A Helping Hand – On Innovations for Rehabilitation and Assistive Technology

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Doctoral Thesis

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To my surprise
**ABSTRACT**

This thesis focuses on assistive and rehabilitation technology for restoring the function of the hand. It presents three different approaches to assistive technology: one in the form of an orthosis, one in the form of a brain-computer interface combined with functional electrical stimulation and finally one totally aiming at rehabilitating the nervous system by restoring brain function using the concept of neuroplasticity. The thesis also includes an epidemiological study based on statistics from the Swedish Hospital Discharge Register and a review on different methods for assessment of hand function.

A novel invention of an orthosis in form of a light weight glove, the SEM (Soft Extra Muscle) glove, is introduced and described in detail. The SEM glove is constructed for improving the grasping capability of a human independently of the particular task being performed. A key feature is that a controlling and strengthening effect is achieved without the need for an external mechanical structure in the form of an exoskeleton. The glove is activated by input from tactile sensors in its fingertips and palm. The sensors react when the applied force is larger than 0.2 N and feed a microcontroller of DC motors. These pull lines, which are attached to the fingers of the glove and thus work as artificial tendons.

A clinical study on the feasibility of the SEM glove to improve hand function on a group of patients with varying degree of disability has been made. Assessments included passive and active range of finger motion, flexor muscle strength according to the Medical Research Council (MRC) 0-5 scale, grip strength using the Grippit hand dynamometer, fine motor skills according to the Nine Hole Peg test and hand function in common activities by use of the Sollerman test. Participants rated the potential benefit on a Visual Analogue Scale.

A prototype for a system for combining BCI (Brain-Computer Interface) and FES (Functional Electrical Stimulation) is described. The system is intended to be used during the first period of recovery from a TBI (Traumatic Brain Injury) or stroke that have led to paresis in the hand, before deciding on a permanent system, thus allowing the patients to get a quick start on the motor relearning. The system contains EEG recording electrodes, a control unit and a power unit. Initially the patients will practice controlling the movement of a robotic hand and then move on to controlling pulses being sent to stimulus electrodes placed on the paretic muscle.

An innovative electrophysiological device for rehabilitation of brain lesions is presented, consisting of a portable headset with electrodes on both sides adapted on the localization of treatment area. The purpose is to receive the outgoing signal from the healthy side of the brain and transfer that signal to the injured and surrounding area of the remote side, thereby having the potential to facilitate the reactivation of the injured brain tissue. The device consists of a control unit as well as a power unit to activate the circuit electronics for amplifying, filtering, AD-converting, multiplexing and switching the outgoing electric signals to the most optimal ingoing signal for treatment of the injured and surrounding area.
Dissertation

Paper I
Maria Asplund, Mats Nilsson, Anders Jacobsson and Hans von Holst
Neuroepidemiology 2009;32:217–228

Paper II
The Soft Extra Muscle System for Improving the Grasping Capability in Neurological Rehabilitation
Mats Nilsson, Johan Ingvast, Jan Wikander and Hans von Holst
Full paper presented at the 2012 IEEE-EMBS International Conference on Biomedical Engineering and Sciences. Accepted for publication in IEEE Xplore.

Paper III
Grip strengthening glove to improve hand function in patients with neuromuscular disorders. A feasibility study.
Mats Nilsson, Annika Fryxell Westerberg, Carl Wadell, Hans von Holst and Jörgen Borg
Submitted to Journal of NeuroEngineering and Rehabilitation.

Paper IV
EEG based control of a brain-computer interface for neuromuscular stimulation
Mats Nilsson, Tobias Nyberg and Hans von Holst
Manuscript

Paper V
An innovative electrophysiological device for rehabilitation of brain lesions
Mats Nilsson, Tobias Nyberg and Hans von Holst
Manuscript

Related Work Not Included
System, device and method for restoration of brain function
Hans von Holst, Tobias Nyberg and Mats Nilsson
Patent application: SE-1300217-5, submission date 2013-03-21
DIVISION OF WORK BETWEEN AUTHORS

PAPER I
Neuroepidemiology 2009;32:217–228
Nilsson and Asplund planned the study and the writing of the paper. Jacobsson from HDR provided the data. Asplund wrote the paper after discussion with Nilsson and under the supervision of von Holst.

PAPER II
The Soft Extra Muscle System for Improving the Grasping Capability in Neurological Rehabilitation
Full paper presented at the 2012 IEEE-EMBS International Conference on Biomedical Engineering and Sciences. Accepted for publication in IEEE Xplore.
Nilsson wrote the paper. Wikander and von Holst introduced the concept and designed the glove together with Ingvast.

PAPER III
Grip strengthening glove to improve hand function in patients with neuromuscular disorders. A feasibility study.
Submitted to Journal of NeuroEngineering and Rehabilitation.
Nilsson, Wadell, Borg and Fryxell Westerberg planned the study. Nilsson, Wadell and Fryxell Westerberg did the tests. Nilsson and Borg wrote the paper under the supervision of von Holst.

PAPER IV
EEG based control of a brain-computer interface for neuromuscular stimulation
Manuscript
Nilsson, Nyberg and von Holst planned the study. Nilsson designed the experiment and wrote the paper under the supervision of Nyberg and von Holst.

PAPER V
An innovative electrophysiological device for rehabilitation of brain lesions
Manuscript
Nilsson, Nyberg and von Holst planned the study. Nilsson and Nyberg designed the experiment. Nilsson wrote the paper under the supervision of Nyberg and von Holst.
The work presented in this thesis has been carried out at the Division of Neuronic Engineering at KTH – Royal Institute of Technology, School of Technology and Health, in Stockholm, Sweden. Some parts of the work have been performed in collaboration with the Department of Mechatronics at KTH, the Department of Neurosurgery at Karolinska University Hospital and the Department of Rehabilitation at Danderyd Hospital (Stockholm, Sweden).

First of all I wish to thank my supervisor Hans von Holst for his everlasting positive attitude and belief in his PhD students as well as his patience when my other duties at KTH demanded my attention. I would also like to thank my co-supervisor Tobias Nyberg for his inestimable support in the last two studies in the thesis. My profound apologies to his family for all the late evenings I’ve made him stay at work to help me in the lab.

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A big thank you also to my parents for bringing me up in an atmosphere of inquisitiveness and always encouraging me to further studies.

Finally I would like to thank all the other nice co-workers I have and have had during my whole time as a PhD student, especially Johnson, Sofia and Maria, who started this journey together with me. We all made it!

Stockholm, March 2013

Mats Nilsson
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1 INTRODUCTION

Medical engineering is the application of engineering principles and design concepts to medicine and biology. It can be used to combine the technological and problem solving skills of engineering with the clinical knowledge and biological science of medicine to improve and renew the healthcare in all aspects. Medical engineering can be applied to all stages of healthcare, from diagnosis via treatment and therapy to rehabilitation.

During the last decades we have seen in Sweden, and most countries around the world, a drastic increase in the life expectancy as well as a decrease in the birth rate, which will have a large impact on the age distribution of the population. Fewer people in working ages will have to support a large group of elderly. Therefore it is of great importance to make diagnosis and treatment of common diseases, as well as rehabilitation, safer and more effective.

The human hand is one of the most complex tools in the nature and vital for our function in the daily life. With gestures with the hands we express, signal and convey messages. We use it for protection, sensory feedback and touch. “The hand is an extension of the brain” (I. Kant, German philosopher). Therefore, loss or reduced function of the hand is a very big burden to the affected person. It is obvious that there are both humanitarian and socio economic reasons for doing research on how to rehabilitate and assist people with reduced hand function.

The aim of this thesis is to introduce new technological aids for use in rehabilitation and assistive technology. These aids can be mechanical, focusing on helping the muscles, or electronic, focusing on helping the nervous system, or a combination of both. Moreover, the thesis focuses on rehabilitation and assistive technology for restoring the function of the hand. Many of the theories and technologies discussed will, however, work with minor modification for other parts of the body as well.

The thesis includes a short introduction to the anatomy, physiology and pathology of the human hand as well as the various parts of the nervous system controlling the hand. It introduces the concept of rehabilitative and assistive tools and discusses the technological considerations needed in constructing assistive devices for the hand. Three different approaches to assistive technology are introduced: one in the form of an orthosis, one in the form of a brain-computer interface combined with functional electrical stimulation and finally one totally aiming at rehabilitating the nervous system by restoring brain function using the concept of neuroplasticity. This is achieved by means of direct electrical stimulation of damaged brain tissue.

To give the full picture of the procedure used for introducing new technology in the field of medical engineering the thesis also includes an epidemiological study based on statistics from the Swedish Hospital Discharge Register and a review on different methods for assessment of hand function.

Five appended papers follow the introduction.
2 Physiological Background

2.1 The Human Hand

The hand (manus) is the name of the extremity of primates located at the end of an arm or forelimb. The hand is the most vital organ for physical manipulation of the environment as well as getting feedback from touching objects. It is used for both gross motor skills, e.g. lifting a heavy object, and fine motor skills, e.g. picking up a small match.

The human hand consists of a broad palm (metacarpus) with 5 digits, attached to the forearm by a joint called the wrist (carpus). The hand has 27 bones. Of these 14 are the phalanges (proximal, medial, and distal) of the fingers. The bone that connects the fingers to the wrist is called the metacarpal. The human has 5 metacarpals in each hand.

The four fingers are used for the outermost performance; they can be folded over the palm which allows the grasping of objects. To distinguish the fingers from each other they have separate names:

- index finger, pointer finger, or forefinger (digitus secundus),
- middle finger or long finger (digitus médius and more commonly digitus tertius)
- ring finger (digitus annuláris)
- little finger (digitus mínimus)

The thumb is located on one side of the hand, parallel to the arm. The thumb can more easily that the other fingers be rotated relative to the palm. One way of distinguishing a proper hand from the forepaws of other mammals is the presence of opposable thumbs. By this is meant the ability to bring the thumb opposite to the fingers, a muscle action known as opposition.

The muscles acting on the hand can be subdivided into two groups: the extrinsic and intrinsic muscle groups. The extrinsic muscle groups are the long flexors and extensors. The reason for them being called extrinsic is the fact that their muscle belly (the thickest part of the muscle) is located on the forearm. To the intrinsic muscle groups are counted the thenar (thumb) and hypothenar (little finger) muscles; the interossei muscles (four dorsally and three volarly) originating between the metacarpal bones; and the lumbrical muscles arising from the deep flexor to insert on the dorsal extensor hood mechanism.

Located on the underside of the forearm are two long flexors controlling the fingers by tendons to the phalanges of the fingers. The deep flexor attaches to the distal phalanx, and the superficial flexor attaches to the middle phalanx. These flexors make it possible to bend the fingers. The human thumb is special in that it has, apart from one long and one short flexor in the thenar muscle group, several other muscles moving the thumb in opposition and thus enabling the grasping grip.
The extensors are located on the back of the forearm and are connected to the fingers in a more complex way than the flexors. The tendons unite with the interosseous and lumbrical muscles to form the extensor hood mechanism. The primary function of the extensors is to straighten out the digits. The thumb has two extensors in the forearm. Also, the index finger and the little finger have an extra extensor, used for instance for pointing.

The combination of these bones and muscles make the articulation of the human hand more complex and delicate than that of comparable organs in any other animal. This extra articulation makes us able to operate a wide variety of tools and devices, as well as achieving a large amount of possible hand gestures.

The articulations are:

- interphalangeal articulations of hand (the hinge joints between the finger bones)
- metacarpophalangeal joints (where the fingers meet the palm)
- intercarpal articulations (where the palm meets the wrist)
- wrist (may also be viewed as belonging to the forearm.)

The hand is also a source for sensory feedback to the body. The fingertips have some of the highest concentrations of nerve endings per area in the body and are thus a great source of tactile feedback. The hands have the most advanced positioning capability of the body. These facts in combination make the hands closely associated with the sense of touch. Each hand, as is the case for other paired organs (eyes, feet, legs), is dominantly controlled by the opposing brain hemisphere [1, 2].

One way of describing the complexity of the hand is to use the concept “degrees of freedom”, in the mechanical meaning of the term, i.e. “any one of the number of ways in which the space configuration of a mechanical system may change”. By this definition a human hand has 27 degrees of freedom (Figure 1). Four of these are in each finger, except for the thumb that has five. The remaining six degrees of freedom is the bending and rotation of the wrist. From combinations of these degrees of freedom the functions of the hand can be described and explained [3, 4].
1. The thumb is the base for the grip function of the hand.
2. The pointer and middle finger combined with the thumb produce the fundamental grip functions.
3. The ring and little fingers adds stability and strength to the grip of the whole hand.

Figure 1. The degrees of freedom of the hand
2.2 The Motor Cortex

The hand is controlled from the motor cortex of the brain. The motor cortex is the region of the cerebral cortex involved in planning, controlling, and executing voluntary movements (Figure 2).

![Figure 2. Topography of the human motor cortex](image)

The various parts of the motor cortex have different tasks in the movement process. The primary motor cortex will generate the neural impulses that are transported to the spinal cord and control the execution of the voluntary movements. The premotor cortex is believed to play a role in the motor control, preparation for and guidance of movement, and also the control of proximal muscles and spatial guidance of reaching. The supplementary motor area (SMA) is coordinating the two sides of the body by internal planning of movement, especially sequences of movement [5]. There are also other brain regions involved in the function of movements and motor function, e.g. the cerebellum and the basal ganglia [1].

The premotor cortex could in turn be divided into four sections: one upper (dorsal) and one lower (ventral). These have each one region in the front of the brain (rostral premotor cortex) and one toward the back (caudal premotor cortex). These are normally described by the acronyms PMDr (premotor dorsal, rostral), PMDc (premotor dorsal, caudal), PMVr (premotor ventral, rostral) and PMVc (premotor ventral, caudal). These different parts are connected with different parts of the movement. PMDc is guiding reaching, PMDr is involved in learning to associate sensory stimuli with specific movements or learning response rules, PMVc has a role in the sensory guidance of movement, and may be involved in the protection of the body by creating a “safety area” around the body by guiding movement with respect to
nearby objects. PMVr is connected to the shaping of the hand in grasping and to interactions between the hand and the mouth. The concept of mirror neurons has been studied in PMVr of monkey brains, discovering that the same neurons are active when the monkey was grasping an object as when it was watching an experimenter doing the same movement, proving that such neurons can be both sensory and motor. They are therefore believed to play a role in the understanding of others by internally imitating the actions [6].

In 1905 Campbell was one of the first making a detailed map of the human motor cortex. The method used was study of amputees. During autopsies it was noted that persons who had lost an arm or a leg would eventually lose parts of the neuronal mass in the corresponding part of the motor cortex. Later studies using electrical stimulation resulted in more detailed mapping. Classic experiments were made by Penfield in 1937, during brain surgery on epileptic patients. A local anaesthetic was given to the patients and then their sculls were opened so that the brain was exposed. Using electrical stimulation to the surface of the brain it was possible to map out the speech areas, in order to prevent the surgeon from damaging the speech circuitry during the operation. These studies enabled Penfield to map out all parts of the cerebral cortex, including the motor cortex. This was illustrated with the classical drawing of the “homunculus” (Figure 3).

![Figure 3. The “homunculus” showing the mapping of the different parts of the brain cortex.](image)

The early research in the field suggested that the connection between the muscle movements could be described in a direct way so that the a neuron in the motor cortex would send an axon or projection to the spinal cord, which in turn would send an axon to a muscle [7]. Thus an active neuron in the cortex would cause a direct contraction in a muscle. The greater the activity in the motor cortex, the stronger the force in the muscle, and each group of muscles would be controlled be a defined point in the motor cortex.
Later research however has shown that each point in the motor cortex will influence a wide range of muscles and joints and that the map has a large tendency to overlap. This effect is most noticed in the premotor cortex and supplementary motor cortex, but can also be noted in the primary motor cortex. This could be the reason that enables animals to learn complicated movements, where the motor cortex gradually adapts to coordinate the muscles [8].

More recent research has been focused on studies of monkey brains [9, 10]. Using electrical stimulation of one side of the cortex it was possible to cause the hand to open and close, grasp things and move them to the mouth and make the arm move in a way similar to reaching. Studies made on several monkeys showed similar mapping in all tests.

Movement of the hand and arm is a complicated procedure and studies has shown that each motor cortex neuron can be correlated to specific movement of the joints and muscles. The speed and direction of the movement as well as the muscle force will also be correlated with specific neuron and the way by which this control is made is still a subject of research [11].

During the second half of the 20th century the concept of neuroplasticity was established, stating that even if the functions of the brain may be located to certain regions, these regions are not confined but may be subject to changes during life, especially during the recovery after an injury [12]. Neuroplasticity may be described at cellular level or as larger-scale changes known as cortical remapping [13]. Both the physical structure and the functional organization of the brain may be changed in this way. The fundamental principle of this is the concept synaptic pruning, stating that the individual connections between the different parts of the brain are constantly removed and recreated. The way this happens depends on how they are used, so that nearby neurons used in the same way become strongly connected while neurons that are used in separate ways will form different maps.

Studies have shown that if a certain part of the cortical map will lose its designated input it may at a later time activate in response to another input. These inputs are normally connected to adjacent parts of the brain. Studies by Merzenich [14] on monkeys where the third digit had been amputated showed that before the amputation there were five distinct areas in the cortical map corresponding to each finger, but two months after the amputation the area connected to the third finger had been invaded by the nearby second and fourth finger areas, while the more distant areas corresponding to the first and fifth finger remained relatively unchanged. The brain is thus not “hard-wired” but may be rewired as a result of both training and response to an injury [15].

The incidence of “phantom limbs” may also involve cortical remapping. This phenomenon occurs in people who have undergone amputation of e.g. hands, arms or legs and can be described as a sensation that an amputated or missing limb (or even an organ, like the appendix) is still attached to the body and is moving appropriately with other body parts (some people also have the feeling that the missing limb is gesticulating while they talk). The majority of such sensations are painful and are known as phantom pains. The missing limb often feels wrongly shaped and placed in a distorted position. The pain is usually intermittent and declines with time. Up until the late 90s it was believed that these sensations were due to signals from the damaged nerve endings that were previously leading to the amputated limb.
These signals should then have been misinterpreted by the brain as pain. Therefore suggested treatment involved second amputations trying to remove the nerve endings. This however often just led to even more sensations and pain from the new stump. In extreme cases surgeons even tried cutting the sensory nerve leading to the spinal cord or removing parts of the thalamus, preventing the signals from the body to reach the brain.

It is now rather believed that these phenomena are due to reorganization in the somatosensory cortex and suggested treatment involves artificial visual feedback using mirror boxes or virtual reality giving the illusion that the patient still has the limb, and thus enabling the patient to move the limb and unclench it from painful positions [16, 17].

2.3 Pathology

Many diseases affect the function of the hand. This thesis focuses on conditions that can’t be successfully treated by chemical drugs but may make the patient in need of assistive tools in the form of exoskeletons, orthoses or protheses. Obvious causes of such conditions would be traumatic loss of the whole or parts of the hand, due to accidents or amputations, e.g. after cancer, but more common are such conditions caused by damages and/or diseases to the nervous system.

Such conditions may originate in the central nervous system (CNS) or in the peripheral nervous systems and the muscles. Table 1 shows the different components of the nervous system. Due to the way the nervous system is constructed and how functions are assigned to its components, lesions in specific areas of the central or peripheral nervous system will show characteristic symptoms and signs. Thus it is possible to trace individual findings or constellations of findings back to the responsible dysfunctional component of the nervous system [18].

Table 1. Components of the nervous system [18]

<table>
<thead>
<tr>
<th>Central</th>
<th>Peripheral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain (not including cranial nerve nuclei)</td>
<td>Cranial nerve nuclei</td>
</tr>
<tr>
<td>Spinal cord (not including anterior horn ganglion cells)</td>
<td>Anterior horn ganglion cells</td>
</tr>
<tr>
<td></td>
<td>Nerve roots</td>
</tr>
<tr>
<td></td>
<td>Brachial and lumbar plexuses</td>
</tr>
<tr>
<td></td>
<td>Peripheral nerves</td>
</tr>
<tr>
<td></td>
<td>Motor end plates</td>
</tr>
<tr>
<td></td>
<td>Muscles</td>
</tr>
</tbody>
</table>
Examples of syndromes on dysfunctions in the nervous system are [18]:

- Central paresis
- Peripheral paresis
- Mono- and hemiparesis
- Polyneuropathy
- Plexus lesion
- Lesion of a single peripheral nerve
- Dysfunction of the neuromuscular junction (motor end plate)
- Myopathy
- Diseases to the spinal cord

Using the criteria in Table 2 it is possible to differentiate central and peripheral forms of paresis. Here the terms “proprioceptive” and “exteroceptive” refers to reflexes responding to stimuli arising within the organism and to stimuli that originate from outside the body, respectively. “Babinski sign” is a neurologic examination based upon the response from the big toe when the sole of the foot is stimulated. “Muscle tone” is the state of muscle tension inside a muscle or muscle group when it is at rest.

Table 2. Characteristics of central and peripheral paresis [18]

<table>
<thead>
<tr>
<th>Feature</th>
<th>Central paresis</th>
<th>Peripheral paresis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proprioceptive muscle reflexes</td>
<td>Increased</td>
<td>Decreased</td>
</tr>
<tr>
<td>Exteroceptive muscle reflexes</td>
<td>Decreased</td>
<td>Decreased</td>
</tr>
<tr>
<td>Babinski sign</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Muscle atrophy</td>
<td>Absent (or mild atrophy of disuse)</td>
<td>Present</td>
</tr>
<tr>
<td>Muscle tone</td>
<td>Increased (i.e. spasticity; not yet present in acute phase)</td>
<td>Decreased</td>
</tr>
</tbody>
</table>
By *monoparesis* we mean isolated weakness of an entire limb or of a major part of it. Some possible causes for this condition are listed in Table 3. Here “fasciculations” mean small, involuntary muscle twitches that can happen to any muscle in the body.

### Table 3. Sites of lesions causing monoparesis, and corresponding clinical features [18]

<table>
<thead>
<tr>
<th>Site of lesion</th>
<th>Clinical features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central nervous system</td>
<td>Spastic paresis (increased muscle tone, increased reflexes)</td>
</tr>
<tr>
<td></td>
<td>No muscle atrophy</td>
</tr>
<tr>
<td></td>
<td>Possibly a purely motor deficit</td>
</tr>
<tr>
<td></td>
<td>(e.g., contralateral leg paresis due to ischemia in the territory of the anterior cerebral artery)</td>
</tr>
<tr>
<td>Anterior horn of spinal cord (chronic lesion)</td>
<td>Paresis of individual muscles with accompanying atrophy and decreased tone</td>
</tr>
<tr>
<td></td>
<td>No sensory deficit</td>
</tr>
<tr>
<td></td>
<td>Possible accompanied by fasciculations</td>
</tr>
<tr>
<td></td>
<td>Decreased proprioceptive muscle reflexes (but may be increased in amyotrophic lateral sclerosis)</td>
</tr>
<tr>
<td>Brachial or lumbar plexus</td>
<td>Mixed sensory and motor deficit</td>
</tr>
<tr>
<td></td>
<td>Decreased muscle tone</td>
</tr>
<tr>
<td></td>
<td>Muscle atrophy, decreased proprioceptive muscle reflexes</td>
</tr>
<tr>
<td></td>
<td>Sensory deficit for all modalities</td>
</tr>
<tr>
<td>Multiple peripheral nerves</td>
<td>Same as in plexus lesions in a single limb</td>
</tr>
<tr>
<td>Muscle</td>
<td>Hardly ever a pure monoparesis; if so, then flaccid</td>
</tr>
<tr>
<td></td>
<td>Purely motor deficit, sometimes with muscle atrophy</td>
</tr>
</tbody>
</table>
Hemiparesis may be due to any of the causes listed in Table 4. Here “Pyramidal tract”, also known as the corticospinal tract, refers to a part of the central nervous system responsible for voluntary movements.

Table 4. Sites of lesions causing hemiparesis, and corresponding clinical features [18]

<table>
<thead>
<tr>
<th>Site of lesion</th>
<th>Clinical features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebrum</td>
<td>Spastic hemiparesis, possibly also involving facial muscles, characterized by:</td>
</tr>
<tr>
<td></td>
<td>Increased muscle tone</td>
</tr>
<tr>
<td></td>
<td>Increased reflexes</td>
</tr>
<tr>
<td></td>
<td>Pyramidal tract signs</td>
</tr>
<tr>
<td></td>
<td>No atrophy</td>
</tr>
<tr>
<td></td>
<td>Usually associated with a sensory deficit</td>
</tr>
<tr>
<td>Brain stem</td>
<td>Spastic hemiparesis, as above</td>
</tr>
<tr>
<td></td>
<td>Face involved or not, depending on level of lesion</td>
</tr>
<tr>
<td></td>
<td>Cranial nerve deficits contralateral to hemiparesis</td>
</tr>
<tr>
<td>Upper cervical spinal cord</td>
<td>Spastic hemiparesis, as above</td>
</tr>
<tr>
<td></td>
<td>Face spared</td>
</tr>
<tr>
<td></td>
<td>Possible ipsilateral loss of position and vibration sense</td>
</tr>
<tr>
<td></td>
<td>and contralateral loss of pain and temperature sense</td>
</tr>
<tr>
<td></td>
<td>below the level of the lesion (Brown-Séquard syndrome)</td>
</tr>
</tbody>
</table>

Polyneuropathy is a condition that usually develops very slowly, over the course of several years and the initial symptoms are normally affecting the lower limbs. At first the abnormalities are purely sensory, like paresthesiae (abnormal, usually nonpainful sensations) in the toes or in the soles of the feet, burning sensations and (occasionally) the feeling of walking on cotton wool. The first objective sign is usually disappearance of the Achilles reflex, followed by weakness as an inability to spread the toes. Later signs involve impairment of cutaneous sensation to touch and weakness in the proximal calf muscles.

When the neuromuscular junction (motor end plate) is the site of dysfunction the result will be a purely motor paresis. The paresis may be of variable severity. However, as in myopathy (see below), sensation remains intact. There is no muscle atrophy.

In myopathy the lesion is directly located in the striated muscle. This will have the effect that the muscle will be subject to paresis, but there will be no sensory deficit. The progress of myopathy is usually quite slow and both sides of the body are affected. The muscles will eventually be atrophied and, in late stages of the illness the corresponding reflexes will be decreased or absent [18].
Many diseases also affect the spinal cord. One example, studied in Paper III, is poliomyelitis, with emphasis on post-polio syndrome. Poliomyelitis is caused by oral ingestion of virus particles from the stool or respiratory secretions of an infected person. In most countries a vaccination program has reduced the incidence of poliomyelitis to almost zero. However, people who suffered from the disease as young may later in life develop post-polio syndrome. This condition shows various symptom complexes but is normally associated with muscular atrophy. This can be diagnosed by electromyography and muscle biopsy. The condition may also lead to fatigability or a more complex constellation of symptoms, including pain, respiratory abnormalities and dysfunctional temperature regulation [18].

Rheumatoid arthritis (RA) is a chronic inflammatory disorder that primarily afflicts flexible joints, although several other organs may also be affected. RA may be a cause for severe loss of mobility and functioning unless adequate treatment is provided. The symptoms include inflammation of the capsule around the joints and excess of the synovial fluid, leading to swelling. Fibrous tissue will then form in the synovium, which eventually will cause destruction of articular cartilage and fusion of the joints, a process known as ankylosis. Since autoimmunity plays a central role in the progression of RA it is characterised as a systemic autoimmune disease. However, its initial causes are unknown.

Another form of arthritis is called osteoarthritis. Like RA it affects the joints, causing pain and swelling. Any joint may be affected, but it is most frequent in hands, spine, knees and hips. The cartilage in the joints will gradually break down; making the bones rub together, something that eventually may damage the joint permanently.

Carpal Tunnel Syndrome (or Median nerve entrapment) affects the carpal tunnel, a narrow passageway of ligament and bones at the base of the hand. This tunnel is the site of tendons and nerves. When the tendons are irritated they may thicken and cause swelling, which makes the tunnel narrow and compress the nerves. This leads to gradually worsened symptoms, like difficulty to grasp objects. This syndrome may have many causes, including RA or other diseases, heredity, wrist injury or monotonous job assignments, like assembly line work. It is more common for women than for men. To prevent nerve damage early diagnosis and treatment is vital.

Tendinitis (or tendonitis) means inflammation of a tendon, most often occurring in the shoulders, elbows or wrists. The joint affected by the inflamed tendon will be the site of tenderness and pain. It is normally caused by overuse of the tendon and/or injuries, but may also be caused by certain diseases like RA. Tendinitis is often described by more popular names, like “tennis elbow”.

12
Cerebrovascular Accident (CVA), more commonly known as “stroke” is a condition characterized by an abrupt onset of neurological symptoms, e.g. loss of sensation or paralysis, arising from the destruction of brain tissue due to lack of oxygen [1]. The reason for the condition may be an obstruction in the blood flow or a rupture of an artery supplying the brain. Depending on what is the reason behind the stroke it is referred to as either ischaemic or haemorrhagic stroke. The ischaemic stroke appears when a thrombus (blood clot) is formed somewhere in the body, often when an artery is damaged by atherosclerosis from a build-up of plaques, and is transported through the bloodstream to the brain. About three-quarters of all stroke cases are ischaemic strokes.

When instead a blood vessel ruptures somewhere in the brain blood will enter the subarachnoid space and a haemorrhagic stroke occurs. Another case is when an artery in the brain ruptures so that the tissue surrounding it is contaminated with blood. This is called a cerebral haemorrhage. Both these types of stroke will cause an increased intracranial pressure in the brain.

A stroke may have various grades of severity, depending on its location. A large stroke may be fatal or cause paralysis, while a smaller stroke may cause weakness in an arm or a leg [19]. Many patients may after a stroke have constant weakness in one side of the body, difficulty of speaking, incontinence, and bladder dysfunction. The condition normally depends on what area of the brain that was damaged and how much tissue that was affected.

The brain tissue in the vicinity of the stroke may be divided into four subtypes: 1. The core (defined as the irreversibly damaged tissue), 2. The penumbra (defined as the severely hypoperfused area that is at risk of infarction, but still may be saved), 3. The oligemia (defined as mildly hypoperfused and with no risk for infarction under normal circumstances) and 4. The hyperperfused tissue (shows an increased cerebral blood flow compared to the contralateral tissue). The penumbra may progress to or escape from infarction. It has been found that survival of the penumbra tissue is the most important factor of recovery after ischaemic stroke [20].

Diaschisis is a sudden loss of function in a portion of the brain connected to a distant, but damaged, brain area. Since the damaged area is connected through neurons to other parts of the brain a physiological imbalance is created and which will disturb the function of the intact parts [21]. The term diaschisis was coined by Constantin von Monakow in 1914 [22]. It should be noted that in diaschisis the dysfunctional tissue is not damaged per se, it is the connections leading to it that have been altered. The common causes for diaschisis are traumatic brain injury or stroke [23].
3 Methods

This chapter describes the different technologies and research methods used in the studies of the thesis.

3.1 Epidemiology

In order to determine where to focus on research in technology and health it is very useful to start with epidemiological studies, i.e. studies of the cause and numbers of injuries and illnesses. In Sweden such studies can in a straightforward way be made using data from the Swedish Hospital Discharge Register (HDR), which gets all data from the different care units. Reporting to HDR has been compulsory on a national level since 1987, and the register therefore contains comprehensive information on all public in-patient care in Sweden, for all Swedish citizens. Four different types of data are registered: patient data, hospital data, administrative data and medical data, including personal identification number, gender, age and area of residence at parish level. The data are structured according to the International Classification of Diseases (ICD). Originally the idea was that this thesis should aim at solutions for patients with peripheral nerve damages, such as neural engineering for the healing of peripheral limbs and nerve interfaces for artificial feedback or neural control of prosthetic limbs, and therefore the epidemiological study in Paper I has its main focus on such injuries.

The term “nerve injury” is very general and involves everything from a slight stretch of a peripheral fibre to the complex and often devastating brain damage. Some peripheral nerve injuries of a less severe kind may heal well providing full recovery of function for the patient, while more severe injuries show poor recovery and may cause lifelong disability.

The data from HDR do not contain information about the severity of the injuries or the outcome of the treatment. For this reason the total time spent in in-patient care was used as a proxy for socio-economic cost and also as an indirect measure of the severity of injuries. In the study described in Paper I data from the years 1998 to 2006 are analysed. To screen the data the selection was made based on three criteria:

- The mean in-patient care time for treatment of this injury was more than a week
- At least 20 patients per year were submitted with this diagnosis
- The total amount of in-patient care days spent on treatment of such injuries per year was more than 100

These criteria were selected on the basis of the following assumptions: 1) There are few injuries, requiring less than a week of hospital care and that are of such substantial grade and severity that they should qualify to be first in line for very advanced prosthetic techniques. 2) Since we are discussing implementation of these techniques for specific applications, that are potentially interesting for the med tech industry, we also want to consider cost effectiveness of such a product. Such devices must naturally be subjected to extensive clinical testing and cost effective before final approval for clinical use.
To be cost effective it is estimated that the number of potential users should be fairly large. In this perspective, 20 patients annually is not a large number, although for scientific purposes, prototype systems tried out on a smaller number of patients would be of great interest, provided that the number of patients using this prototype is large enough for statistical significance of results. Criteria 3 leaves room for injuries that are less than 20, but despite this account for a large proportion of hospital in-patient care, and therefore also can be expected to be of substantial severity, as well as a large contributor to the socio economic costs \[24\]. The incidence of the selected codes and their causing factors, including age and gender distribution, was discussed in detail.

3.2 MECHANICAL AIDS

If the function of the hand is reduced and/or parts of the hand or the whole hand have been lost there are two kinds of technical devices that may help to restore some of the hand’s capacity: exoskeletons (orthoses) and prostheses. In order to as much as possible mimic the function of a normal hand sensors and actuators are used to represent the sense of touch and the muscle action.

Sensors and Actuators

A sensor is a device that measures a physical quantity and converts it into a signal which can be analysed by an observer or by an instrument. The physical quantity may be e.g. temperature or pressure. The sensitivity of a sensor gives information of how much the output of the sensor changes to a certain change in the measured quantity. If the characteristics of the sensor are linear this corresponds to the slope $dy/dx$ of the line. The smaller the changes in the measured quantity are, the higher sensitivity of the sensor is demanded.

Sensors always affect what they measure, e.g. a thermometer measuring the temperature of a hot liquid will cool the liquid while the liquid heats the thermometer. Technological advances in the sensor field include manufacturing sensors on the microscopic scale, what is known as MEMS (Micro Electro Mechanical Systems) technology. Micro sensors of this kind normally have a significantly higher speed and sensitivity compared with macroscopic ones.

When manufacturing a sensor the goal is that it shall:

- be sensitive to the property that is to be measured
- be insensitive to other properties that may affect the sensor
- influence the measured property as little as possible.

Sensors are normally designed to be linear or linear to some mathematical function of the measurement, often logarithmic, i.e. the output signal will be linearly proportional to the value or to a simple function of the measured property.
A typical kind of sensors often used in the field of exoskeletons and prostheses are tactile sensors. The term tactile sensor usually refers to a transducer that is sensitive to touch, force, or pressure. This kind of sensors is used to measure and register interaction between a contact surface and the environment and normally reacts to the physical quantity force. The term tactile refers to the somatosensory system or more commonly the sense of touch. Based on their physical properties tactile sensors can be grouped into a number of types, including piezoresistive, piezoelectric, capacitive and elastoresistive sensors.

Tactile sensors can be constructed as arrays, where each one is called a tactel, and can distinguish a touch at any one of them from a touch at any other one. Tactels have been constructed from metallic capacitive sensing elements, but also from organic materials like conductive rubber.

An actuator is a mechanical device for moving or controlling a mechanism or system. The principle of its operation is that it is powered by a source of energy, normally an electric current, hydraulic fluid pressure or pneumatic pressure, and converts that energy into some kind of motion.

Mechanical actuators operate by either converting rotary motion into linear motion, or vice versa. The conversion can be made using some kind of mechanism, like:

- **Screw**: A nut in the actuator is rotating and making the screw shaft move in a line, or the screw shaft is moving along the line making the nut rotate. The operating principle is the same for the three kinds screw jack, ball screw and roller screw actuators.
- **Wheel and axle**: Hoist, winch, rack and pinion, chain drive, belt drive, rigid chain and rigid belt actuators operate on the principle of the wheel and axle. By rotating a wheel/axle (e.g. drum, gear, pulley or shaft) a linear member (e.g. cable, rack, chain or belt) moves. By moving the linear member, the wheel/axle rotates.

The normal use of actuators in engineering is to introduce or prevent motion. They can also be used to transform an input signal (normally an electric signal) into motion, e.g. in electrical motors. Motors are most often used to induce circular motion. However, by using the screw principle mentioned above they can also be used for linear applications [3, 4, 25].

**Exoskeletons and Orthoses**

An exoskeleton is an artificial device worn outside of the body to protect or assist it. Humans have long used this principle, e.g. suits of armour used for protection in combat. In nature this could be compared to the hermit crabs, the majority of which are obliged constantly to "wear" an empty gastropod shell in order to protect their soft abdomens. A certain form of exoskeletons used in medical contexts is called orthoses. An orthosis is explained as a device which attaches to a limb, or the torso, to support the function or correct the shape of that limb or the spine. Powered exoskeletons have, apart from the framework, a power supply that provides part of or all the activation energy needed for movement of a limb (Figure 4).
There are still many military applications for this. Also, extensive research is currently being done on the medical aspects, both for assisting nursing staff in lifting and carrying patients and in assisting and rehabilitating impaired patients. One example is the training of patients recovering from a traumatic brain injury or a stroke. An exoskeleton could both reduce the number of therapists needed and make the training more uniform, easier to analyse retrospectively and specifically customized for each patient. The most common way of constructing a powered exoskeleton is to use internal combustion engine, batteries or, potentially, fuel cells as power source and a hydraulic system controlled by an on-board computer to transfer the power.

There are many engineering difficulties to overcome when constructing powered exoskeletons. They need to be able to perform rapid and agile movements, and should also be safe to operate without extensive training. The biggest problem is normally the power supply. If the exoskeleton is supposed to sustain a full body normally the power source will only last for a few minutes. In some industrial applications where the exoskeleton is not meant to be used in standalone situations this may be acceptable, but for medical purposes it is not satisfactory. Smaller exoskeletons for a hand or a leg will require less power, but the power supply remains an important issue.

The choice of material for the exoskeleton is also important. Inexpensive and easy to mould materials such as steel and aluminium are desirable. However, steel is heavy and will require more power to assist the wearer, thus reducing efficiency. Aluminium, on the other hand, is lightweight but also not very strong and may not be able to withstand outer strain on the exoskeleton, which could lead to severe injuries for the wearer. The engineers are now targeting more expensive and strong but lightweight materials such as titanium, and using more complex component construction methods, such as moulded carbon-fibre plates. Also organic and textile materials are being used and Paper II in this thesis gives an example of that.
The same problem with power demand and weight applies to the joint actuators. Standard hydraulic cylinders have the advantage of being powerful and precise, but they are also heavy due to the fluid-filled hoses and actuator cylinders. Pneumatics are generally not suitable for precise movement due to their unpredictability since the compressed gas is springy and the length of travel will vary with the gas compression and the reactive forces pushing against the actuator.

Flexibility is another important factor to take into account. Several human joints such as the hips and shoulders are ball and socket joints, with the centre of rotation inside the body, which makes it difficult for an exoskeleton to copy.

Control and modulation of excessive and unwanted movement is also a substantial problem. The control system must be able to react to sudden movements such as tripping or being pushed over. The reaction must be fast and precise to prevent the wearer from falling over. It may however also not be too fast, since that may lead to the assisted motion overshooting the desired position and resulting in contact with a position sensor to move the exoskeleton in another direction, which could lead to uncontrolled oscillatory motion causing injury. Thus the computer control must be able to detect such undesired oscillatory motions and shut down in a safe manner.

Yet an issue is detection and prevention of invalid or unsafe motions. An exoskeleton may never move in a manner that exceeds the range of motion of the human body and tear muscle ligaments. This is both a design and programming problem. The design can consider hinges like the elbow and knee and put limits on the motion so that they e.g. can’t flex backwards, but it is also necessary that not a series of combined movements, that one by one may be harmless, together causes the exoskeleton to collide with itself or the wearer. An ideal powered exoskeleton should be able to computationally track limb positions. From the information the limb movement should be limited so that the wearer does not casually injure themselves through unintended assistive motions, such as when coughing, sneezing, when startled, or if experiencing a sudden uncontrolled seizure or muscle spasm.

Since an exoskeleton normally is constructed of strong and hard materials it usually can’t be worn directly in contact with bare skin. The exoskeleton joints themselves may also be damaged from environment factors such as water, sand and dust, and may need protection from the elements to keep operating effectively. This protection can be accomplished by using fabric suit to enclose the exoskeleton mechanics separate from the user. This suit will then prevent the wearer from pinch hazards as well as acting as a protective layer for the exoskeleton [3, 4, 25].
**Prostheses**

In medicine, a prosthesis, prosthetic, or prosthetic limb (Greek: πρόσθεσις "addition") is an artificial device extension that replaces a missing body part. The missing body parts can have been lost by traumatic injury or be missing from birth (congenital). Prostheses can also be used to assist defective body parts.

The concept of prosthetics have been known for a long time, from the early Egyptians through the Persians where Hegistratus, a soldier, were said to have cut off his own foot to escape his captors and replaced it with a wooden one. In the 16th century development of more functional prostheses began. Götz von Berlichingen, a German mercenary, developed a pair of iron hands that could be moved by relaxing a series of releases and springs. The improvement of prosthetic design has since then gone in pair with amputation surgery.

The most common ways of attaching the artificial limb to the stump of the amputee are by belts and cuffs or by suction. The stump can be either directly fitted into a socket or via a liner that is fixed to the socket either by vacuum (suction sockets) or a pin lock. The liner can be made from a soft material like silicone and thus get a better suction fit. Another method of attaching artificial limbs is called osseointegration. It has been developed not only in order to reduce the pain in the amputee that the stump and socket method often causes, but also create a stable connection point.

The method works by inserting a titanium bolt into the bone at the end of the stump. The bone will eventually attach itself to the titanium and then an abutment is attached to the bolt. This abutment will extend out of the stump enabling the artificial limb to be attached to the abutment. The method has the advantages of providing better control of the prosthetic and enabling the wearer to use it for a longer period of time, but requires that the impact on the limb must not be too large, since the bone may fracture. One interesting feature of this method is a phenomena where the wearer experiences sensation from the artificial limb through the abutment and into the body which is known as osseoperception [26].

In the scope of this thesis the focus will be on prostheses as part of the field of biomechatronics, the science of using mechanical, robotic, devices with human muscle, skeleton, and nervous systems to assist or enhance motor control lost by trauma, disease, or defect. Several components are needed in order for a robotic prosthetic limb to work, i.e. be integrated into the function of the body. Sensors are needed to detect signals from the wearers muscular or nervous systems. To control the device some form of controller inside the device must be able to process that information and combine it with feedback from the limb and actuator, like speed, position and force. This feedback may be provided using force meters and accelerometers. The force and movements normally produced by the muscle will in the prosthesis be mimicked by an actuator.
A myoelectric prosthesis is a prosthesis that reacts to electromyography (EMG) signals, i.e. electrical potential changes from voluntarily contracted muscles. The signals are recorded by electrodes on the surface of the skin of the wearer, analysed and used to control the movements of the prosthesis, such as elbow flexion/extension, wrist supination/pronation (rotation) or hand opening/closing of the fingers. Through advancements in the processor technology it has been possible to get more fine-tuned control of the movement of the prosthesis.

A neural prosthesis works according to the same principle but here the electrodes are attached directly to the nervous system. Due to problem with long term function and the risk of infection with electrodes going through the skin this technique has been more successful for implanted devices such as cochlear implants [27].

![Figure 5. A prosthetic hand (Printed with permission from Uniklinikum Heidelberg)](image)

One way of improving the function of a prosthetic arm or hand is a surgical technique called Targeted Muscle Reinnervation (TMR). It is developed to compensate for the fact that neural control information of the arm is lost during amputation. The TMR technique is used to transfer residual arm nerves to alternative muscle sites, such as the pectoralis major. Once the reinnervation is complete, the EMG signals to control the prosthesis can be measured from the new site instead.

A variety of this technique is called Targeted Sensory Reinnervation (TSR). It is similar to TMR, except that instead of rerouting motor nerves to a new muscle, sensory nerves are rerouted to the skin, e.g. on the chest. The patient will then experience sensory stimulus on that site, such as pressure or temperature, as if it were coming from the amputated limb on the area which the nerve in question originally innervated [28].
3.3 MEASURING BRAIN AND MUSCLE ACTIVITY

Electroencephalography

Electroencephalography (EEG) is the technology used for recording electrical activity on the scalp. This activity is caused by the ionic current flows within the neurons of the brain. The current in one single neuron is far too small to be recorded, so the EEG technology is based on recording the summation of billions of neurons. The EEG technology uses electrodes placed on the scalp or subdural, normally following an international standardised system called 10-20, referring to the relative distance between the electrodes, as shown in Figure 6.

![Figure 6. Placement of electrodes according to the 10-20 system [29]](image)

The voltage can either be measured between two adjacent electrodes or at one single electrode related to a reference electrode, normally placed in the neck or on the chin. The electric potential decreases by the square of the distance, which means that mainly neurons close to the scalp will contribute to the EEG pattern. Different brain activities produce different characteristic wave patterns, traditionally named using Greek letters, as can be seen in Table 5 [30].

<table>
<thead>
<tr>
<th>Type</th>
<th>Frequency (Hz)</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delta</td>
<td>0 - 4</td>
<td>Frontal (in adults)</td>
</tr>
<tr>
<td>Theta</td>
<td>4 - 8</td>
<td>Locations not related to the task at hand</td>
</tr>
<tr>
<td>Alpha</td>
<td>8 - 13</td>
<td>Posterior regions</td>
</tr>
<tr>
<td>Beta</td>
<td>13 - 30</td>
<td>Most evident frontally</td>
</tr>
<tr>
<td>Gamma</td>
<td>30 – 100+</td>
<td>Somatosensory cortex</td>
</tr>
<tr>
<td>Mu</td>
<td>8 - 13</td>
<td>Sensorimotor cortex</td>
</tr>
</tbody>
</table>

Table 5. EEG wave types, their frequency and location
The mu waves are of particular interest in this thesis, since they are found in a band over the motor cortex from ear to ear. The mu waves are connected to motor action in such a way that they are suppressed when a person is performing a motor activity or in some cases while imagining such an activity [31]. The amplitude of EEG signals is normally 10 – 100 μV if measured on the scalp and 10 – 20 mV if measured using subdural electrodes. The EEG data are difficult to interpret and ideally advanced computer-based technology should be used for user-selected montages, scaling vertically and horizontally and filter adjustments [32].

**Electromyography**

A similar type of measurement can be made on skeletal muscles and the technology is then called electromyography (EMG). Electrodes are placed on the muscles and detecting the electrical potential generated by the muscle cells when they are activated by the nervous system. These signals can be used for diagnosing level of activity or medical deficiencies [33]. The amplitude of EMG signals are in the order of 50 μV up to 30 mV and in a frequency range of 7 – 20 Hz, depending on what muscles that are activated. Since EMG signals normally are much stronger than EEG signals it is important to avoid muscle activity in the face during EEG recording, since such face movement may produce artefacts in the measured results.
3.4 Electrical Stimulation

From the fact that both the neurons in the brain and the muscle cells use electrical signals to be activated it is possible to artificially stimulate activity using external current and/or voltage sources. When using this technique for activation of sensorimotor mechanisms the electrical charges should be given in the form of electrical pulses, following three parameters: pulse frequency (f), pulse duration (T) and pulse amplitude (I). Stimulation at low levels, i.e. short pulse duration and low pulse amplitude, activates afferent pathways while stronger stimulation may affect both afferent and efferent pathways [34]. How stimulation pulses can be formed is exemplified in Figure 7.

![Figure 7. Stimulus output trains: (a) Monophasic (b) Asymmetric biphasic (c) Symmetric biphasic (d) Symmetric biphasic with interpulse interval [35]](image)

Neuromuscular Electrical Stimulation (NMES) is defined as the application of electrical current to motor points in the body to artificially contract skeletal muscles. It is known that repetitive movement training of a paretic limb enhances motor relearning. If a stroke survivor does not have the capacity to take part in volitional, active repetitive movement therapy NMES may assist. In motor relearning the NMES may be applied either as cyclic NMES, where the NMES is used to contract paretic muscles at a set duty cycle for a pre-set time period, or as EMG-mediated NMES, where EMG electrodes are used to detect cognitive intent to activate a muscle and the NMES is used to complete or amplify the muscle contraction [75].
Functional Electrical Stimulation is further defined as the application of NMES to facilitate purposeful tasks where normal neural function has been damaged or destroyed, e.g. grasping an object or assisting with walking. FES can be applied using surface, percutaneous or implanted electrodes. The surface electrodes have the advantage of being simple and non-invasive and are thus used for a variety of therapies. Using surface electrodes the size and placing of the electrodes are of great importance. They should be placed directly over the motor points of the muscle. Improper placements may directly affect comfort levels and muscle contraction strength [35].

3.5 BRAIN-MACHINE INTERFACE

Brain-machine interfaces (BMI) or brain-computer interfaces (BCI) uses the electrical signals from the muscles and neurons to communicate with external devices, e.g. by transforming neural commands into motor commands transmitted to robotic arms or other prostheses [36]. To make BMIs be reasonably portable and easy to use, EEG signals are commonly used. Such studies have been successful in studying movement intention. The signals can be recorded on the scalp (EEG), from the cortical surface (ECoG) or within the cortex (local field potentials, LFP) [31].

Electrodes placed as cortical implants pose serious health risks and have rarely been used on humans [37]. However, reconstruction of muscle activities using non-invasive recordings have shown to be difficult since EEG signals normally are quite contaminated by noise, and thus the quality of data is poor compared to data from invasive sensors [38]. Many studies are now being made using this technology for e.g. picture imagining [39], shape recognition [40], manipulating virtual objects or playing games.

Of particular interest for this thesis are the studies being made on using BMI to control paretic limbs. Such studies have been made by among others Tan et al [41], Pfurtscheller et al [42] and Collinger et al [43].

3.6 ASSESSMENT OF HAND FUNCTION

There are various ways of testing the function and performance of the hand. In accordance with guidelines from the World Health Organisation (WHO) health and health-related domains can be classified using “The International Classification of Functioning, Disability and Health”, known more commonly as ICF. The domains are here classified from body, individual and societal perspectives by means of two lists: a list of body functions and structure, and a list of domains of activity and participation. Since an individual’s functioning and disability occurs in a context, the ICF also includes a list of environmental factors. The ICF was officially endorsed by all 191 WHO Member States in the Fifty-fourth World Health Assembly on 22 May 2001(resolution WHA 54.21) [44].
Tests for determining the degree of disability can be related to three components:

- Based on the body function/impairment.
- Based on the ability to perform daily life activities.
- Based on the ability to participate in social activities

**Tests of Grip Strength**

Grip force is a common measurement used in assessment of the hand function. It can be used for various purposes: for evaluating the effectiveness of a treatment, as an indicator of improvement and for determining the patient’s ability to return to normal home activities and employment. The most common measure is maximum grip strength, which however has the limitation that it demands the patient to be motivated to grip at his/her maximum. It also gives little information about the ability of the muscles to sustain the concentration. Thus it is also of interest to measure what happens when a grip is sustained over a period of time [45].

In the Medical Research Council (MRC) scale for muscle strength the patient's effort is graded on a scale of 0 - 5 [46]:

- Grade 5: Muscle contracts normally against full resistance.
- Grade 4: Muscle strength is reduced but muscle contraction can still move joint against resistance.
- Grade 3: Muscle strength is further reduced such that the joint can be moved only against gravity with the examiner's resistance completely removed. As an example, the elbow can be moved from full extension to full flexion starting with the arm hanging down at the side.
- Grade 2: Muscle can move only if the resistance of gravity is removed. As an example, the elbow can be fully flexed only if the arm is maintained in a horizontal plane.
- Grade 1: Only a trace or flicker of movement is seen or felt in the muscle or fasciculations are observed in the muscle.
- Grade 0: No movement is observed.

**Grippit**

Grippit is an instrument used to measure the grip strength of the whole hand and the pinching grip strength. It consists of a dynamometer with two replaceable rods, mounted on a transportable base. An arm guide makes the test situation easy to reproduce (Figure 8). The patient takes a grip of the rods pulling them together and the instrument measures the force produced by the grip. The force transducer is based on strain gauges. The palm and fingers should be completely clasped around the handle. The instrument measures maximum value, mean value and end value of the force and gives the value in Newton. The mean value and the end value give an estimation of the endurance of the patient. The measurement time is controlled electronically and norms are available [45].
Figure 8. The Grippit instrument

**Jamar Dynamometer**

An alternative way of measuring grip strength is the Jamar dynamometer (Figure 9). It was introduced by Bechtol in 1954 and consists of a sealed hydraulic system with adjustable hand spacings that register hand grip force [47].

Figure 9. The Jamar dynamometer

**Tests of Fine Motor Skills**

**Nine Hole Peg Test**

The Nine Hole Peg Test is a timed test the performance of fine motor tasks, commonly used by occupational therapists. The test is very simple and requires that the patient place and removes the pegs from the nine holes in a wooden plate (Figure 10). The time needed to place and remove all nine pegs is measured. Reliability and validity have been assessed and norms are available [48].
Grooved Pegboard Test

A slightly more demanding test of fine motor skills is the Grooved pegboard Test. The pegboard consists of a 10.1 cm by 10.1 cm (5- by 5- in.) metal surface with a 5 by 5 matrix of keyhole-shaped holes in varying orientations. The pegs are 3 mm in diameter and have a small ridge running along its entire length (2.5 cm). At the bottom of the pegboard there is a round receptacle for the pegs (Figure 11). The patients are asked to put all 25 pegs, one at a time, into the holes as quickly as possible and in a prescribed order. It is also common that the test involves removing the pegs, one at a time and in the same order as they were placed, and putting them back in the receptacle. The tests can be done with just the dominant hand or by use of both hands [49].
Tests of Ability to Perform Activities of Daily Living

The Sollerman Hand Function Test

The Sollerman test was developed by the hand surgeon Christer Sollerman in Gothenburg in order to achieve a standardised and objective way of testing seven of the eight most common hand grips without the need for interviews or written surveys of the patients, that often are time-demanding and hard to use in daily care. The test comprises 20 activities of daily living. The patient performs the activities and a therapist observes and documents the results. Examples of test tasks are opening a door using a key, folding a piece of paper, picking coins out of a purse and cutting a piece of clay using ordinary knife and fork [50]. A somewhat modified and shorter version of the Sollerman test is called Grip Ability Test (GAT) [51].

The Barthel Index

The Barthel scale or Barthel ADL index is used widely to assess performance in activities of daily living (ADL) [52, 53]. Data may be collected by observation or by interview. The scale covers ten every day activities. Performance in each activity is rated on a scale and then summated. The activities are summarized in Table 6.

Table 6. The ten activities in the Barthel index [52]

<table>
<thead>
<tr>
<th>Activity</th>
<th>With Help</th>
<th>Independent</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Feeding (if food needs to be cut up = help)</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>2. Moving from wheelchair to bed and return (includes sitting up in bed)</td>
<td>5-10</td>
<td>15</td>
</tr>
<tr>
<td>3. Personal toilet (wash face, comb hair, shave, clean teeth)</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>4. Getting on and off toilet (handling clothes, wipe, flush)</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>5. Bathing self</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>6. Walking on level surface (or if unable to walk, propel wheelchair)</td>
<td>0*</td>
<td>5*</td>
</tr>
<tr>
<td>*score only if unable to walk</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Ascend and descend stairs</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>8. Dressing (includes tying shoes, fastening fasteners)</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>9. Controlling bowels</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>10. Controlling bladder</td>
<td>5</td>
<td>10</td>
</tr>
</tbody>
</table>
The sum score is calculated and the higher the sum, the greater the likelihood of living at home with a degree of independence. If adaptations to the environment are made they should be described in detail and attached to the scale. The scale was introduced in 1965 [54] and has later undergone some modifications.

**DASH**

DASH (Disabilities of the Arm, Shoulder and Hand) is a system presenting a 30-item, self-report questionnaire designed to measure physical function and symptoms in people with any of several musculoskeletal disorders of the upper limb. It is a tool designed to give clinicians and researchers a single, reliable instrument, designed to use to assess movements over any or all joints in the upper extremity. The patient is asked to indicate his/her ability to do certain activities in the week before the test and the answers should be given regardless of how the patients perform the task.

Questions include describing the ability to open a tight or new jar, write, turn a key, push open a heavy door and other daily life activities, but also about how he/she can manage transportation needs and sexual activities. The patient has five answer options (No difficulty, Mild difficulty, Moderate difficulty, Severe difficulty, Unable). The questionnaire also includes questions about the state of pain the patient feels, both in general and performing certain activities and also about weakness and tingling. The answer options to those questions are (None, Mild, Moderate, Severe, Extreme) [55].

**Functional Independence Measure**

The Functional Independence Measure (FIM) is a commonly used assessment instrument based on observation by professionals, who have been trained to use FIM. It is used to rate performance and degree of independence in everyday activities and thus to indicate how much assistance the patient will require to carry out activities of daily living [56]. FIM comprises 13 motor tasks and five cognitive tasks (considered basic activities of daily living). Performance is rated on a 7 point scale, ranging from total assistance (complete dependence) to complete independence. Scores range from 18 (lowest) to 126 (highest) indicating level of function.
The scoring criteria are summarized in Table 7 and the tasks rated include:

- Eating,
- Grooming
- Bathing
- Upper and lower body dressing
- Toileting,
- Bladder and bowel management
- Bed to chair, toilet and shower transfer
- Locomotion (ambulatory or wheelchair level),
- Stairs
- Cognitive comprehension
- Expression
- Social interaction
- Problem solving
- Memory

Table 7. The FIM Scoring Criteria

<table>
<thead>
<tr>
<th>No Helper Required</th>
<th>Helper (Modified Dependence)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Score</strong></td>
<td><strong>Description</strong></td>
</tr>
<tr>
<td>7</td>
<td>Complete Independence</td>
</tr>
<tr>
<td>6</td>
<td>Modified Independence (patient requires use of a device, but no physical assistance)</td>
</tr>
<tr>
<td>3</td>
<td>Moderate Assistance (patient can perform 50% to 74% of task)</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Total Assistance (patient can perform less than 25% of the task or requires more than one person to assist)</td>
</tr>
<tr>
<td>0</td>
<td>Activity does not occur</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Helper (Complete Dependence)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Score</strong></td>
<td><strong>Description</strong></td>
</tr>
<tr>
<td>2</td>
<td>Maximal Assistance (patient can perform 25% to 49% of tasks)</td>
</tr>
<tr>
<td>1</td>
<td>Total Assistance (patient can perform less than 25% of the task or requires more than one person to assist)</td>
</tr>
<tr>
<td>0</td>
<td>Activity does not occur</td>
</tr>
</tbody>
</table>
Tests of General Health Status

EQ-5D

EQ-5D is a standardised measure of health status. It was developed to give a simple and generic measure of health for clinical and economic appraisal. It is applicable in a wide range of health conditions and treatments. It is designed to give both a simple descriptive profile and a single index value for health status that can be used in the clinical and economic evaluation of health care as well as in population health surveys [57]. EQ-5D is mainly designed for self-completion by respondents and can be used in postal surveys, in clinics, and in face-to-face interviews. The version mostly used today consists of one descriptive system and one visual analogue scale (EQ VAS).

The descriptive system includes five dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression). Each dimension has five levels (no problems, slight problems, moderate problems, severe problems, and extreme problems). The patient indicates his/her health state by placing a cross in the box at the most appropriate statement in each of the five dimensions. This procedure results in a 1-digit number expressing the level selected for that dimension. The digits for five dimensions can be combined in a 5-digit number describing the patient’s health state. It should be noted that the numerals 1-5 have no arithmetic properties and should not be used as a cardinal score.

The EQ VAS records the respondent’s self-rated health on a 20 cm vertical, visual analogue scale with endpoints labelled ‘the best health you can imagine’ and ‘the worst health you can imagine’. This information can then be used as a quantitative measure of health as judged by the individual patients [58].
4 RESULTS

The thesis has presented some aspects on rehabilitation and assistive technology focusing on the human hand (Papers II, IV and V) as well as an epidemiological study on the incidence on Traumatic Peripheral Nerve Injuries and Amputations (Paper I). The results of a clinical study on an assistive tool, the SEM Glove, have been presented (Paper III).

4.1 EPIDEMIOLOGICAL STUDY

The results showed that in total during the studied period 11 208 nerve injuries and 4 202 traumatic amputations were reported, thus leaving an incidence rate of 13.9 per 100 000 person-years for nerve injuries and 5.22 per 100 000 person-years for amputations. It should be noted that many injuries are reported in both categories. However, based on the corresponding in-patient care time, most of these injuries could be considered as minor.

There were ten nerve injuries fulfilling the three stated criteria. Among these the most care consuming were brachial plexus injuries, constituting 5.5 % of the total number of peripheral nerve injuries and contributing to 15 % of hospital days spent on peripheral nerve injuries in total. The second and third most common of the selected types of nerve injury were those affecting the radial nerve at upper arm level (347 cases) and injury of peroneal nerve at lower leg level (271 cases). Details on all selected traumatic nerve injuries can be seen in Figure 12.

Complete amputations of body extremities are also relatively rare; the vast majority (81 %) of all amputations are those of fingers, part of hand or wrist, or toes. Since these types of amputations normally not call for any kind of prosthetic solutions they were of minor interest for this study. The reported injuries involving complete loss of hand or foot were in total over the study period 173 cases and 522 cases, respectively. Out of these the most common type was upper extremity amputation between the elbow and wrist (72 cases) and lower extremity amputation between knee and ankle (215 cases). There were only five amputation diagnoses fulfilling the criteria, all of which focused on amputation of lower limbs. Amputations between knee and ankle also alone stand for 17 % of the care time spent on treatment of amputations in Sweden. Details on all selected traumatic amputations can be seen in Figure 13.

In conclusion the most important target for neural engineering techniques would be brachial plexus injuries, since they are both relatively frequent and demands a substantial amount of hospital resources. However, brachial plexus injuries are of a complex nature and there are other injuries, e.g. such more proximal, and thus easier, targets that should be considered as relevant. Based on the data in Paper I such injuries would be those in the radial, peroneal or sciatic nerve. In Sweden, with a population of 9.5 million inhabitants (January 2013), traumatic amputations between knee and ankle, with an average of 23 cases per year, does not constitute a large amount of injuries. However, compared to other amputations it is relatively frequent and technology used for neuroprosthetic legs should most likely be useful for other traumatic amputations.
Figure 12. The selected traumatic nerve injuries constitute 230 traumatic nerve injuries annually in Sweden. A) shows the specific diagnoses and their contribution to these traumatic injuries, B) shows the corresponding number of days (out of 2900 days in total) spent in in-patient care unit on the treatment of these injuries.
Figure 13. The selected traumatic amputations constitute 48 injuries annually in Sweden. A) shows the specific diagnoses and their contribution to these traumatic amputations, B) shows the corresponding number of days (out of 1200 days in total) spent in in-patient care unit on the treatment of these injuries.
4.2 Clinical Study

A feasibility study of the SEM (Soft Extra Muscle) Glove has been made on Danderyd Hospital, using three of the standardized tests described in chapter 3.6; the Grippit test for determining the grip strength, the Nine Hole Peg test for determining the fine motor skills and the Sollerman test for determining general hand functions and activity. Not all patients could perform all parts of the test procedure due to varying hand function as well as concurrent pain and fatigue, but by evaluating case-by-case several conclusions about the usefulness of the glove and the suitable choice of target groups could be made.

Although several limitations were identified, the study indicates a potential for meaningful applications of the glove and thus will encourage further development and testing of the glove. The nine patients who volunteered to participate in the trial were heterogeneous with regard to age, diagnoses, general health condition, and hand function as well as activity level. While age and the diagnoses probably had no impact per se, it is clear that the general condition of the participant and co-morbidities such as pain or fatigue as well as the attitude towards the technology and the test situation had an impact on test performance. However, key determinants were the degree and distribution of the hand paresis and probably also how well compensatory strategies in every-day activities were established.

Both from the participants and the observers point of view, the potential utility of the glove was most obviously illustrated by the performance of the power grip in lifting heavy objects, by the pinch grip in the Nine Hole Peg test and in writing. The performance in these tasks seemed clearly related to the participants overall evaluation of the glove. Obviously, even severely reduced grip strength was compatible with a beneficial effect of the glove in lifting objects. In fact, the two participants with most impaired grip strength reported the best effect. The glove seemed most supportive in tasks that require both certain grip strength and fine motor skills, such as writing. Thus, participants who had problems forming a proper grip, due to impaired strength in one or several fingers, could not utilise the glove. Specifically, the ability to move the thumb independently from the other fingers and to make small adjustments of the pinching grip, turned out to be a crucial factor. Further, participants who had developed and established compensatory movement patterns or learned to use other devices for gripping objects also had problems to use the glove in the test situation. In accordance, participants who had problem forming a proper grip or were used to compensatory movement strategies had low scores for the overall perception of the glove. One additional factor to consider is that activity related pain and fatigue hampered the performance both with and without the glove in some participants. In the study we observed no adverse events or negative side effects that would restrict further trials with the glove as currently designed.
**4.3 Technical Studies**

The SEM Glove has been designed and initially tested in cooperation with the Swedish Public Employment Service, where three people on sick leaves (ages of 25, 61, and 35 years, respectively) were offered the individually adapted SEM gloves for two weeks. Simultaneously, four healthy volunteers tested the SEM Glove system for various leisure activities. The patients improved their individual grasping capacity during workload and felt comfortable with the system applied on their bodies and without any individual problems. The 25 year old female had the capacity to go back to her job as shop assistant with the SEM Glove system on each arm. The system was well tolerated in her daily activities. The 61 year old male improved his grasping capacity substantially although not to the level he had before sick leave. The 35 year old felt clearly helped by the SEM Glove but wore it less frequently due to a sore elbow. Likewise, all of them four healthy volunteers accepted the system without having any difficulties whatsoever and were benefited of the system with regard to strengthening the hand grip during their leisure activity. Further tests are being performed and planned to evaluate future design modifications of the glove.

Within the International standard ISO 9999, Assistive products for persons with disability, the SEM Glove has been classified within the following categories:

- **24 18 03 Devices for grasping.** Products for grasping an object which replace the gripping function of the hands.
- **06 06 07 Hand-finger orthoses.** Devices that encompass the whole or part of the hand and the whole or part of one or more fingers.

A functional prototype for an EEG-controlled surface FES system has been presented and initially tested, using a commercially available headset with EEG electrodes and corresponding software recording and analysing the EEG waves. This device was combined with a designed circuit controlling a robotic hand. The purpose of the set is to give a patient with a paretic limb the possibility to train the ability to control the robotic hand. When the patient has achieved sufficient control the robotic hand can be replaced by electrodes for functional electrical stimulation (FES).

The first test of the prototype was made in the way that one healthy participant (male, 41 years) wore the headset and the experimentalist gave him a set of commands to open and close the robotic hand. In the first test the robotic hand was replaced with a lamp. The details of the experiment are described in Paper IV. The system was set up so that when the participant heard a command his EEG waves were recorded. The participant had been allowed to practice with the system for one hour to make the software recognize two distinct set of EEG waves. The system was then programmed to switch on the lamp when one of the sets of EEG waves were detected and switch it off when the other particular set of EEG waves was detected. If none of the sets were detected the lamp remained unchanged.
Two series of ten commands were tested: one where the participant was looking away and could not see if the lamp was switched on or not and one where the participant was allowed to look at the lamp for visual feedback. In addition the participant’s reaction times to the commands, i.e. the time between the given command and the lighting of the lamp, were noted. This was also done in two series of ten tests: one where the lamp was originally lit and the participant was asked to switch it off and one when the lamp was switched off and the participant was asked to light it as quickly as possible on the command “close” and “open”, respectively. The test results are presented in Table 8.

Table 8. Results from training with a robotic hand

<table>
<thead>
<tr>
<th>Without visual feedback</th>
<th>With visual feedback</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Time (s)</strong></td>
<td><strong>Reaction</strong></td>
</tr>
<tr>
<td>7</td>
<td>Yes</td>
</tr>
<tr>
<td>19</td>
<td>Yes</td>
</tr>
<tr>
<td>27</td>
<td>Yes</td>
</tr>
<tr>
<td>31</td>
<td>No</td>
</tr>
<tr>
<td>34</td>
<td>No</td>
</tr>
<tr>
<td>53</td>
<td>Yes</td>
</tr>
<tr>
<td>62</td>
<td>Yes</td>
</tr>
<tr>
<td>69</td>
<td>Yes</td>
</tr>
<tr>
<td>78</td>
<td>Yes</td>
</tr>
<tr>
<td>83</td>
<td>Yes</td>
</tr>
</tbody>
</table>

An observation that was made is that the times when there was no reaction were those when the commands came with a short interval. The participant were therefore asked to just respond to the command “open” ten times and the reaction time, i.e. the time till the lamp was lit, were noted each time. After that the same procedure was repeated with the command “close” and the time until the lamp was switched off was noted. The mean reaction time for the command “open” was 2.4 s and for “close” the mean reaction time was 2.0 s. The standard deviations were 0.54 and 0.28, respectively.
The test of the system was successful in that a person with a moderate amount of training could learn to control the robotic hand, however with a certain amount of time delay between intent from the participant and action from the robotic hand. This time delay may presumably be possible to reduce by further training and optimization of the software and hardware used, but a certain delay may also be necessary in order to avoid false possible results leading to unintended stimulation. Further studies on a larger set of participants, and also disabled people, are needed in order to fully optimize the system performance.

Further flexibility of a system for restoring function of the nervous system is presented in Paper V in the form of a prototype for recording EEG waves from a healthy part of the brain and, using the same device, sending stimulus pulses to another, damaged, part of the brain. In this way brain recovery will be achieved using the concept of neuroplasticity and the device can be used to give a continuous diagnosis and treatment of the damaged part and hence facilitate the rehabilitation. A first prototype of the system has been designed and constructed and initial tests have been made. Various kinds of electrodes were used to record the signals and the software for analysing the input waves and designing the output stimulus pattern, with respect to frequency, time delay and amplitude, was developed using a FPGA.

Initial studies have been made on measuring the muscle activity produced during eye blinking. The measured values and also a frequency analysis are shown in Figure 14 and Figure 15.

![Diagram of the recorded values, showing eye blinking](image.png)
During the measurements several different kinds of electrodes with varying impedance have been used and thus the voltage values should not be considered as assured and are shown with arbitrary units. A frequency analysis of the recorded signals shows the highest activity in the interval from 10 to 20 Hz, which corresponds to the normal values for myoelectric signals \[59\].

In this prototype the configuration of input/output electrodes is set before the headset is put on. Future development will include extra components and circuitry to enable the same electrodes being used for both recording and stimulation. This will add the feature of self-diagnosis to the system, i.e. the effect of the treatment can be continuously studied by switching the electrodes between output and input (stimulation and recording). Thus, the continued treatment may be modified in real-time using the input from the diagnosis.

Figure 15. Frequency analysis, showing most activity between 10 and 20 Hz
5 DISCUSSION AND CONCLUSIONS

When doing epidemiological studies comparisons of data with results from previous studies must be made with great care, since studies have different selection criteria that will affect statistical evaluations. Epidemiology of nerve injuries and amputations on a national level will naturally also be influenced by national injury prevention programs, gun laws and the participation in armed conflicts [60].

A large number of the amputations registered in the study are not caused by trauma, but are a consequence of peripheral vascular diseases or diabetes. In the USA, it is estimated that trauma accounts for 16 % of all amputation-related hospital discharges [24] and other authors have shown that, depending on country, 25–90 % of all major amputations of lower extremities were associated with diabetes and 30–93 % with peripheral vascular disease [61-63].

The success of an implanted nerve electrode depends on the ability of the nervous system to heal and adjust, and patients subject to traumatic injuries do not in general have other medical conditions that would complicate procedures. Comorbidity was however not studied in this material, and, although such comorbidity is not the primary cause of injury, it could increase the risk of sustaining a traumatic amputation.

The brachial plexus is the most common site of severe upper body peripheral nerve injury (finger and hand level injuries excluded) and stands out as the single most care-consuming of all nerve injury ICD-10 codes studied here. The prognosis is highly dependent on location and severity, but advances in neurosurgical techniques have improved the outlook for patients with this diagnosis [64, 65]. Although brachial plexus injuries might also be more complex to target with neural engineering because of the more complex structure, we have identified a great need for improved treatment.

By virtue of the availability of the HDR, we were able to obtain comprehensive information at a national level about the epidemiology of the included ICD-10 codes. Although reliability of the register is considered to be high, shortcomings have also been reported. Validation of Swedish HDR data on traumatic spinal cord injuries revealed an underestimation of in-patient usage compared to a register on traumatic spinal cord injuries known to be accurate [66]. It could be expected that cases reported in the study were an underestimation, rather than overestimation, of the actual incidence, although the authors found no reason to believe that such underreporting would be selective within the diagnoses studied, but could be expected to be of a random distribution.

Many studies are being made in the field of orthoses and prostheses. There are today several kinds of exoskeletons and prostheses designed for the hand, but there are many problems yet to solve. These problems include weight and power supply for an exoskeleton and mechanics, attachment, control and feedback for a prosthesis. The novel construction of a light-weight orthosis in form of a glove, detachable from the power unit may be a way to overcome this problem.
The aim in the development of the SEM Glove has been to use only standard components and materials. For further improvement it is desirable to use individually constructed sensors where the size and position of the sensors should be individually adjustable. The result of the present development shows the possibility to further support disabled people with new technical innovations aiming at improvements in their daily life activities. A prerequisite is that health care staff and engineers especially from the field of engineering mechatronics merge together more actively in the search for well-designed new technical innovations which may improve disabled people in their neurological rehabilitation. That there are many different applications for this kind of assistive technology was proved in March 2012 when General Motors and NASA presented a prototype of a similar kind of construction, a type of glove to be worn by astronauts, called the K-glove or Robo-Glove [67].

This clinical study aimed at an exploration of the feasibility of a novel glove and thus was restricted to only one test session. Thus, the study design did not allow repeated training sessions with the glove, which would indeed be required in order to further elucidate the potential of the glove to support every-day life. Some minor modifications of the design of the glove might be considered, e.g. to make the glove individually tailored, which would probably make it more comfortable and also help secure optimal positioning of the sensors. Other applications in rehabilitation medicine may be considered and then primarily in other groups of patients with reduced grip strength but preserved ability to open the hand and with preserved sensory function, such as e.g. patients with inflammatory musculoskeletal diseases.

The studies demonstrates the potential value of the SEM Glove for persons with impaired hand function due to neuromuscular disorders with regard to hand function, activity performance and user perceptions. While full mobility in all fingers is one prerequisite for beneficial effects, even severely impaired grip strength is compatible with such effects. These observations may guide further trials designed to evaluate long-term use of the glove in everyday activities.

Cerebral vascular disease (stroke) is the main cause of disabilities in adults [68]. A common effect of both stroke and injuries to the head, neck and the peripheral nerves is reduced manipulation and grasping capability. In Sweden, 30,000 persons per year suffer a stroke and 20,000 persons suffer a head injury [69]. Over the last years a vast number of studies have been focusing on methods for treatment and rehabilitation after stroke and traumatic brain injuries (TBI) [68, 70-72]. Two key features in such studies are brain-computer interfaces (BCI) and functional electrical stimulation (FES).

BCI have traditionally been used mostly for paralyzed and locked-in individuals with no motor control, but could just as well be used for people with just reduced limb function or even as an aid for able-bodied [73]. Several commercial products are now on the market for detecting EEG waves, used to control such devices and studies are being done on possible ways to utilize them [30, 74], as well as on improving the ways to record the EEG signals and increasing the amount of information received, both concerning motor and cognitive signals [75].
Other studies focus on the possibility to use electrical stimulation, in particular neuromuscular stimulation (NMES) to activate paralyzed muscles in precise sequence and amplitude to directly accomplish functional tasks [76]. In such cases the FES systems are meant to provide standing balance, torso control, walking and prevent pressure sores while sitting [77]. Another frequently studied condition is drop foot in hemiplegic gait [78]. It has been shown that FES may also lead to recovery of voluntary power in the corresponding movement, but the mechanism by which this occurs is unclear. It has been presumed that FES may promote adaptive changes in cortical connectivity [79, 80].

In the prototype described in Paper IV these technologies have been combined into one system. The intention is that the system can be used for first use on patients before deciding on a permanent system. A fully developed EEG controlled surface FES system will allow patients getting used to having a neuroprosthesis and learning to control it, something that may improve acceptance of implanted FES. It should also give a quick start to the motor relearning, which would improve both the physiological and psychological state of the patient. It would be desirable to have the later used, maybe implanted, system as compatible to the initial one as possible to allow easy migration between the systems. It has been shown that if a surface stimulator is introduced early after the injury, it increases the likelihood of restoring motor function and the speed of the recovery [34].

The method of using a BCI combined with electrical stimulation has been used on patients suffering from traumatic spinal cord injury [42]. The patient in the study was able to achieve a strong and lasting contraction of the paralyzed muscles in the hand and forearm. For the grasp pattern to be useful it was necessary to use a mechanical orthosis fixing the wrist in a desired position. The FES was then used to stimulate the muscles in the fingers and the hand. To find the best EEG signals that were easy to distinguish the patient had to practice using several types of imagination, e.g. left versus right hand movements. The best results were achieved using the imagination of both feet versus the right hand [42]. It has been seen that the best effect of NMES are found in acute stroke survivors and such with milder impairments, but that the effect in chronic stroke survivors were less enduring [81].

The most important EEG signals for this kind of devices are those in the frequency range of 8-14 Hz, originating from the motor cortex from the brain. Patients not able to move e.g. a paretic hand have been asked to imagine the movement and similar EEG patterns were found. It is of great interest to investigate whether acute stroke patients are able to control a BCI combined with NMES on the wrist and fingers, since those are the most important pre-requisites for useful hand function. Studies have been done where the patients control the movements of the cursor in a simple data program. The cursor is thus used as feedback for the learning process. During such training it is important that the patient is not moving any facial muscles, such as raising an eyebrow, biting or clenching, since such movements have a large effect on the EEG signals and causes artefacts of higher amplitude and frequency than the desired signals [41].
Studies have reported significant improvements in functions as upper limb grasping, standing/walking and ankle dorsiflexion after use of surface FES devices [82]. Patients are however reluctant to try new devices if it is difficult and cumbersome to understand their use. Too complicated user interfaces and bulky constructions must be avoided. The future lies in small easy-to-use devices, preferably based on wireless technology, placed directly on stimulation sites. This will make the systems easier to develop and increase patient acceptance of the systems.

In some cases where the cause of a patient’s condition is based in the nervous system the system presented in Paper V, where the electrical stimulus is directed towards the brain and not the muscles, may be an alternative solution. The system should be possible to use for both patients with ability to move their limbs and such with limited limb movement, e.g. a paretic hand. The reason for this is that it has been shown that actual and imagined movements produce similar EEG patterns [83].

This system should be possible to individually adapt by continuous recording of the brain activity of the individual patients and thus training the system to recognize the specific signal pattern for each user and also adapt and improve the stimulus pattern. During such training sessions a high level of concentration is needed to evoke measurable changes in the EEG pattern and thus each session should not last longer than one hour to avoid mental fatigue.

Many studies have shown that motor tasks including imagery will generate beta oscillations from 20-35 Hz in the representation area of the limb in question and/or in the supplementary motor area (SMA) [84-86]. A point worth noting is however that there is a big difference between the oscillations observed in able-bodied persons and in hemi- or tetraplegic patients. The reason for this difference is that oscillation from persons with ability to move their limbs is observed after termination of the motor task. However, for hemi- or tetraplegic patients the oscillations are detected during execution of the motor task. This needs to be considered when analysing the signals and further research is needed to determine if the same neural networks are involved in both cases [42].

Before using the system the patients should undergo an ordinary EEG examination to determine to what extent patients suffering from a stroke or from diachisis are able to produce a detectable change in the EEG. A minority of the patients may also have permanent trouble using this kind of equipment, since it has been estimated that around 20 % of the population can be described as “BCI-illiterate”, meaning that their motor neurons show too little variation to be of use as signals during EEG measurements [87].

The system described in Paper V has the advantage of being portable, light-weight and easy to use, as well as showing a high flexibility, in that the position of the electrodes for recording and stimulation is easy to adjust and that the FPGA can be reprogrammed for perfectly adapted conditions for the input signals and wave characteristics of the output signals, making it a very suitable tool for continuous training and diagnosis. We believe that the portability is paramount for successful treatment as it increases the wearer time and thus also the length of the treatment.
5.1 General Thoughts on Research in the Field of Medical Engineering

One major problem that occurs in all studies of the kind presented in this thesis is the fact that so much is depending on the choice of patients participating in the study. It is not possible to have a totally objective view, since patients who are believed to be suffering from the same disease or disability still may show very different results in a study. All people are different, in a physiological way so that what is “normal” in one person may be a sign of a disease in another, but also in a psychological way so that their attitude towards the test may strongly affect the outcome. Some patients are really eager to try all kinds of new rehabilitation and assistive aids and put in great effort in making them work, whereas some other are depressed about their condition and feel that nothing can help them. Patients who have recently turned ill are generally more hopeful about their recovery and willing to do all they can in order to speed up the rehabilitation. If the rehabilitation is not very successful their enthusiasm normally drops.

Thus it is necessary to consider many aspects apart from the purely technical when planning such studies and choosing the patient group. When studies are based on results from human beings the experimenter needs to be a bit of an amateur psychologist as well. People who are facing problems with their health every day often need encouragement to try new assisting devices and yet the researcher needs to keep a neutral attitude towards the results.

There are also cases where the combination of technology and medicine can be difficult. A device is constructed based on the condition in healthy people but meant to work for people with some kind of illness. The illness in question may have made the patients loose some ability that were crucial for the function of the device. In a small town like Stockholm it may also be hard to find a large enough group of patients with the desired diagnosis, and thus it may be necessary to use patients with slightly different diagnosis, something that may affect the results.

It is clear that for all kinds of studies on patients there are numerous methodological weaknesses. Examples of such are inadequate blinding, insufficient follow-up data, inequality between patient groups and small sample sizes. Further studies should emphasize on large, multicenter, randomized clinical trials that should be at least single-blinded. Much care should also be taken to finding the right patient groups as well as finding methods of evaluating long-term outcomes, activity limitations and quality of life [81].

These are some of the problems with studies in the field of medical engineering, but also one reason why this research is so stimulating!
5.2 Future Work

For the SEM Glove further studies are needed to show the usefulness of the glove and to improve its construction. It is desirable to make long time studies on a smaller number of people that first have been tested so that it is established that they will be helped from the glove. Some initial tests of this kind have been made in cooperation with the Swedish Public Employment [88]. Clinical studies on patients recovering from e.g. a stroke should also be made to test the glove as a rehabilitating tool for speeding up and facilitating the rebuilding of lost motor and nervous functions.

Another way to go is to modify the construction of the glove so that it takes its input signals from other sources than the sensors in the finger tips and palm. One possible development could be to include myoelectric electrodes to measure intended movements from e.g. muscles around the shoulder. In this way the glove could be used as an aid not only for people with reduced muscle strength, but also for people with a completely paralysed hand. When this step has been taken it is not far to putting the glove on a robotic hand, which would lead to a new kind of prostheses.

For the BCI system in Paper IV the natural step to move on is to study the way the pulses should be formed with respect to frequency, amplitude and time delay to optimize the effect. The placement of the electrodes should also be looked upon. One way would be to use an elastic tube put on the wrist with several electrodes attached and then individually adapt the tube for each patient by choosing which of the electrodes to activate.

The electrophysiological device introduced and presented in Paper V will be subject to further evaluation and modification concerning choice of electrodes and filters as well as the programming of the control unit to achieve a solution as flexible as possible.
6 REFERENCES


