. If slip occurs the system should be able to detect the decreasing height difference between the hand and the cup and increase the stimulation intensity until the cup is no longer slipping out of the hand. With this approach the level of assistance is regulated through every task repetition and can compensate for changes in the users ability.

The initial stimulation intensity is set at 50 % of the individual maximum stimulation intensity. The maximum stimulation intensity is set to fit the individually user of the system, with a overall maximum of 45 mA. At 100 % stimulation intensity the stimulation should only be able to assist and not allow the user to perform the task without exerting voluntary effort in gripping the cup.

To ensure that the distance the intensity regulation is based on is as big as possible, the system should only begin stimulating when the users hand is resting on the table as well as gripping around the cup. Otherwise the user might grip the cup near its top, resulting in a small distance to regulate the intensity on. This could lead to big increments of intensity upon small increments of hand height.



Figure 3.6. The figure shows how the stimulation intensity is regulated once sufficient contact between the hand and the cup is achieved and continuous maintained. a) In the initial grip, the distance between the hand and the top of the cup is 5 cm and the simulation is at 50 % of maximum stimulation intensity. b) The hand have moved upwards, without lifting the cup with it, thereby minimizing the distance between the hand and the top of the cup and the stimulation intensity is increased to apply further assistance to the grip.

- **g**) **Simplicity and user-friendliness:** A simple user interface should be designed where instructions are given to the user on how to perform the task. Instructions should be short and given in steps according to task progress. Markings on where to move the cup from and to can be placed on the table, reducing the need for the user to look on a monitor. The graphical user interface (GUI) could then essentially just consist of a start/stop buttons with a text field to provide instructions on what to do next. Electrode placement can be simplified by incorporating the electrodes into a hand/arm sleeve that is custom made to each user. This would secure correct placement of the electrodes while offering an easy method to place and remove the electrodes.
- h) Motivation: Providing the users with the ability to track their rehabilitation progress is a good means to keep the spirit and motivation high, since it hopefully would show that the time and effort invested in the training is paying off. User motivation can then be achieved through a history section containing information on important task parameters, e.g. mean task duration and the intensity of the electrical stimulation. Another way

to make the training more motivating would be to mimic simple games or challenges that the user is familiar with, such as sudoku or tic-tac-toe. This would however require that the system is able to recognize more complex shapes.

i) Patient safety: The chosen electrical stimulator, NoxiTest IES 230 (see section 7.1) features an external scale amplitude control. This means that the maximum stimulation intensity is hardware regulated, so that even though the software accidentally outputs maximum voltage, the intensity of the applied stimulation is never above the settings of the electrical stimulator. This only limits the amplitude of the stimulation, if the system were to continuously output current (i.e. direct current), the user could sustain considerable harm if stimulation is prolonged. Software safety precautions should therefore be implemented to ensure that the electrical stimulator never can output DC. A National Instruments USB-6229 is used to convert a digital input to an analog output (DAC) which is attached to the analog input of the electrical stimulator. By designing the PC and DAC communication so that the DAC device is dependent on continuously receiving packets of data from the PC it is ensured that stimulation cannot persist in the case of a software or PC crash. An external safety button should be provided to the user, enabling the user to immediately terminate stimulation if needed.

It could happen that the user want to move a stimulation electrode during training due to discomfort or bad electrode skin connection, and end up having an electrode in/on both arms. This could results in that the two electrodes stimulates across the heart, which can cause harm to the user. This can be solved by terminating the stimulation when the electrodes are covered by the shadow of the hand not used for training. When the sensors no longer detect the electrode(s) the stimulation should be terminated.

Implementation \angle

This chapter describes in detail how the different functions were implemented in the system. The system was programmed using MATLAB and flowcharts are utilized to document the code, where green circles represent the start of the flowchart, red circles represent the end, blue diamonds represent decisions and blue blocks represent a process. Several features have been implemented into the program, some of which are not described as a part of the system requirements and system solution in chapter 3. The implementation of the systems main function is documented first in section 4.2. The additional features, which includes an example of how a motivational feature and a calibration tool can be implemented, is documented following the main feature.

4.1 Equipment

The components that were used to realize the purposes described above, and the connections between them, is visualized in figure 4.1. The main program is running on MATLAB 2013a on a PC running Windows 7. The MATLAB program receives depth information from a Microsoft kinect camera. This depth information is analyzed, while information is continuously provided to the user through a monitor. The analysed data is used to control a feedback loop that determines the level of assistance the user is given through electrical stimulation. This feedback loop is implemented by converting the digital output from the MATLAB PC to voltage using a digital to analog converter (DAC) from National Instruments. This voltage is passed on to a stimulation device (NoxiTest) which adjusts the electrical stimulation applied to electrodes on the user, based on the voltage input.



Figure 4.1. Diagram of the components used in the system design and the connections between them.

The list of devices and their specifications is as follows:

- MATLAB PC: Windows 7 Service Pack 1 64 bit, Intel i7 3.5GHz CPU, 8 GB RAM and NVIDIA GeForce GTX 670 graphics adapter. MATLAB R2013a 32 bit.
- Camera: Microsoft Kinect model 1414, serial no. 060452404935, depth resolution 640x480 11-bit integers, RGB resolution 640x480, 30 fps in both depth and RGB cameras, depth operating range of 0.5-5 m [Khoshelham and Elberink 2012]
- NiDAQ: National Instruments USB-6229, serial no. 167A54B, 4 analog output channels with 16 bit resolution, operating range of -10 to 10 V and update rate of 833 kS/s [Instruments 2012].
- NoxiTest: NoxiTest IES 230, serial no. 23013, monopolar stimulation from 0-100 mA with pulse widths between 1μ s and 11 ms [Larsen 2006b;a].
- Electrodes: PALS platinum neurostimulation electrodes, model 879100 3.2 cm circular used as active electrode and model 895240 5x9 cm rectangular used as return electrode.

See section 2.3.3 for more information on the kinect camera and appendix 7.1 and 7.2 for more information on the NoxiTest and NIDAQ.

4.2 Main function

The purpose of the main function, as described throughout chapter 3, is to provide the user with a tool that can assist with gripping a cup while the user moves the cup between two locations.

This section explains how the depth data from the kinect camera is analysed in order to control the electrical stimulation output from the NoxiTest device, while the user moves the cup.

A flowchart covering the general steps in this process, from once the start button in the program is pressed, is shown in figure 4.2. When started, the program receives a frame with depth data from the kinect camera. The program then searches the image for a cup using a circle algorithm. If no cup is found, the analysis of the current frame stops and a new frame is requested from the kinect camera. If a cup is detected in the frame, the program searches the frame for a hand. If no hand is found, the analysis is again stopped for the current frame. If a hand is found the program continues to search for a grip between the detected hand and cup. Analysis continues if a grip is detected, and the program determines where in the three dimensional space the cup is located in order to track the task progress. The program then continues to the stimulation loop which is based upon the cup and hand position in relation to each other. After the initiation or adjustment of the electrical stimulation, the program requests a new depth frame from the kinect camera and the whole process is repeated. The user can at any time stop this process by pressing the stop button. The steps in this process are elaborated in details in the following sections.



Figure 4.2. Flowchart of the main function of the system. The program uses the cup and hand position in a three dimensional space, estimated from depth data from a Kinect camera, to control the applied electrical stimulation.

4.2.1 Initialization

When the program is first initiated, connections are established from the PC to the kinect camera and the NIDAQ. Communication between MATLAB and the kinect camera is made possible through a series of .mex files. Mex files make it possible for MATLAB to execute code written in the C or C++ language. The developers behind the kinect camera have released a library of functions that allows Windows to communicate with the Kinect camera, named OpenNI. By compiling the required mex files for the related C++ files from the OpenNI library, MATLAB is likewise able to retrieve data and send commands to the kinect camera. For information on how to compile the required mex files and establish connection between MATLAB and Kinect. If successful in establishing connections, the program will proceed to create the GUI, seen in figure 4.3.



Figure 4.3. The Graphical User Interface designed for the system. The system features several settings that can be chosen in the left side of the GUI. Shortcuts have been implemented to allow easy saving of data. The bottom row of is used to provide the user with information about the stimulation. The red and blue squares in the view frame (white area) represent the locations the cup are to be moved between.

4.2.2 Data acquisition from Kinect

Data from the kinect image stream is made available as a MATLAB variable through the mxNiDepth mex file. The output is a 2D matrix of 16 bit unsigned integers where each integer

represents the distance from the Kinect camera to the related real world point. After data acquisition the 2D matrix is cropped from 640x480 pixels to 500x320 pixels to reduce the frame size where the tasks are performed and also to lessen the computational requirements. Moving the kinect closer to the table would also result in a smaller task area while maintaining a higher resolution, but the minimum distance supported by the Kinect is about 0.5 m, requiring it to be placed about at least 1 m above the table in order to be measure the distance while lifting the cup [Khoshelham and Elberink 2012]. In this step, the graphics overlaying the kinect stream is also created. Two squares are placed in each side of the camera area acting as the start and finish positions for the task, marked A and B in fig. 4.3.

4.2.3 Detect cup

The kinect camera is placed above the task area, as visualized in figure 3.1 in section 3.2. This setting results in the cup being represented in the images by a filled circle of pixels that all have near equal distance value. Localising the cup in the depth image thus depends on circle recognition for which various methods already have been developed. Many of these methods are based on the circular Hough transform where edges in the image are transformed into a parameter space. Here lines drawn perpendicular from the edge of a circle towards the center will result in a spot of concentrated lines in the center of the circle [Ballard 1981]. MATLAB have a built-in function that uses the circular Hough transform called imfindcircles. The function performs generally well for detecting the cup in the depth images. The Hough transform is however computationally heavy and the processing time is about 0.5 s for each frame on the testing system, which severely limits the usability of this function in a real time system.

It was therefore necessary to develop a custom circle detection algorithm which could perform in real time. Updating the data output from the NiDAQ was after thorough testing limited to a maximum update rate of 10 times per second. This directly limits the rate that we were able to change the stimulation intensity with. To utilize the maximum NIDAQ update rate a minimum frame rate of 10 fps would therefore be required. This limits the execution time of the analysis of each frame to be maximum 100 ms. Considering that the main function would require several additional steps than circle detection, the execution time of the circle detection should not exceed 50 ms.

The general principle in the circle detection algorithm relies a recursive neighbourhood pixel operation, inspired by Eddins [2008]. The idea is that the surface of the cup will always be represented by a linear plane. If one was to know the position of any one pixel that is part of this surface, then the values (distances) of the neighbouring pixels to this pixel would be equal or very close to that of the pixel. The same would be true for the pixels neighbouring the neighbour pixels to the start pixel. If this process was repeated, and all pixels whose value is not within a specified interval of its seed pixel are not considered to be part of the surface, then this process would result in a list of pixels representing the surface of the cup. This would however be largely influenced by the tilt of the cup. A flowchart for this process can be seen in figure 4.8.

In the algorithm a list of 'active pixels' is found, assumed to be part of the surface of the cup. The active pixels are the pixels whose neighbours are to be found. This list initially consists of all pixels in the image with a certain value. This value is calculated as the median of pixel values between the pixel(s) with shortest distance and the shortest distance +8. Here it is assumed that the cup surface is the object closest to the camera. The median value is chosen to get a higher amount of starting active pixels, thereby reducing the number of needed iterations and reducing the risk of starting with a pixel with an outlying height.

In figure 4.4 the situation is visualized where the cup is represented by pixels whose values are between 67 and 73 (grey squares). The surrounding white space represents the table with values 0. The starting active pixels have here been identified as all pixels with a value of 69 (this value is not consistent with the actual median calculation) and they are added to the output list, which is the list of pixels representing the cup. Pixels that are accepted as being part of the cup are marked green on figure 4.4-4.7. The neighbouring pixels (right, left, above and below) of the start active pixels are then found, marked blue on figure 4.5. The values of the neighbouring pixels are then compared to that of the active pixel who they are neighbours to. If the difference in value is 2 or less, the pixels are accepted as being part of the object and they are marked green in figure 4.6. Pixels whose difference in value is larger than 2 are however not accepted, as visualized by the two blue pixels in the left southern corner in figure 4.5 whose values are 0. After 4 iterations all pixels representing the cup have been identified in figure 4.7.

The algorithm have two ways of stopping. Before neighbouring pixels of the active pixels are found, the number of active pixels is read.

First case is if the number of active pixels is zero, meaning that there are no more neighbouring pixels within the value interval nearby. This is the case in figure 4.7. The algorithm then proceeds to analyse the shape of the object that has been found. This shape is parameterized through three properties, circularity, eccentricity and area. Circularity is a function of the area and perimeter and is given by:

circularity =
$$\frac{4 \cdot \pi \cdot \text{area}}{(\text{perimeter + pi})^2}$$

		67	68			
	67	68	69	70		
67	68	68	70	71	72	
68	68	70	71	72	73	
	69	70	71	73		
		70	72			

Figure 4.4. Initial active pixels are found, marked as green squares. Values are not consistent with the actual operation.

		67	68			
	67	68	69	70		
67	68	68	70	71	72	
68	68	70	71	72	73	
0	69	70	71	73		
	0	70	72			

Figure 4.5. Neighbouring pixels, marked as blue squares, to the active pixels are found.

			0			
		67	68	0		
	67	68	69	70	0	
67	68	68	70	71	72	
68	68	70	71	72	73	
	69	70	71	73		
		70	72			

Figure 4.6. Neighbouring pixels, whose height difference are 2 or less from its active pixel, are accepted as new active pixels.

		67	68			
	67	68	69	70		
67	68	68	70	71	72	
68	68	70	71	72	73	
	69	70	71	73		
		70	72			

Figure 4.7. The process is repeated until after 4 iterations, all pixels of the cup have been identified.

Circularity is thus a measure for compactness and a perfect circle will have a circularity of 1. Eccentricity is a measure for how round the perimeter of the object is and a perfect circle will have an eccentricity of 0, and is calculated in MATLAB using the formula:

eccentricity =
$$\frac{2 * \sqrt{\frac{\text{major axis length}^2}{2} - \frac{\text{minor axis length}^2}{2}}}{\text{minor axis length}}$$

where the major and minor axes of the object are the longest and shortest diameter respectively. Both circularity and eccentricity are used to parameterize the object to strengthen the validation process. A square can for instance have a somewhat high circularity (because it is quite compact) whereas the eccentricity is very high (far from a circle). The object is accepted as the cup if circularity is more than 0.50, eccentricity is less than 0.70 and the area is at least 75% of the expected cup area. The expected cup area is determined from the calibration function, see section 4.4. The circularity and eccentricity for the object in figure 4.7 are respectively 0.88 and 0 and would therefore be accepted as a circle (if ignoring the total area parameter).

Second case is if the number of active pixels exceeds a threshold limit, defined as two times the expected cup area, the algorithm terminates and returns an empty array, meaning that the object is too large to be considered the cup. The algorithm is in this case prematurely stopped because the processing time exponentially increases when dealing with large objects. The execution time for the cup detection algorithm is about 9 ms on the test system, fulfilling the requirement.



Figure 4.8. Detailed flowchart of the "cup detected?" process in figure 4.2. The algorithm relies on a recursive neighborhood pixel operation where pixels near a "seed" pixel are identified. The process closely resembles the "magic wand" tool seen in many photo editing programs, but instead of finding pixels of same colour, distance to the kinect camera is used.

4.2.4 Detect hand

After the program have searched the current frame for the cup it proceeds to detect a hand. The hand detection algorithm relies on knowing where the cup is localised in the frame, thus the hand detection algorithm is only run if a cup have successfully been found. A flowchart of the algorithm can be seen in figure 4.9. When run, the algorithm creates a temporary copy of the current image frame. It is then the purpose of the algorithm to separate the pixels in this copy so that pixels that are not constituting the hand is set to zero whereas pixels which could be the hand are set to 1. This separation is initially carried out by setting all pixels that are close (30 units or less above table distance) to the table to zero. All other pixels whose height is above 30 is initially set to 1. By using the pixel index list of the cup as an input parameter to the hand detection algorithm, the cup area can easily be set to zero as the hand cannot be in this area if the cup is successfully detected. Figure 4.10 shows how the image is divided into zeros and ones. The image is then separated into components using the bwconncomp MATLAB function. In this function, groups of pixels that are not connected are considered to be different components and it is possible to retrieve information about the individual components after separation. By looking at the number of pixels that constitute each component, components with an area less of 1000 pixels are deleted. This is done to filter out small objects that cannot resemble a hand. The edge of the remaining components are then identified using the bwboundaries function. Finally the pixel index list and a list of the edge pixels of the remaining components are returned as output.



Figure 4.9. Flowchart for the hand detection algorithm



Figure 4.10. Pixels with a distance value between the point nearest to the camera (red plane) and 30 units above the table (blue plane) are set to a value of 1. Pixels not between this range and pixels constituting the cup, are set to 0.

4.2.5 Detect grip

Grip between the hand and cup can only be detected when both the cup and the hand is successfully detected. The principle in detecting the grip relies on investigating the distance between the pixels constituting the cup and the pixels constituting the hand. When pixels constituting the hand are in a predefined range of the center of the cup, they are considered to be in contact with the cup. This range is defined by two circles that together resemble the "cup circle" which is illustrated in figure 4.12a. The script then finds the pixels that are outside the smaller cup circle, inside the larger cup circle and also part of the hand, marked green in in figure 4.12a. The longest distance that exists between these pixels is then found, marked by a green line in figure 4.12a. Whenever this distance is above a defined threshold, a grip between the hand and cup is considered to be present. If a grip is assumed to be present, the script continues to its second purpose, which is to locate a larger part of the hand that is near the cup. This is done using the same approach as for detecting if a grip exists. Two circles are created, referred to as the hand circles. The pixels outside the smaller hand circle, inside the larger hand circle and part of the hand are found. These pixels are used to determine the distance to



Figure 4.11. Flowchart for the grip detection algorithm

the hand in relation to the cup. The algorithm then returns the two points with the largest distance between them for visual purposes, and also returns the list of pixels of the hand that are near the cup. The flowchart for this algorithm can be seen in figure 4.11.

The radii of the cup and hand circles are determined as a scalar of the cup radius, where the coefficient for each circle is shown above each circle in figure 4.12. The principle with circles is used because of the cone shape of the cup. The circle represented by the top of the cup is smaller than the bottom of the cup. This combined with the shadowing effect created by the top of the cup when gripping the lower part of the cup, contributes to the need for enlarging the area in which the hand is considered to be in contact with the cup. The inner circles of the cup and hand circles are used to subtract pixels that are sometimes falsely classified as being part of the hand or cup. In the case that pixels that actually are part of the cup are classified as being part of the hand, they will be quite close to the cup and could therefore increase the risk of a false grip detection. A large part of the hand that is close to the cup is often shadowed by the cup, therefore the distance of this part of the hand cannot be estimated. Hand pixels close

to the cup are therefore also subtracted from the pixels used in estimating the hand height in relation to the cup.



Figure 4.12. The figure illustrates the principle in the grip detection algorithm. **a**) This part relates to the purpose of deciding whether or not a grip is present. The green area represents the hand pixels that are considered to be in contact with the cup. The green line represents the longest distance between two of these pixels. If this distance is above a threshold, a grip is detected. In this particular case, the distance is greater than the threshold and a grip would be assumed. **b**) Relates to the purpose of finding the hand pixels in a larger area from the cup. The pixels in the blue area are used to determine the hand distance from the Kinect camera. The numbers above each circle is the coefficients used to determine the radius of each circle which is a scalar of the cup radius.

4.2.6 Detect cup location

The stimulation should only be started when the cup is gripped within the starting position, see figure 4.3. If a grip is detected between the hand and the cup, the program therefore proceeds to check what position the cup is in. For this purpose two variables are created, cupStart and cupFinish. cupStart is only set to true when the center of the cup is placed within the finishing position and cupFinish is likewise only true when the cup is placed within the finishing position. The detection of the cup location is based on simple coordinate comparison where the x and y coordinate of the center of the cup is compared against the x and y coordinates of the cup is located just on the border of the specific position, the script would constantly shift between considering the cup to be inside or outside of the position. This could lead to the very undesireable case of electrical stimulation constantly be switched on and off. This problem was solved by creating two squares with different sizes, for both the starting and finishing position. When the cup center is located inside the smaller square, the variable

in question would be switched to on. On the contrary, if the cup is considered to be outside of the larger square, the variable in question would be switched to off. The space between the smaller and larger square therefore acts as a neutral area in which the cup is always considered to be in the position in which it was lastly detected.



Figure 4.13. When the location of the cup is detected, two squares are used to differentiate between both the starting and finishing position. Whenever the cup is inside one of the smaller squares (light green), the variable in question is set to true. Whenever the cup is outside one of the larger squares both variables are set to zero. The neutral area, which is inside the larger square (dark green) but outside the smaller square, is the buffer area in which the variables do not change value. The buffer area is used to avoid fluctuations in the location detection.

4.2.7 Stimulation loop

The stimulation is controlled by sending vectors consisting of zeros and ones to the NiDAQ. The NiDAQ converts this digital signal to an analogue signal with a sampling rate of 5000 Hz. Using the external scale option on the stimulator (described in appendix 7.1), the voltage of the analogue signal determines the stimulation output. Each vector had a length of 400, corresponding to a duration of $\frac{400 \text{samples}}{5000 \text{Hz}} = 0.08 \text{s}$. The vectors are continuously send to the NiDAQ and a number from 0 to 10 is multiplied with each vector to control the stimulation intensity.

After the cup location has been determined, the program controls the stimulation, either by initiating, regulating or stopping the electrical stimulation. A flowchart for the stimulation control can be seen in figure 4.14. The program initially checks if the stimulation is paused, as a maximum duration of stimulation time was one of the system requirements, see section 3.1 requirement e.

If the maximum stimulation duration has been reached and the stimulation therefore is paused, the system will update how much time is left of the pause on the GUI and then proceed to acquire a new frame from the camera and the whole analysis shown in figure 4.2 is repeated until the pause is over. If the stimulation is currently not paused, the algorithm will check if the stimulation is already on.

If stimulation is not being applied and the cup is placed within the starting position, it will initialise the electrical stimulation if the hand height is at a minimum distance. The minimum distance is determined through the calibration tool, see section 4.4. The initial stimulation is gradually increased to a fixed starting percentage using an exponential function. If the cup is not in the starting position or the hand is not at a minimum distance, stimulation will not be initialised and the program proceeds to acquire a new frame from the camera.

If stimulation is already being applied it means that the task previously has been started. The program therefore checks if the cup has been lifted from the table by comparing the current distance of the cup with the distance of the cup at the time stimulation was initially applied. If the current distance is less than a specified value than when stimulation was applied, the cup is considered to have been lifted.

If the cup is not considered to be lifted, the program will regulate the intensity of the stimulation by comparing the distance to the hand with the distance to the cup. The intensity regulation is based on the linear function:

$$\mathbf{y} = \boldsymbol{a} \cdot \boldsymbol{x} + \boldsymbol{b} \tag{4.1}$$

where the variable x is the difference in distance between the cup and the hand for the particular frame.

The constants a and b are determined when the stimulation is initially applied as:

$$a = \left(\frac{\text{startIntensity} - 100}{\text{startHeightDiff} - \text{maxHeightDiff}}\right)$$
(4.2)

$$b = 100 - a \cdot \text{maxHeightDiff}$$
 (4.3)

where the constants are as follows:

- startIntensity: the intensity percentage that the stimulation has been set to start with, default value 50.
- startHeightDiff: the difference in distance between the cup and the hand when the stimulation is initially applied
- maxHeightDiff: value in distance difference where the intensity percentage is maximum, ie. 100, default value 50.

If the cup already has been lifted, the program skips the intensity regulation and checks if the task have been completed, which is fulfilled when the cup is placed inside the finishing position and is placed down on the table. The cup is considered to be placed on the table when the distance to the cup is the same (within a small interval) as the distance to the cup when stimulation was initially applied. When the task has been completed the program saves the following information in an attempt to parameterize the task:

- Stimulation on/off: describes if the stimulation was on or off during the task
- Stimulation intensity: the stimulation intensity in percentage when the cup was lifted
- Completion: describes if the task attempt was successfully or failed
- Time: the time in seconds it took before the task was completed or failed

These data could be used for statistically purposes and show the user improvement over time. After the data has been saved the stimulation is stopped and a pause period is initiated to prevent the user from fatiguing. After this step, one cycle of the program is completed. It therefore retrieves a new frame from the camera and the whole process is repeated. If the task however is not completed, the program will check if the grip is still detected between the cup and hand. This is to prevent stimulation from continuing if for instance the user moves the cup out of the camera area. If the grip is still detected, the cycle ends and a new frame is retrieved. If no grip is detected the stimulation is stopped.



Figure 4.14. Flowchart for the stimulation control algorithm

4.3 Motivational feature

As an attempt to show how a motivational feature could be realised, we implemented the code for a ping pong game into the program. The MATLAB code for the ping pong game was created by Chaudhri [2010]. The game is initially controlled by moving the mouse back and forth. Here the screen coordinates of the mouse is read by MATLAB and the y coordinate is used to control the paddle position. By adapting this to be controlled by the position of the cup in our program instead, it is possible to control the paddle by moving the cup back and forth. The code for converting the cup position into paddle position can be seen in code example 4.1

Code 4.1. Ping pong control

```
1 %% Determine cup position
2 if ~isempty(center) && cupLifted
3 yPosPro = 1/(size(D,1)*0.5)*(center(2)-120);
4 end
```

The position of the cup in the program is basically transformed into a percentile value of a cropped down image frame. The image is cropped so that the paddle reaches the top and bottom before the cup would exit the top and bottom of the depth image, which would cause a loss of control. A screenshot of the ping pong game can be seen in figure 4.15.



Figure 4.15. Screenshot of the ping pong game by Chaudhri [2010] modified to be controlled by the cup position instead of mouse position.

4.4 Calibration tool

The program relies on several parameters to increase the precision of the algorithms documented in section 4.2. To make the program more flexible and easy to setup in different situations, we implemented a calibration tool that can quickly estimate the different parameters needed for the program to perform accurately. The parameters estimated in the calibration are the following:

- tableDistance: the average distance from the kinect camera to the surface of the table
- cupArea: surface area of the top of the cup
- cupDistance: distance from the kinect camera to the surface of the cup
- distanceDifference: distance difference from the top of the hand to the surface of the cup while grasping around the bottom of the cup

The calibration is initiated by selecting the 'calibrate' option under task mode in the GUI. The first parameter to be calibrated is the distance to the table. A screenshot of the GUI while calibrating the table distance can be seen in figure 4.16A-4.16C. The program estimates the table distance by averaging the distance to the table from all the pixels in the depth frame. For this estimation to be accurate, the table must be clear from objects and the camera must be aligned so that the projector and camera angle are perpendicular on the table surface. These requirements are upheld by calculating the variance between the value of all the pixels. If a high variance exists, this would indicate that either an object is present (4.16A) in the camera view or that the camera is misaligned (4.16B). The program will therefore only calibrate the table distance once the variance is at 10 or below (4.16C). The variance is therefore shown on the GUI so that it is possible to continuously adjust the camera position until the variance is below the threshold. The depth image is also continuously updated in a way so that the pixels closest to the camera are black and the pixels furthest away from the camera are white. In this way it is possible to see which way the camera is tilted, as in 4.16B.

When the table distance has been successfully calibrated, the program proceeds to calibrate the remaining parameters, which can be seen on figure 4.16D-4.16F. This is accomplished by creating a graphical square in the middle of the table in which the user is instructed to place the cup while gripping the bottom of the cup (4.16D). When the program detects that the cup is placed within the middle of the square, the program will prompt the user to maintain the position for a moment (4.16E). The program then begins a 4 seconds countdown before it measures the distance to the cup, the surface area of the cup and the distance difference between the hand and the cup (4.16). This countdown is performed so that the user has a moment to adjust and position the hand position accordingly.



Figure 4.16. A) objects are placed around on the table creating a high variance. B) the camera is tilted, creating an imbalance in the depth. C) The camera is aligned correctly and the table is clear of objects and the table distance have successfully been calibrated. D) The user is instructed in placing the cup in the center square while gripping the base of the cup. E) The user is gripping the cup in the square while the program is counting down. F) Countdown has finished and the program saves the parameters into a .mat file.

System test

5.1 Overall system test

The system was tested on five healthy subjects and one unilateral motor impaired subject. The system usability, the optimal electrode placement, maximum stimulation intensity and regulation were qualitatively evaluated on the five healthy subjects prior to testing the motor impaired subject. The cone shaped cup used during task execution had the following dimensions: bottom diameter 9.0 cm, top diameter 5.0 cm, height 16.0 cm and weight 360g.

Healthy subjects

The electrode was placed in a similar manner on the forearm on all the subjects, but the exact location where the best grip assistance was achieved, varied between subjects. The best location was determined as the location where the electrodes did not produce discomfort and activated three or more fingers including the thumb. It was not possible to stimulate all five fingers at once using just a single stimulation channel. The main focus were on flexing the thumb, index finger and middle finger. Feedback from the subjects, visual inspection of the fingers flexing and muscle contraction (evaluated by physical contact from the investigators) were used to evaluate electrode placement. Maximum stimulation intensity varied between 15 and 20 mA, higher intensities were found to be uncomfortable for the subjects.

The healthy subject performed the task equally fast with and without stimulation. Oral and visual feedback from all the subjects expressed that the stimulation did assist in providing a firmer cup grip.

Unilateral motor impaired subject

The test on the motor impaired subject was conducted at a rehabilitation facility in Aalborg. The subject understood the instruction about how the task should be performed and how the intensity could be regulated by sliding the hand up and down the cup. The subject performed the task with and without the assistance of electrical stimulation. Data from only a few tasks executions were recorded due to very rapid muscle fatigue in the motor impaired arm and shoulder. No comparison between the task executed with and without stimulation could be made from data because the subject was too fatigued before actual data could be gathered.

A visual difference was however observed by the three investigators and the therapist present, in which the cup was manipulated in a more steady and controlled manner throughout the tasks when assisted with electrical stimulation. The subject was sensory impaired and had difficulties providing feedback whether or not the stimulation helped assisting the grip during task execution.

The subject had difficulties opening the hand for both gripping and releasing, and often used the less affected hand to place the more affected hand on the cup and to remove it again. It happened that the subject dropped the cup, primarily due to poor initial contact between the hand and the cup (gripping with the fingertips). The cup was not dropped vertically (as expected by the investigators) but instead at an angle. The system cannot detect the cup when the cup is angled too much. If the system cannot detect the cup, the task and the stimulation is terminated.

The subject had difficulties regulating the intensity of the stimulation. When the hand was initially placed on the cup, it was very much fixated at that specific location. If instructed to move/slide the hand smoothly up the cup, it either resulted in the subject lifting the cup or the hand being lifted higher than the cup in one forceful movement. If the hand is located higher than the top of the cup the task and the stimulation is terminated, this is one of the build-in safety mechanisms of the system.

The therapist emphasized on the importance that the subject should not use compensatory movement of the shoulder while performing the task. The system have no mechanisms to detect and prevent undesired shoulder use during task execution.

5.2 Individual component system test

In this section the performance of some of the more important individual components in the system is evaluated.

5.2.1 Cup detection

We evaluated the performance of the cup detection algorithm through 500 frames in which the cup was present. We analysed each frame to see if the cup was correctly detected. This process was repeated for different cup angles and hand height in relation to the cup height. The cup was placed in the middle of the x-axis and just below the middle of the y-axis in the camera view. The angles from 0 - 60 degrees in steps of 5 degrees were tested where 0 corresponds to the cup surface being parallel with the table. The top of the hand was varied between 0 - 7 cm below from the top surface of the cup, so that 0 cm corresponds to the hand being in the same plane as the top surface of the cup. The results for these tests are shown in figure 5.1. The results show that the algorithm is generally very robust with an average correct detection rate of 99.9 % for angles below 40 degrees and height differences greater than 1 cm.



Figure 5.1. Cup detection test of the systems ability to detect the cup when tilted at different angels and different hand height location gripping the cup. a) shows the percentage of frames where the cup is detected when the cup is tilted from 0 - 60 degrees. 0 degrees corresponds to the cup surface being parallel with the table. b) shows the percentage of frames where the cup is detected at different hand height distances in relation to the top surface of the cup. 0 cm corresponds to the hand being in the same plane as the top surface of the cup

5.2.2 Grip detection

The grip detection algorithm was evaluated by measuring the shortest distance from the cup to the hand where the program detected a grip. This is the situation depicted in figure 5.2 A, the distance is approximately 3 cm and is measured from the intersection points (the small blue circles) to the cup detection circle. In situation B a grip is also detected even though the hand is only in partial contact with the cup. In situation C a firm grip is also detected.



Figure 5.2. The figure depicts three different grasping situations that all result in a detected grip. In situation A and B there are none or partial contact with the cup and should not result in the grip detection according to our solution strategy. In situation C the grip is correctly detected.

The results from the grip detection test does not match the requirements from section 3.1e nor complies with the solution strategy in section 3.2e. According to the solution strategy only situation C should result in a grip detection. The reason for this is further elaborated in the discussion.

5.2.3 Stimulation characterstics

In this section it is evaluated if the intensity, duration and frequency of the applied stimulation are consistent with the chosen parameters in section 3.2 solution c. When a voltage of 10 V is output to the stimulator, the current intensity of the stimulation output is the maximum of the current adjustment. During the test the current was set to 10 mA. Using a Hewlett Packard 54600B oscilloscope with a 1000 Ω resistor inserted between the stimulation wires, the expected voltage can be determined using Ohms law:

$$1000\Omega \cdot 0.01A = 10V$$
 (5.1)

Figure 5.3 A shows the characteristics of a single stimulus. Each small dotted rectangle inside the window represents a duration of 200 μ s along the x-axis and 2 V along the y-axis. The oscilloscope measured the peak-to-peak value of the stimulus to be 10.38 V, corresponding to the 10 V calculated from 5.1. The duration of the stimulus was similiar to the x-length of each dotted square which corresponds to a length of 200 μ s. Figure 5.3 B shows the frequency of two consecutive stimuli, in this window each dotted square corresponds to a duration of 5 μ s. Based on the time between the two stimuli, the oscilloscope measured the frequency to be 29.76 Hz, which offhand seems to correspond with the setting of 30 Hz.

However when we investigated the frequency of the signal over a longer duration, seen in window C, the time between each stimuli is unstable. The time between each dotted square is here 20 μ s. We therefore investigated the code that controlled stimulation parameters. The code was initially written for a stimulation frequency of 50 Hz and was later changed to 30 Hz. The frequency was then tested with the oscilloscope and the result was similar to figure 5.3 B. We did however not investigate the signal over a longer time frame.

The mechanism behind the stimulation control is explained in section 4.2.7. A vector length of 400 samples was compatible with a frequency of 50 Hz as each stimulus was separated by $\frac{5000}{50} = 100$ samples. This results in each vector starting with a stimulus elicited in the beginning and followed by stimuli at sample 101, 201 and 301, where the samples in between and up to 400 are zeros. When the next vector is appended, the number of samples between the two vectors is also 100, maintaining the correct frequency.

However, when using a frequency of 30 Hz, there are $\frac{5000}{30} = 167$ samples between each stimulus. When combined with a vector length of 400, a stimulus is initially elicited in the beginning and followed by stimuli at sample 168 and 334. When the next vector is appended, there are only 401 - 334 = 67 samples between the two consecutive stimuli between the two vectors resulting in stimulation frequencies of both 30 Hz and 75 Hz as seen in figure 5.3 C. By increasing the vector length to 500, which corresponds to a duration of 0.1 s, a stable frequency of 30 Hz was achieved, which is seen in 5.3 D.



Figure 5.3. Characteristics of the stimulation output were assessed using an oscilloscope. A) characteristics of a single impulse. B) frequency characteristics of two consecutive stimuli. C) unstable sequence of stimuli. D) stable 30 Hz sequence of stimuli.

Discussion

In the discussion we evaluate if the chosen approach succeed in producing a real time closed loop functional electrical therapy system for use in upper extremity motor rehabilitation. The discussion is divided so the general approach initially is evaluated whereafter the individual requirements stated in section 3.1 are evaluated.

6.1 General system discussion

The task was chosen so that it would be easy to explain, understand and perform. All subjects that were tested understood the task and was able to complete the tasks after a simple explanation. The healthy subjects performed the task in the same manner with or without stimulation. The motor impaired subject did seem to have an increased control when lifting the cup with stimulation compared to without stimulation. The motor impaired subject did however quickly show signs of fatigue after a few task repetitions. This fatigue was reported to be present in both arm regions where the stimulation was applied but especially also in the shoulder region. The therapist observed a high amount of compensatory movement with the shoulder during the task execution. It is therefore difficult to assess whether the fatigue was due to the stimulation or the compensatory movements. Both aspects are however likely to have contributed to the fatigue. To reduce the fatigue arising from the electrical stimulation the ratio of on/off stimulation timings might need adjustment. The maximum on/off ratio used in the tests was 3:2. The rest period between trials was set to a fixed value of 14 seconds, and the maximum stimulation duration was set to 20 seconds. If the task was not completed in 20 seconds, the task was considered incomplete and the stimulation was terminated. A solution could be to regulate each break duration as a function of the latest stimulation duration, for which the ratio is determined on the basis of the individual person fatigue resistance [Baker 2000]. Most FET studies train the participants for sessions of 30 min or more, so a ratio allowing the user to train for a minimum of 30 min, would be desired [de Kroon et al. 2005, Takka et al. 2011, Popovic et al. 2006, Rosewilliam et al. 2012].

An aspect that could have contributed to the fatigue was the faulty implementation of stimulation frequency that was discovered in 5.2.3. The stimulation output was discovered to consist of both 30 Hz and 75 Hz. As described in section 2.2.2 frequencies greater than 30 to 40 Hz have shown to accelerate muscle fatigue [Baker 2000]. Results by de Kroon et al. [2005] indicated however that the stimulation frequency has little influence on the clinical outcome of FET studies. It is therefore unclear how the mixed stimulation frequencies can have influenced the outcome of the system test.

To minimize shoulder compensatory movements, the shoulder could be fixated in a natural position and simple tasks not requiring the involvement of the shoulder could be trained. This might also reduce the fatigue rate of the shoulder, and less affect the overall training intensity.

The motor impaired subject had a small hand and had difficulties placing the hand around the cup. A cup with a smaller sized diameter might have helped the subject not using so much energy and effort on this part of the task. The weight of the cup was comfortable for the motor impaired subject to manipulate, but a cup where the weight could be regulated, is a desired feature that would make it possible to adjust the weight to the individual user level.

If the user of the system is not capable of performing the entire task, shaping principles could be implemented. The task of moving the cup between two locations could be broken down into smaller tasks and trained individually as done with success in CIMT protocols [Morris and Taub 2001, Taub and Morris 2001, Taub and Uswatte 2006]. Performance tracking on the small shaping tasks would allow the user to monitor the progress on each sub.task and work as a motivational factor for further training and improvement.

Additional tasks could be implemented into the system, using the same cup or other objects to be manipulated. After intensive repetitive training of the task of moving the cup between two locations, this particular task would at some point be expected to be mastered. As suggested by Kleim et al. [1998], Plautz et al. [2000], repetitive training of already mastered tasks do not drive the cortical reorganization, as it is the motor re-learning process of training non-mastered tasks, that induce the cortical changes linked to the gain of function.

Using FET in the manner described above could improve the beneficial effects from CIMT by enhancing the users functional capabilities in activities of daily living. This could especially apply to users with severe motor impairments who would not normally benefit significantly from CIMT due to limited capabilities when performing activities of daily living when using the impaired hand [Taub et al. 2002].

6.2 Individual system discussion

Stimulation and electrode placement

Due to hardware limitation in the NoxiTest stimulator, only a monophasic waveform could be used as the stimulation waveform. A symmetrical biphasic waveform could have been a better choice because if its properties to prevent potential skin irritation caused by unequal charge build-up in the excited tissues [Baker 2000].

Electrode placement is a general challenge when developing systems utilizing stimulation, as it is difficult to automatize. An approach to help users place electrodes correctly could be developed using the kinect or a similar camera. By analysing the subjects hand/arm and localise the optimal placement of the electrodes, visual marks on the arm could be shown on the monitor. Another approach that has been reported is the use of small temporary tattoo dots on the users arm to help them locate the optimal placement. These locations can be found in the initial in-clinical rehabilitation phase by the physiotherapists.

The camera could also assist in evaluating the evoked response from the stimulation by analysing the hand movement after stimulation onset. If for instance the camera detects a high level of wrist flexion, it would mean the electrodes are not placed optimally and an alternative placement is suggested.

Finger extension assistance

Even though the cup was shaped like a cone and placed upside down the motor impaired subject had difficulties sliding the hand on and off the cup. Additional stimulation channels could have been used to stimulate extensor muscles in the forearm and hand to assist in opening the hand. FET studies by Popovic et al. [2003; 2004], de Castro and Jr [2000], Popovic et al. [2006] all use the stimulation sequence of first opening the hand to allow the hand to grip an object, close the hand to allow object manipulation and finally open the hand to release the object. Having an additional stimulation channel could have helped the subjects gripping and releasing the cup, but at the expense of making the system and control algorithm more complex.

Assistive stimulation and electrode placement

The effect of the electrical stimulation was largely dependent of the electrode placement. Differences between subjects made correct electrode placement difficult and presented a challenge. Just a small difference in distance of one of the electrodes could result in stimulation of incorrect muscles or the subject experiencing discomfort. Placing electrodes on the motor impaired subject was especially difficult since the subject was unable to provide feedback of how the stimulation felt.

Once the electrodes were correctly placed all subjects did however feel that the stimulation assisted their grip without the intensity of the stimulation leading to discomfort. An increased grip force in the subjects was also experienced by the investigators through physical contact.

Object detection

The stability of the applied electrical stimulation is largely dependent on the program to be able to reliably detect the cup in each frame. If no cup is detected, no further analysis is performed for the current frame. The test of the cup detection in section 5.2.1 showed that the general robustness of the cup detection performed acceptable as long as the cup is being held at an angle lower than 40 degrees and the distance between the top of the hand and top of the cup is at least 1 cm.

The cup detection, during the part of the task where the subjects were to grip the bottom of the cup to initiate the stimulation, worked as expected among both the healthy and motor impaired subject. During this phase the cup surface was always parallel with the table and the hand distance in relation to the cup surface was also sufficient because the program was calibrated to only initiate stimulation when their hand was gripping the lower part of the cup.

During lift the healthy subjects moved the cup reliably and quickly and neither the angle nor the hand distance changed significantly. The motor impaired subject did however show a much more unstable and slower movement during lift compared to the healthy subjects. In some of the trials the movement of the cup was too unstable and the angle of the cup caused the stimulation to be terminated since the cup could not be detected. This cancellation of the task caused confusion to the subject since the subject still tried to position the cup in the finish position, but since the program cancelled the task, the program would wait for the user to put the cup in the starting position to start again. This could however be easily solved by introducing the same pause after a failed task attempt as when a task has been completed.

A more challenging issue is the robustness of the cup detection. Apart from the approach described in section 4.2.3, several other existing methods and methods developed by the project group were tested. Some of these algorithms were more computational efficient but provided lower robustness whereas other approaches provided high robustness but at the expense of very high computational cost (e.g. approaches involving the Hough transform). The proposed method was therefore chosen because of its balanced characteristics of providing robustness while corresponding with the requirement for low computational use.

One way to eliminate the problem of task cancellation after lift-off could be to only stop the task if it is either completed or if maximum time has been reached. Then the angle and distance of the hand would have no influence after lift-off. This would however also remove the possibility of the program stopping the stimulation if the user for instance pulls the arm toward him- or herself. A simple stop button to use in the less affected arm or if the program terminated when no objects are present in the frame at all, could solve that problem. When purely using depth values it is difficult to detect the cup when a hand is closely gripping the top of the cup. It is even quite difficult for the human eye to find the circle in this situation as visualized in figure 6.1. Combining information from the kinect RGB camera to the depth information would add the possibility of using colours to detect the cup. If the cup had a specific colour it would be efficient to detect the cup using colour values. Colour recognition has however the drawback of being largely influenced by light sources and the clothes of the user or other objects present might interfere. A combination of both colour and depth information could provide a very robust cup detection. If the algorithm was unable to detect the cup using depth information it could proceed to attempt to localise the cup using colour information.



Figure 6.1. When relying purely on depth information it can be difficult to distinguish between the cup and the hand when they are close to each other in all three dimensions. In this picture the cup is located between the thumb and the index finger.

The approach for object detection in this system proposal is very specialized and would only work for filled circular objects where a rough estimate of the surface area is known. The general idea behind the system is that it could consist of many different kind of tasks where the object to be interacted with not necessarily is of a circular shape. A more general object detection could be implemented using a classification system based on multiple object properties, such as eccentricity, circularity and area that are used in this system. Training the system to know what property values different shapes would be likely to have, could make the system able to distinguish between several kinds of shapes.

The system currently uses raw depth values and the number of pixels to estimate areas and distances. By converting these values into real world SI units could provide a more general and precise object validation. This conversion could be made using the function shown in figure 2.5 on page 29. Using this conversion the actual area of the object could be estimated without the distance to the object from the camera would influence the estimate.

Voluntary effort

One of the requirements for the system was that it should only apply stimulation if the user exerted voluntary effort toward executing the task. A review by de Kroon et al. [2005] showed that positive rehabilitation results were more common among subjects where stimulation was triggered by voluntary effort than non-triggered stimulation.

The positive effect of voluntary effort combined with simultaneous electrical stimulation might be related to the hypothesis of internal forward dynamic models. The hypothesis states that the brain makes internal models to predict the outcome of all movements [Kawato et al. 1987]. When a motor command is produced in the motor cortex, a copy of the efferent signal is created. This efference copy is used in a forward dynamic model where the brain estimates the incoming sensory feedback as a consequence of the impending actions. This estimated sensory feedback is then compared against the actual feedback arriving from the sensory system, see figure 6.2. If there is a large discrepancy between the estimated sensory feedback and the actual sensory feedback it could mean that an external force is exerted on the individual and attention is needed. The mechanism is thereby believed to be related to how the brain differentiates between self-produced movements and external movements afflicted upon the individual [Wolpert and Flanagan 2009a] and also used to differentiate between internal and external speech [Heinks-Maldonado et al. 2006]. The mechanism is very important for learning new movements and could also be thought of playing a big role when rehabilitating post stroke. But if no efference copy is created, ie. the user is not exerting voluntary effort, but only afferent signals are present, then the mechanism cannot function properly [Wolpert and Flanagan 2009b].



Figure 6.2. An efference copy is created when a motor command is sent from the motor cortex. This copy is used to estimate the sensory feedback arising due to the motor command. The estimated sensory feedback is then compared to the actual sensory feedback. The figure is redrawn from [Miall and Wolpert 1996]

The solution strategy for triggering the stimulation by voluntary movement was to determine when the user has a firm grip around the lower base of the cup. This grip was detected using a distance threshold algorithm based on the pixels intersecting the both the cup and the hand, see section 4.2.5. The test of this approach showed however that false grip assumptions can be made when the fingers are several centimetres from the cup or when the fingers are only partially in contact with the cup. This can lead to the user not gripping the object when stimulation is applied but instead pushing the cup away when prehending the cup. This situation was observed a few times during the test with the motor impaired subject. The technical explanation from the false positive grip detections can largely be due to the tall cone shape of the cup. The top surface area of the cup is quite small compared to the base and as such, the hand will not seem to be in direct contact with the top surface of the cup when the base is gripped. Both shadowing and the placement of the cup in relation to the camera largely affect this. The issue can be seen in three examples in figure 6.3.

Part A depicts the situation when the cup is placed left of the camera. The top of the cup then shadows the left side of the hand while the thumb that is gripping the base of the cup is a large distance from the red circle representation of the cup. In part B the cup is located directly beneath the camera. Here the shadow effect is not present and the hand is generally in close contact with the circle representation. Part C is the situation where the cup is to the right of the camera, again the distance between the hand and circle is enlarged due to the height and shape of the cup.

To solve this problem, the circle representing the cup was enlarged (by a factor of 2.2) to ensure that the hand would in fact be in contact with the cup circle in the analysis. Another way to detect the grip would be desired. Such an approach could involve displacing the hand and cup pixels so that it would appear they were visualized directly beneath the camera. Such a solution would not solve the problem of shadowing but could greatly help in the assessment of hand placement in relation to the cup. Combining information from two depth cameras located on different sides of the task setup could also eliminate or reduce the shadowing problem.



Figure 6.3. The figure depicts the effect by placing the cup differently in relation to the camera. A) The cup is placed left of the camera and the hand/cup contact is difficult to assess. B) The cup is placed directly beneath the camera and the hand/cup contact is easily assessed. C) The cup is played to the right of the camera and the hand/cup contact is again difficult to assess. The way the hand grasped the cup was the same in all three situations.

Suppose a solution was developed that was able to perfectly detect if a grip existed between the cup and hand, it would not necessarily imply that the user is in fact exerting voluntary effort throughout the task. If for instance the cup is too light or the stimulation is too powerful, it would still be possible for the user to lift the cup without providing voluntary effort. That is one of the limitations of the current system design, as it is nearly impossible to detect voluntary muscle contraction using only visual sensors. Detecting voluntary muscle contraction could be realised using other kind of sensors, such as EMG readings, force transducers or accelerometers.

Stimulation intensity regulation

The stimulation intensity was regulated so that the stimulation would fit the user for each task execution. The technical test of the intensity regulation showed that the approach worked as expected and the same did the functional test with the healthy subjects. The test with the motor impaired subject showed however that subject was not able to reliably slide the hand up and down the cup as needed for the regulation to work. It seemed that the passive prehension that was present when the motor impaired subject gripped the lower base of the cup affected the ability to move the hand up and down the cup. If the subject tried to move the hand up the cup to increase stimulation, the cup would be unstably lifted. This could indicate that the weight of the cup may be too low, although increasing the cup weight would probably put even more strain on her already fatiguing shoulder muscles. Decreasing the friction on the surface of the cup without increasing the strain on the shoulder.

It would also be desirable to be able to regulate the stimulation intensity continuously after the cup has been lifted. Several approaches to do this have been investigated by the project group. The linear regulation function described in section 4.2.7 showed however to be too fluctuating to be used in practice when the cup was lifted. This is probably because of a limited precision of the hand and cup distance estimation, where the shadowing effect would have a big impact on the distance estimation based on where in the picture the cup and hand are located. An exponential regulation has also been tested, where small fluctuations in hand/cup distance would result in close to no stimulation adjustments, whereas only larger hand/cup distance variations would result in noticeable intensity regulations. Although this approach did seem to work better than the linear approach during lift off, the fluctuations in the intensity when tilting the cup were considered to be too high.

Other approaches to regulate the intensity could include additional sensors. Pressure transducers built into the cup would be able to reliably assess the gripping forces that are exerted onto the cup. By knowing the weight and size of the cup, a minimum of exerted force required in order to lift the cup could be established and the stimulation intensity could be regulated in attempt to uphold the grip.

6.3 Future perspectives

The system in the current study could be implemented as a tele-rehabilitative option. Rehabilitation of motor impairments is a long and time consuming process, where a great part of the rehabilitation training takes place with a therapist in the clinic. The patient have to travel between the patients home and the clinic to receive in-clinic training. By having the patients do their rehabilitation training from their own home, and only communicate with the therapist when needed, the therapist gain time to do other chores, and the patients no longer have to travel to the clinic and can instead concentrate on the training. The use of a tele-rehabilitation system allows the discharged patients to maintain their training and keep the intensity high since no time consuming traveling is needed. The initial time spend in the hospital, can be used as a training and learning period for the patients to familiarize them self with the tele-rehabilitation system, before the patient will be training at home [Zampolini et al. 2008].
6.4 Summary

An approach has been proposed for designing a motor rehabilitative system that could implement key properties from CIMT and FET. Initial impressions indicated that the system succeded in assisting a motor impaired subject performing a simple task involving the movement of a cup. Current challenges in preparing the system to investigate its validity could include:

- Reducing muscle fatigue arising from electrical stimulation as well as compensatory movements
- Designing different sizes of cups in which the weight can be modified to fit individual users
- Improving the robustness of the technical solution to detect the cup
- Generalising the object recognition solution so that different types of tasks that can be implemented
- Implementation of a technique to reliably assess the user's voluntary effort
- Implementation of a technique to reliably regulate the stimulation based on the user's need

Appendix

7.1 Electrical stimulator

A NoxiTest IES 230 isolated stimulator, see figure 7.1, was used in the project to provide electrical stimulation to subjects forearm. The stimulator provide current in a monopolar setup in the amplitude range from zero to 100 mA. The stimulator can both be controlled directly from its front panel, or externally via the TTL- and Analog input [Larsen 2006b].

Stimulus Control

The stimulator can be set to three different modes of operation, Trig, Gate and Analog. The functionality of the other controls depends on this mode.

Trig: The duration of the stimulus is the dependent on the Pulse width control setting (knob and switch). The pulse width can be set in the interval from 1 μ s to 11 ms. In the Manual mode the amplitude is set via the Current controls and in the External or External scaled mode the amplitude is set via Analog Input at trig time.

Gate: The duration of the stimulus is dependent on the input signal on the TTL input. The stimulus is as long as the TTL input is high (or within current-time limits 7.1). In the Manual mode the amplitude is set via the Current controls and at the External or External scaled mode the amplitude follows the Analog Input.

Analog: The duration of the stimulus is dependent on the input signal. The Analog mode is not available together with the Manual mode and at the External or External scaled mode the amplitude is dependent on the Analog Input signal [Larsen 2006b].

Amplitude Control

The amplitude of the stimulator can be set in three different modes, Manual, External and External scaled.

In the Manual mode the amplitude is controlled by the controls on the front panel (knob and switch). In the External and External scaled mode the analog input signal applied, will affect the amplitude. In both External and External scaled mode a input of zero volt will result in a zero amplitude and the amplitude will increase linearly with the input voltage up till 10 V.



Figure 7.1. The NoxiTest stimulator used in the project.

At External mode a 10 V input will correspond to 10 or 100 mA (depending of the position of the multiplier switch, x1 or x10).

The External scaled mode at 10 V input correspond to the settings on the control panel. If the knob is set to 5.0 mA and the multiplier switch is at x10, then a 3 V input will result in 5.0x10x3/10 = 15 mA [Larsen 2006b].

Isolated Output

The connected electrodes polarity can be changed by the three-position switch (Positive and Negative) relative to the Com socket. The middle position of the three-position switch disable the output. The red LED when lid, indicates out of compliance, meaning that the electrode impedance is too high [Larsen 2006b].

Current-time limit

The Stimulator can deliver current at 20 mA for approximately 200 ms, and at 2 mA the duration of the current is unlimited. This project are not affected by the Current-time limit, since a pulse width of 200 μ s at a maximum of 45 mA, is used. [Larsen 2006b;a]

During stimulation the polarity switch were set to negative. The big return stimulation electrode were connected to the Com port, and the smaller active electrode to the active port.

7.2 National Instruments USB-6229 BNC

The National Instruments (NI) USB-6229 is a multifunction data acquisition (DAQ) module, see figure 7.2. The module is used to bridge a connection between MATLAB to the electrical stimulator, NoxiTest IES 230. The NI USB-6229 have differential BNC analog inputs with 16-bit resolution and a sampling rate of 250 ks/s, and the BNC analog outputs have 16-bit resolution and a sampling rate of 833 kS/s. The analog input and output both have a maximum voltage range from -10 to +10V, meaning that it can operate on the entire range of the electrical stimulator (0-10 V) [Instruments 2012, Larsen 2006b].

The sampling rate of the NI USB-6229 is high enough to be used with the electrical stimulator since a output sampling rate of only 5000 S/s is the minimum requirement. 1 s/200 μ s = 5000 S/s, the pulse width of the stimulation pulse is 200 μ s [Instruments 2012].



Figure 7.2. National Instruments USB-6229 BNC module [Instruments 2012]

Bibliography

- August, K., J. A. Lewis, G. Chandar, A. Merians, B. Biswal, and S. Adamovich (2006). fmri analysis of neural mechanisms underlying rehabilitation in virtual reality: Activating secondary motor areas. In <u>Proceedings of</u> the 28th IEEE EMBS Annual International Conference.
- Baker, L. L. (2000). <u>Neuromuscular Electrical Stimulation: A Practical Guide</u>. Los Amigos Research & Education Institute.
- Ballard, D. H. (1981). Generalizing the hough transform to detect arbitrary shapes. Pattern Recognition 13, 111-122.
- Borenstein, G. (2012). Making Things See. O'Reilly Media, Inc.
- Brennan, D. M., P. S. Lum, G. Uswatte, E. Taub, B. M. Gilmore, and J. Barman (2011). A telerehabilitation platform for home-based automated therapy of arm function. <u>Annual International Conference of the IEEE EMBS</u> <u>33</u>, 1819–1822.
- Brogårdh, C. (2006). Constraint induced movement therapy: influence of restraint and type of training on performance and on brain plasticity. UMEA University Medical Dissertations.
- Chae, J., L. Sheffler, and J. Knutson (2008). Neuromuscular electrical stimulation for motor restoration in hemiplegia. Topics in Stroke Rehabilitation Vol 15 No 5, 412–426.
- Chaudhri, V. (2010, 12). 2-d ping pong game. http://www.dsprelated.com/showcode/53.php. Licensed under a Creative Commons Attribution 3.0 Unported License.
- Chen, S.-C., C.-H. YU, C.-L. LIU, and C.-W. CHEN (2007). Study of functional electrical stimulation by using slip and force sensors for grasping. In 12th Annual Conference of the International FES Society.
- Cheron, G., J.-P. Draye, M. Bourgeios, and G. Liber (1996). A dynamic neural network identification of electromyography and arm trajectory relationship during complex movements. <u>IEEE Transactions on</u> rehabilitation engineering 43, 552–558.
- Corbetta, D., V. Sirtori, L. Moja, and R. Gatti (2010). Constraint-induced movement therapy in stroke patients: systematic review and meta analysis. European Journal of Physical and Rehabilitation Medicine 46, 537–544.
- de Castro, M. C. F. and A. C. Jr (2000). Artificial grasping system for the paralyzed hand. <u>Artificial Organs Vol 24 Nr.</u> 3, 185–188.
- de Kroon, J. R. and M. J. IJzerman (2008). Electrical stimulation of the upper extremity in stroke: cyclic versus emg-triggered stimulation. Clinical Rehabilitation Vol 22 No 8, 690–697.
- de Kroon, J. R., M. J. IJzerman, J. Chae, G. J. Lankhorst, and G. Zilvold (2005). Relation between stimulation characteristics and clinical outcome in studies using electrical stimulation to improve motor control of the upper extremity in stroke. Journal of Rehabilitation Medicine 37, 65–74.
- Donnan, G. A., M. Fisher, M. Macleod, and S. M. Davis (2008). Stroke. Lancet 371, 1612–1623.
- Dromerick, A., C. Lang, R. Birkenmeier, J. Wagner, J. Miller, T. Videen, W. Powers, S. Wolf, and D. Edwards (2009). Very early constraint-induced movement during stroke rehabilitation (vectors). <u>Neurology Vol 73 No 3</u>, 195–201.

- Duncan, P. W., L. B. Goldstein, R. D. Horner, P. B. Landsman, G. P. Samsa, and D. B. Matchar (1994). Similar motor recovery of upper and lower extremities after stroke. Stroke Vol 25, 1181–1188.
- Eddins, S. (2008, 02). Neighbor indexing, http://blogs.mathworks.com/steve/2008/02/25/neighbor-indexing-2/. Blog.
- Enderle, J., S. M. Blanchard, and J. Bronzino (2005). Introduction to Biomedical Engineering. Academic Press.

for hjerneskade, V. (2007). Tema: Apopleksi – rammer hver 7. dansker. Fokus Vol 14 No 2, 1–32.

- Freeman, C. T., E. Rogers, A.-M. Hughes, J. H. Burridge, and K. L. Meadmore (2012). Iterative learning control in health care: Electrical stimulation and robotic-assisted upper-limb stroke rehabilitation. <u>IEEE CONTROL</u> SYSTEMS MAGAZINE, 18–43.
- Guerra-Filho, G. B. (2005). Optical motion capture: Theory and implementation. RITA XII.
- Hakkennes, S. and J. L. Keating (2005). Constraint-induced movement therapy following stroke: A systematic review of randomised controlled trials. Australian Journal of Physiotherapy Vol 51, 221–231.
- Han, B. S., S. H. Jang, Y. Chang, W. M. Byun, S. K. Lim, and D. S. Kang (2003). Functional magnetic resonance image finding of cortical activation by neuromuscular electrical stimulation on wrist extensor muscles. <u>American</u> Journal of Physical Medicine & Rehabilitation 82, 17–20.
- Heinks-Maldonado, T. H., S. S. Nagarajanban, and J. F. Houde (2006). Magnetoencephalographic evidence for a precise forward model in speech production. Neuroreport 17, 1375–1379.
- Horch, K. W. and G. Dhillon (2002). Neuroprosthetics: Theory and practice. World Scientific Publishing Co Pte Ltd.
- Instruments, N. (2012). Ni usb-6229 bnc: 16-bit, 250 ks/s m series, integrated bnc, external power. http://sine.ni.com/nips/cds/print/p/lang/da/nid/203866.
- Ito, K., M. Tsukamoto, and T. Kondo (2008). Discrimination of intended movements based on nonstationary emg for a prosthetic hand control. In <u>Communications, Control and Signal Processing, 2008. ISCCSP 2008. 3rd</u> International Symposium on.
- Johansen-Berg, H., H. Dawes, C. Guy, S. M. Smith, D. T. Wade, and P. M. Matthews (2002). Correlation between motor improvements and altered fmri activity after rehabilitative therapy. Brain 125, 2731–2742.
- Jorgensen, H. S., H. Nakayama, H. O. Raaschou, and T. S. Olsen (1995). Recovery of walking function in stroke patients: The copenhagen stroke study. Archives of Physical Medicine and Rehabilitation 76, 27–32.
- Jørgensen, H. S., H. Nakayama, H. O. Raaschou, J. Vive-Larsen, M. Støier, and T. S. Olsen (1995). Outcome and time course of recovery in stroke. part ii: Time course of recovery. the copenhagen stroke study. <u>Archives of Physical</u> Medicine and Rehabilitation Vol 76, 406–412.
- Kandel, E. R., J. H. Schwartz, and T. M. Jessell (2000). Principles of nerual science. McGraw-Hill Medical.
- Kawato, M., K. Furukawa, and R. Suzuki (1987). A hierarchical neural-network model for control and learning of voluntary movement. <u>Biological Cybernetics</u> 57, 169–185.
- Khoshelham, K. and S. O. Elberink (2012). Accuracy and resolution of kinect depth data for indoor mapping applications. Sensors 12, 1437–1454.
- Kleim, J. A., S. Barbay, and R. J. Nudo (1998). Functional reorganization of the rat motor cortex following motor skill learning. Journal of Neurophysiology Vol 80, 3321–3325.
- Larsen, K. (2006a, November). Technical specifications: Isolated stimulator, noxitest ies 230, "noxistim". https://smiold.hst.aau.dk/manuals/techman/noxistim/techspec.html.
- Larsen, K. (2006b, November). Users guide: Isolated stimulator, noxitest ies 230, "noxistim". https://smiold.hst.aau.dk/manuals/techman/noxistim/usrguide.html.

- Latham, N. K., D. U. Jette, M. Slavin, L. G. Richards, A. Procino, R. J. Smout, and S. D. Horn (2005). Physical therapy during stroke rehabilitation for people with different walking abilities. <u>Archives of Physical Medicine</u> and Rehabilitation 86, 41–50.
- leung Chan, M. K., R. K. yu Tong, and K. Y. kwan Chung (2009). Bilateral upper limb training with functional electric stimulation in patients with chronic stroke. Neurorehabilitation and Neural Repair Vol 23 No 4, 357–365.
- Li, J., J. Yang, Z. Xu, and J. Peng (2012). Computer-assisted hand rehabilitation assessment using an optical motion capture system. In Image Analysis and Signal Processing (IASP), 2012 International Conference on.
- Liepert, J., H. Bauder, W. H. R. Miltner, E. Taub, and C. Weiller (2000). Treatment-induced cortical reorganization after stroke in humans. Stroke Vol 31, 1210–1216.
- Liepert, J., W. Miltner, Bauder, M. Sommer, C. Dettmers, E. Taub, and C. Weiller (1998). Motor cortex plasticity during constraint-induced movement therapy in stroke patients. Neuroscience Letters 250, 5–8.
- Magnenat, S. (2010, 11). Open kinect imaging information. http://openkinect.org/wiki/Imaging_ Information.
- Meadows, P. (1991). Portable electrical stimulation systems. In IEEE AES Systems Magazine.
- Miall, R. C. and D. M. Wolpert (1996). Forwardmodels for physiological motor control. <u>Neural Networks Vol 9 No 8</u>, 1265–1279.
- Mitobe, K., M. Saitoh, and N. Yoshimura (2010). Analysis of dexterous finger movements for writing using a hand motion capture system. In <u>Virtual Environments Human-Computer Interfaces and Measurement Systems</u> (VECIMS), 2010 IEEE International Conference on.
- Morris, D. M. and E. Taub (2001). Constraint-induced therapy approach to restoring function after neurological injury. Topics in Stroke Rehabilitation Vol 8 Nr. 3, 16–30.
- Nudo, R. J. (1999). Recovery after damage to motor cortical areas. <u>Current Opinion in Neurobiology Vol 9 No 6</u>, 740–747.
- Nudo, R. J. (2007). Postinfarct cortical plasticity and behavioral recovery. Stroke Vol 38 No 2, 840-845.
- Nudo, R. J. and G. W. Milliken (1996). Reorganization of movement representations in primary motor cortex following focal ischemic infarcts in adult squirrel monkeys. Journal of Neurophysiology 75, 2144–2149.
- Nudo, R. J., B. M. Wise, F. SiFuentes, and G. W. Milliken (1996). Neural substrates for the effects of rehabilitative training on motor recovery after lschemic infarc. Science Vol. 207 No. 5269, 1791–1794.
- Packman-Braun, R. (1988). Relationship between functional electrical stimulation duty cycle and fatigue in wrist extensor muscles of patients with hemiparesis. Physical Therapy 68, 51–56.
- Page, S. J., P. Levine, S. Sisto, Q. Bond, and M. V. Johnston (2002). Stroke patients' and therapists' opinions of constraint-induced movement therapy. Clinical Rehabilitation 16, 55–60.
- Park, S.-W., A. J. Butler, V. Cavalheiro, J. L. Alberts, and S. L. Wolf (2004). Changes in serial optical topography and tms during task performance after constraint-induced movement therapy in stroke: A case study. Neurorehabilitation and Neural Repair Vol 18 No 2, 95–104.
- Peckham, P. H. and J. S. Knutson (2005). Functional electrical stimulation for neuromuscular applications. <u>Annual</u> Review of Biomedical Engineering 7, 327–260.
- Plautz, E. J., G. W. Milliken, and R. J. Nudo (2000). Effects of repetitive motor training on movement representations in adult squirrel monkeys: Role of use versus learning. Neurobiology of Learning and Memory Vol 74, 27–55.
- Popovic, D. B., M. B. Popovic, T. Sinkjær, A. Stefanovic, and L. Schwirtlich (2004). Therapy of paretic arm in hemiplegic subjects augmented with a neural prosthesis: A cross-over study. <u>Canadian Journal of Physiology</u> and Pharmacology 82, 749–756.

- Popovic, M., T. Thrasher, M. Adams, V. Takes, V. Zivanovic, and M. Tonack (2006). Functional electrical therapy: retraining grasping in spinal cord injury. Spinal Cord 44, 143–151.
- Popovic, M. B., D. B. Popovic, T. Sinkjær, A. Stefanovic, and L. Schwirtlich (2003). Clinical evaluation of functional electrical therapy in acute hemiplegic subjects. <u>Journal of Rehabilitation Research and Development Vol. 4 No.</u> <u>5</u>, 443–454.
- Ro, T., E. Noser, C. Boake, R. Johnson, M. Gaber, A. Speroni, M. Bernstein, A. D. Joya, W. S. Burgin, L. Zhang, E. Taub, J. C. Grotta, and H. S. Levin (2006). Functional reorganization and recovery after constraint-induced movement therapy in subacute stroke: Case reports. Neurocase: The Neural Basis of Cognition Vol 12 No 1, 50–60.
- Rosewilliam, S., S. Malhotra, C. Roffe, P. Jones, and A. D. Pandyan (2012). Can surface neuromuscular electrical stimulation of the wrist and hand combined with routine therapy facilitate recovery of arm function in patients with stroke? Archives of Physical Medicine and Rehabilitation 93, 1715–1722.
- Rushton, D. N. (2003). Functional electrical stimulation and rehabilitation—an hypothesis. <u>Medical Engineering &</u> Physics 25, 75–78.
- Sawaki, L., A. J. Butler, X. Leng, P. A. Wassenaar, Y. M. Mohammad, K. S. Sarah Blanton, D. S. Nichols-Larsen, S. L. Wolf, D. C. Good, and G. F. Wittenberg (2008). Constraint-induced movement therapy results in increased motor map area in subjects 3 to 9 months after stroke. Neurorehabil Neural Repair Vol 22 No 5, 505–513.
- Schaechter, J. D., E. Kraft, T. S. Hilliard, R. M. Dijkhuizen, T. Benner, S. P. Finklestein, B. R. Rosen, and S. C. Cramer (2002). Motor recovery and cortical reorganization after constraint-induced movement therapy in stroke patients: A preliminary study. Neurorehabilitation and Neural Repair Vol 16 No 4, 1–13.
- Schuhfried, O., R. Crevenna, V. Fialka-Moser, and T. Paternostro-Sluga (2012). Non-invasive neuromuscular electrical stimulation in patients with central nervous system lesions: an educational review. Journal of Rehabilitation Medicine 44, 99–105.
- Seitz, R. J., T. Hildebold, and K. Simeria (2011). Spontaneous arm movement activity assessed by accelerometry is a marker for early recovery after stroke. Journal of neurology 258, 457–463.
- Sheffler, L. R. and J. Chae (2007). Neuromuscular electrical stimulation in neurorehabilitation. <u>Muscle Nerve Vol 35</u> No 5, 562–590.
- Shi, Y. X., J. H. Tian, K. H. Yang, and Y. Zhao (2011). Modified constraint-induced movement therapy versus traditional rehabilitation in patients with upper-extremity dysfunction after stroke: A systematic review and meta-analysis. Archives of Physical Medicine and Rehabilitation 92, 972–982.
- Smith, G. V., G. Alon, S. R. Roys, and R. P. Gullapall (2003). Functional mri determination of a dose-response relationship to lower extremity neuromuscular electrical stimulation in healthy subjects. Experimental Brain Research 150, 33–39.
- Sterr, A., T. Elbert, I. Berthold, S. Kölbel, B. Rockstroh, and E. Taub (2002). Longer versus shorter daily constraintinduced movement therapy of chronic hemiparesis: An exploratory study. <u>Archives of Physical Medicine and</u> Rehabilitation 83, 1374–1377.

Sundhedsstyrelsen (2011). Hjerneskaderehabilitering - en medicinsk teknologivurdering; hovedrapport.

- Takka, I. M., K. Pitkänen, D. B. Popvic, R. Vanninen, and M. Könönen (2011). Functional electrical therapy for hemiparesis alleviates disability and enhances neuroplasticity. <u>Tohoku Journal of Experimental Medicine Vol.</u> <u>225 Nr. 1</u>, 71–76.
- Taub, E., J. E. Crago, L. D. Burgio, T. E. Groomes, E. W. Cook, S. C. Deluca, and N. E. Miller (1994). An operant approach to rehabilitation medicine: Overcoming learned nonuse by shaping. <u>Journal of the Experimental</u> Analysis of Behavior 61, 281–293.
- Taub, E., J. E. Crago, and G. Uswatte (1998). Constraint-induced movement therapy: A new approach to treatment in physical rehabilitation. <u>Rehabilitation Psychology Vol. 43 No. 2</u>, 152–170.

- Taub, E., N. E. Miller, T. A. Novack, E. W. Cook, W. C. Fleming, C. S. Nepomecuno, J. S. Connell, and J. E. Crago (1993). Technique to improve chronic motor deficit after stroke. Arch Phys Med Rehabil 74, 347–354.
- Taub, E. and D. M. Morris (2001). Constraint-induced movement therapy to enhance recovery after stroke. <u>Current</u> Atherosclerosis Reports 3, 279–286.
- Taub, E. and G. Uswatte (2006). Constraint-induced movement therapy: Answers and questions after two decades of research. NeuroRehabilitation 21, 93–95.
- Taub, E., G. Uswatte, and T. Elbert (2002). New treatments in neurorehabilitation founded on basic research. <u>Nature</u> reviews, Neuroscience Vol 3 No 3, 228–236.
- Taub, E., G. Uswatte, D. K. King, D. Morris, J. E. Crago, and A. Chatterjee (2006). A placebo-controlled trial of constraint-induced movement therapy for upper extremity after stroke. Stroke 37, 1045–1049.
- Taub, E., G. Uswatte, and R. Pidikiti (1999). Constraint induced movement therapy: A new family of techniques with broad application to physical rehabilitation a clinical review. Journal of Rehabilitation Research & Development Vol. 36 No. 3.
- Truelsen, T., B. Piechowski-Jozwiak, R. Bonita, C. Mathers, J. Bogousslavsky, and G. Boysen (2006). Stroke incidence and prevalence in europe: a review of available data. European Journal of Neurology 13, 581–598.
- van der Lee, J. H., R. C. Wagenaar, G. J. Lankhorst, T. W. Vogelaar, W. L. Deville, and L. M. Bouter (1999). Forced use of the upper extremity in chronic stroke patients: Results from a single-blind randomized clinical trial. <u>Stroke 3</u>, 2369–2375.
- Wei, X., N. J. Rijkhoff, W. A. Santa, J. A. Anderson, P. Afshar, W. J. Schindeldecker, K. E. Wika, N. D. Barka, and T. J. Denison (2011). Functional electrical stimulation as a neuroprosthetic methodology for enabling closed-loop urinary incontinence treatment. Neural Engineering (NER). 5th International IEEE/EMBS Conference, 650–654.
- Wieloch, T. and K. Nikolich (2006). Mechanisms of neural plasticity following brain injury. <u>Current Opinion in</u> Neurobiology Vol. 16, 258–264.
- Wittenberg, G. F., R. Chen, K. O. B. Kenji Ishii, E. Taub, L. H. Gerber, M. Hallett, and L. G. (2003). Constraint-induced therapy in stroke: Magnetic-stimulation motor maps and cerebral activation. <u>Neurorehabil Neural Repair Vol</u> 17, 48–57.
- Wittenberg, G. F. and J. D. Schaechter (2009). The neural basis of constraint-induced movement therapy. <u>Current</u> Opinion in Neurology 22, 582–588.
- Wolf, S. L., S. Blanton, H. Baer, J. Breshears, and A. J. Butler (2002). Repetitive task practice: A critical review of constraint-induced movement therapy in stroke. The Neurologist Vol. 8 No. 6, 325–338.
- Wolf, S. L., C. J. Winstein, J. P. Miller, E. Taub, G. Uswatte, D. Morris, C. Giuliani, K. E. Light, and D. Nichols-Larsen (2006). Effect of constraint-induced movement therapy on upper extremity function 3 to 9 months after stroke: the excite randomized clinical trial. The Journal of the American Medical Association Vol 296 No 17, 2095–2104.
- Wolpert, D. M. and J. R. Flanagan (2009a). forward models. Oxford Companion to Consciousness, 295-296.
- Wolpert, D. M. and J. R. Flanagan (2009b). Motor prediction. Current Biology Vol 11 No 18, 729-732.
- Zampolini, M., E. Todeschini, M. B. Guitart, H. Hermens, S. Ilsbroukx, V. Macellari, R. Magni, M. Rogante, S. S. Marchese, M. Vollenbroek, and C. Giacomozzi (2008). Tele-rehabilitation: present and future. <u>Ann Ist Super</u> Sanità 44, 125–134.