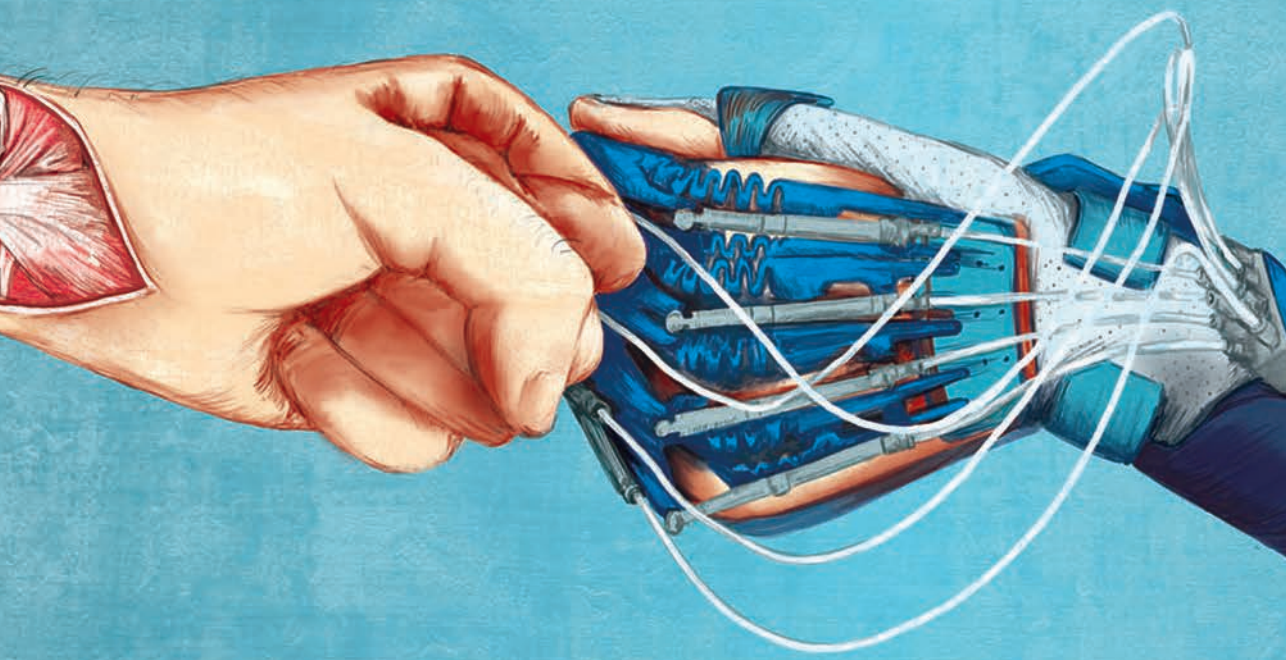
HAND

NEURO-MOTOR CHARACTERIZATION

AND MOTOR INTENTION DECODING

in Duchenne Muscular Dystrophy



Kostas Nizamis

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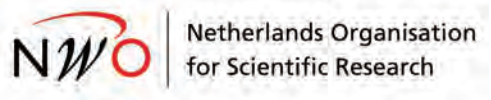

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TO ALL THE PEOPLE WHO SUPPORTED ME
IN THIS LONG PROCESS,

BUT ESPECIALLY TO MY FAMILY

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SUMMARY

Duchenne muscular dystrophy is a neuromuscular progressive disease that affects mainly males. The disease leads to progressive loss of muscle strength and results in limited mobility for the affected individuals. Individuals with DMD, subsequently lose their ability to be self-dependent and maintain social participation. While their life expectancy increased, due to their dependency on caregivers and lack of interaction with the environment, their quality of life remains poor. It is therefore important, to enable individuals with DMD to use their own limbs for as long as possible.

Assistive technologies are identified as means to achieve this goal, with an immediate effect, unlike the alternative options (i.e. pharmaceuticals) that target more long-term goals. Wheelchair mounted robotic manipulators are currently used by individuals with DMD. However useful; they still do not promote active user participation. Arm and trunk orthoses have been developed to assist individuals with DMD, by increasing their reachable workspace and allowing environment manipulation. However, the hand is crucial in manipulating this environment. Since, the disease affects the proximal muscles first, maintenance of the hand function of individuals with DMD did not receive much attention. Currently, the clinically applied protocols focus on passive stretching of the distal muscles and resting hand splints during sleep.

The need for a multi-level and multi-disciplinary approach for the treatment of the hand function of individuals with DMD, assisted using technology, has already been pointed out in previous studies. In the Symbionics project, we aimed for the development of a hand orthosis that adapts to the user, either by design or control or a combination, and is natural to control.

In this dissertation, we present our effort to characterize the hand neuro-motor function of individuals with Duchenne muscular dystrophy (DMD) and decode hand motor intention for controlling an active hand orthosis. We characterized the hand related cognitive-motor performance, created a tool to measure hand and wrist kinematics and studied the high-density surface electromyograms (HD-sEMG) in the forearm. Additionally, we explored the human-machine interfaces typically used in bionic limbs, and we concluded that surface electromyography (sEMG), combined with an admittance controller, is a novel and viable way to decode hand motor

intention of individuals with DMD. Based on the hand characterization, we systematically develop an active hand orthosis (SymbiHand) and an effective way to decode hand motor intention. The SymbiHand was then tested with an individual with DMD, and yielded promising results. It successfully assisted the participant's hand during a hand related task and resulted in lower effort and increased grasping force output.

The goal of this dissertation is "*the characterization of the neuro-motor function of the hand, the decoding of hand motor intention decoding and the implementation of this in an active hand support for individuals with DMD.*" To this end, several research questions were formulated and investigated:

I. Can we characterize the hand neuro-motor function of individuals with DMD?

In order to systematically develop an active hand orthosis, first we decided to characterize the neuro-motor function of the hand of individuals with DMD. This characterization was split in three levels: 1) Cognitive-motor performance characterization, 2) the creation of a reliable tool for characterizing hand kinematics and 3) the characterization of forearm electromyograms. The combination of these three studies created a neuro-motor profile for individuals with DMD.
We first characterized the hand cognitive-motor performance of individuals

- We found a statistically significant difference between individuals with DMD and healthy controls. This deterioration in performance was more clear when the simultaneous use of more than three fingers was needed to complete the task.
- In terms of the task related workload, we found that there was no statistically significant difference between healthy participants and participants with DMD.
- The results indicate that there is indeed a statistically significant difference in hand motor-cognitive performance between healthy individuals and individuals with DMD. This suggests the need for an active hand orthosis to offset this difference.

with DMD. To achieve the first level of characterization we employed a systematic analysis on multi-finger cognitive-motor performance of individuals with DMD by employing a visuo-motor task, which was performed by both healthy and affected individuals.

Due to contractures, individuals with DMD have decreased active and passive range-of-motion (ROM) in the hand compared to healthy individuals. The ability to measure and evaluate the degree of hand ROM impairment is important for creating customized effective treatment and for the development of a customized active hand orthosis. Currently measurement of finger ROM is performed with the use of the goniometer, resulting in a time-consuming process of questionable reliability, while the hospital visiting time of an individual with DMD is quite valuable. We investigated the use of the Leap motion sensor, as an alternative to the goniometer.

- We found that we can measure kinematic data reliably between measurements and with a large decrease in measurement time.
- Despite the low agreement between the two methods, such a technology can: measure finger movements dynamically, help to combine hand treatment with virtual or augmented reality and serve as means of measuring during active use of the fingers.
- Such an approach can be used to monitor the changes in active ROM of individuals with DMD over time and evaluate interventions targeting robotic assisted hand rehabilitation.

The hand function of individuals with DMD can directly benefit from the use of technology. To this end, the Symbionics collaboration aimed to develop an active hand orthosis. A crucial component for the control of such a device is the effective decoding of hand motor intention. The decision to consider sEMG for the decoding of hand motor intention, was motivated by recent previous studies in individuals with DMD, where sEMG was used for decoding arm motor intention. This led to the question of how feasible this approach is for the forearm muscles of individuals with DMD. To answer this, we characterized the forearm sEMG of healthy and affected participants, using a high-density sEMG grid around the forearm during wrist and hand tasks.

- We found that the participants with DMD exhibit lower dimensionality, a decreased repertoire of spatially distinct activations, and an increase in overall activation effort compared to the healthy participants. However, they can repeatedly perform the same activation pattern.
- We also found that when using a pattern recognition algorithm, their offline accuracy performance, while lower than the healthy participants, is still more than 80% for the classification of seven different gestures.
- This indicates that sEMG based hand motor intention decoding is feasible for individuals with DMD.

II. Can we identify a feasible way to decode hand motor intention in real-time in order to control an active hand orthosis for individuals with DMD?

A crucial component for the control of active devices is the effective decoding of motor intention. This topic has been extensively addressed in the field of bionics limbs and prosthetics. Acknowledging this fact, we performed an extensive search of the state-of-the-art techniques used for decoding upper limb motor intention in that field and discussed the results with respect to our target population and our specific application.

- We found that the most common approaches for decoding motor intention include surface electromyography (sEMG), impedance/admittance control and body powered control.
- Based on the opinion of experts in each of the three approaches, we concluded that for individuals with DMD the use of sEMG seems promising, especially in combination with approaches such as an admittance controller, to allow for another level of control customization.
- We used the conclusions of this study to develop hand motor intention methods for individuals with DMD.

We evaluated in practice how feasible sEMG is, for real-time control of hand and wrist motion with an individual with DMD. In this case we compared two broadly used approaches for myoelectric control, namely sequential direct control (DC) and pattern recognition (PR) control. The classified tasks were divided in 1- and 2-degree-of-freedom (DOF).

- We found that, despite the nature of DMD as a muscle degenerative disease, sEMG signals were still sufficient for myocontrol.
- We found that for both 1- and 2-DOF tasks and control approaches there was no statistically significant difference in the performance between the healthy participants and the participant with DMD.
- We also found that, DC performed better with the 1-DOF task as expected. For the 2-DOF task PR control was significantly better than DC, however less robust to changes in forearm orientation.
- Both approaches were combined with an admittance controller to allow for further customization of the control.
- We found that the participant with DMD used different admittance parameters than the healthy participants, indicating the need for a customized support.

Subsequently, we used DC to decode hand motor intention of one participant with DMD and enable him to control the SymbiHand. DC was combined with an admittance model and the participant was able to control the opening and closing hand motion of the SymbiHand. The participant was asked to perform a force tracking computer task with and without the SymbiHand.

- We found that the participant was able to open and close his hand with lower effort, indicated by a large decrease in sEMG activation.
- His grasping force was also increased by a factor of three at only one third of the SymbiHand's capacity and there was no change in force tracking performance.
- This case study has demonstrated that the SymbiHand combined with sEMG and an admittance controller, is able to provide active hand assistance to a participant with DMD.

We concluded that current hand treatment, aiming to delay the effects of the disease in individuals with DMD, might not be able to maintain hand motor performance. Such training can be further enhanced by multi-finger training. Additionally, the Leap motion sensor shows potential to contribute to the development of hand treatment protocols, as it can be used with patients in a clinical setting and assist the fast assessment of hand related impairments. We explored and confirmed the feasibility of high-density sEMG to characterize and decode hand motor intention in individuals with DMD. The subsequent application of myocontrol methods for real-time decoding of hand motor intention, demonstrated that for single degree of freedom tasks direct control is the advised approach. Direct control was further tested with a participant with DMD wearing the SymbiHand and showed the potential of this device to enhance hand function and reduce fatigue while performing ADL tasks for individuals with DMD.

SAMENVATTING

Duchenne spierdystrofie is een progressieve neuromusculaire aandoening die met name voor komt bij jongens. De ziekte zorgt voor progressieve spierzwakte en leidt tot een beperkte mobiliteit. Mensen met DMD worden daardoor afhankelijk van anderen en zijn niet meer in staat om sociaal te blijven participeren. Alhoewel de levensverwachting van mensen met DMD toeneemt, zorgt de afhankelijkheid van anderen ervoor dat de kwaliteit van leven laag blijft. Daarom is het belangrijk om ervoor te zorgen dat mensen met DMD zo lag mogelijk hun eigen handen kunnen blijven gebruiken.

Technologie is een mogelijk middel om dit doel te bereiken met een direct effect, in tegenstelling tot alternatieven (zoals medicijnen) die zich richten op de lange termijn. Op rolstoel gemonteerde robotachtige manipulators worden momenteel gebruikt door personen met DMD. Maar hoe nuttig deze ook zijn, ze bevorderen geen actieve gebruikersparticipatie. Arm- en romporthesen zijn ontwikkeld om voor mensen met DMD een grotere werkruimte creëren. Echter is de hand cruciaal bij het manipuleren van deze omgeving. Omdat de ziekte eerst de proximale spieren treft, kreeg ondersteuning van de handfunctie tot nu toe weinig aandacht. Klinisch toegepaste protocollen richten zich voornamelijk op passief rekken van de distale spieren en het gebruik van nachtelijke handspalken.

De behoefte aan een multilevel- en multidisciplinaire aanpak voor de behandeling van de handfunctie van mensen met DMD middels technologie, is in eerdere studies naar voren gekomen. In het Symbionics-project hebben we ons gericht op de ontwikkeling van een handorthese die zich aanpast aan de behoefte van de gebruiker en intuïtief aan te sturen is.

In dit proefschrift presenteren we onze bevindingen met betrekking tot aansturing van de hand bij mensen met DMD en de intentie voor het besturen van een actieve handorthese. We karakteriseerden de prestaties van de handaansturing, creëerden een hulpmiddel om de beweging te meten in de klinische praktijk. Spieractiviteit in de onderarm is bestudeerd middels high-density oppervlakte elektromyografie (EMG). Uit studies in bionische ledematen is gebleken dat oppervlakte EMG, gecombineerd met een admittance controller, de een nieuwe en werkbare manier is om handmotorintentie van mensen met DMD te decoderen. Een actieve handorthese (SymbiHand) is ontwikkeld, evenals

een effectieve methode om de intentie van de handbewegingen te herkennen uit oppervlakte EMG. Eerste testen van de SymbiHand door een persoon met DMD leverde veelbelovende resultaten op. De orthese was in staat de hand van de persoon te ondersteunen, en resulteerde in een lagere inspanning en een verhoogde grijpkracht.
Het doel van dit proefschrift is "*het karakteriseren van de handfunctie, het herkennen van de intentie van de handbeweging en de implementatie daarvan in een actieve handondersteuner voor mensen met DMD.*"
Een aantal onderzoeksvragen werd hiervoor geformuleerd.

I. Kunnen we de handfunctie van mensen met DMD karakteriseren?

Om systematisch een actieve handorthese te ontwikkelen, moesten we eerst de aansturing van de handfunctie van individuen met DMD karakteriseren. Dit was opgesplitst in drie niveaus: 1) De cognitief-motorische prestatie, 2) het in kaart brengen van handbewegingen en 3) de karakterisatie van onderarm elektromyogrammen. De combinaties van deze drie studies creëerden een neuro-motor profiel voor elk persoon met DMD.

We hebben eerst de cognitieve motorprestaties van personen met DMD gekarakteriseerd. Hiervoor is visuomotorische taak gebruikt, die werd uitgevoerd door zowel gezonde personen als personen met DMD.

- We merkten op dat personen met DMD statistisch significant slechter presteerden dan de gezonde personen. Deze verslechtering was duidelijker wanneer het gelijktijdig gebruik van meer dan drie vingers gevraagd werd.
- Wat betreft de ervaren moeilijkheid van de taak, vonden we geen statistisch significant verschil tussen gezonde deelnemers en deelnemers met DMD.
- De resultaten geven aan dat er inderdaad een statistisch significant verschil is in de cognitief-motorische prestatie tussen gezonde individuen en personen met DMD. Dit bevestigt de noodzaak van een actieve handorthese.

Door contracturen bij mensen met DMD is het actieve en passieve

bewegingsbereik in de hand verminderd in vergelijking met gezonde personen. Het vermogen om het bewegingsbereik van de hand te meten is belangrijk voor het evalueren van een op maat gemaakte actieve handorthese. Momenteel wordt het bewegingsbereik van de vingers gemeten met behulp van een goniometer, wat resulteert in een tijdrovend proces van twijfelachtige betrouwbaarheid. We onderzochten het gebruik van een optische Leap motion sensor als alternatief voor de traditionele benadering.

- We hebben vastgesteld dat we herhaalbaar kunnen meten met een grote afname van de meettijd.
- Ondanks de lage overeenkomst tussen de twee methoden kan de sensor gebruikt worden voor: het meten van dynamische vinger bewegingen en het combineren van behandeling met virtual of augmented reality en tegelijkertijd de beweging van de vingers meten.
- Deze sensor kan worden gebruikt om de progressie van het actieve bewegingsbereik bij mensen met DMD te monitoren en interventies te evalueren die gericht zijn op robot-geassisteerde revalidatie van de hand.

De handfunctie van mensen met DMD kan direct baat hebben bij het gebruik van technologie. Daartoe was samenwerking binnen Symbionics gericht op de ontwikkeling van een actieve handorthese. Een cruciaal onderdeel voor de besturing van een dergelijke inrichting is het herkennen van de intentie van de handbeweging. De beslissing om oppervlakte EMG te gebruiken voor het herkennen intentie, werd gemotiveerd door recente onderzoeken bij personen met DMD, waarbij oppervlakte EMG werd gebruikt voor herkennen van de intentie van armbewegingen. Dit leidde tot de vraag hoe haalbaar deze benadering is voor de onderarmspieren. Om deze vraag te beantwoorden, hebben we met hoge dichtheid de oppervlakte EMG van de onderarm gekarakteriseerd bij gezonde en aangedane deelnemers, tijdens pols- en handbewegingen.

- We merkten op dat de deelnemers met DMD minder onderscheid vertonen tussen patronen van verschillende bewegingen en een toename van de algehele activatie-inspanning laten zien vergeleken met de gezonde deelnemers. Ze kunnen echter herhaaldelijk hetzelfde activeringspatroon uitvoeren.
- We ontdekten dat offline de intentie minder goed herkend kon worden dan bij gezonde deelnemers, maar dat dit nog bij meer dan 80% van zeven verschillende bewegingen goed lukte.
- Dit betekent dat oppervlakte EMG geschikt is om bij mensen met DMD de intentie van handbewegingen te herkennen.

II. Kunnen we een haalbare manier identificeren om handmotorintentie in real-time te decoderen voor de aansturing van een actieve handorthese voor mensen met DMD?

Een cruciaal onderdeel voor de besturing van actieve apparaten is het herkennen van de intentie voor handbewegingen. Dit onderwerp is uitgebreid behandeld in relatie tot bionische ledematen en prothesen. We hebben uitgezocht wat de meest geavanceerde technieken zijn die werden gebruikt voor het herkennen van de intentie van bewegingen van de bovenste ledematen in dat veld. Deze resultaten hebben we in de context van onze doelpopulatie en onze specifieke toepassing bediscussieerd.

- De meest voorkomende benaderingen voor het herkennen van de intentie zijn: oppervlakte EMG, impedance/admittance control en door het lichaam aangedreven.
- Op basis van de mening van experts in drie benaderingen, concludeerden we dat voor mensen met DMD het gebruik van oppervlakte EMG veelbelovend lijkt, vooral in combinatie met admittance control, om een extra niveau van controle mogelijk te maken.
- We hebben de conclusies van deze studie gebruikt om hand-motorintentie methoden te ontwikkelen voor mensen met DMD.

We hebben we in de praktijk getest hoe haalbaar oppervlakte EMG is voor de real-time controle van hand- en polsbeweging met een persoon met DMD. In dit geval hebben we twee breed gebruikte benaderingen voor myo-elektrische besturing vergeleken, namelijk sequentiële directe controle (DC) en patroonherkenning (PH) controle. De geclassificeerde taken waren onderverdeeld in 1 en 2 vrijheidsgraden.

- We merkten op dat, ondanks de aard van DMD als degeneratieve spierziekte, EMG-signalen nog steeds voldoende waren voor myocontrole.
- We stelden vast dat er voor zowel 1 als 2 vrijheidsgraden geen statistisch significant verschil was in de prestaties tussen de gezonde deelnemers en de deelnemer met DMD.
- Zoals verwacht vonden we dat DC beter presteerde met de taak met 1 vrijheidsgraad. Voor de taken met 2 vrijheidsgraden was de PH-controle aanzienlijk beter dan DC, maar minder robuust voor veranderingen in de oriëntatie van de onderarm.
- Beide benaderingen werden gecombineerd met een admittance controller om verder personaliseren mogelijk te maken.
- Voor de deelnemer met DMD waren andere admittance parameters nodig dan voor de gezonde deelnemers, wat aangeeft dat er behoefte is aan ondersteuning op maat.

Vervolgens gebruikten we DC om de intentie van handbewegingen bij een deelnemer met DMD te herkennen en hem in staat te stellen de SymbiHand te besturen. DC werd gecombineerd met een admittance model en de deelnemer kon de hand openen en sluiten met de SymbiHand. De deelnemer werd gevraagd om een computertaak uit te voeren die gebaseerd was op krachten, met en zonder de SymbiHand.

- We stelden vast dat de deelnemer in staat was om zijn hand te openen en te sluiten met een lagere inspanning, wat bleek uit een grote afname in EMG-activiteit.

- Zijn grijpkracht werd ook driemaal verhoogd met slechts een derde van de capaciteit van de SymbiHand en er was geen verandering in de prestatie van de kracht-volg taak.
- Deze casestudy heeft aangetoond dat de SymbiHand in combinatie met oppervlakte EMG en een admittance controller actieve handondersteuning kan bieden aan een deelnemer met DMD.

We concludeerden dat de huidige handbehandeling bij mensen met DMD mogelijk niet in staat is om de prestaties van de handmotor te behouden en dat dynamische training met meerdere vingers moet worden overwogen. Een dergelijke training kan verder worden verbeterd door gebruik van de Leap-bewegingssensor, die potentie heeft om bij te dragen aan de ontwikkeling van behandelprotocollen, gebruik bij patiënten in een klinische omgeving en het snel beoordelen van hand gerelateerde stoornissen. We evalueerden oppervlakte EMG als een manier om intentie van handbewegingen te herkennen bij mensen met DMD en vonden dat dit een haalbare manier is om dat te bereiken. De daaropvolgende toepassing van myocontrol-methoden voor real-time herkennen van de intentie van handbewegingen toonde aan dat voor taken met één vrijheidsgraad directe besturing een goede benadering is. Directe controle werd verder getest met een deelnemer met DMD die de SymbiHand draagt en toonde de potentie van dit apparaat om de handfunctie te verbeteren en vermoeidheid te verminderen tijdens het uitvoeren van ADL voor personen met een DMD.

CHAPTER 1

GENERAL INTRODUCTION

The human hand is a very complex and versatile instrument; a powerful tool for interacting with the environment and being able to manipulate it [1]. The use of the hand enables the individual to live independently and being socially active [2]. This is evident by the fact that the hand is being studied by a vast spectrum of sciences including, anthropology, philosophy, linguistics, engineering, haptics and cognitive and clinical neuroscience. Individuals with Duchenne muscular dystrophy (DMD), however, due to severe muscular weakness caused by the lack of dystrophin [3] live for many years without this instrumental function which hinders their social participation [4] and decreases their quality of life [5].

Currently, new emerging technologies in the field of robotic exoskeletons encourage the belief that exoskeletons can be of use for individuals with DMD and partially restore their progressively diminished hand function [6]. The functionality of the legs is effectively supported using wheelchairs. The Flextension A-Gear project [7], developed passive and active arm supports for individuals with DMD [8]. Currently, the Symbionics 2.1 [9] explored the feasibility of an active support for the trunk and the neck of individuals with DMD. The eNHANCE collaborative effort explores the integration of arm and hand active support, together with behavioral modelling in order to predict the user motor intention [10] for individuals with Stroke and DMD. This work presents the effort by Symbionics 1.3 [11] to characterize the hand of individuals with Duchenne muscular dystrophy (DMD), and decode hand motor intention for controlling an active hand orthosis.

The current part presents a general overview of the disease, followed by a description of the current state of the art in assistive devices for individuals with DMD and the ongoing research on active assistive devices and motor intention decoding in DMD. Finally, the goal of Symbionics 1.3 and a description of the roadmap we followed to reach that goal, together with the outline of this dissertation are presented.

1.1 DUCHENNE MUSCULAR DYSTROPHY

Background

DMD belongs in a group of inherited muscular dystrophies, that affect the muscles with fiber degeneration, and it is the most common and severe form of those [12]. The first registered case was reported in 1836; however, it was not identified as muscular dystrophy [13]. In 1852, there were the first indications on how it is genetically transmitted through females, but it only affects males [14]. DMD was first described by the French neurologist Guillaume Duchenne and subsequently his name was given to the disease due to his significant contribution [14]. Since then and until the 80's when the dystrophin gene was discovered [15], little was known about what causes DMD. Nowadays, we know that DMD is an X chromosome-linked progressive neuromuscular disease, which is passed on by the mother [3]. The mother is referred to as acarrier, and despite rarely expressing any symptoms, can transmit the mutation to the son.

Pathophysiology

The dystrophin protein is one of the many proteins involved in muscle cell processes and the gene that encodes dystrophin (which constitutes the largest gene known [15]), is located in the X chromosome [16]. Despite its low occurrence (constitutes around 0.002% of the proteins found in striated muscle) plays a very important role for the integrity of the muscle cells membrane [16]. The lack of dystrophin that characterizes DMD, contributes to cellular instability and the progressive leak of intracellular components [16], which results in increased levels of creatine kinase (CK), used to diagnose DMD [17]. Individuals with DMD suffer from progressive severe muscular weakness which affects skeletal, respiratory and cardiac muscles [18]. Regarding the extremities, proximal muscles are the first to be affected [18]. Dystrophin is moreover distributed in the smooth muscle and in the brain as well, leading to mental deficiencies in several individuals with DMD [19], associated with low average IQ [20].

Epidemiology

DMD is the most common form of muscular dystrophy, with an incidence of 1 out of 4000 live male births [5]. The prevalence of DMD is reported to range from 1.9 to 10.9 individuals per 100.000 males [17]. Regarding the

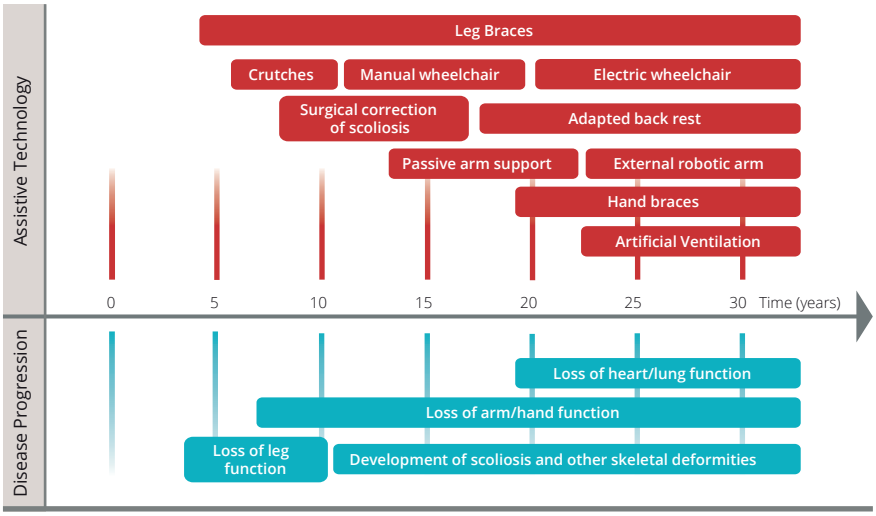

Figure 1.1 ***This figure shows the progression of the disease that hinders crucial bodily functions and the parallel technological interventions that aim to counter the disease symptoms. Adapted from [8].***

mortality rates of DMD, technology advances and improved standards of care, significantly increased the life expectancy of individuals with DMD [21], as reported by also by recent meta-analysis on DMD mortality studies [17]. This is expected to lead to an increased number of adults living a longer time, yet with significant impairment and strong dependency on caregivers [22] or external aids [23].

Progression Pattern

Cognitive Function - The presence of dystrophin in the cerebellum and the hippocampus in the brain and its decrease in the brains of individuals with DMD causes cognitive weakness [15]. According to Cotton et al. [20], showed a great heterogeneity in IQ scores from 14 to 134, illustrating that there are individuals with DMD that are highly intelligent. However, the average IQ of the 1200 individuals that participated in his study was 80, showing a "low average". Both language related IQ and motor and visual performance related IQ, remain relatively stable and unaffected by the progression of the disease [20]. Additionally, individuals with DMD present short-term memory deficits [15], impaired ability in processing visual information [24] and even individuals without any obvious intellectual

disability, present a deficit in implicit learning [25], affecting their ability to learn complex information in a subconscious manner.

Physical Function - Despite the high clinical heterogeneity that is present in the progression of individuals with DMD [26], according to Lobo-Prat [8] there is a disease progression pattern (Figure 1.1). The main components of this pattern include the early onset of ambulatory difficulties around the age of 5-6 and the loss of independent ambulation by the age of 12-14 [17]. Subsequently, the trunk gets affected and scoliosis develops mainly due to the wheelchair confinement [15] and also cardiac and respiratory functions are affected [17]. Around the age of 7 the arm is affected and lastly, around the age of 20 the hand and wrist [27]. Individuals with DMD often adopt awkward postures in order to compensate for their muscle weakness or adopt less energy consuming strategies in order to reduce their burden [15]. This leads to the disuse of their limbs and results in the developments of muscle shortage and joint contractures [28], that subsequently lead to further disuse.

Quality of Life - Quality of life presents a very important aspect in the life of individuals with DMD [29]. The extended life expectancy achieved for individuals with DMD has led in them being able to acquire paid jobs and actively participate in society [15]. They can use computers and even live independently, and this happens more frequently in the last years, and it is accompanied by the ability to start a relationship and even a family [15]. This was achieved mainly via technological aids and the fact that individuals with DMD are increasingly treated as functional members of the society [15]. From the previous, it becomes clear that quality of life of individuals with DMD is tightly linked to their functional independence. In line with that, the extension of the life expectancy of individuals with DMD which leads to further deterioration of hand and wrist function now becomes an important issue, as their loss can result in lower social participation and independence and subsequently in lower quality of life [2]. However, the results from studies trying to systematically assess the quality of life of individuals with DMD are rather inconclusive and the need for a better assessment is more essential than ever [17].

Treatment

The development of systematic treatment guidelines, multidisciplinary approaches and recent technological advancements, has led to impressive improvements in the way DMD is treated [17], [21], [30], [31]. However, individuals with DMD are currently not treated uniformly across the world, or even within the same continent or country, as it is evident from the variable treatments that are reported by Ryder et al. depending on each country [17].

Cure - To this point, there is no cure for DMD. Most cure seeking approaches focus on targeting the problem in the dystrophin gene [32] by gene therapy [33], exon skipping [34], stop codon read-through [35] and gene repair [36], with numerous exciting clinical trials currently underway [37]. Recently, a study was published in ***Science,*** with very promising results on a canine model. In this study, researchers were able to use CRISPR gene editing technology to restore dystrophin expression in a dog model [38].

Medical Treatment - Medical treatments currently aim at delaying the process of the disease rather than curing it. The most common medical treatment for DMD includes the use of corticosteroids [17], in order to prolong ambulation [30]. Moreover, supplements such as carnitine, aminoacids, anit-inflamatories and anti-oxidants are being used; however, there is a complete absence of data supporting such treatments [30].

Respiratory and Cardiac Treatment - Nocturnal ventilation for respiratory management in later stages of the disease has been shown to increase life expectancy as it reduces complications, occurring from the weakening of respiratory muscles [31]. The main reason for DMD mortality is cardiac arrest. It is currently treated by frequent assessments of the heart function and efforts to manage cardiomyopathy and ensure cardiovascular health. In the later stages, anticoagulation therapy is also suggested [31].

Surgical Treatment - Various surgical interventions are employed for individuals with DMD. Lower-limb joint contracture in the ankle and knee are often treated with corrective surgery in order to increase range-of-motion (ROM). Moreover, scoliosis is often treated with posture corrective surgery around the age of 10 (Figure 1.1). Finally, gastrostomy for the better

nutritional support and tracheostomy for ventilation, are considered in later stages [31].

Physical Therapy - Less invasive interventions include physical therapy. Physical therapy for DMD aims mainly in the passive stretching and positioning of the limbs, in order to facilitate muscle extensibility and prevent joint contractures [30]. Individuals receive regular stretching of their ankle, knee and hip, during bot ambulatory and non-ambulatory phases. Later, and in accordance with the progression pattern, they also receive stretching of the shoulder and elbow joints and finally of the wrist and fingers [31].

Exercise - It is recommended, that individuals with DMD, should avoid eccentric and high resistance training exercises [39]. However, new guidelines, promote the use of sub-maximal aerobic exercise and gentle functional strengthening such as swimming-pool exercises [31]. Studies on the benefit of sub-maximal exercises have often contradictory conclusions. Several of them report limited or no benefit; however, there is a clear lack of controlled studies on many exercise related parameters, which would give a more clear view on the benefits of exercising [40]. More recent studies showed the beneficial effect of assisted bicycle training in delaying functional deterioration in individuals with DMD [28] and also similar benefits were observed for the upper extremity [41], [42].

Treatment Costs - A disease like DMD is treated in a multi-disciplinary way as described and many aspects of the disease are a subject of intervention or therapy. This results in a high cost of the current treatment for individuals with DMD, which increases with the disease progression [17] and a lot of time allocation for different check-ups in every hospital visit. Additionally, powered wheelchairs [43] combined with passive (e.g. the WREX from JAECO orthopedic, USA [44] or the TOP from Focal Meditech, The Netherlands [45]) or active arm supports (e.g. JACO robotic arm from Kinova, Canada [46] or the iArm from Exact Dynamics, The Netherlands [47]), further increase the disease related costs. These costs are shaping the current health and social care for DMD and increase the burden for both the patients and the healthcare providers.

1.2 COMMERCIALLY AVAILABLE ASSISTIVE DEVICES FOR INDIVIDUALS WITH DMD

Assistive devices can serve to reduce rehabilitation and physical therapy costs, invasive interventions and enhance physical therapy while providing functional benefits [6].

Legs and Trunk

Ambulation problems are treated mainly with the use of wheelchairs (powered or not) [31]. In many cases resting ankle foot orthoses (AFOs) and knee ankle foot orthoses (KAFOs) are worn during the night to prevent contractures [31]. During the late ambulatory and non-ambulatory phase AFOs are also prescribed for daily use to wheelchair users. If contractures in the lower extremity are not severe, a passive standing device or a power standing wheelchair can be used to enhance mobility [31]. When deformations occur in the spine, due to wheelchair confinement, trunk orthoses or custom-made back rests for wheelchairs are recommended [8].

Arms

The arm function in DMD is in the early stages of the disease mainly assisted with passive arm supports with elastic elements and subsequently with actively adjustable passive arm supports to compensate for the increasing effect of gravity [8]. Active arm supports are not broadly used by individuals with DMD. This is mainly due to their bulkiness that results in social stigmatization, and their inability to support daily tasks [8]. Thus, the most common aids to compliment or substitute the arm function of individuals with DMD are external robotics devices that are usually wheelchair mounted and operated by a joystick [8].

Hand and Wrist

As mentioned earlier, the distal function of the upper extremity is the last to be affected in DMD. This has resulted in a lack of systematic research and any significant breakthrough towards active hand and wrist supports. The currently clinically used supports are resting splints (Figure 1.2A), which are aiming in the preservation of the flexibility of the long finger flexors and the prevention of contractures [31]. Those are worn during the night and do not provide any immediate dynamic or

functional support [31]. The most recent hand orthosis for individuals with DMD found in literature includes the development of a new resting passive orthosis [48] for the wrist and the hand (Figure 1.2B). This study emphasized the treatment of the wrist and the thumb separately (unlike the common practice), and reported promising results, regarding joint mobility and joint contracture delay.

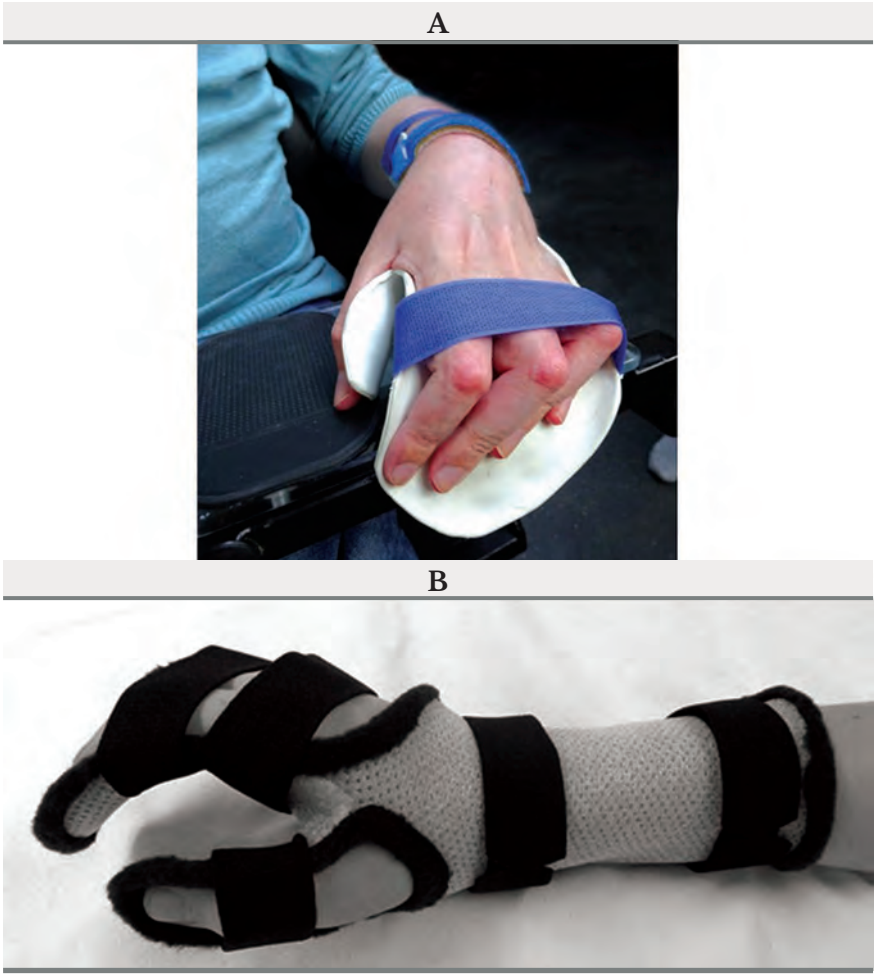

Figure 1.2 A) A commercially available hand splint currently prescribed to individuals with DMD, in order to prevent flexion contractures and preserve flexibility in the hand. B) A passive orthosis for individuals with DMD, that aims to preserve range of motion (adapted from [48]).

1.3 RESEARCH ON ACTIVE SUPPORT FOR INDIVIDUALS WITH DMD

Currently most of the assistive devices used for individuals with DMD are passive resting orthoses [31], however, the benefit of active support is already identified and according to experts can have a beneficial effect [6] and in some cases active assistive devices are already prescribed [8], [31]. In the previous years, DMD received a lot of research attention, mainly in the Netherlands and the United Kingdom and also in the United States of America, with the local Parent Organizations, being very active [49]–[51]. This led to a variety of research projects that aimed to develop supportive technologies in the form of wearable exoskeletons, for various functions that are affected by the disease.

Arm and Hand Support

The eNHANCE project is a European Horizon 2020 project, with its main partners in Enschede and London [10]. The main objectives of this project include the development of technologies for the enhancing and training of the upper extremity motor function, of individuals with physical disabilities. Within its scope, a complete arm and hand mechatronic support is being developed for individuals with Stroke and DMD. This device aspires to be intuitively controlled by means of a multi-modal system including eye tracking, sEMG, motion sensors and interaction forces. A secondary function will be the assessment and real-time characterization of the user and the user's behavior, in order to create a personalized control model for each user.

The Flextension A-Gear project [7] was a national Dutch project, which aimed at the development of an arm exoskeleton for individuals with DMD [8]. The main breakthroughs of this project were the passive and active A-Gear arm orthosis and the A-Arm (Figure 1.3). The passive and active A-Gear, both yield five degrees of freedom (DOFs). The A-arm is an active planar support with two DOFs. In the Flextension project, interaction force and surface electromyography (sEMG) were investigated as potential candidates for the intuitive motor intention decoding of arm movements. Both methods showed merit for individuals with DMD and were deemed worthy for further investigation [8].

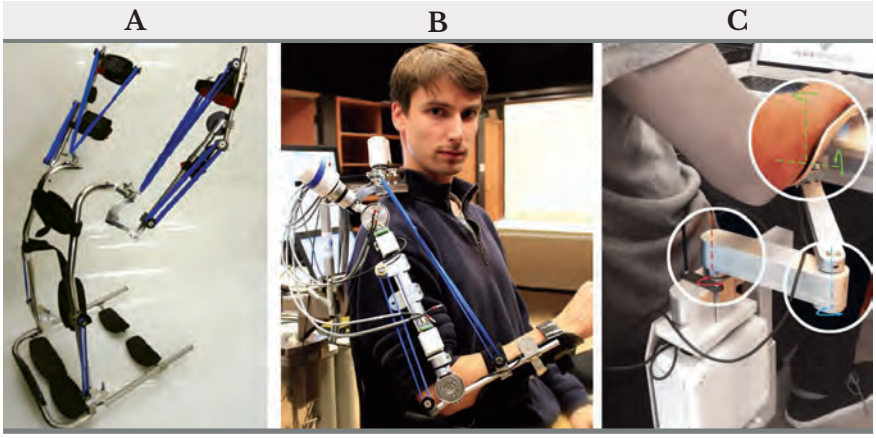

Figure 1.3 A) The passive A-Gear (adapted from [296]*). B) The active A-Gear. C) The A-Arm planar arm support (adapted from* [297]*).*

Trunk and Neck Support

The promising results of the Flextension project, have led to the need for further investigation of assistive robotic technologies for individuals with DMD. For a person to be able to functionally exploit the arm movements, movement of the trunk is necessary to increase the reachable workspace, while the neck is needed to provide visual feedback of the arms position. As the disease progresses individuals with DMD experience difficulties with the active control of their trunk and neck muscles. This leads to deformities, scoliosis and inability to voluntarily increase the reachable arm workspace. This problem was addressed by the Symbionics 2.1 project [9]. The aim of this project was to develop wearable robotic exoskeletons, for the dynamic and intentional assistance of the trunk and the neck of individuals with DMD and integrate it with the Flextension A-gear to further enhance its functionality. A first passive trunk support prototype (Figure 1.4A) was developed and evaluated by Mahmood et al. [52], while an active one (Figure 1.4B) was developed and evaluated by Verros et al. [53]. Both evaluations were performed with healthy participants.

1.4 MOTOR INTENTION DECODING IN DMD

A crucial component for the control of active devices is the effective decoding of motor intention. This requires methods to interface the user with the device in a robust and intuitive way. Currently in DMD, this is mainly achieved via a joystick attached on a powered wheelchair table, which controls the wheelchair and additional devices attached to it.
Regarding individuals with DMD, a recent number of studies by Lobo-Prat et al. [8] focused on the motor intention decoding of the arm. Force and sEMG were identified as promising methods to decode motor intention in individuals with DMD. Despite the unintuitive concept of using muscular signals to decode motor intention in a group of individuals suffering from a muscular disease, myocontrol has shown potential and even more surprising for individuals with DMD, where the disease was in later stages [54]. sEMG signals with enough merit for motor intention decoding, were identified even in a very late stage individual with DMD [55].

Regarding the trunk, Verros et al. [53] have evaluated force and sEMG as potential candidates for decoding trunk motor intention in individuals with DMD. They illustrated the merit of force, sEMG and joystick as potential control interfaces for an active trunk support. However, the study was performed only with healthy individuals.

Polygerinos et al. [56], showed promising results in terms of the

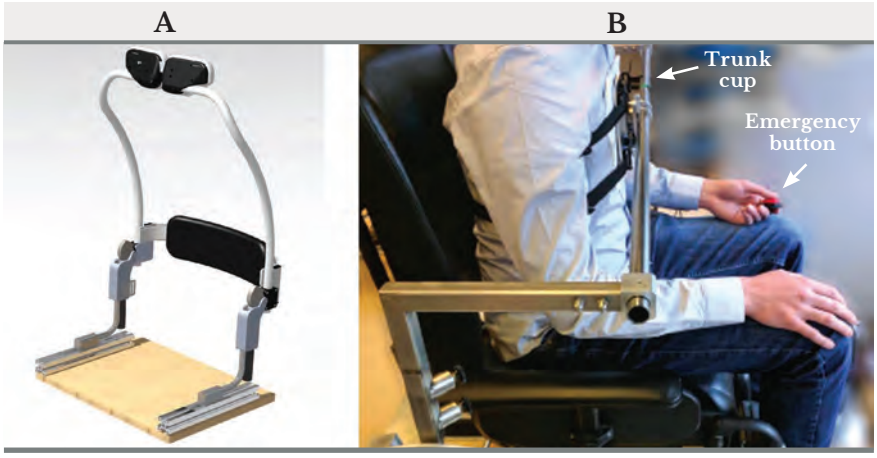

Figure 1.4 Prototype of a A) passive (adapted from [52]*) and an B) active trunk support (adapted from* [53]*) for individuals with DMD.*

functional decoding of motor intention from the hand/wrist with one individual with muscular dystrophy, in order to control a soft robotic glove. Additionally, Vogel et al [57], performed a study with a participant with spinal muscular atrophy, were he successfully decoded in real-time coordinate arm and hand motions for controlling a virtual robotic arm. However, the findings of both studies do not explicitly refer to DMD, but to similar conditions.

1.5 EXISTING ACTIVE HAND ORTHOSES

A recent comprehensive review by Bos et al. [1], gathered and organized the collective endeavors in the development of active hand orthoses worldwide. This effort was performed in order to discuss design choices and create a framework for the development of such devices. The results reveal a significant acceleration in the development of active hand orthoses. This becomes evident as more than half of the 165 devices being identified in total, have been developed in the past 7 years. Another interesting result is that the majority of the identified devices, aim to provide in house rehabilitation or help with ADL. However, only in rare cases pathologies like muscular dystrophy are specifically addressed in literature, with most of the devices being developed for post-stroke rehabilitation [1]. If the specificities found in the hand function of individuals with DMD or other muscular dystrophies, are not addressed, such groups may fall short in specialized devices compared to more prevalent groups like stroke survivors [1].

1.6 PROBLEM DEFINITION

From the aforementioned literature, a few problems and limitations regarding research on the hand function of individuals with DMD were identified. Similar to the trunk and the neck movement, the hand is an integral component of the distal upper extremity, which allows the interaction with the immediate environment and object manipulation. The functionality of the arm cannot be properly assisted, when the hand is not properly supported.

- It is evident, that due to technological and medical advancements, more and more individuals with DMD will reach the stage that hand

is affected and will live for decades with that impairment.

- This will directly affect their independence and the independence related quality of life, as well their ability to be socially active. Additionally, the costs for rehabilitation and the time needed to address all different functional issues related to the progression of the disease will increase
- Currently, ambulation is adequately supported using wheelchairs. The arm is sufficiently researched, and arm supports are translated into the market. There are active efforts to combine these with a trunk and neck support.
- However, all these efforts aim at increasing the ROM of the arm and enable a larger reachable space, without addressing the function of the distal part of the arm, namely the hand. Without the ability to use the hand and the wrist, the increased reach of the arm is not sufficient by itself to results in a functionally used limb.
- The wrist and hand functions are currently substituted by external wheelchair mounted robotic devices that do not promote user involvement, and thus results in disuse. Disuse is proved to results in the fastest development of contractures and in reduction of muscle flexibility and thus ROM.
- Currently the most common clinical treatments for the hand, include passive resting hand splints, which are worn during the night, to preserve functional ROM and muscle flexibility.
- Existing active hand orthoses have been focused on more prevalent patient groups like stroke survivors and fail to address the specificities of DMD.
- The current research towards motor intention decoding for the active hand support for individuals with DMD, shows modest results and it is limited.

1.7 SYMBIONICS 1.3

At the end of 2014, the Symbionics 1.3 [11] project started in order to address the active support of the hand and wrist functions, in individuals with DMD. We believe that robotic exoskeletons are the solution, to the progressively deteriorating hand function this population is experiencing. Hence, we developed a hand exoskeleton that is natural to control in

order to raise the quality of life and social acceptance and participation of individuals with DMD. According to Bos et al. [1], most existing active hand orthoses, are targeting stroke survivor rehabilitation and therefore, there is currently a gap in the development of hand orthoses specifically for individuals with DMD.

Developments

The development of the hand orthosis for individuals with DMD was split in two different approaches. Considering the comprehensive effort of Bos et al. [1] to structure the currently available solution space for the development of hand orthoses, we developed two prototypes. The first prototype [58] that was developed (Figure 1.5A), aimed at a very light-weight design and a low-profile (the device is close to the fingers). The force transmission mechanism was based on a novel concept, using tape springs, which contributes to a low weight and profile hand orthosis, which underactuates all fingers. In its current form, this orthosis supports only the index and middle fingers. The mechanism showed promising results by being able to transmit a high force output. However, this prototype was not tested with an individual with DMD, by the time this thesis was submitted. The second prototype (Figure 1.5B) orthosis [59] is based in the use of miniature hydraulics to transmit mechanical work and underactuate all fingers. The initial design of the prototype was based on commercially

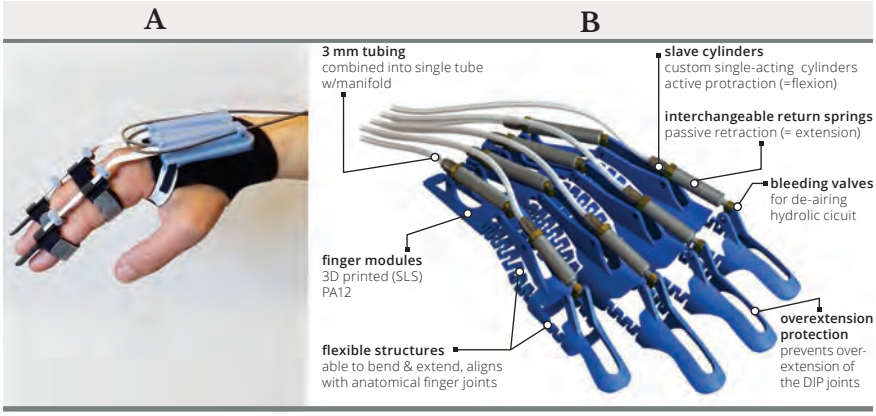

Figure 1.5 A) The first prototype developed in the Symbionics 1.3 project. Its design is based on a novel tape spring mechanism. B) The second prototype (SymbiHand). This design is based on the concept of miniature hydraulics

available components and 3-D printing [59], resulting in a low weight hand orthosis (150 g). Later, it was extended with the use of customized components with a new weight of 213 g and was named SymbiHand. In its current state, the SymbiHand orthosis can support four fingers. Every finger is supported by a separate finger module, which can be attached and detached at will. This creates a highly modular hand orthosis. This is an important requirement for the donning and doffing in individuals with DMD, especially in the case of contractures and stiff fingers, were a glove like design would be insufficient. This prototype was evaluated for its capacity to provide the needed bandwidth for hand movements [59] and it was further tested with an individual with DMD (Chapter 7). Both prototypes developed within the Symbionics 1.3 project, lack a thumb and a wrist module.

Team Composition and Roles

The main research team of Symbionics 1.3 (Figure 1.6) was composed by eleven members, working in two Universities and one company. Ronald A. Bos, a PhD student in TU Delft, was responsible for the exploration of novel mechanisms and components, that led to the development of the SymbiHand orthosis for individuals with DMD (Figure 1.5B), under the supervision of Just L. Herder and Dick H. Plettenburg. Similarly, Claudia J. W. Haarman, a

Figure 1.6 ***The Symbionics research team with all the projects and (almost) all the members of the project's user committee. The highlighted people are those directly involved in Symbionics 1.3 project.*** *From left to right:* ***Leo Hoogendoorn (TMSi), Jan koudijzer (Festo), Ronald Bos (TU Delft), Dr. Dick Plettenburg (TU Delft), Claudia Haarman (UTwente), Kostas Nizamis (UTwente), Prof. Bart Koopman (UTwente), Henry van der Valk (NWO/TTW), Elizabeth Vroom (Duchenne Parent Project), Arjen Bergsma (UTwente). The picture was taken at the kickoff meeting of the Symbionics project.***

PDeng student in UTwente and Hankamp Rehab, was responsible for the development of the first prototype, using a novel tape spring mechanism (Figure 1.5A), under the co-supervision of Freek Tönis and Herman van der Kooij. Finally, I was responsible for the characterization of the hand/wrist neuro-motor function, and the development of hand/wrist motor intention decoding methods for individuals with DMD, and their implementation in the two prototypes, working closely with Noortje H. M. Rijken, under the supervision of Bart F.J.M. Koopman, Massimo Sartori and Arjen Bergsma. All the members of the team were closely collaborating for the duration of this project in an optimal way and all individual developments were successfully combined to create two prototypes. Additionally, to the main research team, several specialists and clinical experts were involved, providing their useful clinical perspective and assisting with the testing of our developments with individuals with DMD. Last but not least, via the help of the Duchenne Parent Project in the Netherlands, we were able to hold focus groups and involve as many as possible individuals with DMD in our thinking process. This gave incredible insights for the design of the two prototypes and ensured their relevance regarding the wishes of their future users.

1.8 RESEARCH OBJECTIVES AND QUESTIONS

Current hand supports available for individuals with DMD, are passive resting splints, which are worn over night. It is evident that they cannot offer dynamic and functional support of the hand and enhance user participation. When the hand function is lost or heavily impaired, individuals with DMD use external, wheelchair mounted robotic devices, to interact with their immediate environment and manipulate objects. An active hand support, such as the SymbiHand can provide adequate assistance and enable individuals with DMD, to perform hand related tasks of their own volition with the active use of their own hands. In order to control such a device in a natural way, we need a successful way to decode hand motor intention of the user and additionally, we need insights in the neuro-motor function of the hand of individuals with DMD.

The goal of this dissertation is "***the characterization of the neuro-motor function of the hand, the decoding of hand motor intention decoding and the implementation of this in an active hand support for individuals with DMD.***" To this end, several research questions were formulated and investigated.

Research Questions

I. Can we characterize the neuro-motor hand function of individuals with DMD? Part I (Chapters 2-4)

II. Can we identify a feasible way to decode hand motor intention in real-time in order to control an active hand orthosis for individuals with DMD? Part II (Chapters 5-7)

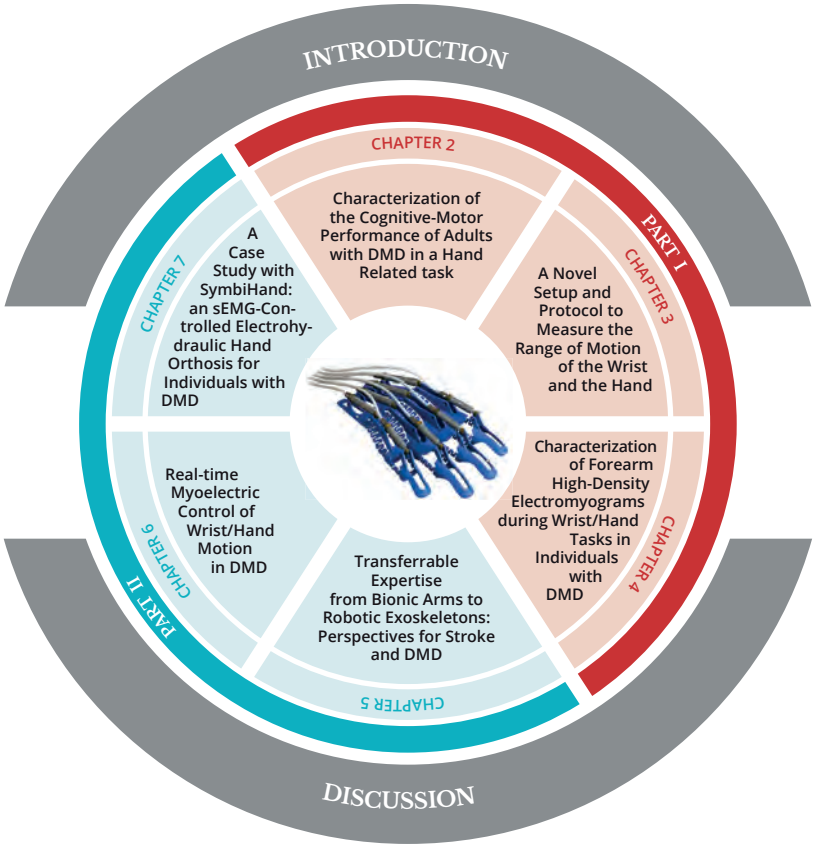

Figure 1.7 *Overview of the parts corresponding to the research questions and the chapters of this dissertation*

1.9 OUTLINE OF THIS DISSERTATION

All the chapters of this dissertation (excluding the introduction and discussion), were written as full journal papers. Figure 1.7 shows the diagram of the outline of this dissertation.

PART I

HAND NEURO-MOTOR CHARACTERIZATION IN DUCHENNE MUSCULAR DYSTROPHY

This part describes the studies we performed, to gain insights into the hand neuro-motor function of individuals with DMD. A three-level characterization was performed, including cognitive-motor performance characterization (Chapter 2), the creation of a reliable tool for measuring hand kinematics to characterize the hand ROM in DMD (Chapter 3) and the characterization of forearm electromyograms (Chapter 4). All studies were performed both with healthy and DMD participants, except the study described in Chapter 3, in which only healthy participants took place. The systematic characterization of the hand neuro-motor function of individuals with DMD gave us insight in the level of impairment in the hand and the characterization of forearm electromyograms, motivated our choices, regarding the feasibility of sEMG for motor intention decoding as described in in part II.

Chapter 2 CHARACTERIZATION OF THE COGNITIVE-MOTOR PERFORMANCE OF ADULTS WITH DUCHENNE MUSCULAR DYSTROPHY IN A HAND RELATED TASK

The main assumption in our project was that individuals with DMD need active hand assistance. However, it is not clear how different individuals with DMD are compared to healthy individuals regarding their hand function. This chapter presents a systematic analysis on dynamic multi-finger, cognitive-motor performance of individuals with DMD, by employing a visuo-motor task, in order to give insight in their residual hand

function. This study was performed with three participants with DMD and eight healthy participants, in order to serve as a healthy baseline for the purposes of comparison. Additionally, the healthy participants performed seven sessions and we assessed the training effects. Task related cognitive-motor performance was evaluated using information transfer rate (ITR) and task perceived workload.

Chapter 3 A NOVEL SETUP AND PROTOCOL TO MEASURE THE RANGE OF MOTION OF THE WRIST AND THE HAND

It is known that due to contractures and muscle stiffness, individuals with DMD experience a decreased active and passive ROM in the hand compared to healthy individuals. This can make the customization and fitting of an active hand orthosis challenging. Currently measurement of finger ROM is performed with the use of the goniometer, resulting in a time-consuming process of questionable reliability, when the hospital visiting time of an individual with DMD is quite valuable. This chapter describes our assessment of the validity and reliability a commercially available optical sensor (Leap Motion) for the fast and reliable measurement of active hand ROM in DMD. We used the Leap Motion sensor to measure the active hand/wrist ROM of 20 healthy adults for all the DOFs in the arm and wrist.

Chapter 4 CHARACTERIZATION OF FOREARM HIGH-DENSITY ELECTROMYOGRAMS DURING WRIST-HAND TASKS IN INDIVIDUALS WITH DUCHENNE MUSCULAR DYSTROPHY

The decision to consider sEMG for the decoding of hand motor intention was motivated by recent previous studies in individuals with DMD, where sEMG was used for decoding arm motor intention [8]. This led to the question of how feasible this approach for the forearm muscles of individuals with DMD is. To answer this, we characterized the forearm sEMG of healthy and affected participants, using a high-density sEMG grid around the forearm, during wrist/hand tasks. This study was performed with three participants with DMD and eight healthy participants, which served as a healthy baseline for the purposes of comparison. The results of this study motivated directly the studies described in part II of this dissertation.

PART II

HAND MOTOR INTENTION DECODING IN DUCHENNE MUSCULAR DYSTROPHY

This part was directly motivated by the previously conducted studies as described in part I, and it is dedicated to our studies for the identification of a feasible motor intention decoding method, to control an active hand orthosis for individuals with DMD. This part was also broken into three levels. Firstly, we explored motor intention detection approaches commonly used in bionic limbs and offered our perspective on their use in robotic exoskeletons for individuals with DMD (Chapter 5). Secondly, inspired by the work described in chapters 4 and 5 we identified myocontrol as a promising motor intention decoding approach and tested its real-time application in individuals with DMD, without (Chapter 6) and with a robotic hand exoskeleton (Chapter 7).

Chapter 5 TRANSFERRABLE EXPERTISE FROM BIONIC ARMS TO ROBOTIC EXOSKELETONS: PERSPECTIVES FOR STROKE AND DUCHENNE MUSCULAR DYSTROPHY

This chapter presents our perspective on the useful knowledge that exists in the field of bionic arms regarding motor intention decoding, and how this could be translated in the field of robotic exoskeletons. Different human-machine interfaces (HMIs) are described in this chapter with concrete applicative examples of hybrid HMIs in two selected clinical scenarios including post-stroke and Duchenne muscular dystrophy individuals. Furthermore, the chapter presents a perspective on new avenues for the translation of robotic exoskeletons that inspired our choices for motor intention decoding described further in part II of this dissertation.

Chapter 6 REAL-TIME MYOELECTRIC CONTROL OF WRIST/HAND MOTION IN DUCHENNE MUSCULAR DYSTROPHY

In this chapter, we describe a study where we applied and compared two broadly used approaches for myoelectric control, namely sequential direct

control (DC) and pattern recognition (PR) control. The classified tasks were divided in 1- and 2-degree-of-freedom (DOF). Additionally, we combined myocontrol with an admittance model as described in Part I. This study was performed with one participant with DMD and ten healthy participants, which served as a healthy baseline for the purposes of comparison. The results of this study motivated directly the study described in chapter 7.

Chapter 7 A CASE STUDY WITH SYMBIHAND: AN SEMG-CONTROLLED ELECTROHYDRAULIC HAND ORTHOSIS FOR INDIVIDUALS WITH DUCHENNE MUSCULAR DYSTROPHY

This chapter presents our case study of the SymbiHand orthosis with one individual with DMD. sEMG was identified as a motor intention decoding method and its feasibility was verified as described in Chapter 5. This myocontrol method and its combination with an admittance model as discussed in Chapter 2 were tested in real time, as described in Chapter 6. We applied the knowledge gained in those previous studies and applied a direct control paradigm in our case study with the SymbiHand, combined with an admittance model. The participant with DMD was able to control the opening and closing hand motion of the SymbiHand while performing a force tracking computer task.

Chapter 8 DISCUSSION

The final chapter of this dissertation discusses each of the research questions, elaborates on the lessons learned and finalizes with the future directions for hand motor intention decoding in DMD and the new research avenues that were created by answering the research questions.

PART I

HAND NEURO-MOTOR CHARACTERIZATION IN DUCHENNE MUSCULAR DYSTROPHY

2

CHARACTERIZATION OF THE COGNITIVE-MOTOR PERFORMANCE OF ADULTS WITH DUCHENNE MUSCULAR DYSTROPHY IN A HAND RELATED TASK*

Kostas Nizamis, Wouter Schutte, Jan J. Grutters, Jasper Goseling,
Noortje H. M. Rijken and Bart F. J. M. Koopman

ABSTRACT

Duchenne muscular dystrophy (DMD) is a progressive degenerative muscle disease, affecting, among others, the upper extremities. Effective hand rehabilitation can improve the hand function of individuals with DMD. To reach this goal, we first need to gain more insight into the hand cognitive-motor performance of individuals with DMD. This is the first study employing a systematic analysis on multi-finger, cognitive-motor performance of individuals with DMD. For this purpose, we propose an active dynamic visuo-motor task. The task employed six visual stimuli, a subset of which was activated at each trial. The stimuli were activated with a frequency of 1, 2, 3 and 4 Hz. Eight healthy participants and three participants with DMD performed the task. Additionally, the healthy participants performed seven sessions, and we assessed the training effects. Task-related cognitive-motor performance was evaluated using information transfer rate (ITR) and perceived workload. Regarding ITR, healthy participants performed significantly better than DMD participants; however, this was more evident for trials involving more than three fingers. Workload showed no difference between the healthy and the DMD groups. Healthy participants significantly improved their performance during training. Our results suggest that hand rehabilitation of individuals with DMD should consider multi-finger dynamic training. However, additional research with more individuals with DMD is needed for further generalization of our conclusions.

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2.1 INTRODUCTION

Duchenne muscular dystrophy (DMD) is an X chromosome-linked recessive neuromuscular disease, affecting mainly males. It is diagnosed in childhood, affecting approximately 1:5000 births [60]. In 2013, the population of individuals with DMD in The Netherlands was 420 [61]. Duchenne is caused by mutations in the dystrophin gene that encodes the protein dystrophin, causing its absence or defect [30]. Individuals with DMD suffer from progressive muscle weakness which leads to physical disability, high dependency on caregivers, and shortened life expectancy [62].

Due to advances in health care over the past few years, life expectancy has gradually increased, and currently individuals with DMD can reach the age of 40 [30]. The number of adults with DMD will grow substantially as future therapies, though not necessarily curing, will retard the disease, thus increasing the existing DMD population [22]. Although their lifespan has increased, their hand function remains limited, especially after the age of ten [63]. Individuals with DMD may live longer with impaired hand function, and therefore will be unable to perform basic activities of daily living (ADL) for decades [64].

Still, the main clinically applied hand treatment for individuals with DMD includes physical therapy [22] and passive hand splints [48]. These aim at maintaining a large active range-of-motion (ROM) for the fingers and the wrist and slowing the development of contractures. Furthermore, studies investigating hand function in DMD concern the remaining hand ROM and strength [63], [65], but not dynamic finger performance.

Individuals with DMD can benefit from active-hand-assistive technology that can provide continuous passive motion (CPM) or support

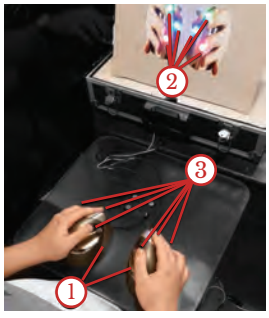


Figure 2.1 A participant with DMD, while using the portable setup with the proposed method, during the visuo-motor task (trial of 6 stimuli at 1 Hz). 1) Vertical mice with three buttons each. 2) LEDs: one for each index finger, middle finger, and thumb of each hand. The LEDs are also color coded: green for the index, red for the middle, and blue for the thumb; and 3) the number of fingers involved in this trial.

their movement based on their intention [6]. In the Symbionics project [11], we are developing a wearable active-hand-assistive device with an intuitive control interface for individuals with DMD. To this end, we have studied the ability of individuals with DMD to control their hand during a visuo-motor task. To the best knowledge of the authors, there is currently no detailed and systematic analysis of the cognitive-motor, multi-finger performance of individuals with DMD. Such a detailed analysis is needed to finally understand how, compared to healthy controls, individuals with DMD can perform. More insight into their hand cognitive-motor performance may enable the development of customized rehabilitation with the use of wearable active-assistive devices.

We employed a visuo-motor task including the use of six fingers. Motor performance was measured via information transfer rate (ITR) [66]. ITR provides a way of quantifying the mutual information exchange between a human and an interface and has important ramifications for the design of human-machine interfaces [66]. The ITR measurement in combination with a visuo-motor task were inspired by the work of Klemmer et al. [67], who sought to assess and optimize ITR in healthy participants during a visuo-motor task. Their participants had to respond by pressing the correct button(s) to five visual stimuli (a subset of those was provided at each time). Five different stimuli presentation frequencies were included in their study, ranging from 1 to 5 Hz. We also decided to measure the perceived workload imposed on the participant by the task, in order to gain an indication of the cognitive performance during the task [68]. The observation of both ITR and workload can show the optimal trade-off between cognitive and motor performance, as related to the task.

In a previously conducted pilot [69], we found that healthy participants and a participant with DMD were able to perform the visuo-motor task. However, the person with DMD showed a lower absolute performance in the task compared to healthy participants. The present study was conducted with eight other healthy participants who performed seven training sessions and two more individuals with DMD. In this study, we wanted to (I)compare the task performance of individuals with DMD to a healthy baseline performance, (II)analyze their motor performance together with their cognitive effort using a Pareto analysis and (III)study the effects of training on the task-related cognitive-motor performance in the healthy controls.

2.2 MATERIALS AND METHODS

Participants

The experiment was carried out by eight healthy adults (six male and two female), ranging from 19-24 years in age, without any hand-related impairment, and three adults with DMD (aged from 20-25). We included participants with different levels of hand function. Participant 1 (DMD 1, 20 yrs. old) was able to functionally use his hand, and minimal contractures relevant to finger movement were observed. Participant 2 (DMD 2, 21 yrs. old) was able to use his hands functionally, but he experienced a decrease in strength. Minimal contractures relevant to finger movement were observed. Lastly, participant 3 (DMD 3, 25 yrs. old) was not able to use his hands for grabbing a pen and was experiencing strong fatigue during the use of his hand. Extensive contractures relevant to finger movement were observed. All participants were capable of clicking the buttons and performing the experiment. The Medical Ethics Committee of Twente decided that this study did not require an ethical approval regarding the healthy participants (Protocol number: K17-51). The study was conducted according to the ethical standards given in the Declaration of Helsinki in 1975, as revised in 2008. For the participants with DMD, the Medical Ethics Committee of Twente approved the study design, the experimental protocol, and the procedures (Protocol number: NL59061.044.16). Both healthy and DMD participants were informed via a letter and signed a consent form prior to the experiment.

Materials and Data Acquisition

The setup (Figure 2.1) used for this experiment was developed at the University of Twente. It consists of a suitcase that contains all the components. The task consisted of a stimulus of blinking (ON/OFF) LEDs to which a participant had to respond by clicking mouse buttons that corresponded to LEDs that are ON. The LEDs were placed in a wooden board in front of the participant in an intuitive position (Figure 2.1). Two vertical mice, one right- and one left-handed, were used as an interface. The LEDs changed state synchronously over time with a frequency of 1,2,...,4 Hz, depending on the trial. The LEDs were ON or OFF with equal probability, independently of each other. The number of LEDs involved in a trial ranged from 1 to 6. The fingers involved were index, middle, and thumb of both

hands. Performing all stimuli subsets for each of the four frequency steps results in a visuo-motor task with 24 different trials. After every trial, the perceived workload was verbally scored by the participants on a 1-20 scale [70]. The setup was chosen to enable the task for individuals with DMD and to resemble a game, since gaming can make the setup more familiar [71].

Based on previous studies on finger independence [72], finger involvement in functional grasps [73], and results on a grasp analysis questionnaire for individuals with DMD, we decided to include the thumb, index, and middle finger of both hands for the analysis of hand performance.

A real-time computer (myRio, National instruments Inc.) was used to control the visual stimuli for the participants. The same computer performed data acquisition, digitizing the mice signals at a sampling frequency of 24 Hz. All the data of the trials were logged. All electrical components were secured on the hollow part of the suitcase and protected by a wooden board. The LEDs and the mice had custom-made connectors, allowing for a quick set-up of the device to enhance its overall portability.

Experimental Procedure

The participants were placed in a chair in front of the setup (Figure 2.1). The protocol was explained to the participants, and they could become familiar with the device until they felt comfortable starting the experiment. The task included 24 trials, containing all combinations of four stimuli frequencies (1-4 Hz, with a step of 1 Hz) and simultaneous components (1-6 stimuli). We grouped the trials based on the number of simultaneous stimuli (six groups with four stimuli frequencies). To avoid for order effects in our results, the group order was randomized per participant. Prior to each trial, the participant was informed about the frequency and the number of stimuli. After every trial, the participant was asked to score the perceived workload [70] on a visual analogue scale, where zero was a very low workload and 20 very high. This assessment technique was chosen because it is very simple to perform and reported as sensitive as multi-dimensional workload assessment techniques such as NASA-TLX [74]. Strong fatigue effects are often observed for individuals with DMD. Hence, for the participants with DMD, fatigue was also scored on a 10-point scale. If there was a reported score of above two, the participant took a short break (10 min), in order to make sure fatigue did not affect the results.

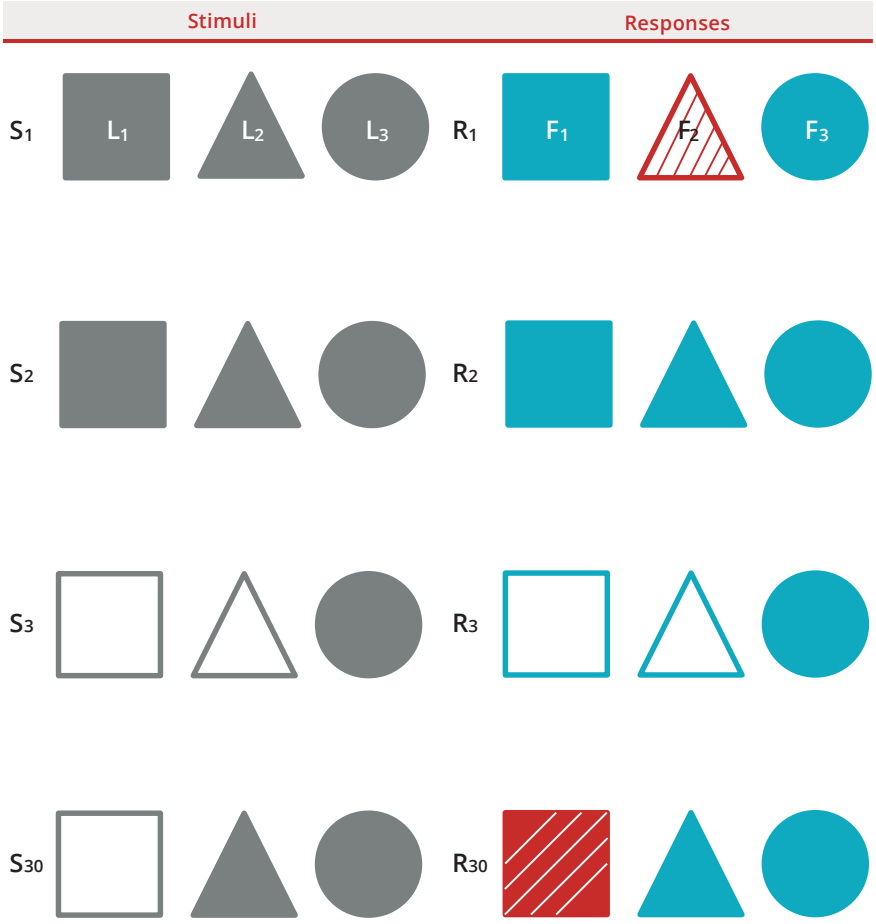
Each trial had a duration of 30s, and, for each trial, a certain number of LEDs was used. For each stimulus in a trial, each LED involved was on or off with equal probability. The participants were instructed to click the button(s) based on the visual stimuli and to try to avoid random clicks. An example of a trial can be seen in Figure 2.2. The order of finger recruitment is right and left index finger, right and left middle finger and right and left thumb, meaning that a trial including, for example, three fingers would be performed by the right and left index and the right middle finger. Healthy participants performed the task seven times over a period of three weeks, in intervals of three days.

Data Analysis

The first step in the data analysis was to determine for each component in each stimulus if the correct response was given. Note that each stimulus was offered for $1/F$ seconds, where F was the frequency of the trial. Every trial had a fixed duration of 30 s; therefore, the response signal per finger was divided into $30 \cdot F$ adjacent intervals of $1/F$ seconds. We assumed that the response to a stimulus was given in the corresponding interval, which we will refer to as a window. Since there was a response delay (incurred by both the participant and the experimental setup), we needed to offset the start of the windows. This offset was different for each participant and each trial, but it was taken as a constant within a trial. The offset was determined by computing for various values of the offset and the total number of correct responses in a trial. The offset was then fixed to the value that maximized the number of correct responses.

Every participant's performance was assessed in terms of ITR and perceived workload. A brief explanation of the metrics is given in Table 2.1

ITR is defined as the mutual information [75] between stimulus and response [66], [67]. We estimated the ITR per finger by counting the number of occurrences of each stimulus (on/off) – response (click/no click) pair.



T = 30 seconds
F = 1 Hz
Number of Stimuli (Ns) = F • T = 30
Number of Stimuli Components (Nc) = 3

Figure 2.2 An example of a trial (three fingers at 1 Hz). In this example, we assume three LEDs (here shown as different shapes) blinking. Solid shapes mean LED on and click. Non-solid shapes mean LED off and no-click. As we have three LEDs for each stimulus, the responses come from three fingers responding to each LED. Red (with stripes) indicates a wrong and blue (no stripes) a correct response. Note here, that a click when there is no stimulus provided is equally wrong to a no-click when a stimulus is provided. In this example, we assume 30 stimuli with a frequency of 1 Hz (1 stimulus/second).

Table 2.1 Performance Metrics

Metric	Short Description
ITR (bits/sec)	The amount of mutual information between stimuli and responses [66].
Perceived Workload	Workload imposed by the visuo-motor task on the participants. It is assessed using a uni-dimensional assessment technique [70]

These numbers provided the maximum likelihood estimate of the probability of these pairs occurring in a trial and an estimate of ITR_{finger}, the ITR per finger per stimulus, as:

$$ITR_{finger} = \sum_{i\in\{on,off\}} \sum_{j\in\{noclick,click\}} I\left(n_i, n_j, n_{ij}, N_s\right), \quad (1)$$

$$I\left(n_i, n_j, n_{ij}, N_s\right) = \begin{cases} \frac{n_{ij}}{N_s} \log_2\left(\frac{n_{ij} N_s}{n_i n_j}\right) & for\ n_{ij} > 0 \\ 0, & otherwise \end{cases} \quad (2)$$

$$ITR_{est} = F \cdot \sum_{1}^{N_c} ITR_{finger} \quad (3)$$

$$n_i = \sum_{j\in\{noclick,click\}} n_{ij} \quad (4)$$

$$n_j = \sum_{i\in\{on,off\}} n_{ij}, \quad (5)$$

where ***nij*** is the number of times event (*i*,*j*) occurs, ***Ns*** is the total number of stimuli provided in the trial and ***Nc*** the number of stimuli components. To illustrate, in a trial at 2 Hz, ***N***=30·2=60. The ITR_{finger} was summed over all fingers and multiplied with the frequency to obtain the total ITR_{est} in a trial, expressed in bits/sec. Note that, for the summation to be valid, we assumed that responses are independent across fingers.

The provided information (PI) per trial refers to the amount of bits/sec that we provide the participant via the visual stimuli. This was calculated as:

$$PI_{trial} = F \cdot N_c \tag{6}$$

Statistical Analysis

All statistical tests were performed following the guidelines proposed by Marshall et al. [76], depending whether the groups we wanted to compare were normally distributed or not and whether they were independent or paired. To check for the normality assumption, we used the Shapiro-Wilk test.

All the data used for the statistical analysis will be available online as a complimentary file to this article. To compare ITR (Shapiro-Wilk test for normality, healthy p = 0.337 and DMD p = 0.260) and workload (Shapiro-Wilk test for normality, healthy p = 0.545 and DMD p = 0.730) between healthy and DMD participants, we performed an independent t-test.

Furthermore, we wanted to compare healthy and DMD participants for each trial. To do this, we treat the ITRs of our healthy participants as observations from a "healthy" population that was normally distributed with a mean and a variance different per trial. For each trial and each DMD participant, we considered the null hypothesis that the ITR of the DMD participant was an observation from the ITRs of the healthy population. Based on this, we computed the lower-tailed p-value, corresponding to the test that the ITR of the DMD participant was significantly smaller than the ITR of healthy participants. The computation of the p-value was done according to [77], i.e. specifically for the situation that we were comparing a single case with a control sample.

For the assessment of training effects on ITR and workload (Shapiro-Wilk test for normality, $p > 0.05$ for all sessions for both ITR and workload), repeated measures ANOVA was used together with a Bonferroni post-hoc test.

The statistical tests were performed with SPSS (IBM SPSS Statistics 24).

Additionally, we performed a Pareto optimization analysis to illustrate the trade-off between ITR and workload. The trials in which the ITR cannot be improved without increasing the workload are called Pareto optimal [78]. We used this analysis to compare healthy and DMD participants as well as to visualize the effects of training.

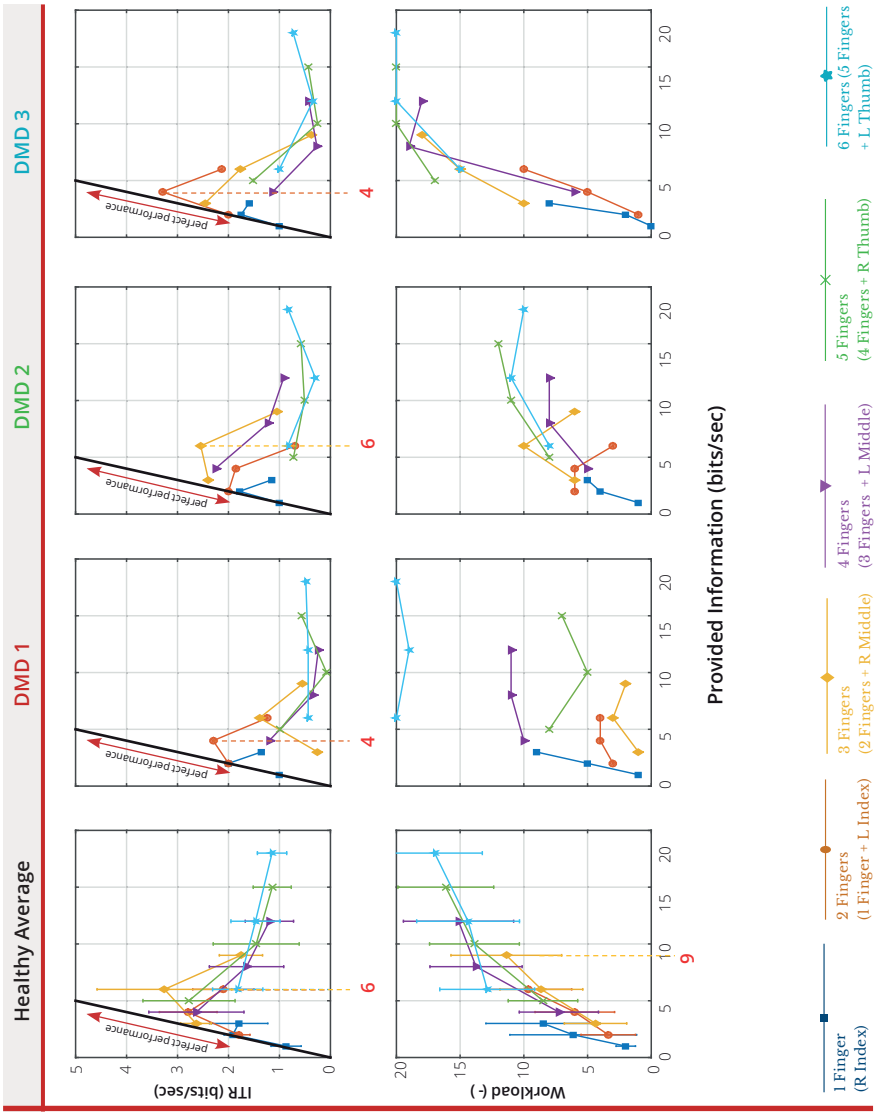


Figure 2.3 The results for all participants. For the healthy group, average mean and standard deviation are plotted for each trial. Provided information can depict more than one trial at the same point. For example (top left plot), 6 bits/sec can represent the second yellow data point (three fingers · 2 Hz), the third orange data point (two fingers · 3 Hz) and the first light blue data point (6 fingers · 1 Hz). The diagonal line represents perfect performance (where provided information is equal to ITR). The DMD participants are placed in order of age from the youngest to the oldest.

2.3 RESULTS

After a first analysis of the recorded data, we noticed that trials of 4 Hz showed very small ITR. This was probably because the participants were not able to cope with these trials in a meaningful way, and mostly random clicking was observed. Therefore, we decided to exclude the 4 Hz trials from the data analysis and the visualization of the results.

Healthy vs. DMD

Figure 2.3 shows the results of ITR and workload as a function of the provided information for all participants. Figure 2.4A summarizes, together with Table 2.2, the statistical analysis performed on each metric between the healthy and DMD participants. Figure 2.4B shows a per trial comparison between healthy and DMD participants for ITR. Figure 2.4A shows for all participants the optimal trials found from the Pareto analysis.

ITR - The highest mean ITR value for the healthy participants was achieved for the three fingers-2 Hz trial. DMD 1 achieved a maximum ITR at two fingers-2 Hz trial. His maximum ITR was the lowest achieved among the DMD participants (2.30 bits/sec). DMD 2 achieved a maximum ITR for three fingers-2 Hz, similar to the healthy average and DMD 3 achieved maximum for the two fingers-2 Hz trial. His maximum (3.29 bits/sec) was the highest value among the DMD participants as well as higher than the mean ITR of the healthy participants (3.25 bits/sec). We can see that healthy participants and DMD 2 achieved the highest ITR at 6 bits/sec of provided information while DMD 1 and DMD 3 at 4 bits/sec.

A difference was identified for ITR (ANOVA, p=0.002) between healthy and DMD participants. A comparison per trial (Figure 2.4B) revealed that the difference between healthy and DMD participants increases when more fingers are involved.

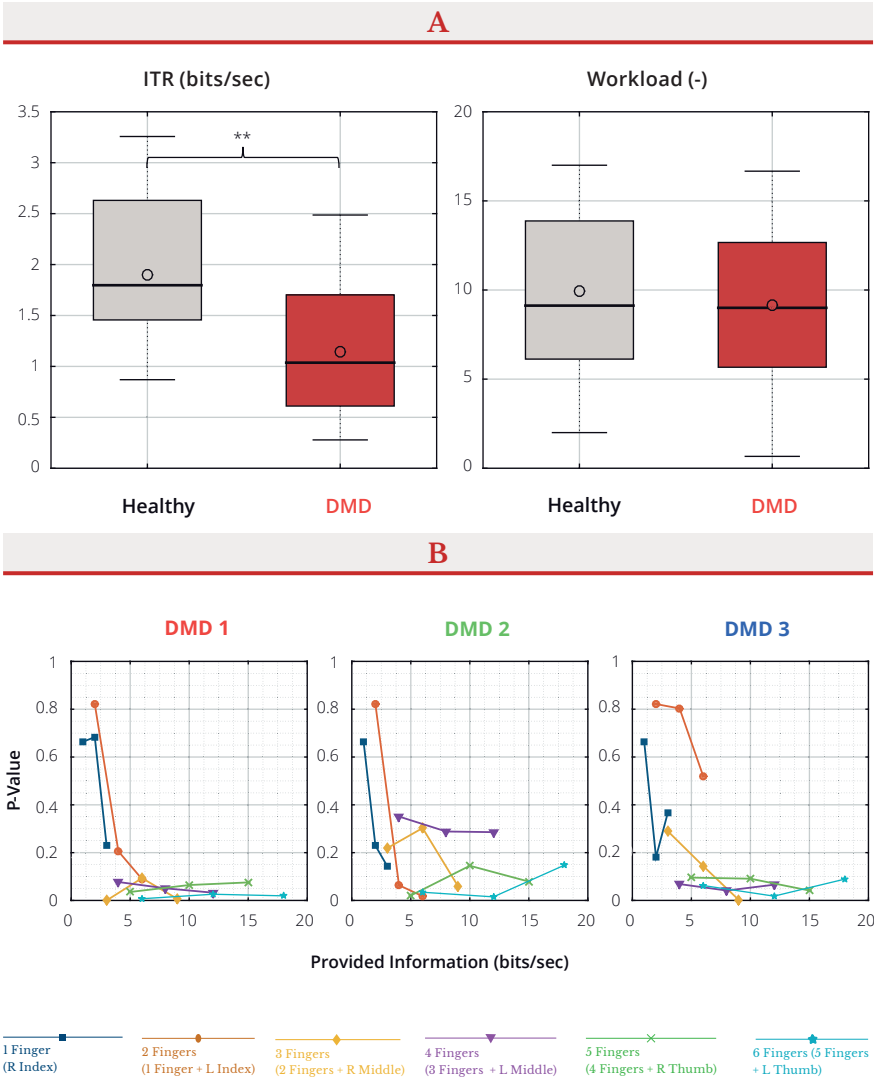


*Figure 2.4 A) Box plots of average ITR and workload during the first session of the healthy group and the DMD participants. The average ITR of eight healthy participants over the 18 trials (1-3 Hz) and the average ITR of 18 trials per DMD participant are shown. Horizontal lines represent the median while circles represent the mean values. * indicates a significant difference at the level of p<0.05, ** indicates p<0.01 and *** indicates p<0.001. B)The differences between the healthy and every DMD participant per trial, regarding ITR.*

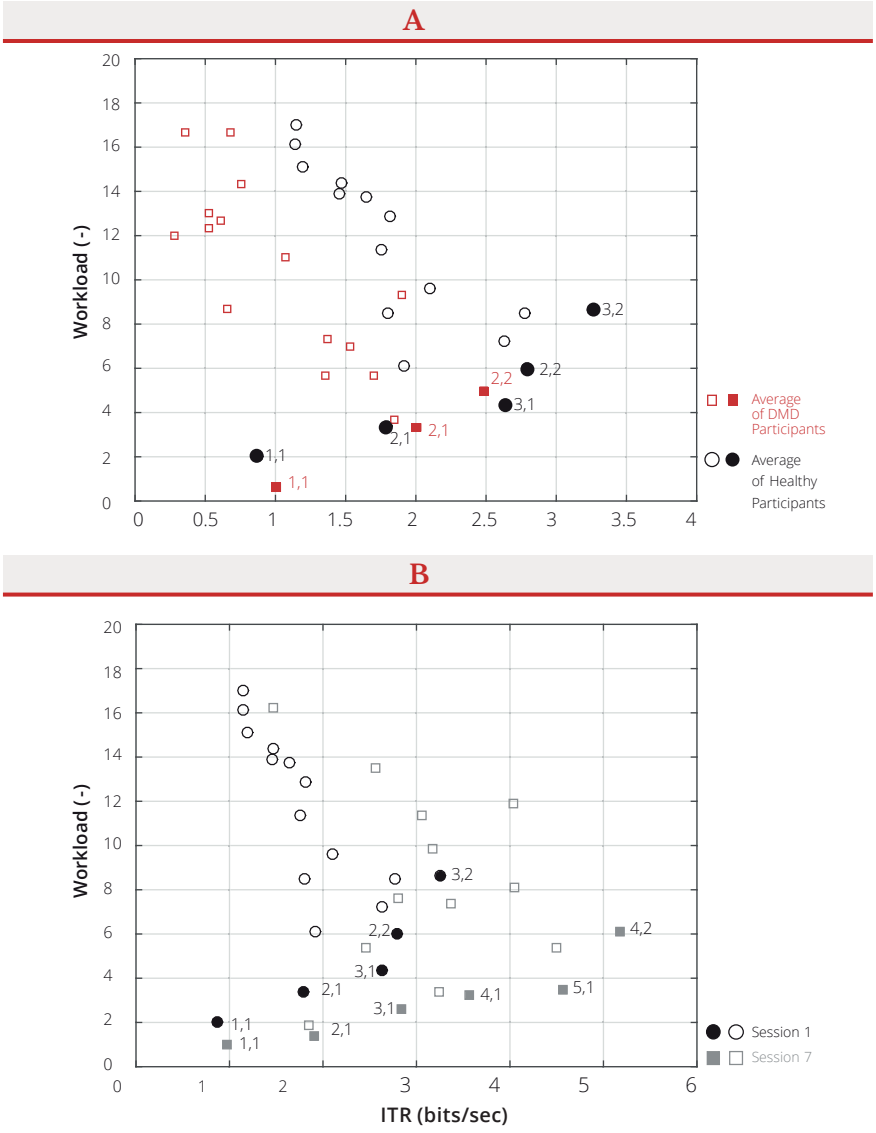


Figure 2.5 The trade-off between ITR and workload. The first number is the number of fingers and the second is the frequency. Solid shapes indicate Pareto optimal trials. Optimal is a trial from which we cannot go to higher ITR without also raising the workload. (A) Pareto optimal trials of healthy participants for the first session together with the optimal trials of DMD participant, and (B) the shift in Pareto optimal trials after seven sessions for the healthy participants.

Workload - For workload, no statistically significant difference was found between healthy and DMD participants. Average scores appeared to be slightly lower for DMD 1 and 2, whereas DMD 3 scored slightly higher (Figure 2.3). Trends were comparable to the healthy group for all DMD participants. Generally, 3 Hz trials with large number of fingers were experienced the hardest, whereas the 1 Hz trials (with low number of fingers) were experienced as the easiest. However, DMD 1 showed a different workload pattern from all the other participants.

Pareto Analysis - The Pareto analysis (Figure 2.5A) shows the optimal trials with respect to the trade-off between ITR and workload. Optimal is a trial from which we cannot go to higher ITR without also raising the workload. Healthy and DMD participants showed similar performance. The trials of one finger at 1 Hz and two fingers at 1 and 2 Hz were common optimal trials among healthy and DMD participants. However, healthy participants also showed optimal trials for three fingers at 1 and 2 Hz.

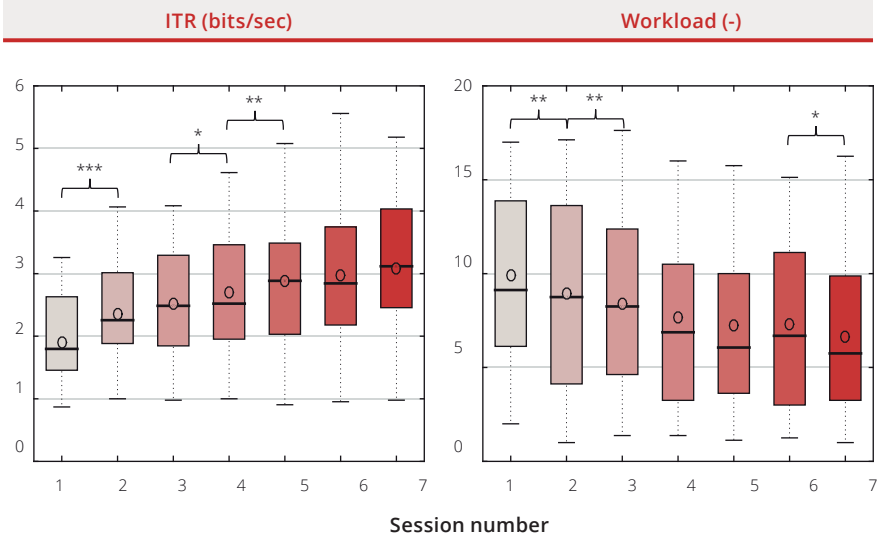


*Figure 2.6 Box plots of average ITR and workload during the training period of seven sessions for the healthy participants. The values per session are averaged over all healthy participants and all trials. Horizontal lines represent the median while circles represent the mean values. * indicates significant difference at the level of p<0.05, ** indicates p<0.01, and *** indicates p<0.001.*

Table 2.2 **Summary of the means with standard deviations and the statistical tests.**

	Metric/Participant	Healthy	DMD
ITR (bit/sec)	Mean (± std)	1.9 (±0.67)	1.14 (±0.65)
	Independent t-test	**p = 0.002**	
Work-load (-)	Mean (± std)	9.9 (±4.57)	9.1 (±4.69)
	Independent t-test	p = 0.621	

	Metric/Session	1	2	3	4	5	6	7
ITR (bit/sec)	Mean (± std)	1.9 (±0.67)	2.3 (±0.81)	2.5 (±0.92)	2.7 (±1.03)	2.8 (±1.16)	2.9 (±1.15)	3.0 (±1.12)
	One-way RM ANOVA				**p = 0.02**			
	Comparisons	1-2	2-3	3-4	4-5	5-6	6-7	-
	Bonferroni test	**p < 0.001**	p = 0.084	**p = 0.014**	**p = 0.009**	p=0.161	p=0.173	-
Workload (-)	Mean (± std)	9.9 (±4.57)	8.9 (±5.28)	8.3 (±5.06)	7.6 (±4.65)	7.2 (±4.44)	7.2 (±4.55)	6.6 (±4.45)
	One-way RM ANOVA				**p < 0.001**			
	Comparisons	1-2	2-3	3-4	4-5	5-6	6-7	-
	Bonferroni test	p = 0.155	p = 1.000	p = 0.039	p = 1.000	p = 1.000	p = 0.445	-

Bold p-values indicate a significant difference at the p=0.05 level.

Training

Figure 2.6 and Table 2.2 summarize the results of the statistical analysis performed in each metric to show the results of training. Figure 2.5B shows the change in the optimal trials due to training. There were significant improvements between the seven sessions for each metric, suggesting a learning effect.

ITR and workload - There was significant improvement for ITR between sessions 1 and 2 (p=0.001), 3 and 4 (p=0.014) and 4 and 5 (p=0.009). The participants reached a steady state for ITR in day 5 (ITR = 2.8±1.16 bits/sec). Workload was also significantly different between sessions 3 and 4 p=0.039, workload was 8.38±5.06 and 7.66±4.65, respectively).

Pareto Analysis - In Figure 2.5B, we can see that, after seven sessions, different trials became optimal. These were trials with four fingers at 1 and 2 Hz (4,1 and 4,2) and five fingers at 1 Hz (5,1). The trials with two fingers and three fingers at 2 Hz were no more optimal after the training was completed and the number of optimal trials increased from five to six.

2.4 DISCUSSION

Number of Participants and Protocol

Due to the low density of the DMD population, we aimed to include only three participants. Therefore, our conclusions must be regarded with caution. Individuals with DMD often experience strong fatigue effects. We took this into account, adjusting our protocol accordingly. We monitored their fatigue throughout the experiment and offered them breaks when needed. The results regarding task performance reported here cannot be attributed to motor performance alone. With the introduction of the workload evaluation after every trial, we aimed to capture the cognitive effort and analyze it together with motor performance. Regarding our participants, DMD 1 had inconsistent and unexpected workload scores (for example, all five finger trials scored lower than four finger trials). This may indicate that he suffers from cognitive issues, which may partly explain the lower task performance that we found for this participant.

Healthy vs. DMD

We found a significant difference in task performance between healthy and DMD, only for ITR. The Pareto analysis revealed similarities for trials of one and two fingers. However, healthy individuals had optimal trials also for three fingers. By analyzing the ITR per trial, we found also that those similarities in task performance are mainly for one up to three fingers. Recent studies with individuals with DMD have shown that no use of their limbs is disuse [79]. Therefore, we believe that the disuse of their fingers probably made it difficult for them to retain performance similar to healthy individuals for more than three fingers.

Training

In order to determine if and where there can be any improvement on the experimental task, we performed a training measurement consisting of

seven sessions. We observed significant improvement in both metrics, indicating better motor performance and lower cognitive effort as a result of a short training period. There are two ways to increase ITR. One is by increasing the number of stimuli components and the other by increasing the stimuli frequency. According to our results, participants were able to improve the number of stimuli components (fingers) that could (successfully) be processed, rather than an increase in frequency. We found that our participants, after training, reached the maximum ITR scores at the frequency of 2 Hz. This corresponds to the results of Klemmer et al. wherein the highest ITR values were at 2.4 Hz [67].

Keeping the limitations of individuals with DMD in mind, we did not perform a training study with them, in order to cause the least inconvenience possible to our participants. However, we believe that, despite the progressive deterioration of their hand function, individuals who retain some functionality may also improve in a time frame of three weeks, since motor learning does not change as a result of the disease [80]. A recent study showed that individuals with DMD experience even stronger training effects than healthy controls during a computer task, and they can acquire and retain motor learning improvements after training [81]. Hence, we assume improvement of their motor performance, similar to what we observed for healthy individuals. However, the visuo-motor task used in our study requires substantial cognitive processing. This can be seen in the Pareto analysis, where trials that require a lower cognitive effort yield higher task performance. Individuals with DMD mainly experience motor impairments (primarily muscle weakness), but a large number of individuals with DMD also experience cognitive impairments and impaired ability in processing visual information [24]. A recent study showed that even individuals with DMD without intellectual disability have a deficit in implicit learning [25]. Therefore, we cannot assume that individuals with DMD will also improve due to implicit learning that will lead to lower cognitive effort.

Implications of the Study

The results of this study are particularly relevant given the lack of systematic analyses concerning the cognitive-motor hand performance of this specific population. They are also relevant given the expected increase in DMD population and the related need to introduce customized

hand rehabilitation for individuals with DMD [22] and a multidisciplinary approach to create preventive measures and interventions for the rehabilitation of individuals with DMD [30], [31].

As suggested by Wagner et al. [65] and as shown by Weichbrodt et al. [48], rehabilitation for individuals with DMD should aim for the retardation of the progress of the disease and the preservation of certain motor performance. Currently, passive stretching of muscles [22] and resting hand splints during sleep [48] are clinically used for the hand rehabilitation of individuals with DMD. In 2010, Bushby et al. [31] proposed a new set of care guidelines with additional therapeutic options for multi-disciplinary hand rehabilitation of the DMD population. Those aim to extend traditional rehabilitation with the use of technology [41]. They also suggest the use of active devices. The development of such a device is the project goal of the Symbionics project [11].

Based on the current training results of the healthy controls, we believe that individuals with DMD may improve their motor-related performance of four and five fingers already within a few weeks. Additionally, the differences in task performance indicate that healthy adults can achieve higher cognitive-motor performance related to the control of the hand, especially for more than three fingers. This can be linked to disuse of fingers in the DMD population [79] and to the modest results of current hand rehabilitation. Therefore, we believe, in line with the recommendation by Bushby et al. [30], [31] and Jansen et al. [79], that early multi-disciplinary rehabilitation of individuals with DMD should involve dynamic multi-finger rehabilitation and promote use, in order to help them retain a higher cognitive-motor hand performance. This can be complemented by active-hand devices for home rehabilitation in combination with gaming, similar to what was done by Amirabdollahian et al. [82] for stroke rehabilitation. In this way, the user will actively participate in the rehabilitation process and may be motivated to use his own fingers more. Additionally, more effective hand rehabilitation can enable the use of sophisticated hand orthoses, which can provide daily assistance to individuals with DMD.

2.5 CONCLUSION

We compared the cognitive-motor performance of healthy and DMD individuals during a hand-related visuo-motor task and analyzed this together with the perceived workload. We also studied the training effects related to the repeated application of our protocol. Individuals with DMD showed an overall lower task performance compared to the healthy. However, this was mainly seen when more than three fingers were involved. Both metrics showed improvement when training was provided. However mainly over the number of fingers involved rather than the frequency. Dynamic multi-finger training may help, together with the use of active-assistive devices, to reduce finger disuse and improve hand-related cognitive-motor performance. Regardless of the low number of participants with DMD included in this study, we gained useful insights into the cognitive-motor hand performance of individuals with DMD, related to our task. In order to generalize our results, additional research with more individuals with DMD is needed. In the future, we will apply our conclusions in the design of customized hand rehabilitation for individuals with DMD, in combination with an active-hand-assistive device.

A NOVEL SETUP AND PROTOCOL TO MEASURE THE RANGE OF MOTION OF THE WRIST AND THE HAND*

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ABSTRACT

The human hand is important for the performance of activities of daily living which is directly related to quality of life. Various conditions, such as Duchenne muscular dystrophy (DMD) can affect the function of the human hand and wrist. The ability to assess the impairment in the hand and the wrist by measuring the range of motion (ROM) is essential for the development of effective rehabilitation protocols. Currently the clinical standard is the goniometer. In this study we explore the feasibility and reliability of an optical sensor (Leap motion sensor) in measuring active hand/wrist ROM. We measured the hand/wrist ROM of 20 healthy adults with the goniometer and the Leap motion sensor, in order to check the agreement between the two methods and additionally, we performed a test-retest of the Leap motion sensor with 12 of them, to assess its reliability. The results suggest low agreement between the goniometer and the leap motion sensor yet showing a large decrease in measurement time and high reliability when using the later. Despite the low agreement between the two methods, we believe that the Leap motion sensor shows potential to contribute to the development of hand rehabilitation protocols and be used with patients in a clinical setting.

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3.1 INTRODUCTION

The human hand is one of the most complex and versatile anatomical structures in the human body [83] and plays an important role in a person's ability to interact with the environment. Reduced functioning of the hands may occur for example as a consequence of increasing age [84], traumatic injuries such as amputation of a finger or thumb [1], [85], diseases on the nervous system like carpal tunnel syndrome, stroke and Parkinson's disease [86], or diseases that affect the muscle, like in neuromuscular diseases [87]. Hand function impairments can restrict the independence of the affected individual and thus quality of life [1], [88]. To evaluate the level of dysfunction and to guide adequate therapeutic strategies, reliable assessment of hand function and joint range of motion (ROM) is important [89].

We are specifically interested in disabilities of the upper extremity related to Duchenne muscular dystrophy (DMD). DMD is a neuromuscular disease affecting around 1:5000 male births worldwide [60]. Mutations in the dystrophin gene, lead to progressive muscular weakness and disability due to loss of skeletal muscle strength [62]. This includes the muscles in the forearm that control the movements of the hand and wrist and first signs of muscle loss are already visible in the late ambulatory stage [64]. Lately, interventions are proposed for assisting the hand function of people with DMD such as passive hand/wrist orthoses [48]. These are complimentary to physical therapy already aiming to preserve as much functionality as possible [90]. In the Flextension-Symbionics project we are currently developing an active hand exoskeleton in order to actively assist the hand function of people with DMD [11].

For the measurement of ROM in clinical practice, goniometry is widely used [89]. Different types of joints require different types of goniometers, in terms of size and shape. In general, goniometers are low-cost, lightweight and portable. However, its intrarater reliability depends on the experience of the rater and interrater reliability is quite low [91] and not consistent over time [92]. With a goniometer, only one joint at a time can be measured, making the procedure for the whole hand time-consuming for both the rater and the participant [93].

Throughout the last years, new techniques have been developed that enable dynamic analysis of kinematics of the hands. Such techniques

may have potential for objective clinical evaluation of the ROM of hand and fingers. Motion tracking devices can measure dynamic parameters through cameras [94], gloves [88], [95]–[97] or by attaching sensors to the skin of the user [98], [99]. However, most of these instruments are expensive, take a lot of time to setup or are difficult to don and doff by people with hand deformities or severe muscle weakness, like in DMD. Pham et al. developed a non-contact camera-based system that showed very promising results for the tracking of the finger MCP, PIP and DIP joints [100]. However, the price of that camera is still relatively high, and the proposed system is not currently commercially available.

The Leap motion sensor is able to detect hand kinematics through the use of three infrared emitters and two small cameras incorporated in one sensor. It already has a wide range of applications related to hand gesture recognition, such as manipulation of robots [94], human-computer interfaces [101] and gaming [102]. Because the Leap motion sensor does not require contact with the individuals' hands or the use of markers, assessments can be performed fast. Furthermore, it is a low-cost solution and it can minimize significantly measurement time since more than one joint can be measured simultaneously. It has been indicated that due to internal constraints of hand angles estimation, the leap is not a promising sensory modality for clinical practice [100]. However, a recent study showed promising results for the finger MCP joints using the Leap motion sensor [103].

In this study, we propose a new clinical assessment protocol using off the shelf, low-cost components, namely the Leap motion sensor (Leap motion Inc.) and Brekel software (Brekel Pro Hands 1.27). We measured the maximal active voluntary angles of fingers, thumb and wrist in twenty healthy participants with no hand impairments. The goal of this study is to evaluate the accuracy and reliability of the Leap motion sensor for measuring hand and wrist ROM by 1) comparing the active ROM of the wrist, hand and fingers measured using the Leap motion sensor to goniometer measurements and 2) determine the test-retest reliability of the Leap motion ROM measurements.

3.2 MATERIALS AND METHODS

Study participants

Twenty healthy persons participated in the study (all right-handed, 20-26 years old, 8 males and 12 females). None of the participants had previous traumas (e.g. bone fractures) of their hands or fingers. Twelve of the participants were re-measured with the Leap motion sensor. The Medical Ethics Committee of Twente decided that this study does not require a medical ethical approval (K17-41). The study was conducted according to the ethical standards given in the Declaration of Helsinki of
1975, as revised in the year 2008. All participants were informed via a letter and signed a consent form prior to the experiment.

Materials and Data Acquisition

The measurement setup consists of four components. The Leap motion sensor, a software package to obtain and record the hand and wrist ROM from the Leap motion sensor (Brekel Pro Hands 1.27), a Matlab based graphical user interface to instruct the participants on how to perform the movements and analyze the data and a mechanical setup for positioning the arms of a person (Figure 3.1).

The Leap motion sensor is a low-cost consumer-grade camera system with three infrared emitters and two cameras. Data from the Leap are recorded with a rate of up to 300 frames per second (fps). The Leap sensor includes a controller and it has its own coordination system and skeletal model of the human hand. It has a field of view of about 150 degrees and approximately up to 600 mm above the device, which enables 3D tracking of the hands.

Based on a pilot measurement, we determined the following conditions to be optimal for Leap motion use: The distance between the controller and the participant's hands, and the orientation of the hand itself, are crucial to avoid occlusion and aliasing. The best performance was achieved when the distance above the sensor was kept between 14 and 24 cm, which is also in accordance with previous literature [104]. The suggested starting finger configuration is with spread fingers [105]. However, people with DMD may have difficulties spreading the fingers.

We found no influence of the starting finger configuration on the quality of the recorded data. Regarding the light, optimal recordings were

achieved when the artificial light in the room was switched off and the curtains were closed. Regarding jewelry, watches and clothing, the most optimal recording quality was achieved when the arms were uncovered.

To record the data from the leap sensor, the software application 'Brekel Pro Hands v1.27' (Brekel [105]) was used. This application enables recording of motion of up to two hands and forearms using a Leap controller. The displayed data distinguish the left and right side and the position and orientation values for each joint and fingertips of the digits, elbow, wrist and palm are recorded in 3D.

To check and save the data provided by the Brekel application of each participant and also to serve as a visual cue for the participant with respect to the movement they had to perform, we created a Graphical User Interface (GUI) in MATLAB (R2016b, The MathWorks, Inc.), presented in Figure 3.1. The raw data of the orientation of the joints were stored in separate *.csv files which were stored in Matlab by the GUI as *.mat files. Data were captured with a rate of 115 fps. A low-pass 2nd order Butterworth filter with a cutoff frequency of 2 Hz, similar to the one used by Lanari Bó et al. [106] was used to smooth the raw joint angle data.

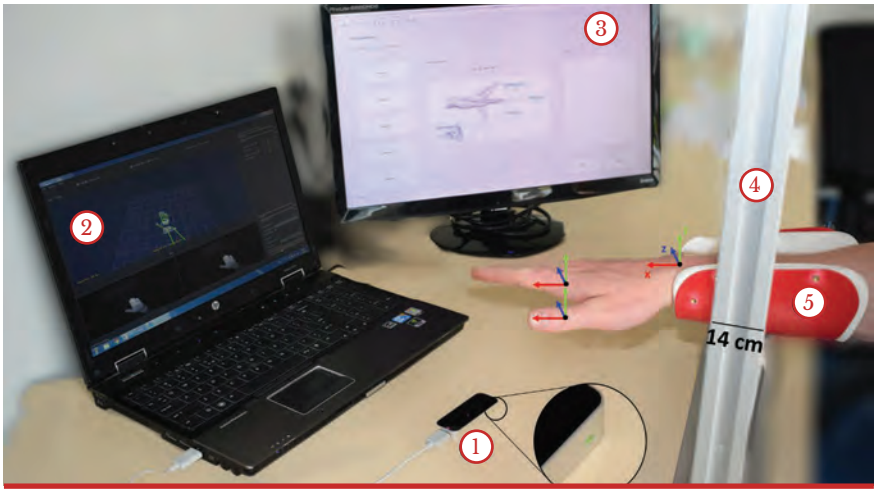

Figure 3.1 Experimental setup. 1) The controller of the Leap sensor. The green light indicates that the controller is on. 2) Brekel Pro Hands application in real-time, on the host computer. 3) The Guide User Interface shows which movement the participant should do. 4) The platform with 5) arm support at a distance of 14 cm from the table's surface, where the participant should place his forearm.

Figure 3.2 *Representation of one trial of each movement the participants need to perform. All movements start at the neutral position. The movements are: (a) flexion and extension of the wrist; (b) radial and ulnar deviation of the wrist; (c) pronation and supination of the wrist; (d) flexion and extension of the MCP and IP joints of the thumb; and (e) flexion and extension of the MCP, PIP and DIP joints of the four fingers.*

A setup with arm supports was constructed to allow participants to rest their arms above the Leap sensor (Figure 3.1). The positioning of the arm support is adjustable vertically and horizontally. The preferred forearm of the participant was placed on the arm support. The arm support was set such that the lower arm of the participant was resting in a comfortable position, and the hand was placed above the Leap motion sensor in the center of the body. The setup allowed for the unrestricted completion of the wrist, fingers and thumb. Since the movements of the joints are with respect to the local coordinate frame (Figure 3.1) performed in 2D, only rotation values of one axis were considered for each joint. The angles of the joints were measured by the Brekel software around the local x, y, z axes of every joint (Figure 3.1).

Experimental protocol

For assessments with the Leap, from the initial resting position, participants were asked to actively move their fingers and maximally perform one by one the following five movements with their hand and wrist: flexion/extension of the fingers (MCP, PIP and DIP) by making a fist and then extending, flexion/extension of the thumb (MCP and IP), by flexing the thumb maximally in a plane parallel to the palm and subsequently try to touch the palmar side of the little finger's MCP, radial/ulnar deviation of the wrist, pronation/supination of the forearm and flexion/extension of the wrist (Figure 3.2). The participants had to repeat each movement three times, while resting their arm on the arm support (Figure 3.1). The mean of

Figure 3.3 Goniometers used in this study: (a) Rolyan finger goniometer with loose-fitting hinge; (b) Devore pocket goniometer; and (c) universal goniometer with full-circle body.

the 3 repetitions was used for the data analysis.

To obtain the angles manually with the goniometer, the raters of this study were trained by an experienced clinical evaluator to measure the angles for the different joints. Three different goniometers, which varied in size, were used to measure the joint angles (measured in degrees). To measure the angles of the DIP joint of the fingers and IP joint of the thumb, a plastic Rolyan finger goniometer with loose-fitting hinge (Figure 3.3a) was used. It has a resolution of 2° increments, and ranges from 30° of hyperextension to 120° of flexion. To measure the angles of the MCP and PIP joints of the fingers and MCP joint of the thumb, a plastic Devore pocket goniometer (Figure 3.3b) with a resolution of 1° increments, and a reading range of 180° was used. To assess the wrist joint, a plastic universal goniometer with full-circle body (Figure 3.3c) with a resolution of 2° increments was used.

All 20 participants performed one measurement with the Leap and one with the goniometer, consisting of three repetitions per measuring methods. Additionally, 12 of them performed an additional measurement (also with three repetitions) with the Leap sensor two weeks after the first one. This was done to assess the test-retest reliability of the Leap measurements. Flexion/extension of a total of 14 finger joints (MCP, PIP and DIP for the 4 digits and MCP and IP of the thumb) and three degrees of freedom of the wrist (pronation/supination, radial/ulnar deviation and flexion/extension) were measured with each measurement methods (Figure 3.3). All flexion angles, together with pronation and radial deviation were taken as positive, while extension angles, ulnar deviation and supination were taken as negative. The accuracy of the evaluation protocol was defined as the agreement between the Leap motion sensor and the goniometer. The reliability of the assessment was defined as the consistency of the

measure with repeated observations by the Leap motion sensor.

The time-consumption (in minutes) is recorded for both techniques as the amount of time that was needed to perform the measurement (including the three repetitions) for each method. The time that was needed for preparation of the participant and the setup was not considered in this. was not considered in this. The time was measured using a stopwatch.

Statistical analyses

Minimum and maximum active joint angles measured with Leap motion sensor and goniometer are compared using Bland-Altman plots and quantified by the mean difference and limits of agreement. Compared to previous similar studies [100], we avoided the use of Intraclass Correlation Coefficient (ICC) analysis. Our choice was motivated by the fact that there are no standard values for acceptable reliability using ICC [107] and that we had low variability in maximum flexion and extension angles between our participants, which disables the use of correlational analysis. It has been suggested that correct use of ICC as a rule of thumb includes the acquisition of at least 30 heterogeneous samples when conducting a reliability study [107]. We first calculated the difference of the mean between the Leap motion sensor and the goniometer and, between test and retest for every individual joint. One sample t-tests were performed to check if these differences of means differ significantly from zero. Differences of means were normally distributed. Only 8 out of the 68 differences, moderately violated the assumption of normality, as assessed by Shapiro-Wilk's test ($p < 0.05$. However, the one sample t-test is quite robust to moderate violations of normality [108]. The statistical analysis was performed with IBM SPSS v24. All the data used for the statistical analysis are available online as a complimentary file to this article.

3.3 RESULTS

Evaluation of the Leap motion sensor

All participants performed all the movements and all data were collected successfully with both the Leap sensor and the goniometer. Mean values and standard deviations of both the goniometer and Leap measurements can be found in Table 3.1, together with the mean difference between measurements.

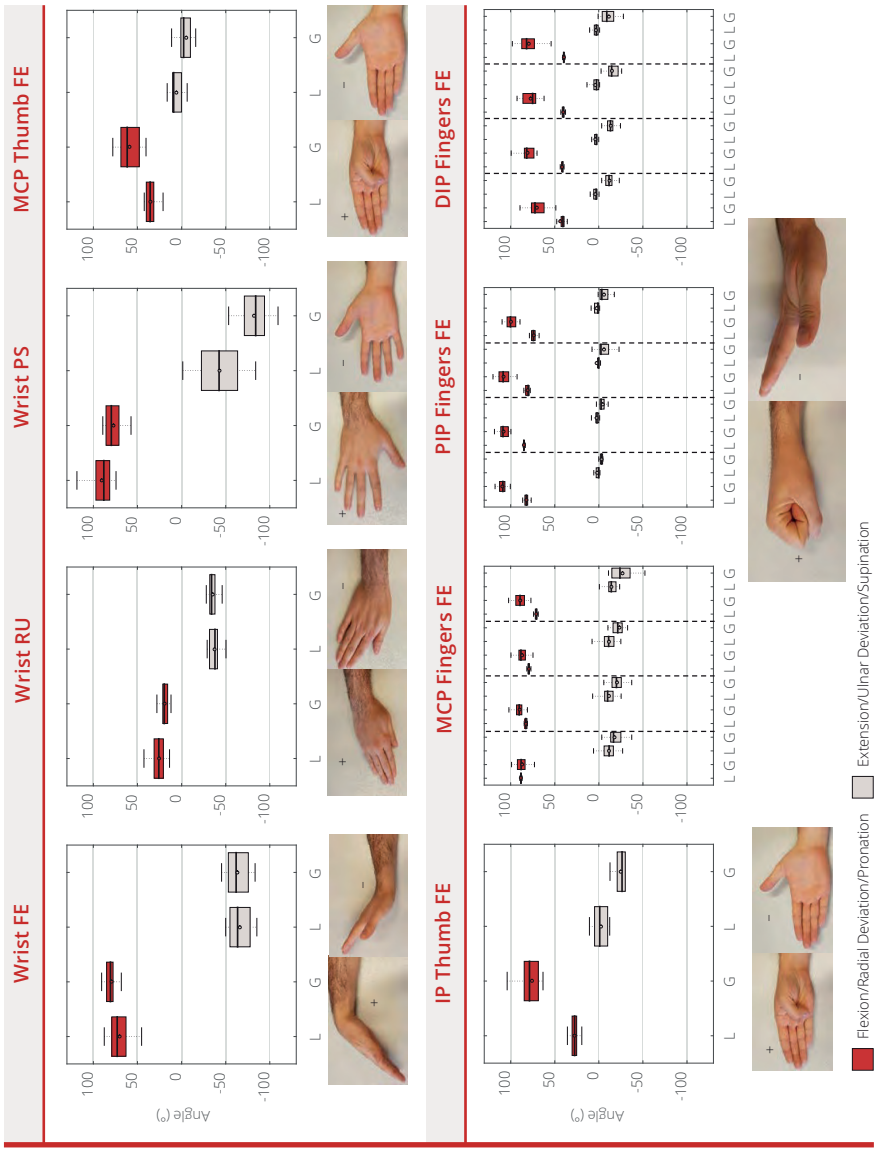

Figure 3.4 *Boxplots of the maximal and minimal values of all the joints measured with the Leap motion sensor and the goniometer. L: Data from the Leap motion sensor; G: Data from the goniometer; FE: Flexion/Extension; RU: Radial/Ulnar deviation; PS: Pronation/Supination; For the fingers, the order is index, middle, ring, little, from left to right. For every pair of boxplots, flexion/radial deviation/pronation is left and extension/ulnar deviation and supination right.*

One sample t-test p-values for comparing the mean differences to zero for every joint measured are reported in Table 3.1. Results are also displayed graphically with boxplots (Figure 3.4). From this figure, it becomes clear that for the wrist, the leap and goniometry results are quite comparable. MCP angles are also comparable but differences seem to increase when moving from index to little finger and from proximal to distal joints. Overall, the mean flexion angles of most joints are underestimated when measured with the Leap motion sensor. Furthermore, all finger joints showed smaller standard deviations for the Leap motion sensor results compared to the goniometer results.

Maximum extension measured with the goniometer reveals negative values for all joints, which indicate hyperextension. Leap results also show hyperextension in some of the joints, but most extension angles are less extreme compared to the goniometer results. When measured with the leap, DIP and PIP joints never go below zero.

Based on the statistical analysis, we found satisfactory agreement between the goniometer and the Leap motion sensor only for three movements. These are wrist extension, index MCP flexion and ulnar deviation. In Table 3.1, it is shown that for these movements the 95% CI for the mean difference is small and it includes zero (Figure 3.5). The one sample t-test p-values, for these three movements do not show a statistically significant difference for the mean difference between the goniometer and the Leap motion sensor from zero.

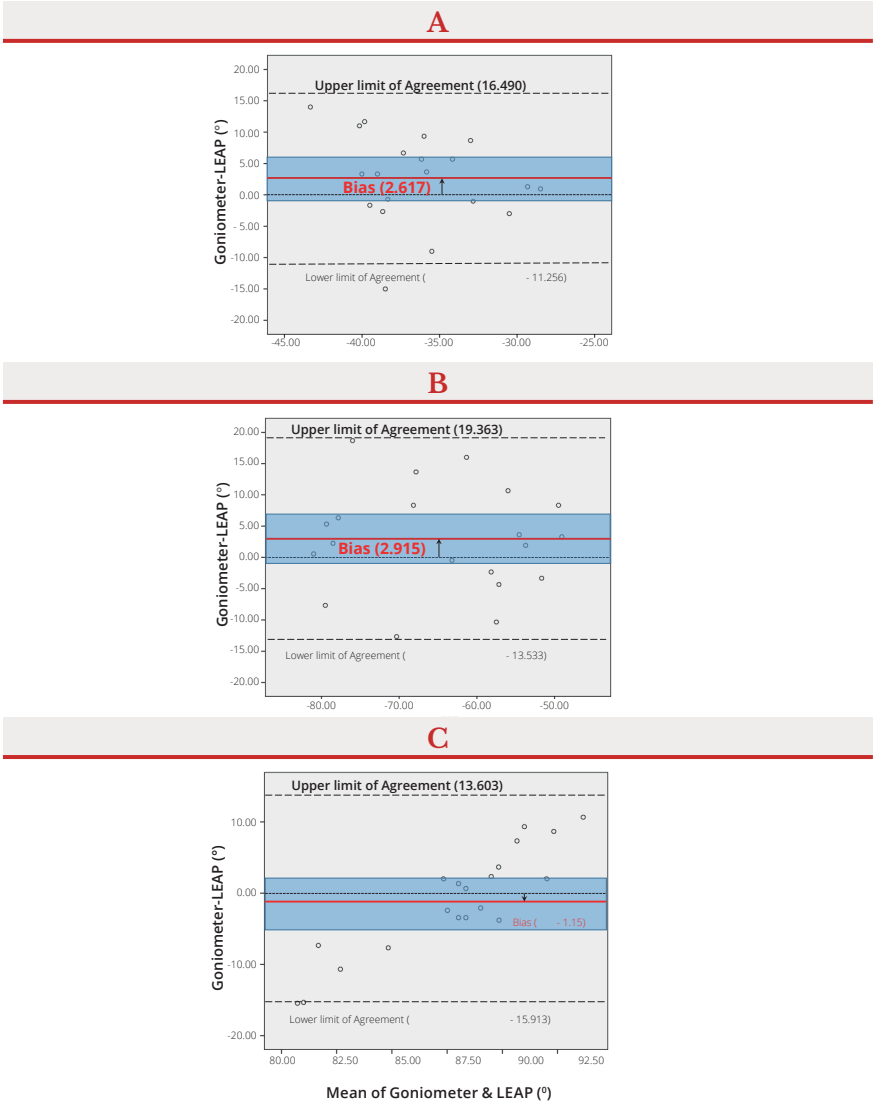

*Figure 3.5 Bland-Altman plots of A. wrist ulnar deviation, B. wrist extension and C. Index finger MCP flexion. The y –axis shows the difference, while the x-axis the mean between goniometer and Leap motion sensor for every participant (20 participants/dots). The red line shows the mean difference (bias) for the two measurement techniques. The blue shaded area is the 95% CI for the mean difference. For these three movements the line of equality (line crossing zero) is included inside the shaded area. The two dashed lines show the limits of agreement (±1,96*SD), between the two measurement techniques.*

Table 3.1 Maximum joint angles measured with goniometer and Leap for all joints in all directions of movement.

Joint	Direction	Mean gonio (sd)	Mean Leap (sd)	Mean Diff	95% CI of Mean Diff	One Sample t-test (2-tailed)
Wrist	Radial dev	19(4)	26(9)	-7	-11;-2	0.007
	Ulnar dev	**-35(5)**	**-38(6)**	**3**	**-1;6**	**0.115**
	Pronation	77(10)	90(12)	-13	-19;-7	< 0.001
	Supination	-82(16)	-43(24)	-39	-51;-26	< 0.001
	Flexion	79(8)	70(14)	9	4;14	0.001
	Extension	**-63(12)**	**-66(12)**	**3**	**-1;7**	**0.137**
Thumb MCP	Flexion	59(13)	36(6)	24	18;30	< 0.001
	Extension	-5(15)	6(7)	-11	-17;-5	0.001
Thumb IP	Flexion	76(16)	28(4)	48	40;56	< 0.001
	Extension	-25(6)	-2(8)	-23	-27;-18	< 0.001
Index MCP	**Flexion**	**87(7)**	**88(2)**	**-1**	**-5;2**	**0.501**
	Extension	-18(9)	-11(8)	-7	-11;-3	0.003
Index PIP	Flexion	109(5)	82(2)	27	24;30	< 0.001
	Extension	-3(4)	2(3)	-5	-8;-3	< 0.001
Index DIP	Flexion	70(11)	43(9)	27	21;33	< 0.001
	Extension	-12(6)	4(3)	-16	-19;-13	< 0.001
Middle MCP	Flexion	90(6)	83(1)	7	4;10	< 0.001
	Extension	-21(9)	-11(8)	-10	-14;-5	0.001
Middle PIP	Flexion	108(6)	85(2)	23	21;26	< 0.001
	Extension	-4(6)	3(3)	-7	-10;-3	< 0.001
Middle DIP	Flexion	81(8)	41(2)	39	36;43	< 0.001
	Extension	-14(6)	4(4)	-17	-21;-14	< 0.001
Ring MCP	Flexion	87(8)	80(1)	8	4;11	< 0.001
	Extension	-23(9)	-11(9)	-12	-17;-7	< 0.001

Table 3.1 Continued

Joint	Direction	Mean gonio (sd)	Mean Leap (sd)	Mean Diff	95% CI of Mean Diff	One Sample t-test (2-tailed)
Ring PIP	Flexion	108(7)	81(2)	27	24;30	< 0.001
	Extension	-6(10)	2(4)	-8	-14;-3	0.003
Ring DIP	Flexion	77(9)	40(1)	37	32;41	< 0.001
	Extension	-15(8)	4(4)	-19	-23;-15	< 0.001
Little MCP	Flexion	89(7)	71(2)	18	15;22	< 0.001
	Extension	-27(13)	-14(6)	-13	-19;-6	< 0.001
Little PIP	Flexion	100(6)	74(3)	26	23;29	< 0.001
	Extension	-6(10)	2(3)	-8	-13;-4	0.001
Little DIP	Flexion	79(12)	40(2)	40	34;45	< 0.001
	Extension	-11(9)	3(4)	-15	-19;-11	< 0.001

Means and standard deviations (sd) are given. Mean differences, 95% Confidence Intervals for the mean differences and the p-value for the one sample t-test of comparing the mean difference to zero are given. Bold letters indicate the joints and movements for which the two measurement techniques reached a good agreement. The Bland-Altman plots for these joints are illustrated in Figure 3.5.

Test-retest

Test-retest assessment of Leap measurements was done with 12 of the 20 participants. The results are reported in Table 3.2 and visualized with boxplots in Figure 3.6. During the retest assessments, again small standard deviations were found, especially for finger joint flexion results. The statistical analysis revealed that for all movements assessed, small differences were present between test and retest values. Furthermore, for all movements except little finger DIP flexion, a difference of zero was within narrow 95% CI of the mean difference. Broader 95% CI were found for pronation/supination and wrist flexion/extension, however still including zero within them.

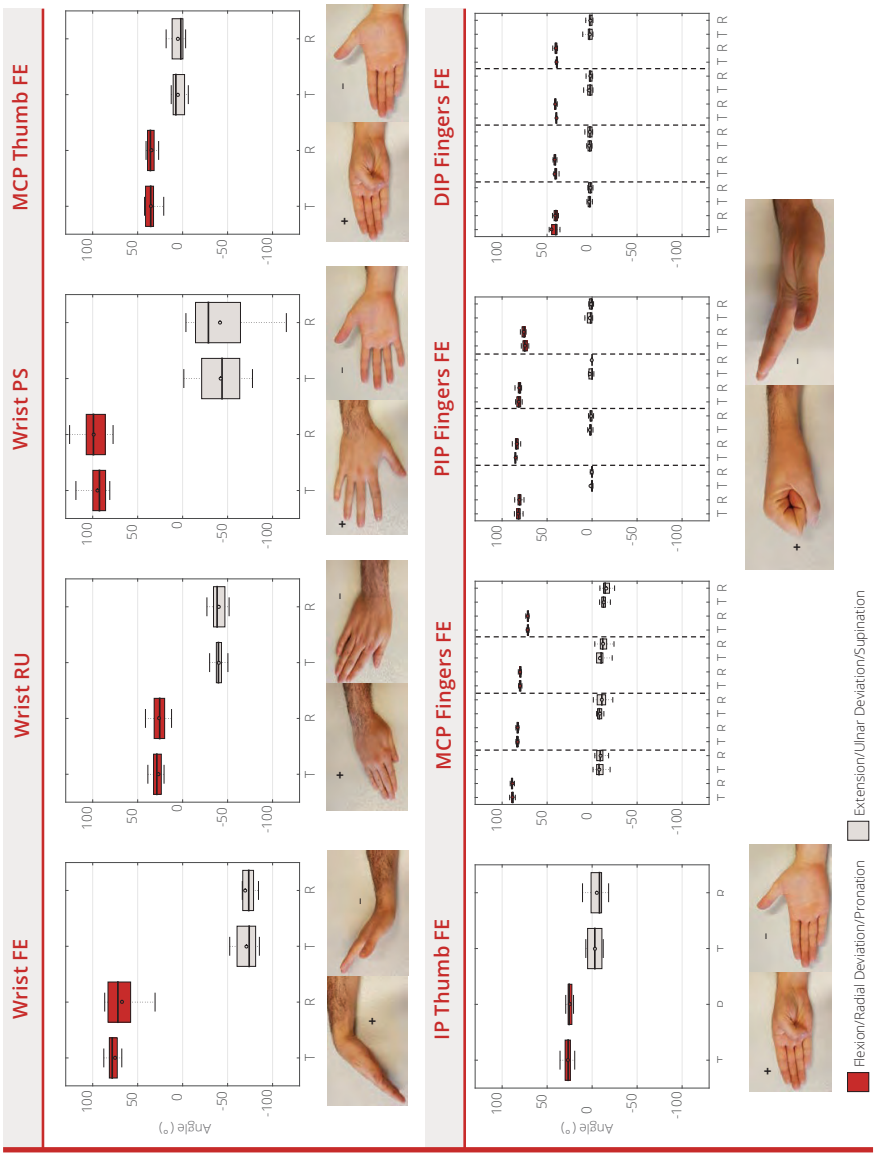

Figure 3.6 Boxplots of the maximal and minimal values of all the joints measured with the Leap motion sensor test and retest. T: Test data from the Leap motion sensor; R: Retest data from the Leap motion sensor; FE: Flexion/Extension; RU: Radial/Ulnar deviation; PS: Pronation/Supination; for the fingers, the order is index, middle, ring, little, from left to right. For every pair of boxplots, flexion/radial deviation/pronation is left and extension/ulnar deviation and supination right.

Table 3.2 Test and retest maximum joint angles for all joints in all directions of movement.

Joint	Direction	Mean Leap test (sd)	Mean Leap retest (sd)	Mean Diff	95% CI of Mean Diff	One Sample t-test (2-tailed)
Wrist	Radial dev	27(9)	26(8)	1	-7;8	0.798
	Ulnar dev	-40(5)	-40(8)	0	-6;5	0.888
	Pronation	95(12)	99(15)	-4	-13;6	0.413
	Supination	-42(25)	-41(35)	-1	-23;21	0.939
	Flexion	75(11)	67(18)	8	-7;22	0.270
	Extension	-71(12)	-70(14)	-1	-10;7	0.724
Thumb MCP	Flexion	35(6)	34(5)	1	-3;4	0.757
	Extension	5(7)	6(8)	-1	-7;6	0.862
Thumb IP	Flexion	27(4)	25(3)	2	-1;6	0.214
	Extension	-3(8)	-5(9)	2	-5;9	0.507
Index MCP	Flexion	88(2)	88(2)	0	-2;2	0.891
	Extension	-8(7)	-9(5)	1	-2;4	0.537
Index PIP	Flexion	82(3)	81(3)	1	-1;3	0.380
	Extension	1(4)	0(2)	1	-2;4	0.467
Index DIP	Flexion	45(12)	41(2)	4	-3;11	0.249
	Extension	3(3)	2(2)	1	-1;4	0.198
Middle MCP	Flexion	83(1)	83(1)	0	-1;1	0.597
	Extension	-9(7)	-11(6)	2	-1;6	0.194
Middle PIP	Flexion	85(2)	84(3)	1	-1;4	0.255
	Extension	2(4)	1(2)	1	-1;4	0.300
Middle DIP	Flexion	41(3)	41(2)	0	-3;2	0.768
	Extension	3(4)	2(3)	1	-2;4	0.474
Ring MCP	Flexion	80(1)	80(1)	0	-1;1	0.884
	Extension	-8(9)	-12(6)	4	-2;9	0.183
Ring PIP	Flexion	81(2)	81(2)	0	-1;2	0.584
	Extension	2(5)	0(2)	2	-2;6	0.300
Ring DIP	Flexion	40(1)	41(1)	-1	-3;0	0.109
	Extension	3(4)	2(2)	1	-2;4	0.401
Little MCP	Flexion	71(1)	71(1)	0	-1;1	0.848
	Extension	-13(6)	-16(5)	3	-1;6	0.130

Table 3.2 Continued

Joint	Direction	Mean Leap test (sd)	Mean Leap retest (sd)	Mean Diff	95% CI of Mean Diff	One Sample t-test (2-tailed)
Little PIP	Flexion	75(3)	76(2)	-1	-3;0	0.122
	Extension	3(3)	1(2)	2	-1;4	0.183
Little DIP	**Flexion**	**39(2)**	**40(2)**	**-1**	**-2;-0**	**0.041**
	Extension	3(3)	2(2)	1	-1;3	0.389

Means and standard deviations (sd) are given. Mean differences, 95% Confidence Intervals for the mean differences and the p-value for the one sample t-test of comparing the mean difference to zero are also reported. Bold letters indicate the joints and movements for which the test retest did not reach a good agreement.

Measurement Time

Using the goniometer took on average 32:65 minutes per participant, with a standard deviation of 10:86 minutes. With the use of the Leap motion sensor, the rater was able to measure on average every participant within 7:22 minutes, with a standard deviation of 2:47 minutes.

3.4 DISCUSSION

Rationale

In this study we aimed to evaluate the accuracy and reliability of the Leap motion sensor together with a novel protocol, to measure the ROM of the wrist and finger joints. To the authors' best knowledge, this is the first study to assess accuracy and test-retest reliability of this system for hand and wrist joint angles measurement. This was done by comparison of the Leap motion sensor to the current clinical standard for hand and wrist angle measurements; the goniometer. Additionally, test retest reliability of the Leap motion sensor was examined. Using goniometry as the golden standard for evaluating the accuracy of the Leap motion sensors is questionable. Other high precision optical techniques, such as cameras with reflective markers could be used for a more meaningful comparison. However, goniometry is the current clinical standard, and there is a plethora of studies related to measurements, protocols and different goniometers

[91]. Moreover, comparable studies evaluated new and existing sensors and measurement protocols against the goniometer, reporting promising results and significant reduction in measurement time, yet asking for further improvements in measurements protocols [100], [103], [109].

Leap vs. Goniometer

Most joints revealed minimal agreement between the results of the goniometer and the Leap motion sensor (Table 3.1). This may be explained by several different protocols were used to assess the finger ROM for each measurement technique. Using the goniometer, individual joint movements were assessed, whereas all fingers moved together for the assessment of finger flexion and extension during the Leap measurement. This may have resulted in some discrepancies between reachable angles, between the two techniques. However, we do not believe that the differences we found can be only attributed to this aspect. With the goniometer we measured the dorsal side of the hand and wrist (center of rotation outside of the joint), while the Leap motion sensor estimates the center of rotation inside the joint. In participants with protruding knuckles this can results in measurement differences between the two techniques. Moreover, while using the goniometer sometimes the rater is slightly pushing the measured joints and it is not clear to what extend these results in measurement of passive instead of active ROM.

The disagreement in the results can also be attributed to the internal constraints of the Leap motion sensor. The system does not only rely on what the cameras can visualize, but also on the accuracy of the internal hand model. We noticed an increasing disagreement, while moving from proximal to more distal joints of the fingers. This can be attributed to the constraints of the Leap motion sensor, such as the coupling between the MCP and the DIP joint ($\theta_{DIP} = 2/3\ \theta_{MCP}$). This inherent coupling in the model, might explain the big disagreement for especially the thumb joints, between the two methods. In all cases, we noticed the participants' thumb moving with a larger ROM in reality than the movement of the virtual thumb in the screen. Furthermore, the Leap motion sensor estimated rather than measure joint angles when occlusion was occurring. This may also explain the small standard deviations of the Leap results, whereas goniometer standard deviations were larger. Based on our results, we believe that the Leap motion sensor does not seem able to measure

reliably at the extreme angle values for the measured joints (maximum and minimum angles). Since occlusion mainly occurred in the extreme flexion movements, the fact that we have measured maximum flexion and extension may have affected the results. This can also be observed in Figure 3.5c, where the difference between the two measurement techniques increases proportionally to the mean angle. Occlusion issues can be solved by using multiple Leap motion sensors. Placidi et al. [110] used 2 Leap motions sensors for tracking the position of the hand in 3D, resulting in reduced occlusions and without inducing further complications.

The use of goniometry and especially interrater assessments of finger ROM is also questionable with people suffering from hand related conditions, and would likely only produce less reliable measures [92]. The results of goniometric measurements indicate that it is difficult to show any change of a joint motion of less than 5° to 10° for most joints measured by the same tester [92]. Therefore, the Leap motion sensor should be evaluated as a viable alternative.

Test vs. Re-Test

Regarding the test-retest reliability of the Leap motion sensor, we found a good agreement for all measured joints, except the DIP of the little finger. This result is probably due to the fact the Leap motion sensor, relies mostly to an estimation of the DIP rather than to the optical tracking. Most 95% CI have a span from 2° to 14°. This is similar to the reported intrarater reliability of the goniometer, which is reported to be from 1.5° and up to 10° [91]. For the wrist measurements, we can see a lower agreement and larger 95% CI between test and retest measurements, especially for pronation/supination and wrist flexion/extension (Table 3.2).

Time Consumption

Using the goniometer the rater needed on average 32:65 minutes per participant. With the use of the Leap motion sensor, the rater was able to measure more joints at the same time, reducing measurement time to 7:22 minutes per participant. It can be assumed that more experienced raters can perform goniometric measurements in less time, however they would hardly be able to reach similar times to the Leap motion sensor measurements, without compromising accuracy. In addition, this study

measured only one hand, while the Leap is able to measure two hands simultaneously, which could reduce the time consumption compared to the goniometer even further. In clinical practice, time is a very important aspect, as less time-consuming processes can allow the therapist to spend time with more patients, the patients to spend less time at the clinic and the overall costs to be reduced [111].

Lessons learned

Regarding the wrist flexion/extension, we realized that the visibility of the elbow during the measurement, is important for the estimation of the wrist flexion/extension and pronation/supination angles. In our measurement protocol, due to the arm support (Figure 3.1) we used for our set-up, the elbow was occluded from the Leap motion sensor. Similarly, even after clear instructions to our participants to only pronate and supinate by moving their forearm, we believe that the large 95% CI is due to shoulder rotations during the assessment of this movement. More strict and uniform protocols can give more consistent and reliable measurements, regarding the wrist joint. This is currently also the case for the goniometer, where proper training and consistency in measurement technique are also important for therapists in order to perform reliable measurements [91].

Implications for clinical use

Although we have seen some clear advantages of using the goniometer over the Leap motion sensor there are also many advantages of using the Leap motion sensor over the goniometer, which could be especially useful in a clinical setting. Measurements with the Leap motion sensor are less time consuming and can also be used to assess dynamic and submaximal joint angles instead of only static and maximal joint angels. In addition, the Leap motion sensor is like the goniometer low-cost and no pre-calibration is required. Furthermore, no contact with the hand of the patient is required, which makes measuring with the Leap motion sensor less invasive, and possibly less painful than measurements with the goniometer. In addition, Leap motion measurements are in comparison to goniometer measurements much less dependent on the experience of the rater, which improves overall objectiveness and applicability of the method. Consequently, we think that the Leap motion sensor is a promising device for clinical use, but the applicability in people with limited hand

function should still be investigated. The further development of the Leap motion sensor and future advances in technology can potentially offer a solution to occlusion and estimation of joint angles issues.

We believe that in the future, the Leap motion sensor can be used in combination with virtual or augmented reality together with gaming in order to motivate and enhance hand and wrist rehabilitation. This together with the ability of the Leap to measure joint angles at the same time, can enable evaluation of such futuristic interventions at the same time. Moreover, the low cost and the portability of the sensor, can allow the use of it for home rehabilitation and further reducing rehabilitation costs [111].

3.5 CONCLUSION

We performed an evaluation of the accuracy of the Leap motion sensor in comparison with the goniometer for 20 healthy participants. Additionally, we assessed the test-retest reliability of the sensor with 12 healthy participants. Our results give insight into the accuracy and reliability of this system and based on those results, we think the Leap motion sensor has potential to be used in clinical and research settings in the future. However, improvements have to be made in the measurement protocol and additional research is required to fully determine the optimal use of the Leap motion sensor. We were especially interested in the potential of the Leap motion sensor to evaluate the level of dysfunction and to guide adequate therapeutic strategies with people with DMD. Therefore, reliable assessment of hand function and joint ROM is important. At this point the Leap motion sensor cannot yet be used in this context, without further research in people with DMD. Future research should focus on the adjustment of the protocol in order to improve data acquisition and quality. Standardized protocols to set up and use the device must be established in order to ensure a reliable performance of the leap motion sensor, which will also add to the intra- and interrater reliability. Additionally, it is important to evaluate the performance of the Leap motion sensor for submaximal angles and assess the effect of the addition of an extra Leap motion sensor to solve occlusion issues. We believe that the current results contribute to further development of clinical protocols to use the Leap motion sensor in a clinical setting with patients.

4

CHARACTERIZATION OF FOREARM HIGH-DENSITY ELECTROMYOGRAMS DURING WRIST-HAND TASKS IN INDIVIDUALS WITH DUCHENNE MUSCULAR DYSTROPHY*

Kostas Nizamis, Noortje H.M. Rijken, Robbert van Middelaar, João Neto, Bart F.J.M. Koopman and Massimo Sartori

ABSTRACT

Duchenne muscular dystrophy (DMD) is a genetic disorder that results in progressive muscular degeneration. Recent medical breakthroughs increased the life expectancy of individuals with DMD; however their quality of life decreased due to their increasing dependence on caregivers. Unimpaired hand/wrist function is central for independence. In this context, robotic exoskeletons can effectively assist this function and raise the quality of life of individuals with DMD. Such devices, require the accurate decoding of motor intention, which for the hand/wrist, is commonly achieved via high-density surface electromyography (HD-sEMG). However, due to the absence of any systematic analysis of the forearm muscle activations of individuals with DMD, there is no evidence about their difference from healthy individuals and the feasibility of HD-sEMG, for decoding hand/wrist motor intention. This study characterized for the first time, the forearm electromyograms of three individuals with DMD while performing seven hand/wrist related tasks and compared them to eight healthy individuals. We looked into the spatial distribution of HD-sEMG patterns using principal component analysis (PCA), the repeatability and the amplitude distributions. Additionally, we used an offline machine learning approach, in order to compare the feasibility of myocontrol for people with DMD. Our analysis showed a decreased repertoire of spatially distinguishable HD-sEMG patterns for people with DMD compared >>

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<< to the healthy participants.Additionally, the participants with DMD experienced higher normalized and lower absolute activations compared to the healthy. However, the ability of the DMD participants to produce repeatable HD-sEMG patterns was comparable to that of healthy participants and the same holds true for their offline myocontrol performance. Our findings suggest that despite the muscle tissue degeneration, the number of spatially distinguishable patterns, repeatability activation distribution and myocontrol performance of the DMD individuals, however different, were still comparable to that of the healthy individuals. This can lead to further developments for the intuitive myoelectric control of active hand exoskeletons for individuals with DMD.

4.1 INTRODUCTION

Duchenne muscular dystrophy (DMD) is an X chromosome-linked recessive neuromuscular disease and it is diagnosed in childhood and has an incidence of 1 out of 4000 living male births [5]. The absence of dystrophin causes progressive weakness of skeletal, respiratory and cardiac muscles, and leads to severe physical disability and shortened life expectancy [62]. Improved standards of care and the recent introduction of assisted ventilation, in the later stages of the disease, increase the life expectancy of individuals with DMD [21]. This has led to an increase in the number of adults with DMD [22] experiencing low quality of life and an increased dependency on external aids [23] and caregivers [4].

Wearable devices such as hand/wrist exoskeletons can provide a functional solution by assisting individuals with DMD in performing activities of daily living (ADL) [6]. However, to this point, dynamic active hand support of individuals with DMD remains a challenge [22] and passive hand orthoses [48] present the main clinical way of hand and wrist treatment of individuals with DMD. Bushby et al. [30], [31], suggest that the treatment of individuals with DMD should become more complete and multi-disciplinary and promote the use of technology. However, in order to control such devices accurately, motor intention decoding presents an important challenge [112].

The clinical golden standard currently for non-invasive motor intention decoding [113], control of robotic devices [114] and characterization of muscle activity [115] is surface electromyography (sEMG). Despite

the fact that sEMG is broadly used in amputee research [115]–[118], to characterize forearm activity, in degenerative disorders such as DMD, there is a lack of understanding on how these individuals activate their forearm muscles to achieve functionally relevant tasks. DMD presents a challenging case study, due to its progressive nature and the fact that it affects mainly the muscle function.

High-density sEMG (HD-sEMG) is a non-invasive technique that collects high resolution myoelectric signals from many monopolar electrodes [119]. It has been shown that HD-sEMG can provide an improved way, compared to past approaches, to define where the electrical activity of motor unit is best represented [115]. This information can be used to create heat-maps (Figure 4.1) with the spatial distribution of HD-sEMG amplitudes during different hand/wrist related tasks [118]. Such heat-maps can capture distinct HD-sEMG patterns associated to specific tasks, variations in amplitude and repeatability of each task over a period of time. They can also be used to characterize motor control strategies and explore applications for myocontrol when combined with currently used machine learning classification techniques [120].

In this paper, we characterize for the first time, the HD-sEMG electromyograms of three individuals with DMD during seven hand-wrist related tasks and compare with a baseline of eight healthy participants. Our study is motivated by the absence of a systematic and detailed analysis of forearm muscle activations in individuals with DMD and how they compare to healthy individuals. We use for the first time HD-sEMG heat-maps combined with principal component analysis (PCA) to spatially characterize their hand/wrist motor control. We additionally characterize the task related amplitude distributions and their ability to produce repeatable and distinguishable HD-sEMG patterns as those present central requirements for the control of robotic exoskeletons. Lastly, we use machine learning classification to investigate their potential for myocontrol. Repeatability, spatial distribution and distinguishability of HD-sEMG patterns together with offline classification performance are important requirements that can provide with a better understanding of DMD motor control with regard to robotic applications. This will assist the development of an intuitive motor decoding paradigm for the control of the wearable active hand exoskeleton [59] we have developed in the Flextension Symbionics project [121] for individuals with DMD.

4.2 METHODS

Participants

The experiment was carried out with eight healthy adults, ranging from 20-24 years in age, without any hand-related impairment, and three adults with DMD, aged from 20-25 (Table 4.1). The participants with DMD were chosen to have different levels of hand function and therefore induce a high functional variability. Participant 1 (DP1, 22 yrs. old) was able to use his hands functionally and no contractures relevant to hand/wrist movement were observed clinically. Participant 2 (DP2, 20 yrs. old) was able to functionally use his hand, but he experienced a decrease in strength and minimal contractures relevant to hand/wrist movement. Participant 3 (DP3, 25 yrs. old) was not able to use his hands at all and was affected by immediate onset of fatigue during its use. Extensive contractures relevant to finger movement were observed and only minimal movement of the fingers was possible. All participants were able to perform the experimental protocol. The Medical Ethics Committee of Twente approved the study design, the experimental protocol, and the procedures (Protocol number: NL59061.044.16). The study was conducted according to the ethical standards given in the Declaration of Helsinki in 1975, as revised in 2008.

Setup and Signal Acquisition

The setup (Figure 4.1) included several components, and it was designed to record HD-sEMG signals from the forearm in a repeatable and systematic way. Muscular activity was measured with a 128-channel amplification system (REFA 128 model, TMS International, Oldenzaal, The Netherlands). We used 64 monopolar electrodes around the forearm to acquire the raw monopolar sEMG signals. The signals were recorded with a gain of 26.55 without filtering and sampled with a frequency of 2048 Hz, and digitally converted with a 24-bit conversion (a resolution of 0.018 μV per bit, 300mV dynamic range). The acquisition software (TMSi Polybench) was executed in a host laptop. A computer screen was used to provide visual feedback of the task to the participants.

The fitting of the electrodes was done similar to what was done by Daley et al. [118] to normalize the locations of the electrodes to each participants arm circumference in order to account for different forearm

thicknesses (Table 4.1). The inter-electrode distance in the longitudinal direction of the forearm was kept constant at 2 cm which is the minimum recommended inter-electrode distance for minimizing cross-talk [122]. The choice to not normalize to the forearm length was motivated by the fact that the majority of the superficial muscles that can be measured in the forearm are spread along the circumferal direction, while the longitudinal direction is the direction of their muscle fibers. Hence the spatial differentiation in muscular activity, while performing hand and wrist motions, was expected to be larger along the circumferal direction. Two researchers were responsible for the fitting of the electrodes. First, we cleaned the skin of the dominant forearm of the participant carefully with alcohol. Then we measured the forearm length from the lateral epicondyle until the styloid process of the ulna and the forearm circumference at 20% of the forearm length from the elbow (Figure 4.1). The participant had to wear a perforated sleeve (Figure 4.1) with equally placed holes and elastic only along the circumferal direction, to ensure that the electrode placement was standardized for all participants. We used a non-permanent marker to mark the skin of the participant (Figure 4.1) and then visually inspect the markings, before applying the electrodes.

Conductive gel was applied to each of the 64 electrodes with a syringe and they were subsequently attached to the forearm. The first row of electrodes was placed above the line between the lateral epicondyle and the styloid process of the ulna and the last row below, in such a way that that line, lies exactly in the middle between the two rows of electrodes (Figure 4.1). The first electrode was attached starting at the 20% of the forearm length, from the elbow. Electrodes were placed from distal to proximal, and in anti-clockwise direction (from the perspective of a right-handed participant). This way, electrodes 1-32 were placed over the dorsal side (mostly extensor muscles) and 33-64 over the ventral side (mostly flexor muscles) of the forearm. The reference electrode was placed at the distal end of the forearm, over the head of the ulna.

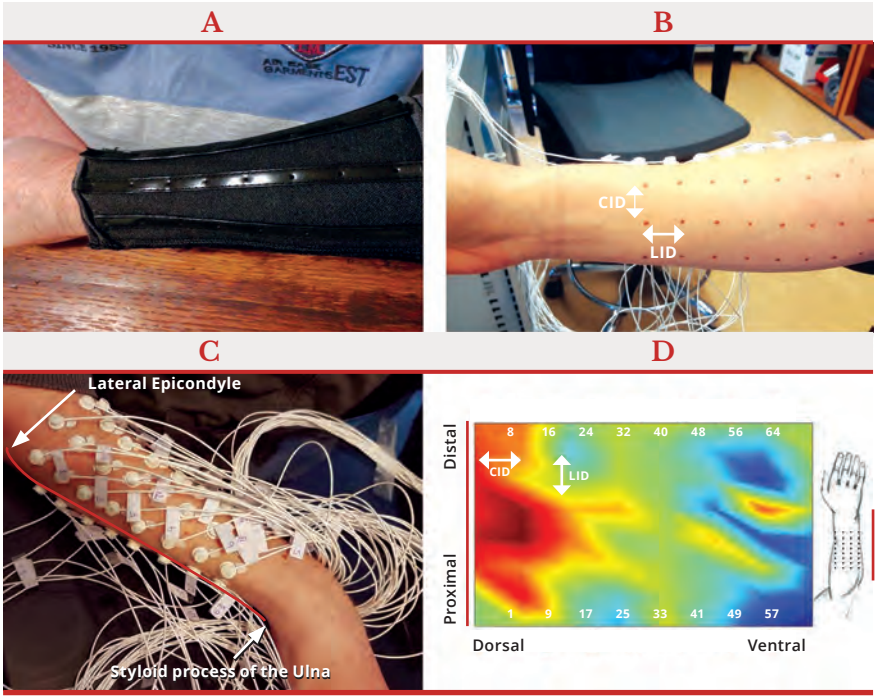


Figure 4.1 *The figure shows the process of the electrode placement. A) the flexible custom-made sleeve that was used for marking the skin of the participant. The sleeve is flexible only around the circumferal direction and stiff along the longitudinal direction of the arm. B) The marked skin of the participant. The longitudinal inter-electrode distance (LID) is fixed at 2cm (L), while the circumferal inter-electrode distance (CID) depends on the forearm width of each participant. C) The participant with all the 64 electrodes placed. The virtual line that connects the lateral epicondyle and the styloid process of the ulna was used as the border between the dorsal and ventral side of the forearm. The placement of the electrodes starts right above this line, with electrode number 1 placed proximally (at 20% of forearm length from the elbow) and 8 distally. The rest of the electrode rows are placed counter-clockwise as someone is looking at his right arm. D) This way electrodes 1-32 were placed over the dorsal side (sketch) and 33-64 over the ventral side of the forearm.*

Table 4.1 Participant Information.

Participant	Age (yrs.)	Sex	Dominant Arm	Forearm Length (20%)	LID (cm)	At 20% of forearm length from the elbow	
						Forearm circumference (cm)	CID (cm)
HP1	21	M	R	26 (5.2)	2	27	3.38
HP2	21	F	R	23 (4.6)	2	24	3
HP3	21	F	R	28 (5.6)	2	26	3.25
HP4	24	F	R	26 (5.2)	2	27	3.38
HP5	22	F	R	22.5 (4.5)	2	23.5	2.94
HP6	21	F	R	24 (4.8)	2	25	3.13
HP7	20	F	R	24 (4.8)	2	26	3.25
HP8	21	F	R	25 (5)	2	29	3.63
DP1	22	M	R	27.5 (5.5)	2	28	3.5
DP2	20	M	L	23 (4.6)	2	27.5	3.4
DP3	25	M	R	22 (4.4)	2	21	2.63

HP denotes the healthy participants and DP the participants with DMD.

Experimental Protocol

Participants performed seven different gestures involving hand and wrist motions (Figure 4.2). The chosen gestures induced: hand open/close, thumb flexion/extension, wrist flexion/extension and index extension. These were chosen as they involved the most frequent activities of daily living (ADL) [123]. First each participant was instructed to perform all gestures without constraints (dynamic) as forcefully as possible in a single recording. This way, we recorded the maximum voluntary contraction (MVC) for every electrode across all gestures. For every gesture 10 repetitions of three-second contractions were performed, together with 10 repetitions of three-second resting periods between the contractions (Figure 4.2). The participants were instructed to perform all movements in a comfortable fashion, in order to avoid forceful contractions that may elicit co-contractions of antagonist muscle groups.

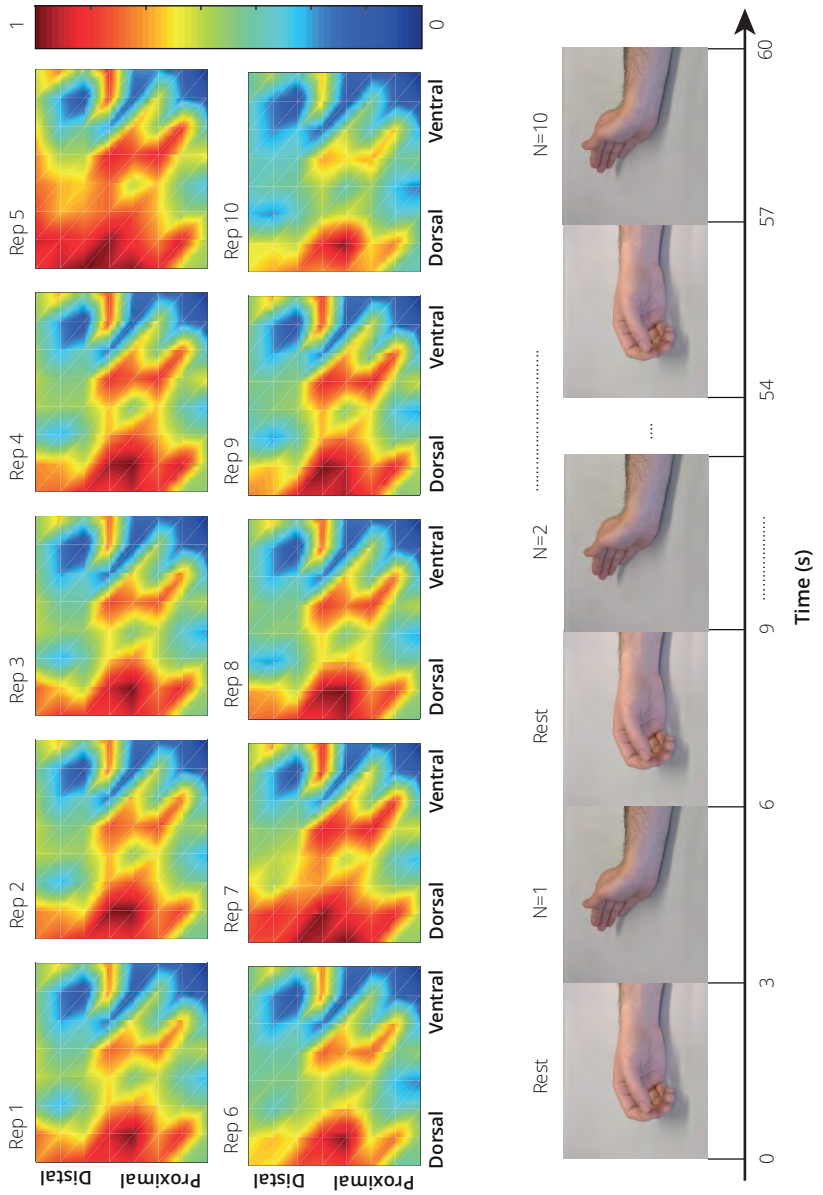


Figure 4.2 *The 10 repetitions of DP3 for wrist extension that were used to acquire the average map. The lower part shows an example of the protocol followed to record the data. In this example the participant was instructed extend his wrist for 3 seconds and then rest for 3 seconds. This was repeated 10 times. The same procedure was followed for all the 7 gestures.*

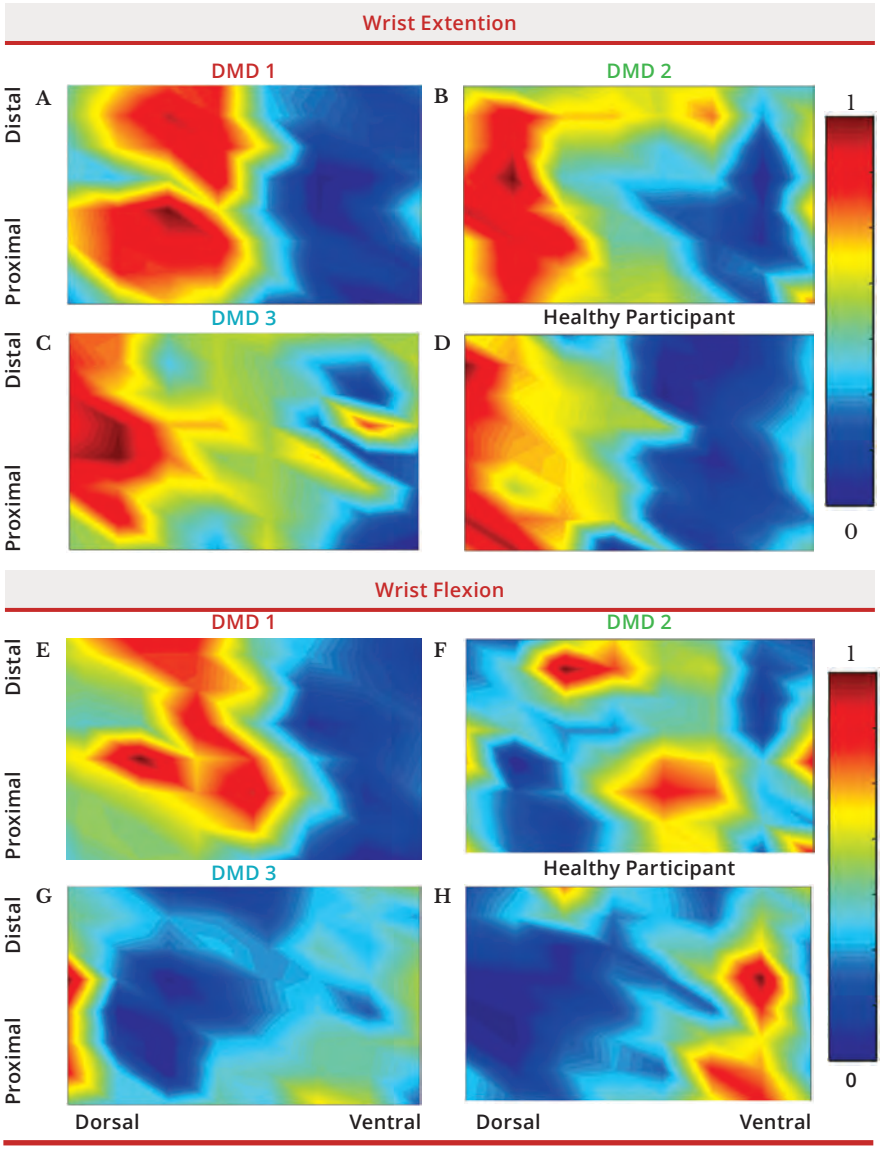


Figure 4.3 *The heat-maps of 2 representative gestures for the 3 participants with DMD and one healthy participant. Sub-figures A-D show wrist extension heat-maps for DP1 (A), DP2 (B), DP3 (C) and HP6 (D). Sub-figures E-G show wrist flexion heat-maps for DP1 (E), DP2 (F), DP3 (G) and HP6 (H). Regarding wrist extension, all participants exhibit similar activation patterns. However, for wrist flexion there is higher variability in the activation patterns within participants.*

The timing of the gestures was dictated with the use of visual feedback. The visual feedback illustrated which gesture had to be performed, and it instructed the participant when to perform the gesture and when to relax. Additionally, the measurements were performed in the morning in order to avoid effects of the end-of-the-day fatigue, especially for the participants with DMD. Furthermore, the participants had short breaks between gestures in order to rest.

Signal Processing and Analysis

The raw sEMG signals were processed offline in order to compute the envelopes for each of the 64 electrodes per gesture and per participant. First the raw data were filtered with a band-pass filter (4^{th} order Butterworth, F_c = [20-450] Hz). Additionally, a 50Hz notch filter was used to remove the power line noise. The signals were subsequently rectified and filtered with a low-pass filter (3^{th} order Butterworth, F_c = 2 Hz). Every envelope was segmented, according to the acquisitions protocol, to ten contractions and non-contraction resting periods (each lasting approximately three seconds) and normalized. A threshold was selected to define the onset of the activity and the next 3s after the onset were chosen as a contraction period. The threshold was defined as the time that the where the signal exceeded 10 standard deviations of the baseline (non-contraction) activity. The maximum value of the MVC envelope per electrode was used as a normalization value for each electrode. Faulty channels were replaced by linear interpolation of their surrounding neighboring channels (8-neighbourhood). Different local conditions were applied to faulty electrodes placed in the longitudinal extremes (less than 8 neighboring channels).

Every three-second contraction segment was further segmented in one-second segments, by keeping only the middle second of the contraction to record steady state activity. For every electrode the average of this one-second steady state contraction was calculated and used to construct 10 heat-maps per gesture (Fig. 2). For the visual inspection of the forearm activity per gesture, we constructed activity heat-maps by averaging the 10 repetition heat-maps (Figure 4.3).

Data Analysis

We analyze the data to assess myoelectric pattern repeatability, absolute and normalized activation distribution, observe motor control strategies

and explore possibilities for myocontrol in an offline setting for both healthy and DMD participants. The datasets generated for this study are stored in the 4TU repository [*https://data.4tu.nl/*], and will be available online after the publication of this study (DOI: 10.4121/uuid:f252f933-90be-4543-9c13-3c4efe208052).

Motor Control-Repeatability - The degree of repeatability across repetitions per participant was calculated using square Pearson correlation. The coefficient was extracted among the 10 repetitions per gesture and per participant.

Motor Control-Activations Distribution - The distribution of activations between healthy and DMD was calculated via the maximum normalized and absolute activations.

Motor Control-Dimensionality - The 10 heat-maps were subsequently used to construct one average heat-map per gesture per participant (Figure 4.3), that was used for the motor control analysis. We quantified differences in motor control between the healthy and DMD participants, via a principal component analysis (PCA) [124] to the gesture heat-maps per participant. For every participant, we performed a PCA to the concatenation of the sEMG heat-maps of all gestures per participant. The number of principal components (PC) needed to reconstruct the original seven gesture heat-maps was identified per participant by means of the variance explained (VE) and it was the number of PC that summed together explained more than 90% of the total variance. This number was used to explore the repertoire of orthogonal and uncorrelated sEMG patterns produced by the two groups of participants.

Myocontrol - We explored participants' myocontrol performance via an offline pattern recognition algorithm in the raw segmented data of each participant. We used a linear discriminant analysis (LDA), to recognize each of the gestures performed. The ten steady state segments for every gesture were concatenated and created a 10s vector. We trained the classifier, by extracting four time-domain features [125] (Mean Absolute Value, Zero Crossing, Slope Sign Change and Waveform Length) from the raw segmented data. We chose for a feature extraction window of 200ms (with an overlap of 100ms), which is within acceptable range for real-time

myoelectric applications [126]. The classifier was validated with a three-split Monte Carlo validation approach [127]. Each time a different part of the segmented data was used for training (always 70%) and testing (always 30%). The average offline classification accuracy of these three trainings was used as the classification accuracy per participant. Additionally, we tested how the offline classification accuracy per participant is affected by the number of gestures it has to classify.

All signal processing and data analyses were performed in Matlab 2018b software (The MathWorks Inc., USA)

4.3 RESULTS

Motor Control-Repeatability

As illustrated in Figure 4.4, both healthy and DMD individuals exhibited high and comparable correlation. The coefficient was 0.89±0.12 (mean ± std) for DMD and 0.89±0.13 for healthy participants between repetitions. An example of the ten repetitions for a DMD participant can be seen in Figure 4.2. The number of unique comparisons between 10 repetitions is 45 multiplied by the 7 gestures, makes 315 unique comparisons per participant. That explains the total of 2520 events in the healthy histogram compared to the 945 in the DMD (Figure 4.4).

Motor Control- Activations Distribution

Figure 4.5 shows the maximum absolute and normalized muscular activation distributions for both participant groups. The maximum normalized activation was on average higher for the DMD (0.7±0.4), than for the healthy participants (0.3±0.2). The maximum value observed for participants with DMD was 2.1 (DP3) and the minimum 0.3 (DP1), while for healthy were respectively 1.2 (HP1) and 0.05 (HP8). The maximum absolute activation of the DMD participants was on average 35±19 μV, while for healthy participants it was 89±358 μV.

The maximum value observed for participants with DMD was 108 μV (DP2) and the minimum 18.6 μV (DP3), while for healthy were respectively 628 μV (HP1) and 8.5 μV (HP8). Due to the difference in the number between the healthy and DMD participants, we have fewer repetitions for the DMD (7 gestures multiplied by 10 repetitions per participant, which means 210 for the DMD versus 560 for the healthy).

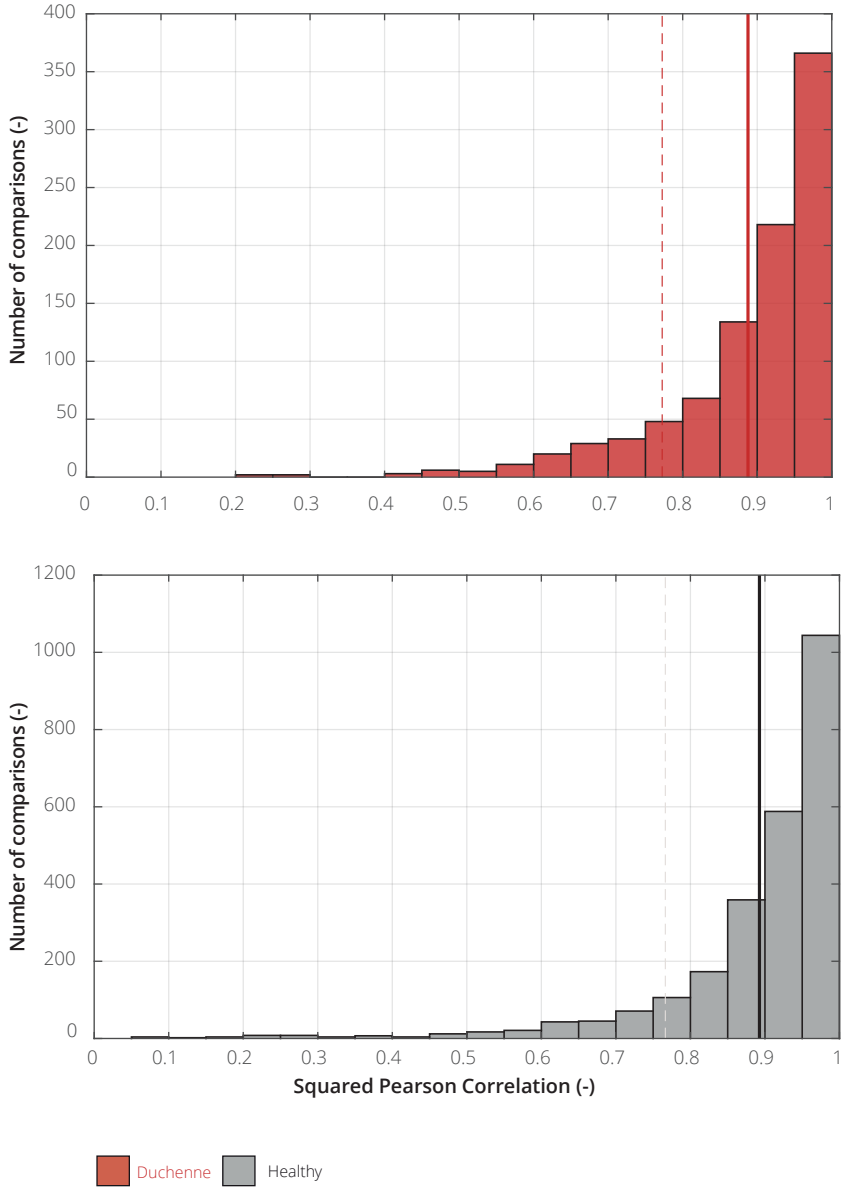


Figure 4.4 *The square Pearson correlation between the 10 repetitions for all gestures and for all participants. High correlation shows similarity between the repetitions and thus high repeatability. Both healthy and DMD participants achieved similarly high repeatability on the tasks. The full vertical lines represent the mean and the dashed the standard deviation.*

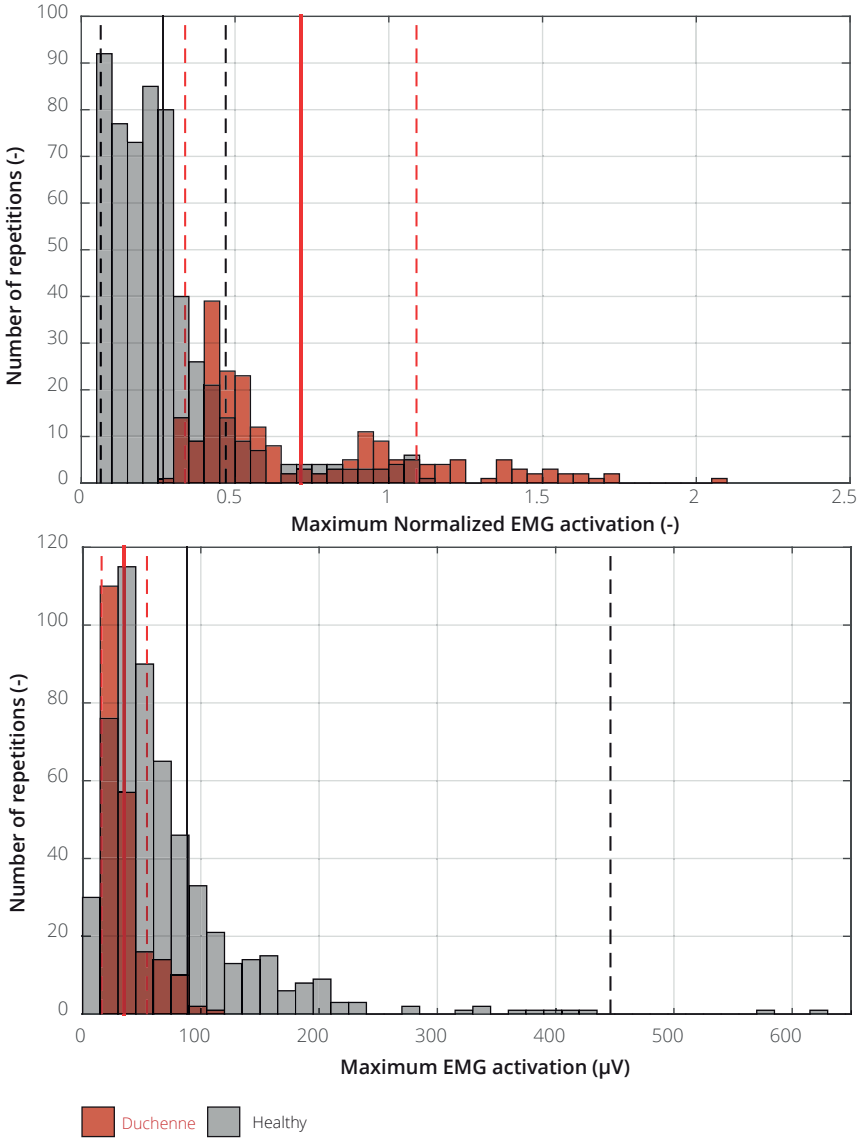


Figure 4.5 *The maximum normalized (left) and absolute (right) activation for each of the 10 repetitions of each gesture for all participants. Healthy participants generally performed the tasks with low levels of maximum normalized activation, while participants with DMD showed higher levels of maximum normalized activation during the tasks. However, the maximum absolute activations were higher for the healthy participants. The full vertical lines represent the mean and the dashed the standard deviation.*

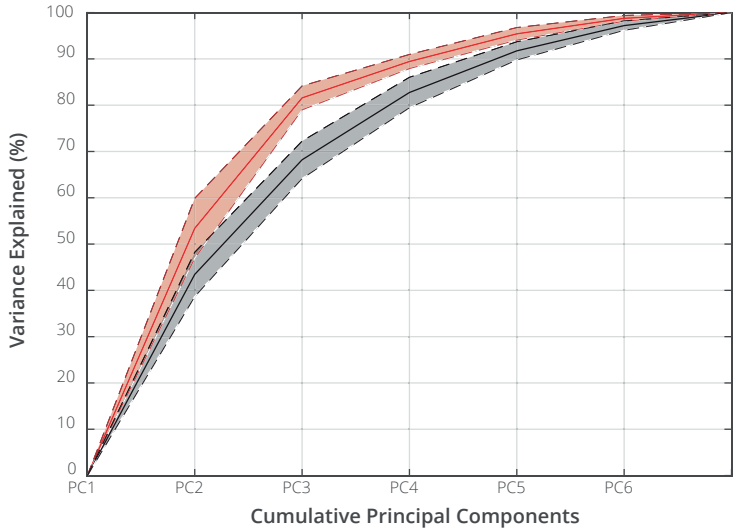


Figure 4.6 *The percentage of variance explained as a function of the number of cumulative principal components (PC). More than 90% of the variance (blue dashed line) of the data of the participants with DMD is explained by three PC, while for the healthy by four. The full lines represent the mean and the dashed the standard deviation.*

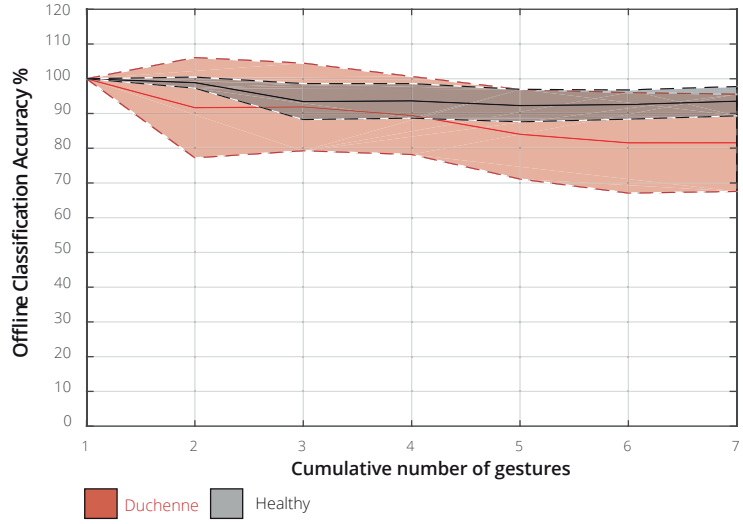


Figure 4.7 *The difference in average offline classification accuracy for healthy and DMD participants, as a function of the gestures needed to be identified by the LDA classifier. The full lines represent the mean and the dashed the standard deviation.*

Motor Control-Dimensionality

The participants with DMD used on average three PC to explain 90% of the total variance of the seven gestures (see Figure 4.6). The same variance was explained on average by four PC for the healthy participants. The total number of PC that explained 100% of the variance of the original data was six for both participant groups.

Myocontrol

The LDA classifier was trained using the seven gestures. Figure 4.7 shows the results of the offline classification accuracy as a function of the gestures that had to be recognized. The average offline classification accuracy of the DMD participants was always lower than the average of the healthy participants. When all the gestures are included, this accuracy reaches 93.6±4.2% for the healthy and 81.6±14% for the DMD participants. The offline accuracy reaches a steady state at five gestures for the participants with DMD, while for the healthy participants, this happens at three.

4.4 DISCUSSION

In this study, we measured HD-sEMG activity from the forearm of 8 healthy and 3 DMD participants, during seven hand/wrist related tasks. Using the information we performed a detailed analysis in order to characterize the differences in motor control and myocontrol capabilities between the two groups of participants.

The three participants with DMD, showed clear differences with respect to motor control, compared to the healthy population and also between each other, probably due to the different stages of the disease each one was experiencing.

Despite the consequences of muscular degeneration and minimal hand/wrist motion (DP2, supplementary video); the myocontrol potential for the DMD participants is present and comparable to the healthy participants. However, the existing differences, due to the specificities of individuals with DMD need to be addressed, while developing myocontrol algorithms.

Motor Control-Repeatability

The results showed that repeatability was intact for the participants with DMD and comparable to the healthy participants (Figure 4.4). This is an

important requirement for robust and repeatable pattern recognition based myocontrol [128].

Motor Control-Activations

Participants with DMD exhibit lower maximum absolute activations and higher maximum normalized activations compared to the healthy participants (Figure 4.5). This shows that participants with DMD operate close to their maximum effort in order to perform simple hand/wrist related tasks, and yet they produce lower absolute sEMG activity. This result, together with the fact the most progress participant (DP3) presented simultaneously the maximum normalized and the minimum absolute sEMG activity, agrees with previous studies stating that the disease progression results in lower absolute sEMG amplitude [55] and also in higher effort and fatigue [129]. The distinctly higher maximum absolute and normalized activations of HP1, can be attributed to the fact that he is the only healthy male participants. According to recent studies on upper extremity muscles, males exhibit higher activations compared to females [130] and additionally adopt different motor control strategies [131].

Motor Control-Dimensionality

Healthy participants (Figure 4.6) exhibit a higher degree of dimensionality, as expressed by the larger repertoire of orthogonal and uncorrelated sEMG patterns they can produce across the seven hand/wrist related gestures. The healthy population is using four PC to explain 90% of the variability in the original data, while DMD participants use three, except DP1 that is also using four. This may provide another indication (together with variability in maximum activation) of how the progress of the disease affects motor control, since DP1 is the least affected participant. The decrease in dimensionality may be partially attributed to the increased level of co-contractions that we observed in the DMD participants, when performing the tasks. Co-contractions may be elicited by the effort of the participants to stabilize their wrist during the tasks. Let it be noted here, that for the totality of the participants, the maximum number of PC is six. This indicates a redundancy in the selected gestures space, as it shows that the seven gestures can be decomposed to six orthogonal and uncorrelated sEMG patterns, which can explain 100% of the variability in the original data instead of seven.

Application for Myocontrol

According to our results there is potential for HD-sEMG for the robust decoding of hand/wrist motor intention in individuals with DMD. This can enable individuals with DMD to control a high-tech hand orthosis with multiple degrees of freedom (DOF). However, there was a noticeable decay of the LDA offline classification performance, when more gestures were added for the participants with DMD, which was larger than the one for the healthy participants (Figure 4.7). However, despite the lower performance, the classification performance is on average larger than 80% for all the seven gestures and more or equal to 90% for up to four gestures. Together with the ability of the DMD participants to create repeatable HD-sEMG activation patterns, this result shows the potential of myocontrol for decoding of hand/wrist motor intention.

The current performance of classification could be improved with the development of DMD tailored classification algorithms, which will consider the specificities of the disease. Such specificities are the progression of the disease, the low sEMG signal to noise ratio [55] and the differences in the motor control strategies employed by individuals with DMD. The observed lower spatial dimensionality in the HD-sEMG, may also suggest the compression of the data before classification, due to the lower variability. However, more research with individuals with DMD is necessary, before any definitive conclusions can be reached.

Limitations of the study

We included in our study three participants with DMD with large functional variability in order to explore a larger spectrum of the disease. However, our study is limited by the low number of participants with DMD. This is an unavoidable limitation due to the low number of available participants. We also intended to comply with the ethical and legal standards while conducting our study, by not recruiting participants that are already involved in other studies at the same time. Hence, our conclusions need to be taken as indicative until research is performed with more participants, which will allow for more general and strong conclusions.

Additionally, we did not monitor the level of contraction during the conduction of the measurements. We explicitly asked our participants to perform all movements comfortably, but we did not control this condition. However, it is known from the literature that different contraction levels

elicit a small shift in the main activity area, however not significantly altering the spatial distribution of HD-sEMG in the forearm [115].

Future Work

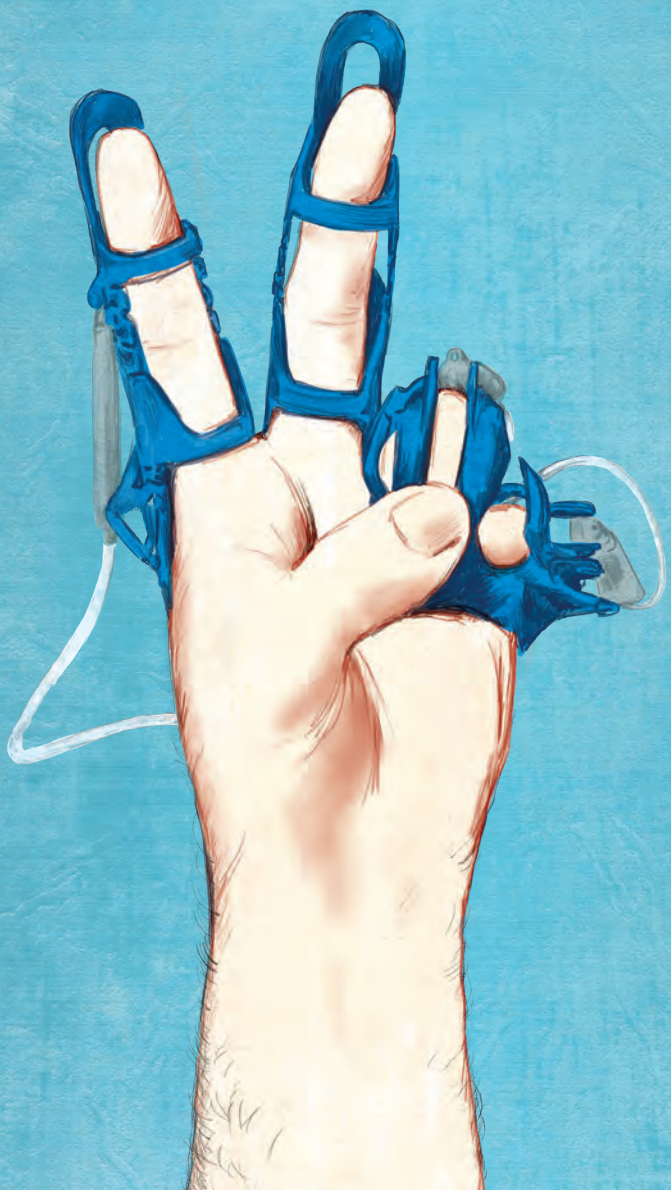
Future work will evaluate the generalization of our protocol with more participants with DMD, in order to investigate further the characterization of forearm electromyograms for individuals with DMD and come to more general conclusions, regarding this very diverse population. Moreover, we are interested in the exploration of online classification performance implemented outside of the lab, in order to simulate daily use. The results of this study together with the future studies will be further used for the development of myocontrol algorithms for the robust control of an active hand exoskeleton [59], developed within the Flextension-Symbionics project [121] for individuals with DMD.

4.5 CONCLUSION

We characterized the forearm electromyograms of three individuals with DMD and compared to eight healthy individuals. For the first time, we have a systematic analysis on how the disease affects the spatial distribution of HD-sEMG pattern in the forearm and the repeatability and activation distribution of these patterns. Additionally, we explored the potential for the myocontrol, be the offline decoding of motor intention from the forearm muscles of individuals with DMD. We performed this study in order to get a better understanding of DMD hand/wrist motor control with regard to exoskeleton applications. The results show that the disease decreased the repertoire of spatially distinguishable HD-sEMG patterns for the individuals with DMD and increased the muscle activations related to them. However, the ability of the participant with DMD to repeatedly produce the same HD-sEMG was intact and the potential of their muscle signals for myocontrol comparable to the healthy individuals. Future studies will focus on testing sEMG for the real-time decoding of hand/wrist motor intention with individuals with DMD. Moreover, we will implement and test the feasibility of sEMG control with a new active hand exoskeleton for individuals with DMD.

PART II

HAND MOTOR INTENTION DECODING IN DUCHENNE MUSCULAR DYSTROPHY



5

TRANSFERRABLE EXPERTISE FROM BIONIC ARMS TO ROBOTIC EXOSKELETONS: PERSPECTIVES FOR STROKE AND DUCHENNE MUSCULAR DYSTROPHY *

Kostas Nizamis, Arno H. A. Stienen, Derek G. Kamper, Thierry Keller, Dick H. Plettenburg, Elliott J. Rouse, Dario Farina, Bart F. J. M. Koopman and Massimo Sartori

ABSTRACT

Upper extremity function is affected by a variety of neurological conditions. Robotic exoskeletons offer a potential solution for motor restoration. However, their systematic adoption is limited by challenges relative to human intention detection and device control. This position paper offers a focused perspective on this topic. That is, on how knowledge gained from the design and implementation of human-machine interfaces (HMIs) for bionic arms can benefit the field of rehabilitation exoskeletons. Three broadly used HMIs in bionic arms are here investigated including surface electromyography, impedance and body-powered control. We propose that combinations of these HMIs could push forward upper extremity exoskeleton development. In this context, we provide concrete applicative examples in two selected clinical scenarios including post-stroke and Duchenne muscular dystrophy individuals. The discussed solutions can open new avenues for the translation of robotic exoskeletons in a large set of clinical settings and enable a class of exoskeleton technologies that could support a broader range of impairment and disease types.

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5.1 INTRODUCTION

The ability to perform coordinated arm-hand movements relates to the quality of life, as well as to social participation and acceptance [2]. As we manipulate objects primarily through our hands, neurological injuries and disorders affecting the upper extremity [2] highly impair one's ability to interact with the external world. In this context, robotic exoskeletons have been long developed for restoring impaired motor functions [1], [132], due to their potential in promoting active user participation [133], independence [134] and potential suitability for home rehabilitation [135].

The research field of robotic exoskeletons has been growing rapidly [1], [132], [136], resulting in an explosion of wearable assistive and rehabilitation technologies [137]. However, demonstrated functional and clinical impact is still limited. Kinematic compatibility and the additional weight imposed on the existing limb by a robotic exoskeleton are important factors limiting robotic exoskeleton use. The development of soft exosuits, aims to easier fitting and lightweight designs that require less energy to use [138], [139]. Additionally, the lack of a rigid frame simplifies sensor placement, and prevents extra strains to the body of the user. However, soft exosuits result in a limited amount of support compared to rigid robotic exoskeletons [138]. Bos et al. [1] identified forty-six hand exoskeletons intended for use as daily assistive devices, yet most of them did not reach the market. Moreover, Maciejasz et al. [136] concluded that the results of the clinical evaluation of robotic exoskeleton-aided therapy are sparse. Additionally, despite the large research performed in the last 30 years [140], the effectiveness of robotic therapy over conventional physiotherapy is modest [136], [141], especially in people with neuromuscular injuries (e.g. stroke) or progressive impaired function (e.g. Duchenne muscular dystrophy or DMD). Important causes are the slow translation of robotic exoskeletons from laboratories to clinical setting, where clinical trials can further assess their efficacy [136], and the fact that the broad use of exoskeletons for daily or home use has not been consistently translated from the laboratory to the clinic [82], [142], [143]. Additionally, the lack of natural and intuitive human-machine interfaces (HMI), presents an important challenge for the future, indicating that the use of robotic exoskeletons in the real world requires significant improvements before it can be realised [134] [144].

On the other hand, the field of bionic arms has undergone substantial scientific and technological advances with direct clinical and market impact. Prosthetic procedures, such as targeted muscle re-innervation (TMR) [145] and osseointegration, greatly improved surface electromyography (sEMG)-based decoding and device control [146] as well as donning/doffing [147] and stability of the bionic arms fixation. Such procedures have opened up new opportunities for HMI. In the case of people with brachial plexus injury, where a robotic exoskeleton would be the preferable (minimally invasive) technology, elective amputation and use of a bionic arm is sometimes preferred [148]. In this way, people with critical injuries can substitute a non-functional limb with a highly functional bionic limb, indicating that bionic technology is more mature to enhance functional recovery.

Robotic exoskeletons such as the MyoPro elbow/wrist/hand orthosis [149], [150] and the SaeboGlove [151] are commercially available. However, in terms of HMIs, they are less advanced compared to commercial bionic limbs, which are driven by pattern recognition myocontrollers [152], [153] or biomechanical models [154], enabling multiple degrees-of-freedom (DOF).

Given the close relation and overlap between bionic arms' and robotic exoskeletons' HMIs (see Section 5.2), this paper proposes a focused perspective for how expertise and technological advancements in bionic arms could be translated to the developing field of arm-hand exoskeletons. We trust that the development of such a roadmap will lead to a new class of wearable robots that can seamlessly cooperate as a natural extension of the human body.

In this paper, we first introduce three key technologies well established in current HMIs for bionic arms including sEMG, impedance and body-powered control. Second, we propose how HMIs can be translated to exoskeletons. Third, we introduce relevant clinical scenarios that can benefit from the use of exoskeletons, including stroke and DMD. These key scenarios allow distinguishing between exoskeletons used for rehabilitation or restoration (i.e. stroke scenario) and those used for functional replacement, i.e. assistive technologies for daily use (i.e. DMD scenario). Finally, we discuss how these technologies can be combined in order to be used for the presented clinical scenarios. This provides new perspectives on how exoskeletons can be interfaced to individuals with neuromuscular impairments.

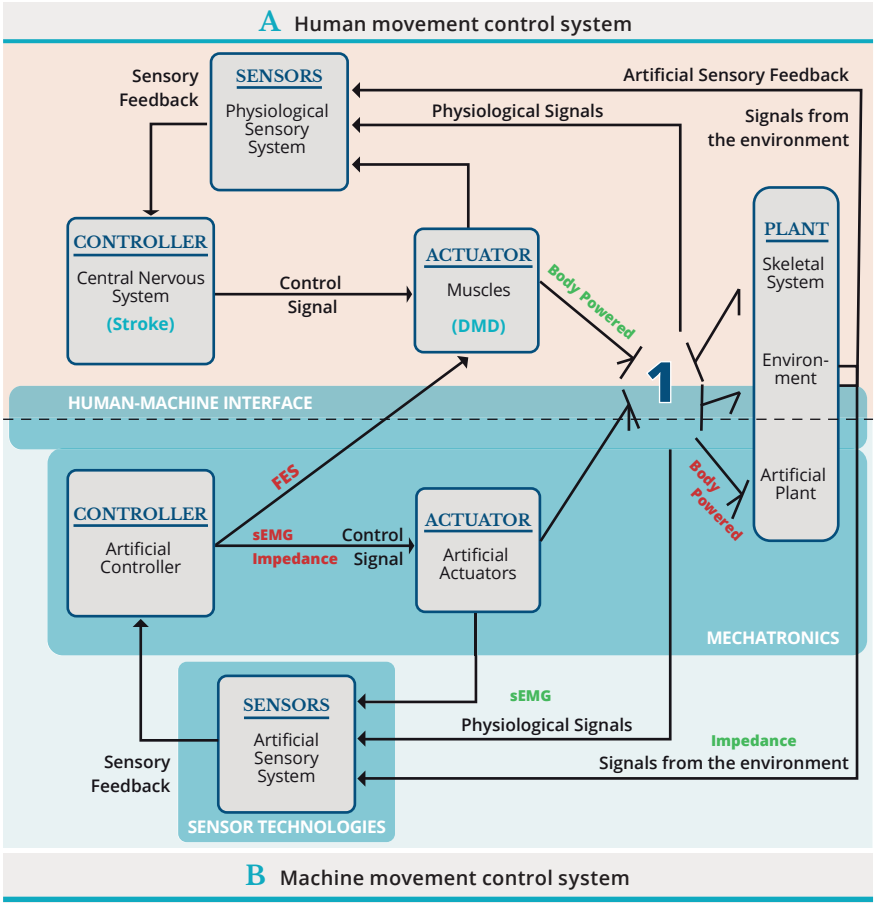

Figure 5.1 This figure illustrates A) the human movement control system together with B) the machine movement control system. The machine movement control system can be a robotic exoskeleton or a bionic limb. With light blue are noted the two clinical cases discussed in this paper. DMD affects the muscles, and stroke causes central nervous system disorders. With red and green we can see the interaction between each of the three human-machine-interfaces discussed and the human, plus functional electrical stimulation (FES). The input signal (motor intention detection) and resulting interaction is noted in green and red, respectively. The three major components of bionic arms and robotic exoskeleton systems are highlighted in the machine movement control system. The mechatronics consist of the controller, actuator and the device (bionic limb or robotic exoskeleton), the sensor technologies refer to the artificial sensory system and the human-machine interface includes the flow of information between the human movement control system and the machine movement control system. Adapted from [168].

5.2 FOCUSED PERSPECTIVE

Learning from Bionic Arms

Research on prosthetic arms goes back for centuries [155], reaching a strong impact on the market [156]. Arm exoskeletons share a similar design and functional features to current bionic arms, yet underline unique and distinctive attributes, i.e. exoskeletons act in parallel to the impaired limb, rather than replacing it. Figure 5.1 shows differences at the HMI level across bionic arms and exoskeleton technologies. The human movement control system (Figure 5.1A) and the machine movement control system (Figure 5.1B) act in parallel to each other for exoskeletons but in series for bionic arms. In this context, we argue that the transfer from bionic arms to exoskeletons should focus on the HMI level.

The term HMI refers to methodologies for the identification of the user's intent to move from biological signals (i.e. surface electromyograms or sEMG) or body force and position data and its translation into robotic commands. Numerous invasive [157], [158] and non-invasive [159]–[164] interfaces were developed in the past and applied to both bionic arms [157]–[161], [163], [164] and exoskeletons [44], [162], [165]–[167]. There are different levels of interfacing with the human [168] (Figure 5.1). Myocontrolled bionic arms [159], [160] interface with residual muscle tissues replacing the missing limb. There are also bionic lower limbs that interface with the musculoskeletal plant via impedance control [161], [162] (utilising the interaction between the user and the robotic limb) or via body-powered control [163], [164] (by using an intact limb to mechanically control a bionic limb). Neuroprostheses are available to stimulate muscles or nerves [157], [158] to elicit movement in the impaired limb.

Clinical Scenarios

In this position paper, we rely on two representative key clinical scenarios including stroke [169] and DMD [170]. [170]. For both scenarios there is a clear need for active support and robotic exoskeletons present a feasible solution. However, despite this similarity both conditions present clear differences at the HMI level. Stroke represents a class of conditions where the affected individual needs to re-learn how to use their limbs, thus requiring HMIs providing minimal assistance in order to facilitate motor learning. On the other hand, muscular dystrophies are characterized

by a progressive loss of muscle strength, with no potential for motor function restoration, thus requiring HMIs providing maximal assistance to postpone tissue degeneration. By discussing extensively those distinct neuromuscular deficiencies we cover a large HMI spectrum which, if addressed properly, would enable a class of exoskeleton technologies that could support a broader range of impairments and disease types.

Stroke: It is caused by a lesion in the central nervous system or CNS (Figure 5.1) and results in loss of motor capacity [169]. According to a recent study by the world stroke organization, it has an incidence of 35-909 per 100,000 people per year worldwide [171] and the observed acceleration in the ageing population is expected to raise these numbers [171]. Stroke results in motor impairment with a level of similarity to other neurological conditions including multiple sclerosis (MS) [172] and spinal cord injury (SCI) [173], i.e. early fatigue onsets, spasticity, paresis, muscle contractures and rigidity, reduced mobility and musculoskeletal coordination and mechanical tissue changes [174]. Hence, exoskeleton technologies effectively supporting stroke rehabilitation could have a broader impact on other clinical scenarios, i.e. SCI and MS.

Exoskeletons targeting stroke individuals are designed for rehabilitation of the impaired motor function [137]. Currently, static splints are used for increasing range of motion and preventing contractures [175]. However, although highly prescribed by doctors, these are reportedly ineffective [176] and uncomfortable for long-term use [177]. Active exoskeletons are also broadly for clinical or home rehabilitation [1].

For stroke patients, exoskeletons are controlled via assistance-as-needed strategies to enable the active participation of individuals during the rehabilitation process [178], [179].

DMD: It is an X chromosome-linked progressive neuromuscular disease (Figure 5.1) which leads to physical disability and shortened life expectancy [62]. There is currently no therapy developed for DMD. Nevertheless, recent technological advances have significantly increased the life expectancy of people with DMD [21]. Due to this fact, the population of individuals with DMD is expected to significantly increase in the near future [22]. DMD presents a representative case for other existing muscular dystrophies as it is the most common and severe form of muscular dystrophy [180], with an incidence of 1 out of 4,000 male births [5].

People with DMD need exoskeletons to maintain tissue integrity. This can be achieved by the decrease of detrimental mechanical load on their muscle tissues in order to minimise contractures and joint deformities that develop due to disuse of the limb [65]. There is evidence that people with DMD can greatly benefit from the use of arm exoskeletons [6], thereby promoting the use of the upper limb. Even more importantly, DMD individuals need devices to assist function in daily living for a prolonged period of time [64]. Regarding the hand, the only exoskeletons systematically adopted in people with DMD are passive splints [48]. These aim at maintaining a large active range-of-motion for the fingers and the wrist and slow the development of contractures.

Muscular dystrophies present a different scenario than stroke as the disease is progressive. While short-term therapeutic benefits may be seen with the use of a device, the primary focus is on providing as much assistance as possible. Thus, the exoskeleton should minimise the effort of the user to enable activities of daily living.

Key Technologies in human-machine systems

Whether for exoskeletons or bionic arms, an HMI should enable the robust identification of the user's movement intent and translate it into machine commands. In the remainder of this section, we introduce three HMI technologies as well as the use of functional electrical stimulation (FES), which we selected for their potentials. These selected technologies will be combined together in Section 5.3 to compose HMIs specifically tailored for stroke and DMD.

sEMG control - Myocontrol is broadly used in bionic arms [113], [114]. Direct sEMG control [181] is typically combined with co-contraction to enable switching across DOF. However, it has been reported as an unintuitive approach providing limited gains in functionality [113]. More advanced approaches rely on two main techniques [182]. The first is model-free machine learning [183]. The second emerging one is the model-based approach using musculoskeletal modelling [184]–[186]. Machine learning uses multi-channel sEMG recordings in conjunction with model-free algorithms in order to achieve higher functionality and control over more DOF. In this context, pattern recognition [187] (classifying a finite number of movements based on features of the sEMG signals) and regression

[188] (continuous mapping of sEMG signals to kinematic variables) are currently used for the control of bionic arms. However, training in a specific spatiotemporal condition using machine learning does not necessarily translate into another [189]. The combination of such approaches with biomechanical models can overcome this limitation [184], as recently demonstrated [185], [186].

Pros and cons: The benefit of myocontrol techniques is that they allow for the user's intent to be detected before the movement actually takes place and even if no mechanical movement is possible [184]. This way, it is possible to synchronise the actual muscle contraction to the movement of a device, thus making the combined movement more intuitive [113]. On the other hand, sEMG can be contaminated by electromagnetic interference, skin perspiration and fatigue [190], and movement and crosstalk artefacts [191]. The use of sophisticated machine learning techniques is reportedly low for more challenging 'outside the lab' conditions [113] as it requires significant set-up and training time. Also, myoelectric bionic arms tend to be rejected by the user due to unpredictability in their response [192].

Impedance control - Impedance and admittance control govern the relationship between position and force (torque) rather than controlling either position or force explicitly, where admittance is the inverse of impedance. The impedance control approach was originally proposed by N. Hogan [193] and has had widespread success in wearable robotic technologies for the lower extremity. For example, Herr et al. have used impedance control to govern the behaviour of their bionic ankle and knee, which have had promising clinical results [76],[77]. Furthermore, Goldfarb et al. have implemented impedance control in their robotic leg, which has provided a rich foundation of work on the development of many aspects of robotic legs [196],[197]. Impedance control is particularly useful for lower extremity bionic limbs because it permits mechanical dynamics between the body centre of mass and the ground, governed by the multi-joint mechanical impedance of the robotic hardware. Thus, impedance control circumvents the use of high-gain position-controlled mechanisms, which would cause the wearer to 'ride' the robotic leg or exoskeleton. This approach contrasts the control of upper limb robotics; bionic arms have traditionally used muscle sEMG as a command signal, which often controls

the velocity of the joint or grasp mode [160], [198], [199].

Pros and cons: One unique characteristic of impedance-based control schemes is that they enable mimicking the compliance of the musculoskeletal system. Knowledge of how impedance is regulated during movement forms the foundation of a biomimetic impedance control approach, which can be implemented in the control of exoskeletons and bionic arms. The impedance control framework is the only control strategy that permits the ability to match human regulation of kinetics, kinematics, and impedance, simultaneously. However, further studies are needed to ascertain the value of the biomimetic impedance framework, both in bionic limbs and exoskeletons. This case is dominated by lower extremity bionic limbs. Upper extremity bionic limbs are stiff mechanisms controlled using sEMG thresholding or pattern recognition.

Body-powered control - To control a bionic arm, it is important that the user can provide a proper feedforward signal. Equally important is that the user receives a proper feedback signal. This was already pointed out by Norbert Wiener in 1948 [200]. The human hand has excellent control; there is a wealth of effectors and of afferent information (muscle spindles and Golgi-tendon organs) providing excellent (proprioceptive) feedback. In body powered bionic arms, shoulder movements are most commonly harnessed to provide the intent of the motion. The shoulder muscles involved provide proprioceptive feedback. The bionic arm user can learn how the position of the shoulder and/or the upper arm at the unaffected side is a measure for the opening width of the bionic arm. Equally, the user can learn to interpret the forces perceived on the shoulder as a measure for the applied pinch force of the bionic arm.

Existing control methods include harnessing body movements, cineplasty [201], muscle bulging [202], myo-electricity, and myo-acoustics [203]. New control methods explored include peripheral nerve interfaces [204] and brain-computer interfaces [205].

Pros and cons: Given the need for feedback, only harnessing body movements, cineplasty, and peripheral nerve interfaces are feasible control methods. Research in body-powered bionic arms focusses on lowering the operating forces to enhance force and displacement perception. For all options, the design of a servo mechanism is

instrumental [206]. All that is said for bionic arms applies to robotic exoskeletons as well – it is all about how a human being can control a machine. Closed-loop control is also a necessity here. However, body powered prosthesis, are quite limited in the number of DOFs that they can restore and actively control.

Functional electrical stimulation (FES) - FES is broadly used together with robotic exoskeletons [207]–[210]. Transcutaneous FES is integrated with exoskeletal structures in which the exoskeleton takes a double function: i) it carries the electrodes; ii) it stiffens or stabilizes the joints that cannot be well controlled by FES alone. A typical example of such a transcutaneous FES upper extremity exoskeleton is the Bioness Inc. H200, a device that has been used in clinical applications for almost two decades. Current challenges for the seamless integration of all these technologies into an intelligent exoskeleton for unassisted hand grasp are mainly on the material side on stretchable electronics, the electrode-skin interface, and personalization.

Pros and cons: For the upper limb, recent reviews concluded that FES is a promising technology for rehabilitation in combination with robotic exoskeletons [211] and that FES systems reduce spasticity and improve the range of motion and the quality of life of people with stroke [212]. To the authors' best knowledge, there is no evidence of FES being used with individuals with DMD to assist in functional movements of the upper limb. However, there are studies [213]–[215] on the therapeutic effects of FES for people with muscular dystrophies, but with controversial and sometimes contradicting results. It is therefore important to approach this idea with the appropriate caution since it is known from the literature that exercises imposing high mechanical stress and eccentric muscle contractions can be harmful to individuals with DMD [39].

5.3 THE PROPOSED POSITION

In the previous sections, we described three key HMI components currently used in bionic arms (sEMGs, impedance control and body-power schemes) and neuro-prostheses (FES). Here, we discuss our position regarding their combined use and translation into robotic exoskeletons as an intervention for the clinical scenarios discussed previously.

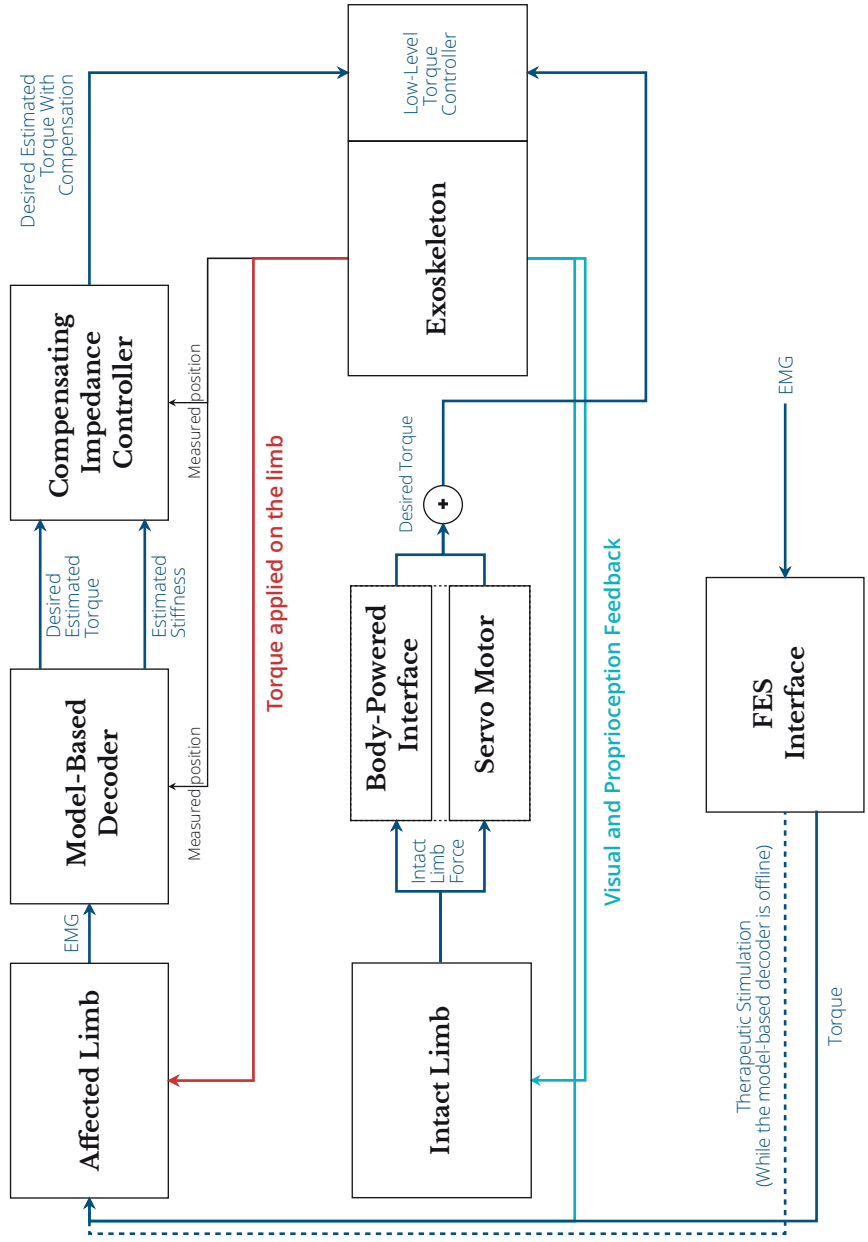

Figure 5.2 This figure illustrates the proposed control diagram for stroke, including a body powered interface together with sEMG and impedance. All the separate elements are described in detail in Section Position for stroke case-scenario.

Position for stroke case-scenario

Figure 5.2 shows the conceptual design of a stroke-specific HMI scheme. The user intent is estimated by means of sEMG from the affected limb [159], [160]. In stroke patients with residual proprioception, this provides a level of closed-loop control. The sEMG signals are directed together with position information from the robotics exoskeleton to a model-based decoder [146], which provides an estimate of the desired torque in the limb's joints. This allows the implementation of control strategies in which the participant is supported as little as needed and proportionally to residual force, central for neuroplasticity [113]. Moreover, this allows the estimation of joint stiffness, as previously shown, and therefore establishes closed-loop controllers operating in the impedance/admittance domain [216]. An impedance compensation controller receives the estimated torque and stiffness from the model and also position information from the exoskeleton. In this way, it can be directly controlled from the sEMG-decoded stiffness and compensate for altered joint mechanics due to tissue structural changes [174],[216]. This can be achieved by a position-based compensator. The impedance compensation controller needs to be calibrated beforehand in order to compensate for joint-stiffness induced torques, similar to the active stiffness compensation proposed by Lobo-Prat et al. [217]. Additionally, the impedance compensation controller can be used to provide active gravity compensation including weight compensation of handheld objects. The final desired estimated torque is directed to a low-level torque controller and the outcome torque is applied to the limb by the exoskeleton. For individuals with hemiparesis, body-power technology can be used to harness the functionality of the non-impaired side and further enhance the active participation of the user. In the case of more impaired participants, the torque provided by the non-impaired limb can be amplified by the addition of a servo motor (Figure 5.2). In this case, the desired torque is also directed to a low-level torque controller and the outcome torque is applied to the limb by the exoskeleton. We propose the use of electrical stimulation (ES) as a means to improve upper limb functionality by reducing muscle contractures and spasticity while improving coordination [218]. This is also reported to happen in cases of MS [219] and SCI [220], however, for the lower limb. With such use of FES, we can optimise the use of the robotic exoskeleton by the human.

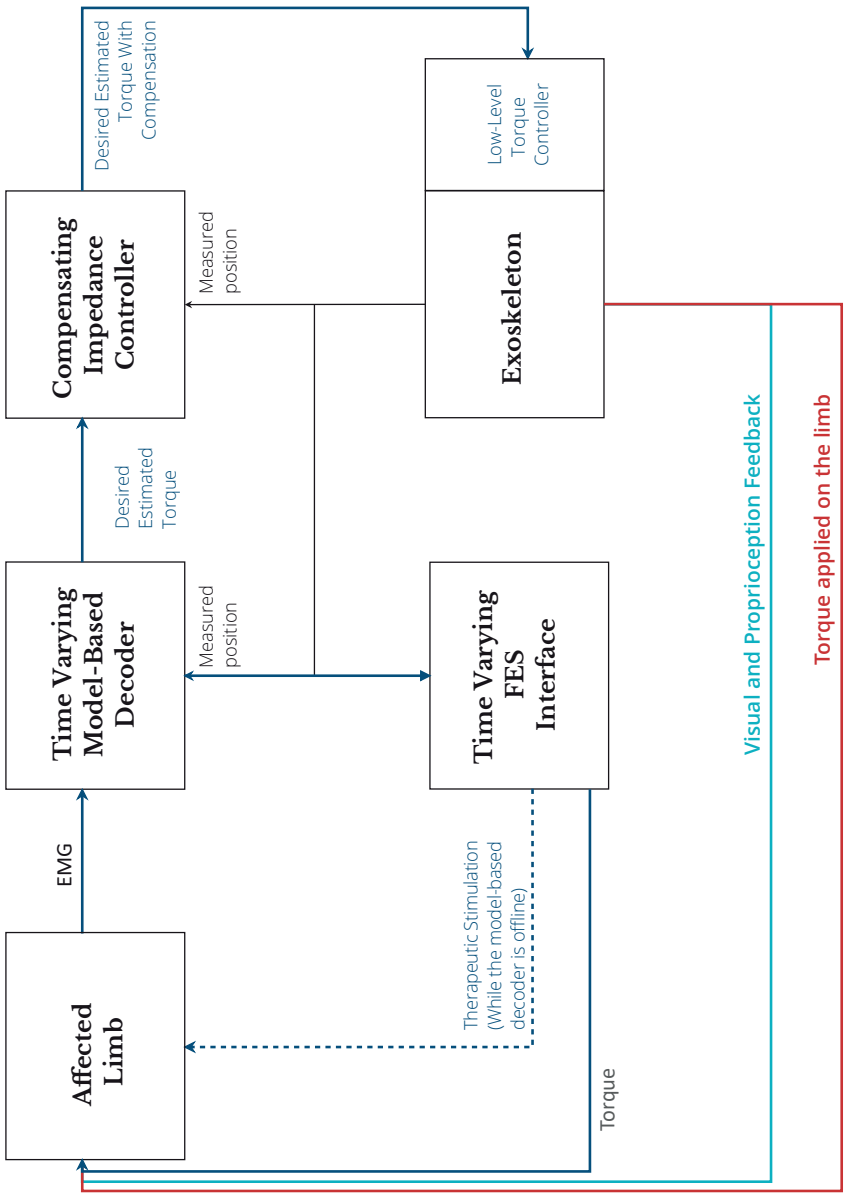

Figure 5.3 This figure illustrates the proposed control diagram for DMD. In this case, we combine sEMG with a time-varying biomechanical model (due to the progressive nature of the disease) and impedance control. All the separate elements are described in detail in Section Position for DMD case-scenario.

Position for DMD case-scenario

Figure 5.3 shows the DMD specific HMI scheme. Similar to what we proposed previously for stroke, the user and the robotic exoskeleton interface by the means of sEMG of the affected limb. Closed-loop sEMG control is achievable in DMD with residual proprioception [221]. We propose to combine sEMG with a virtual impedance/admittance model similar to [217], [222]. sEMG signals are directed together with position information from the robotic exoskeleton to a time-varying model-based decoder [146], which estimates the desired torque in the limb's joints. The model-based decoder adapts with time (time-varying) to the progress of the disease. This can be done via multi-scale mechanobiology models characterizing cellular-to-organ scale musculoskeletal adaptations [223], [224]. The impedance compensation controller will receive the estimated torque and stiffness from the model and also position information from the exoskeleton. This can be achieved by a position-based compensation similar to the one applied to abnormal joint stiffness induced forces by Lobo-Prat et al. [217]. The impedance compensation controller needs to be calibrated beforehand in order to compensate for such parasitic forces and torques, due to abnormal joint stiffness. Additionally, the impedance compensation controller can be used to provide active gravity compensation. The torque estimated by the model-based sEMG decoder is algebraically added to the torque estimated from the compensatory impedance controller and will be sent to the low-level torque controller. The outcome torque will be applied by the exoskeleton to the affected limb.

The therapeutic ES will act when the sEMG-impedance hybrid is offline. The interaction between the sEMG model-based decoder and the ES module will have a dual nature. First, it tells the ES module how much exercise is needed based on the quality of the sEMG measurements. Second, it will indirectly affect the performance of the model-based decoder by improving muscle quality. The ES module can be integrated into the robotic exoskeleton to enhance portability.

5.4 DISCUSSION

This position paper presents two HMI designs for addressing distinctive clinical scenarios including stroke and DMD. For both scenarios, the proposed designs include different combinations of sEMG, impedance control, and body-powered technology in combination with FES. The technologies discussed in this paper covered three crucial objectives for the control of bionic limbs: 1) the connection to the human body (sEMG) 2) the control of actuators (impedance/admittance) and 3) usage of the residual limb capabilities (body-powered). In this context, FES enables establishing neuroprostheses for upper extremity function restoration as a stand-alone [218] or in combination with a robotic exoskeleton [225]. Therefore, FES is the optimal starting point for investigating new concepts of integration between bionic prosthetics and robotic exoskeleton technologies. The HMI type considered in our position paper aims to operate at a lower level than cognitive HMIs. Our proposed HMIs aim to interface wearable robots with the human neuromuscular system via the recording and processing of bio-electrical information.

Additional HMI technologies exist that were not covered by this paper [168]. Common non-invasive HMIs include brain-computer interfaces like electroencephalography [226] (EEG), and near-infrared spectroscopy [227]. At the muscle level, interfaces like mechanomyography [203] and sonomyography [228] aim at providing alternatives to sEMG. Last but not least, HMI such as eye tracking, tongue interfaces and joysticks have been heavily used for the control of bionics [168]. Those have a clear disadvantage of sacrificing one function to support another.

In addition to HMI, there are a number of issues already addressed in bionic arms, which can enhance the adoption of exoskeleton technologies. Effortless donning and doffing of an external device can have a positive effect on a user's satisfaction and presents an aspect already well-studied for bionic arms. Moreover, cosmetic gloves and artificial skin ensure a natural appearance and thus enhance the acceptability of such devices. Exoskeletons can benefit from the successful examples already set for bionic arms. The fact that amputees may have specific surgeries performed to improve fit (like osseointegration) or bionic arm control (like TMR) suggests that surgical procedures could become available for individuals using exoskeletons.

Such procedures could also restore sensory feedback in people with Stroke or DMD, when impaired; similar to what is done for amputees [229]. This is important for the upper limb, as the sense of touch and proprioception is central for object manipulation [230]. Additionally, the restoration of sensory feedback enables natural closed-loop control (Section 5.3) and improves fine motor control in terms of coordination and dexterity [231]–[233]. However, it is important to consider that while amputees might have the level of commitment to consider invasive surgery, paretic patients or muscular dystrophy patients may not have it. In these neurological conditions, it is not uncommon that sensory feedback and proprioception may be restored through non-invasive ways, such as rehabilitation [234] or that are not even impaired [235], [236].

5.5 CONCLUSION

This position paper offers a focused perspective on the development of personalized HMI schemes to enhance upper extremity function via robotic exoskeletons for the cases of stroke and DMD. We believe that the use of the proposed schemes can help the development of better HMI schemes for users of robotic exoskeletons of the upper limb, enhance function and daily use of such devices, and inspire more research towards the development of hybrid HMI.

Next to HMIs, there are a number of issues already addressed in bionic limbs, which can enhance the adoption of exoskeleton technologies. Effortless donning and doffing of an external device can have a positive effect on a user's satisfaction and presents an aspect already well-studied for bionic limbs. Moreover, cosmetic gloves and artificial skin ensure a natural appearance and thus enhance acceptability of such devices. Exoskeletons can benefit from the successful examples already set for bionic limbs. The fact that amputees may have specific surgeries performed to improve fit (like osseointegration) or bionic limb control (like TMR) suggest that surgical procedures could open to possibilities for individuals using exoskeletons.

6

REAL-TIME MYOELECTRIC CONTROL OF WRIST/HAND MOTION IN DUCHENNE MUSCULAR DYSTROPHY*

Kostas Nizamis, Anil Ayvaz, Noortje H.M. Rijken,
Bart F.J.M. Koopman and Massimo Sartori

ABSTRACT

Duchenne muscular dystrophy (DMD) is a genetic disorder that induces progressive muscular degeneration. Currently, the increase in DMD individuals' life expectancy is not being matched by an increase in quality of life. The functioning of the hand and wrist is central for performing daily activities and for providing a higher degree of independence. Active exoskeletons can assist this functioning but require the accurate decoding of the users' motor intention. These methods have, however, never been systematically analyzed in terms of DMD. This study evaluated direct control and pattern recognition, combined with an admittance model. This enabled customization of myoelectric controllers to one DMD individual and to ten healthy participants during a target-reaching task in 1- and 2- degrees of freedom (DOF). We quantified real-time myocontrol performance using target reaching times and analyzed the differences between the healthy individuals and the DMD individual. Our findings suggest that despite the muscle tissue degeneration, the myocontrol performance of the DMD individual was comparable to that of the healthy individuals in both DOFs. Our results can lead to further developments for the intuitive myoelectric control of active hand exoskeletons for individuals with DMD.

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6.1 INTRODUCTION

Duchenne muscular dystrophy (DMD) is the most common form of muscular dystrophy in male children, affecting 1 in 4,000 individuals worldwide [5]. DMD is caused by a gene mutation that compromises the production of dystrophin protein, the absence of which causes progressive weakness in the skeletal, respiratory and cardiac muscles. This leads to severe physical disability and shortened life expectancy [170]. Boys with DMD become increasingly dependent on external aids in their daily activities due to the progressive paresis and the loss of functional ability [23]. However, over the last two decades, life expectancy has improved significantly due to improvements in healthcare, with the current estimate being around 40 years [30]. This has led to a significant increase in the number of DMD adults living with severe physical impairments who have a strong dependency on care [4].

Functional interaction with the world heavily relies on hand manipulation, a central element for every individual in performing the activities of daily living (ADL) [237]. However, the dynamic support of hand functioning in individuals with DMD remains a challenge [22].

Here, wearable robotic devices, such as hand exoskeletons, can provide a solution. A recent study showed that the overnight use of passive hand orthoses helps preserve the passive range of motion in

Figure 6.1 The participant with Duchenne muscular dystrophy controlling a virtual cursor in 1 and 2 degrees-of-freedom, while resting his arm on his wheelchair.

terms of wrist extension and thumb abduction [48]. The usage of active hand exoskeletons could further assist DMD individuals in terms of tackling a greater range of motor tasks [62] as this would enable dynamic movements with the active participation of the user [54].

For the intuitive and robust control of active hand exoskeletons, accurate decoding of the user's intention is the primary challenge [112]. A clinically viable way to enable robust control involves the use of surface electromyography (sEMG) [113], [114], [238], [239]. Various sEMG-based control methods have been developed to decode the hand motor intention of the user, with direct control (DC) [112], [240] and pattern recognition (PR)-based control [199] being the most common. While regression [188] and model-based approaches [184], [185] are being developed, they are not yet broadly considered being clinical standards. DC is broadly used with upper extremity prostheses [214], [241], while common PR classification methods include linear discriminant analysis (LDA), support vector machines (SVM), fuzzy approaches, regression and multi-layer perceptron (MLP) [242].

Importantly, there is lack of systematic analyses on the feasibility of forearm sEMG as a source of control signals for active hand exoskeletons in individuals with DMD. However, two studies involving participants suffering from other forms of muscular dystrophy [56], [57] showed promising results in terms of the functional decoding of motor intention from the hand/wrist. Meanwhile, the performance of sEMG control was recently compared to force control with an active planar support for the

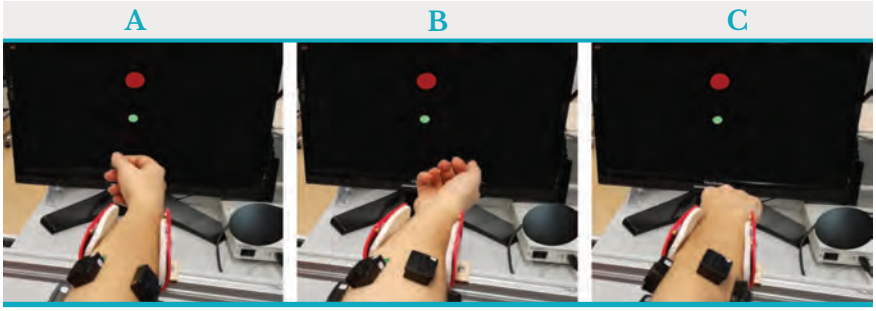

Figure 6.2 A healthy participant performing the experiment. Participants controlled a cursor in 1-DOF and 2-DOF target reaching tasks while their arm was supported by the arm support. Forearm can be seen in three different configurations: Neutral (A), this forearm orientation is the midpoint between supination and pronation, supination (B) and pronation (C).

shoulder and elbow in DMD individuals [54]. Here, it was shown that both methods can decode intended arm movements. However, the possibility of decoding wrist-hand movements was not explored.

In this paper, we make the first attempt to evaluate the real-time sEMG decoding of wrist-hand motor intention on one DMD individual and ten healthy control individuals. We compare sequential DC and PR as potential sEMG control methods and provide an analysis of their differences. For this study, our PR method incorporates an MLP, while both our approaches combine myocontrol with a first-order admittance model [54], which allows for the manipulation of the interface virtual dynamics and a subsequent further tailoring of the control across all the participants. This is beneficial, especially in terms of the participant with DMD, who is expected to have different assistance requirements than the healthy participants. Finally, we directly test the system outside of the lab at the DMD individual's home. This is particularly important since the mid-term objective is to control a hand exoskeleton for daily home use. Real-time myocontrol, admittance modelling and out-of-the-lab use are central requirements for the function-related use of assistive technology in DMD sufferers' everyday lives.

6.2 METHODS

Participants

The experiment was carried out with ten healthy adults (seven males and three females) aged between 20 and 33 who have no hand-related impairment, and one male adult with DMD of age 25 (Table 6.1) who is unable to use his hands in terms of simple tasks such as, for example, holding a pen. The DMD individual consistently experiences early onset fatigue and extensive hand/wrist related contractures and had a Brooke score of 5 (cannot raise hands to the mouth, but could use his hands to hold a pen or pick up pennies from the table). The Medical Ethics Committee of Twente approved the study design, the experimental protocol and the procedures, while all the participants were fully informed about the study through a letter and subsequently provided written informed consent (Protocol number: NL59061.044.16). Each participant took part in two sessions, where they performed the proposed target-reaching task with each myocontrol method.

Experimental Setup and Signal Acquisition

The experimental setup is shown in Figure 6.2. During the experiment, each healthy participant was seated in a chair in front of a computer screen, with their arm placed on a soft foam-padded arm support on the table. Meanwhile, the DMD participant was similarly positioned, while his arm rested on the arm support of his wheelchair. Six dry, active sEMG, bipolar electrodes (Trigno Lab, Delsys, USA) were placed around the dominant forearm of each of the participants.

Table 6.1 Participant Information. HP denotes the healthy participants and DMD the participant with Duchenne.

Participant	Age (years)	Dominant Hand	Condition
HP1-HP10	20-33	1 Left / 9 Right	Healthy
DMD	25	Right	DMD

Firstly, one electrode was placed on the muscle belly of the flexor carpi ulnaris (FCU), and one on the muscle belly of the extensor carpi ulnaris (ECU). The co-contraction of the FCU and the ECU was used in order to switch between degrees-of-freedom (DOF) during DC for the healthy participants. Meanwhile, the other four electrodes were placed in between, equidistantly, while for the DMD participant, an extra electrode was added to his gastrocnemius muscle. This was used as a trigger to switch between DOFs during DC (blue line in Figure 6.4), since he could not co-contract his forearm muscles in a controlled fashion and without experiencing fatigue. Prior to the electrode placement, the skin was cleaned with alcohol to ensure optimal electrode-skin impedance, while the sEMG signals were obtained through the use of a real-time computer (xPC Target 5.1, MathWorks Inc., USA). The analogue-to-digital conversion was performed using a National Instruments card (PCI-6229, National Instruments Corp., USA) at a sampling frequency of 1 kHz with a 16-bit resolution, while a National Instruments USB-data-acquisition device (6259, National Instruments Corp., USA) was used to record the offline data for the training of the MLP. The controllers were also running on the real-time computer and were sending position commands through UDP/IP communication to a Windows-powered PC in order to control the position of the cursor.

Experimental Protocol

A screen-based target-reaching task was employed in this study to evaluate the performance of the two myocontrol methods. The experiment consisted of two sessions, one for each of the different myocontrol methods compared. Both DC and PR were coupled with admittance control (see Section Myoelectric Control). At the beginning of each session, the maximum voluntary contraction (MVC) of each participant was recorded. Each session was performed in three different forearm orientations – neutral arm position, supination and pronation – to assess myocontrol robustness (Figure 6.2). For each session and forearm orientation, myocontrol tasks were performed both for the 1-DOF and the 2-DOF tasks (Figure 6.3). Both the 1-DOF tasks and the 2-DOF tasks included four target locations. For targets 1-4, the participants had to move only in 1-DOF for every trial, while for targets 5-8 they had to sequentially move in 2-DOF (Figure 6.3). Each task was repeated one time per forearm orientation. Between tasks, the participants were provided with rest periods of five to ten minutes, depending on the degree of muscle fatigue. Each task consisted of eight targets with ten trials per target. Meanwhile, each target appeared ten times and the order of appearance was that shown in Figure 6.3.

The order of the evaluation of the myocontrol methods and the forearm orientations was randomised across the participants in order to avoid order effects. Each trial began with the appearance of a target on the screen, where the participants were then instructed to move the cursor as fast as possible from its initial position (centre of the screen) to the target and to keep it there for two seconds. The cursor returned to its initial position upon trial completion and the next trial would then start in two seconds. The participants first familiarised themselves with each myocontrol method before starting each session. For every target, the first two trials were discarded and were not included in the statistical analysis to account for learning.

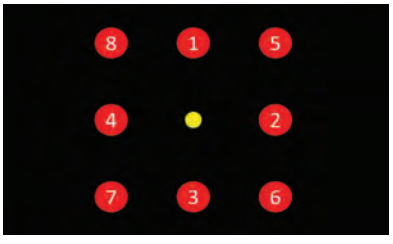

Figure 6.3 Locations of all possible targets (red) shown by their target number, and the cursor (yellow). Targets 1-4 were performed in 1-DOF and targets 5-8 in 2-DOF. Each trial was accepted as successful when participants kept the cursor inside the target for 2 seconds.

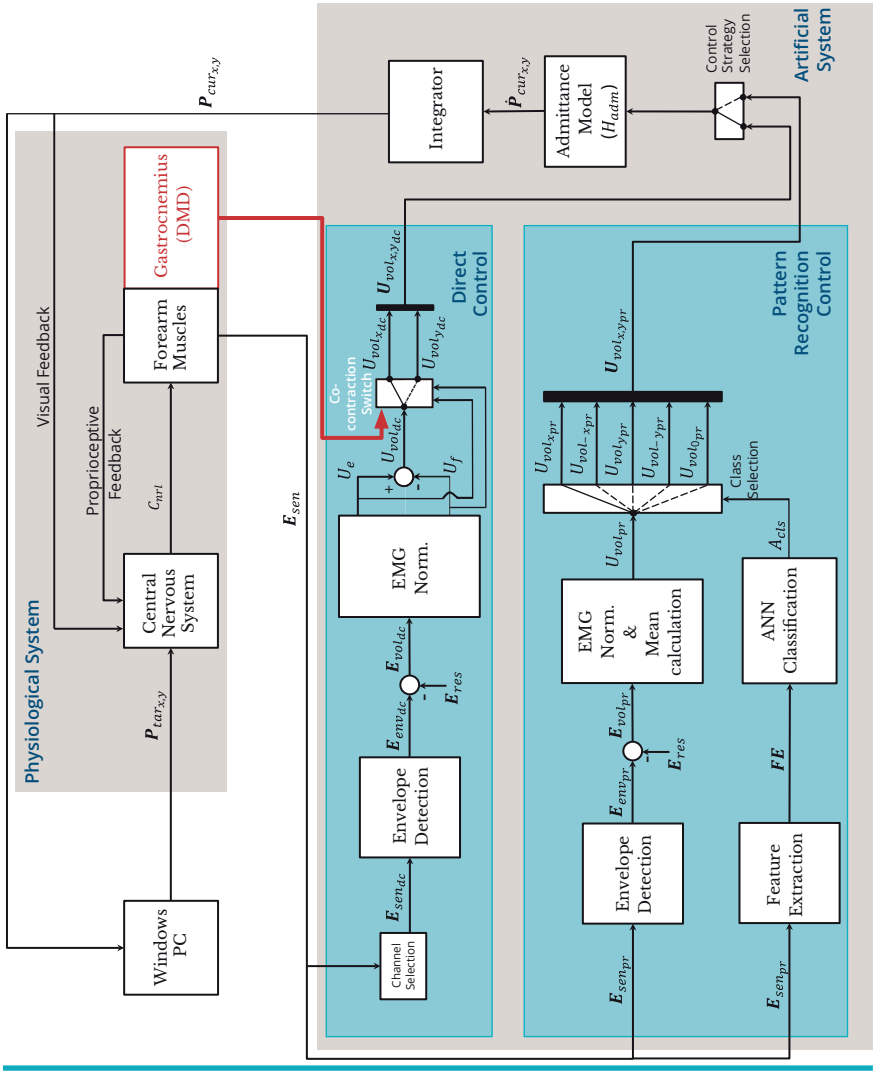

Figure 6.4 Diagram of implemented control methods adapted from Lobo-Prat et. al. [54]. Bold font style symbols indicate vectors and regular font style symbols indicate scalars. The upper section represents the physiological system (participant), while the lower section represents the experimental system. To perform a movement participant first see the target on the screen ($P_{tarx,y}$). The target is generated by a python script running in the host computer. This generates a neural command (C_{nrl}) with their central nervous system, which results in muscle activation at forearm muscles where sEMG signals (E_{sen}) are measured. Intention of the user is decoded from these sEMG signals. >>

<< In direct control the sEMG signals (E_{sendc}) are measured from agonist/antagonist muscle pair from forearm (Flexor Carpi Ulnaris/Extensor Carpi Ulnaris) and the resting sEMG (E_{res}) is subtracted to acquire the voluntary sEMG (E_{voldc}). The signal is normalized to the maximum voluntary contraction (MVC) and control signals are generated from each muscle (U_e,U_f). A voluntary control signal (U_{voldc}) is obtained by subtracting the control signal of the flexor muscle from that of the extensor muscle (reverse for left handed participants). A co-contraction switch, was used to alternate DOF. In case of the DMD participant, an electrode in the gastrocnemius was used to switch (red line). In pattern recognition control sEMG signals (E_{senpr}) are measured from six electrodes placed on forearm (hexagonal grid). Time domain features (FE) were extracted from measured sEMG signals and these features were then used by ANN classifier to identify the movement class (Acls). This class is then used to select the final control signal ($U_{volx,ypr}$). This control signal (U_{volpr}) is the normalized envelope of the six electrodes. In both control methods the estimated voluntary forces are used as input to a first order admittance model (H_{adm}) that resembles the dynamics of a mass-damper system. The resulting velocity of the cursor ($\dot{P}_{curx,y}$) is send to an integrator ($P_{curx,y}$) and then to the windows PC to control the position of the cursor on the screen. This motion was sensed by the participants proprioception and by visual feedback and was used to generate new neural commands to reach new target positions ($P_{tarx,y}$).

For the DMD individual, the experiment was conducted only at one forearm orientation (pronated, see Figure 6.1) and included targets 1, 2, 6, 8 (2 for 1-DOF and 2 for 2-DOF, Figure 6.3). This was dictated by the need to comply with ethically viable standards in terms of avoiding the onset of extensive contractures that would result in pain with the pronation and supination contractions. The reduced targets were chosen in order to capture the maximum variability of movements (e.g. targets 1 and 2 required opposite movements, as did targets 6 and 8).

Myoelectric Control

In order to perform a movement, the participants were presented with a target appearing on the screen. This generated a neural command within their nervous system, which resulted in the subsequent activation of the forearm muscles (E_{sen}) that was measured via dry surface electromyography (sEMG) electrodes. Raw sEMG signals were initially digitally filtered with a second-order Butterworth high-pass filter with a 20Hz cut-off frequency to reduce any movement artefacts.

The envelopes were calculated through full-wave rectification of the signal and the subsequent application of a fourth-order Butterworth low-pass filter with a 2Hz cut-off frequency [112]. The envelopes were normalised to the MVC. This measure was taken at the beginning of each session and was the average maximal contraction over three seconds. Normalised-filtered sEMG signals were then used to estimate the control signal ($\mathbf{U}_{volx,y}$) for both the pattern recognition (PR) method and the direct control (DC) method.

DC method - Both degrees-of-freedom (DOF) on the x-axis and the y-axis were controlled using the sEMG from an antagonistic muscle pair. Here, two out of the six electrodes that were placed on the forearm were used, that is, the one on the muscle belly of the flexor carpi ulnaris (FCU), and the one on the muscle belly of the extensor carpi ulnaris (ECU). The envelopes of the sEMG signals ($\mathbf{E}_{envdc}$) were detected, while the voluntary sEMG signals (E_{voldc}) and the voluntary control signals (U) for flexion or extension were calculated using the following equations:

$$E_{voldce,f} = E_{envdce,f} - E_{reste,f} \tag{1}$$

and

$$\mathrm{U}_{e,f} = \frac{E_{voldce,f}}{E_{mvcdce,f}} \tag{2}$$

$E_{envdce,f}$ denotes the processed sEMG envelope signal per electrode placement site (flexor or extensor). For the DC method, the MVCs were acquired by asking the participants to maximally extend and flex their wrist for 3 seconds. Finally, mode switching between different DOFs was achieved through the co-contraction of the FCU and the ECU. For the participant with Duchenne muscular dystrophy (DMD), an extra electrode was added to his gastrocnemius muscle. This was used as a trigger to switch between DOFs (blue line Figure 6.4), since he could not co-contract his forearm muscles in a controlled fashion and without experiencing fatigue. The use of the switch determined the final voluntary normalised control signal ($\mathbf{U}_{volx,ydc}$) that served as input to the admittance model and was calculated with the following equation:

$$\mathbf{U}_{voldc} = U_e - U_f \tag{3}$$

Wrist flexion involved moving the cursor left/down and wrist extension involved moving it right/up.

PR method - A pattern recognition artificial neural network (ANN) myocontrol method was implemented using MATLAB's Neural Network Toolbox (The MathWorks Inc., Natick, MA) for the following motion classes: hand close and open; wrist flexion and extension; and no motion. Each motion class corresponded to a different DOF movement of the cursor (see Table 6.2). The method chosen in this study was a multilayer perceptron method – which is one of the most popular PR classification methods [243] since it yields high classification accuracy compared to other commonly used PR methods [242] – with one hidden layer consisting of ten neurons.

For the training of the supervised classification algorithm, sEMG signals were collected prior to the PR session during five repetitions of two-second comfortable contractions for each motion class. The classifier was trained with the use of five commonly used time-domain features: root mean square, mean absolute value, number of zero crossings, slope sign changes and waveform length [244]. The features were extracted using a window of 250ms (which is within an acceptable range for real-time myoelectric applications) [126] with an overlap of 125ms. During the experiment, when the classifier decoded the intention of the user (direction of the cursor), the normalised mean of the envelopes of all six electrodes was used to create a velocity signal proportional to the overall muscle activity, as is presented in the following equation:

$$\mathrm{U}_{volpr} = \frac{E_{volpr}}{E_{mvcpr}} \tag{4}$$

E_{volpr} denotes the mean of the envelopes of the six electrodes and E_{mvcpr} the mean of the envelopes of the six electrodes during the MVC. For the PR method, the MVCs were acquired by asking the participants to maximally co-contract their forearm muscles for 3 seconds. The input to the admittance model ($\mathbf{U}_{volx,ypr}$) was a vector with five elements (motion classes). One element was equal to the U_{volpr} and the remainder equal to zero (depending on which motion class was decoded).

The velocity of the cursor ($\dot{\mathbf{P}}_{curx,y}$) as predicted by the admittance controller was subsequently processed via a forward Euler integrator in order to obtain the desired position ($\mathbf{P}_{curx,y}$), which was used to control the virtual cursor.

For both myocontrol methods, the participants practiced the target-reaching task prior to the experiment in order to grasp the motion mapping (Table 6.2). In the case of the ANN, the machine learning algorithm was re-trained in case any participant was not comfortable with the control of the cursor (low responsiveness, misclassifications and fatigue).

Table 6.2 Mapping of limb motion to cursor motion during PR and DC myocontrol

Myocontrol Method	Participant	Cursor Left	Cursor Right	Cursor Up	Cursor Down
Pattern Recognition	Right Handed (S1-S5, S7-S10)	Wrist Flexion	Wrist Extension	Hand Open	Hand Closed
	Left Handed (S6)	Wrist Extension	Wrist Flexion	Hand Open	Hand Closed
	DMD	Hand Closed	Hand Open	Wrist Extension	Wrist Flexion
Direct Control	Right Handed (S1-S5, S7-S10)	Wrist Flexion	Wrist Extension	Wrist Flexion	Wrist Extension
	Left Handed (S6)	Wrist Extension	Wrist Flexion	Wrist Extension	Wrist Flexion
	DMD	Wrist Extension	Wrist Flexion	Wrist Extension	Wrist Flexion

Admittance Model

Both myocontrol methods were used in combination with a first-order admittance model (H_{adm}) (Eq.1), which received the sEMG estimated control signal $\mathbf{U}_{volx,y}$ as input and outputted the cursor velocity ($\dot{\mathbf{P}}_{curx,y}$).
where A is the virtual mass related parameter and B is the virtual damping

$$\mathrm{H}_{adm} = \frac{\dot{\boldsymbol{P}}_{curx,y}(s)}{\boldsymbol{U}_{volx,y}(s)} = \frac{1}{\mathrm{A}s + B} \tag{5}$$

related parameter. For the healthy participants, the parameters of the admittance model were fixed *a priori* based on pilot trials and were left unchanged for all of them (Table 6.3). Meanwhile, for the DMD participant, the parameters were fine tuned. While we initially asked the DMD participant to perform the experiment with the same parameters as the healthy

participants, this proved to be too fatiguing for him. Subsequently, we adjusted the parameters according to his feedback through trial and error (Table 6.3).

Table 6.3 Admittance model parameter values

Parameter	S1-S10	DMD
A (Mass Related)	$6.6 \cdot 10^{-4}$ kg	$5 \cdot 10^{-4}$ kg
B (Damping Related)	$4 \cdot 10^{-4}$ Ns/m	$6 \cdot 10^{-4}$ Ns/m

Performance Metrics and Statistical Analysis

Reaching time was used to analyse the reaching performance of the participants. The dataset, generated for this study, including all reaching times for all participants, is stored in the Mendeley Data repository, and will be available online after the publication of this study (DOI: 10.17632/tn8zn77fh5.1). Reaching time was defined as the time needed to reach the target as it appeared on the screen, starting from the moment the target appeared. The two seconds of settling time, inside the target were not included in the reaching time. The performance metrics were averaged across all the healthy participants for every trial of every target per session. Since the performance metrics were not normally distributed (Shapiro-Wilk normality test, $p \leq 0.05$), the non-parametric Wilcoxon signed-rank test for dependent data was used to perform the comparisons between the different forearm orientations and the myocontrol methods for the healthy participants (see Figure 6.5 below). The significance level was set at $p \leq 0.05$. The same test was used to compare the myocontrol methods for the DMD participant. For the comparison between the healthy participants and the DMD participant, a matching subset of the healthy data was used to adjust the analyses to the different protocols. The average reaching times of the healthy participants per repetition and per target were calculated and compared with the results of the DMD participant. To perform the statistical comparison, we used the non-parametric Wilcoxon rank-sum test for independent data.

6.3 RESULTS

Healthy Participants vs. DMD Participant

This subsection presents the results of the comparison between the reaching times of the DMD participant and those of the healthy population for both myocontrol methods in a matching subset of targets (see Figure 6.5A and Table 6.4 below). We compared the performance differences

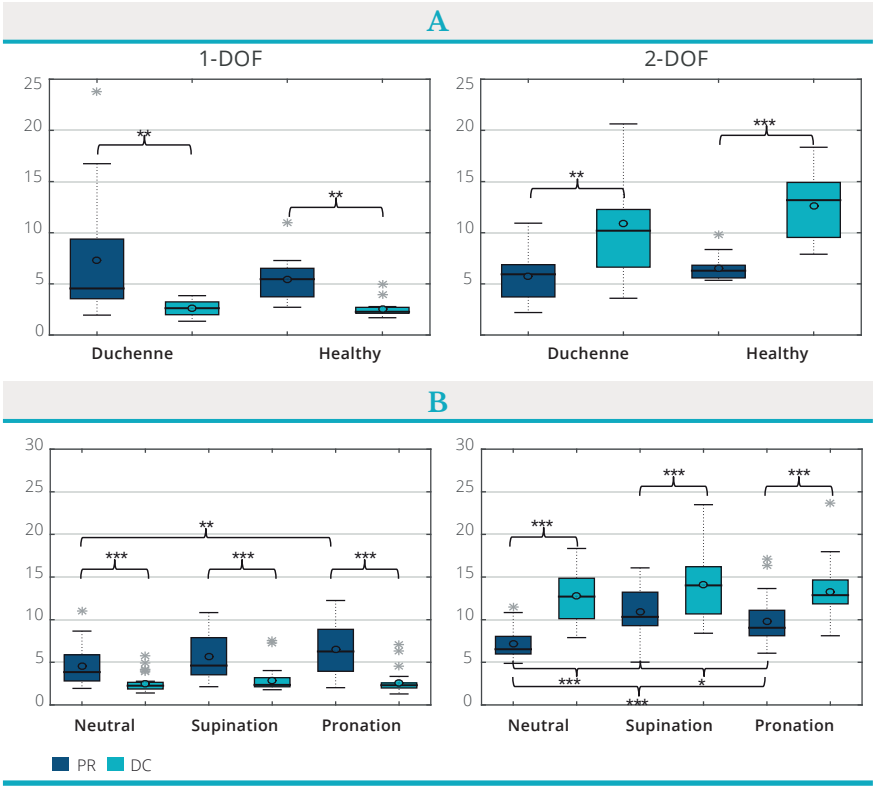

*Figure 6.5 Boxplots and non-parametric Wilcoxon tests of the reaching time for all participants. and 2-DOF tasks were compared separately. Each forearm orientation was plotted with both PR and DC method. A) Since the participant with DMD performed half of the targets, we compare his data with a subset of the healthy data and the samples per boxplot are 16. B) The boxplots consist of the average reaching time of the ten healthy participants. Since every DOF includes four targets and each target was performed 8 times, we have 32 samples per boxplot. Lines represent the mean values and circles the median. Significant differences marked with stars; *P < 0.05, **P < 0.01, ***P < 0.001.*

Table 6.4 Reaching time in seconds (means±std) for all participants.

		Reaching Time (s)					
	Myocontrol Method	PR			DC		
	Orientation	Neu	Sup	Pro	Neu	Sup	Pro
Healthy	**1-DOF task**	4.6±2.1	5.6±2.8	6.5±2.9	2.5±1	2.9±1.3	2.6±1.2
	2-DOF task	7.1±1.7	10.9±2.9	9.8±2.8	12.8±3	14.1±3.8	13.3±3.2
DMD	**1-DOF task**	7.3±6	-	-	2.6±0.8	-	-
	2-DOF task	5.7±2.4	-	-	10.9±6.6	-	-
Healthy Subset	**1-DOF task**	5.4±2.1	-	-	2.5±0.8	-	-
	2-DOF task	6.5±1.2	-	-	12.6±3.4	-	-

The reaching times for the last eight trials of targets 1-4 are averaged for the 1-DOF task and those of targets 5-8 are averaged for the 2-DOF task.

between healthy and DMD, for each control method and DOF (four comparisons in total).

1-DOF tasks - No significant difference was observed between the healthy participants (reaching time of 5.4±2.1s for PR and 2.5±0.8s for DC) and the participant with DMD (reaching time of 7.3±6s for PR and 2.6±0.8s for DC) for both myocontrol methods ($p = 0.926$ for PR and $p = 0.491$ for DC).

2-DOF tasks - No significant difference was observed between the healthy participants (reaching time of 6.5±1.2s for PR and 12.6±3.4s for DC) and the DMD participant (reaching time of 5.7±2.4s for PR and 10.9±6.6s for DC) for both myocontrol methods ($p = 0.287$ for PR and $p = 0.094$ for DC).

Admittance model personalisation - Table 6.3 shows the parameters for the admittance model for the healthy population and the DMD participant. The latter was more comfortable with a lower virtual mass related parameter

than the healthy population (A = $6.6 \cdot 10^{-4}$ kg and A = $5 \cdot 10^{-4}$ kg respectively). The virtual damping-related parameter was higher for the participant with DMD (B = $6 \cdot 10^{-4}$ Ns/m) than for the healthy population (B = $4 \cdot 10^{-4}$ Ns/m).

DC vs. PR

This subsection presents the results of the comparison between the two myocontrol methods for the healthy control participants and the DMD participant. We compare the performance of the healthy participants and the participant with DMD separately, for each control method and DOF (4 comparisons, see figure 6.5A). In addition, it illustrates the effect of forearm orientation on the performance of both myocontrol methods (see Figure 6.5B and Table 6.4). Here, we compare the performance of the healthy participants between the two control methods for each DOF (6 comparisons) and the performance differences for each control method across different forearm orientations per DOF (12 comparisons in total).

1-DOF tasks - The reaching time during DC (2.5±1s) was significantly lower than that with PR (4.6±2.1s) in the neutral forearm orientation ($p < 0.001$). In the supinated and pronated forearm orientations, DC (2.9±1.3s and 2.6±1.2s respectively) also showed a significantly lower reaching time ($p < 0.001$) than PR (5.6±2.8s and 6.5±2.9s respectively). PR was significantly higher ($p = 0.002$) in the pronation orientation (6.5±2.9s) than in the neutral position (4.6±2.1s). No other differences were found in terms of reaching times among the three forearm orientations, for both myocontrol methods. For the DMD participant, the reaching time during DC (2.6±0.8s) was significantly lower ($p = 0.003$) than during PR (7.3±6).

2-DOF tasks - The reaching times of the healthy participants were significantly different for the two myocontrol methods, with PR revealing significantly lower ($p < 0.001$) reaching times than DC in neutral (7.1±1.7s and 12.8±3s, respectively), supinated (10.9±2.9s and 14.1±3.8s, respectively) and pronated forearm orientation (9.8±2.8s and 13.3±3.2s, respectively). Similarly, for the DMD participant, the reaching time for PR (6.5±1.2s) was significantly lower ($p = 0.008$) compared to that for DC (12.6±3.4s). In terms of PR, there were significant differences in reaching times with the three forearm orientations of the healthy participants. Both the supinated (10.9±2.9s) and the

pronated (9.8±2.8s) forearm orientations resulted in longer reaching times ($p<0.001$) than with the neutral orientation (7.1±1.7), while there was also some difference between the two ($p = 0.033$). In terms of DC, there was no significant difference among the different forearm orientations.

6.4 DISCUSSION AND CONCLUSION

In this study, we tested two myocontrol admittance-based methods and evaluated them among ten healthy participants and one participant with DMD using virtual target-reaching tasks. Despite the muscular degeneration, the DMD individual displayed a comparable myocontrol performance in relation to the healthy individuals. Moreover, our proposed admittance model enabled the setting of appropriate virtual dynamics for the DMD participant, facilitating a myocontrol capacity catered to the patient's needs. This suggests that a personalised myocontrol scheme can successfully decode intention in DMD sufferers despite the degeneration in the underlying muscle tissues.

The participant with DMD was able to control the cursor on the screen with success using both the DC and the PR methods. However, for mode switching in DC, the participant with DMD used a switch placed on the gastrocnemius muscle, since controlling the switch via the co-contraction of his forearm muscles was rather fatiguing and thus presented a challenge for us. Similar to the healthy population, the DMD individual exhibited lower reaching times while using DC for 1-DOF and PR for 2-DOF. While the reaching times of the DMD participant for 1- and 2-DOF were similar to those of the healthy participants, this might be attributed to the fact that the former performed a reduced version of the experimental protocol used for the healthy population, which allowed for comparable cognitive and physical demands. Nevertheless, the results suggest that the DMD participant was able to perform the requested tasks and that both myocontrol methods were both comfortably and successfully used. This is a promising result for the further investigation of the presented myocontrol methods as potential ways to decode hand/wrist motor intention in individuals with DMD, since the successful decoding of their intention will enable them to control active hand exoskeletons.

The use of an admittance model in combination with sEMG can provide an advantage for DMD, since it offers an additional level of customisation that is absent in most conventional myoelectric control methods. Table 6.3 shows that the individual with DMD required a different level of assistance than the healthy participants. In fact, the former preferred a lower parameter A (related to the virtual mass) and a higher parameter B (related to the virtual damping). This enabled him to move the cursor in a less fatiguing way (lower virtual mass) and to achieve stable myocontrol (higher virtual damping). We expect that in future studies, a person-specific adaptation of both parameters (virtual mass and damping-related parameters) will be required in order to allow some adjustment in terms of the level of the individual needs of each participant with DMD, which can vary according to the level of disease progression and the rehabilitation measures received.

In terms of the 1-DOF targets, all the healthy participants performed better in all forearm orientations during DC, without any decline in performance, which was in contrast to the PR test. However, during the 1-DOF tasks in PR, the participants were able to move the cursor in both DOFs, which was not the case for DC, meaning this may have resulted in a slightly overestimated performance of the DC. During the 2-DOF tasks, all the participants performed better during PR than during DC in all forearm orientations. For the DC, a co-contraction switch was implemented for alternating between the DOFs.

The switching between the DOFs that was required for DC control appeared to be unintuitive for several healthy participants, which was reflected in the higher reaching times for DC during the 2-DOF tasks. Hence, the reaching times for DC may have been slightly underestimated, given that PR allowed the participants to perform uninterrupted movements. However, PR dropped in performance when the participants had to perform the task while in the supination or the pronation position, while DC proved to be unaffected by any such orientation changes. This can be attributed to the fact that during any forearm rotation, the muscles moved under the skin while the sEMG electrodes stayed in place, making it difficult for the PR algorithm to generalise (it was trained in neutral orientation). Additionally, we believe that it was cognitively demanding for the participants to adjust to the fact that the direction of movement of the wrist/hand was not directly related to the direction of movement

of the cursor in the pronated or supinated orientation. Although this was also the case for DC, we expect that the negative effect on reaching time would be smaller here, since the different movements were de-coupled (co-contraction switch). The appearance order of the targets during the target-reaching tasks for both the DOF and the myocontrol methods was not randomised (they always appeared sequentially in their numerical order: 1-4 for 1-DOF and 5-8 for 2-DOF). While this may have created a learning effect throughout the experiment, we do not believe this presents a major concern since the directions of the targets were alternating one after another, and, as a result, the participants had to perform different movements to reach the target. Moreover, this setting was applied in all the conditions tested, meaning it affected them all in equal measure.

The participant with DMD consistently experienced early fatigue onset throughout the tests. However, the modification in the protocol ensured that enough trials were performed with the appropriate variability for extracting useful insights while ensuring any ethical requirements were met. Nonetheless, our research was limited due to the low number of available participants with DMD. Hence, our conclusions must be regarded with some caution as a higher number of participants would be required to ensure they are appropriately robust. With regard to the different forearm orientations, it is not clear whether they have a similar effect with individuals with DMD as they do with healthy individuals. In fact, it was reported that this effect has significantly lower consequences for transradial amputees [245].

Future work should involve an evaluation of the effect of forearm orientation in hand/wrist motor intention decoding with individuals with DMD. Despite its limitations, our study indicates that for the decoding of simple 1-DOF motions of the hand, DC demonstrates significantly better performance (more than two times faster) than PR. In contrast, in terms of 2-DOF tasks, DC performs significantly worse than PR, albeit that the former still results in a more robust performance across different forearm configurations. In future work we must implement these myocontrol methods and validate their use with an active hand exoskeleton [59].

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A CASE STUDY WITH SYMBIHAND: AN SEMG-CONTROLLED ELECTROHYDRAULIC HAND ORTHOSIS FOR INDIVIDUALS WITH DUCHENNE MUSCULAR DYSTROPHY*

Ronald A. Bos*, Kostas Nizamis*, Bart F.J.M. Koopman, Just L. Herder, Massimo Sartori and Dick H. Plettenburg

ABSTRACT

With recent improvements in healthcare, individuals with Duchenne muscular dystrophy (DMD) have a prolonged life expectancy, and it is therefore vital to preserve their quality of life. Hand function plays a central role in maintaining independence while performing activities of daily living. For this purpose, we developed a novel dynamic hand orthosis called SymbiHand, in which the user's hand motor intention is decoded by means of surface electromyography, which enables the control of an electrohydraulic pump for actuation. Mechanical work is transported and distributed using a hydraulic transmission and differential mechanism. Interaction forces are then redirected with flexible structures for a comfortable force interaction. This paper outlines SymbiHand's design and, for the first time, a case study with an individual with DMD. Results show that SymbiHand was able to increase the participant's grip strength from 2.4 to 8 N at 35% of the actuator's capacity. During a force-tracking task that used grasping force as input, muscular activation was decreased by more than 40% without compromising task performance. These results suggest that SymbiHand has the potential to decrease overall muscular activation and increase grip strength for individuals with DMD, adding to the hand a total mass of no more than 213 g. Changes in mass distributions and an active thumb support are necessary for improved usability, in addition to a larger-scale study in order to generalize its assistive potential.

* *This chapter has been submitted as: Ronald A. Bos*, Kostas Nizamis*, Bart F.J.M. Koopman, Just L. Herder, Massimo Sartori and Dick H. Plettenburg "A Case Study with SymbiHand: an sEMG-Controlled Electrohydraulic Hand Orthosis for Individuals with Duchenne Muscular Dystrophy", March 2019 (under review)*

7.1 INTRODUCTION

Duchenne muscular dystrophy (DMD) is a progressive neuromuscular disease and is the most common form of muscular dystrophy, affecting approximately 1 in 5000–6000 live births [17], [64]. It results in severe disability, a strong dependence on care [29], and a subsequent decline in functional abilities [23]. Recent scientific advances have increased the life expectancy of individuals with DMD up to 40 years [30], leading to an increase in the number of adults with DMD living with severe physical impairments and decreased functionality [4].

The hand plays a central role in performing activities of daily living (ADL), and its use is related to an increased quality of life in individuals with DMD [237]. Despite this, hand treatment for such individuals presents moderate results [22]. Current state-of-the-art includes hand physical therapy [22] or the use of passive hand splints during the night, which preserves the passive range of motion of the wrist and thumb [48]. Assistive devices such as dynamic hand orthoses, however, can improve the quality of life of individuals with DMD and enhance their social participation [6]. Evidence is increasingly highlighting the need

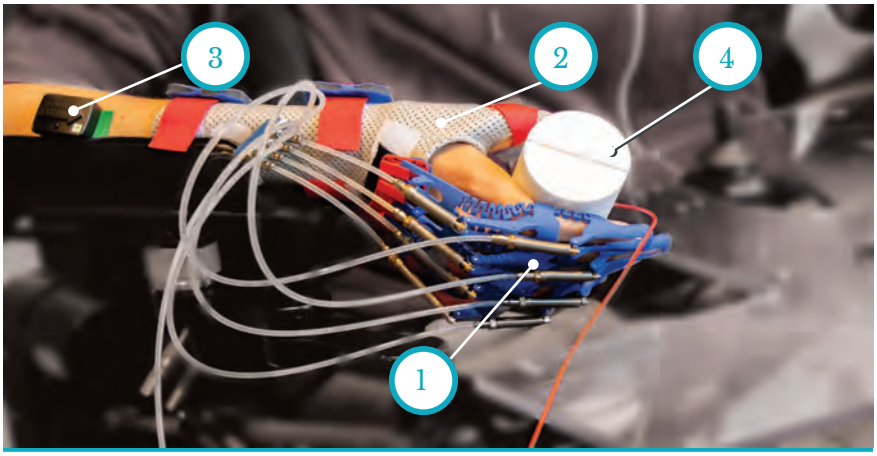

Figure 7.1 The participant with DMD grasping the sensorized object while wearing the SymbiHand orthosis. 1) SymbiHand, consisting of four finger modules. 2) The thermoplastic hand splint, used to stabilize the wrist and thumb while providing an anchoring surface for the four finger modules. 3) Wireless sEMG sensor, placed on the extensor digitorum communis muscle. 4) The cylindrical sensorized object, used for measuring grasping force.

for a comprehensive and multidisciplinary treatment of the current rehabilitation of individuals with DMD [30], [31] that favors the use of dynamic hand orthoses.

Dynamic hand orthoses require a robust and intuitive way of decoding the user's intention and controlling the resulting mechanical output [112]. Surface electromyography (sEMG) presents a well-established method of decoding the motor intention of a user [113] and is broadly used to enable the control of active hand orthoses [1]. Direct sEMG control was successfully tested in the past with individuals with DMD, combined with a first-order admittance model, to control active arm orthosis [54], [165]. However, to the authors' best knowledge, there is no evidence of the use of this approach for the real-time decoding of hand motor intention with individuals with DMD. This concept is applied for the first time in the current study in combination with a new dynamic hand orthosis.

The hand orthosis' design is based on a hydraulic transmission, flexible structures, and a self-adaptive grasp. The hydraulic components have been customized for a more low-profile mechanism and improved pressure resilience. Additionally, a custom hydraulic piston pump has been made to provide the required hydraulic pressure. In combination with the sEMG control strategy, the combined system is called SymbiHand.

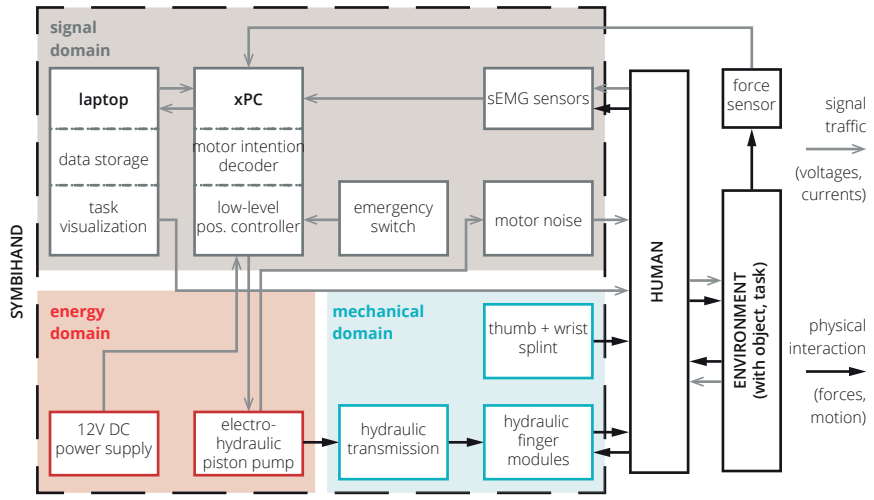

Figure 7.2 System overview of the different components of SymbiHand, subdivided into a signal, energy, and mechanical domain.

The objective of this study is to assess SymbiHands' potential to actively assist the hand function of individuals with DMD. To this end, we conducted a case study with one participant with DMD. The primary purpose of SymbiHand is to augment the grasping force of the user and additionally reduce the muscular activation needed to open and close the hand. This can help to extend the hand functionality of the user and delay the onset of fatigue while performing ADL.

7.2 METHODS

Participants

One 23-year-old male participant, diagnosed with DMD, took part in this study. He had not used hand splints in the past, and his dominant right arm was actively assisted by an arm support (TOP/HELP, Focal Meditech, Tilburg, Netherlands). He had a Brooke score [246] of 5 (cannot raise hands to the mouth, but could use his hands to hold a pen or pick up pennies from the table), and a Performance of Upper Limb (PUL) score [247] of 8 (0 on the shoulder dimension, 1 on the elbow dimension, and 7 on the wrist/hand dimension). Minimal contractures relevant to finger movement were observed, and the range of motion (ROM) of the fingers was quite well preserved. However, he was experiencing early fatigue onset and a substantial decrease in grasping force.

The study design, experimental protocol, and procedures were approved by the Delft Human Research Ethical Committee (HREC) under ID 482. The study was conducted according to the ethical standards given in the Declaration of Helsinki of 1975, as revised in 2008. The participant was informed via a letter and signed a consent form prior to the experiment.

SymbiHand

A picture of the manufactured prototype of SymbiHand worn by the participant is shown in Figure 7.1 and a video of the participant controlling the SymbiHand in real-time in [248]. The total mass on the hand was 213g, where Table 7.1 shows a more detailed mass distribution. The piston pump assembly, which includes the master cylinder, had a mass of 526g.

SymbiHand consists of components in the signal, energy, and mechanical domain [1]. Figure 7.2, shows how each component is categorized in these domains. SymbiHand aids the user in performing

tasks by exchanging signals and physical interactions with the user, who, in turn, interacts with the environment. The intention of the participant was decoded in real time with the use of direct sEMG control, combined with a first-order admittance model and enabled voluntary opening/closing of the hand orthosis. A sensorized cylindrical object (Figure 7.1) was utilized to measure the grasping force, which was used as input for a force-tracking task in real time). The following paragraphs describe the key components in more detail.

Signal domain - In this study, direct sEMG control [112] was used to decode a one degree-of-freedom (DOF) hand motion (open/close). After cleaning the participant's skin with alcohol to enhance signal quality, two dry wireless electrodes (Trigno, Delsys Inc., Natick, MA, USA) were put in place, one above the muscle belly of the extensor digitorum communis (EDC) and one above the muscle belly of the flexor digitorum superficialis (FDS). The two sEMG signals were used to decode the hand opening-closing motor intention of the participant and enable the direct sEMG control of the orthosis. The EDC signal (Figure 7.1) corresponded to hand opening and the FDS to hand closing. The same sEMG signals were used to measure muscular activation during the task.

The lower part of Figure 7.3, presents a detailed diagram of the signal processing. Raw sEMG signals were initially digitally filtered with a high-pass filter (2nd order Butterworth filter, $f_{c,hp}$ =20Hz) to reduce any movement artefacts. The envelopes of the sEMG signals $\mathbf{E}_{env}$ were obtained by applying full-wave rectification and a low-pass filter (4th order Butterworth filter, $f_{c,lp}$=2Hz). The offsets of both the EDC and FDS envelopes were corrected by subtracting the resting sEMG envelope ($\mathbf{E}_{res}$), which was measured while the participant was completely relaxed. The resulting signals ($\mathbf{E}_{vol}$) were subsequently normalized to their own maximum voluntary contraction (MVC) value. Lastly, the normalized extensor envelope (U_{EDC}) was subtracted from the normalized flexor envelope (U_{FDS}) in order to create the normalized sEMG control signal (U_{vol}). This was multiplied by a conversion gain of 1N in order to acquire the estimated force (F_{est}), which served as input to a first-order admittance model similar to that carried out by Lobo-Prat et al. [54]:

$$H_{adm} = \frac{1}{As + B} \quad (1)$$

Here, ***A*** represents the parameter related to virtual mass (10^{-4}kg) and ***B*** the parameter related to virtual damping (10^{-2}Ns/m). The values were chosen in accordance with the participant's preferences and determined during a pre-trial. The manipulation of the virtual dynamics with the help of the admittance model, aimed to create a responsive (dictated by mass yet stable (dictated by damping) interaction between the user and the device. The admittance model expected a force (estimated from the sEMG signals) as an input, i.e., a normalized signal that is negative for hand opening and positive for hand closing. The output of the admittance model was the reference velocity for the motor (V_{ref}) based on the participant's intention. The reference position was obtained through integration (P_{ref}) and was sent to the low-level position controller (Figure 7.2 in the signal domain and Figure 7.3)

The grasping force was measured in real time with the use of a sensorized cylindrical object (Figure 7.1). For this purpose, a miniature S-beam load cell (FH04086, FUTEK Advanced Sensor Technology, Irvine, CA, USA) was incorporated in a 3D-printed cylindrical object with a diameter of 60 mm. The measured grasping force was normalized to the maximum voluntary force (MVF) produced by the participant and used for the visualization of the force-tracking task. The object included an indentation where the thumb could be placed in order to ensure that the grasping force direction was aligned with the axis of the load cell.

The analog signals of the sEMG electrodes and the force sensors were measured with the use of a real-time computer (xPC Target, MathWorks Inc., Natick, MA, USA) and by means of a data acquisition card (PCI-6229, National Instruments Corp., Austin, TX, USA). The analog data was converted to a digital signal with a 16-bit resolution and at a sampling frequency of 1 kHz.

Energy domain - A custom electrohydraulic piston pump was made to convert electrical energy from the power supply into mechanical work in the form of hydraulic pressure. The pump was able to create pressures well up to 5.0 MPa. However, because of the frailness of the fingers among individuals with DMD, and thus to reduce the risk of harming the participant, the current to the piston pump was limited to approximately 35% of the motor's maximum continuous current. This way, pressures could not exceed 1.5 MPa during the study.

Figure 7.3 shows the working principle of the electrohydraulic pump. It used a 12V DC motor (118743, RE25 10W, Maxon Motor AG, Sachseln, Switzerland) to move a spindle drive via a belt transmission. The spindle was directly connected to the piston of the master cylinder with an 8 mm bore diameter and was able to generate pressure in a closed hydraulic circuit. The spindle drive's travel distance was limited with mechanical stops at 60 mm, which resulted in a maximum fluid displacement of 3 mL. The linear velocity of the spindle was limited to 10 mm/s (i.e., flowrate of 0.5 mL/s, 6 s for full flexion/extension). This value was, after a few trials, chosen by the participant as the maximum velocity that gave him a feeling of stable and safe control.

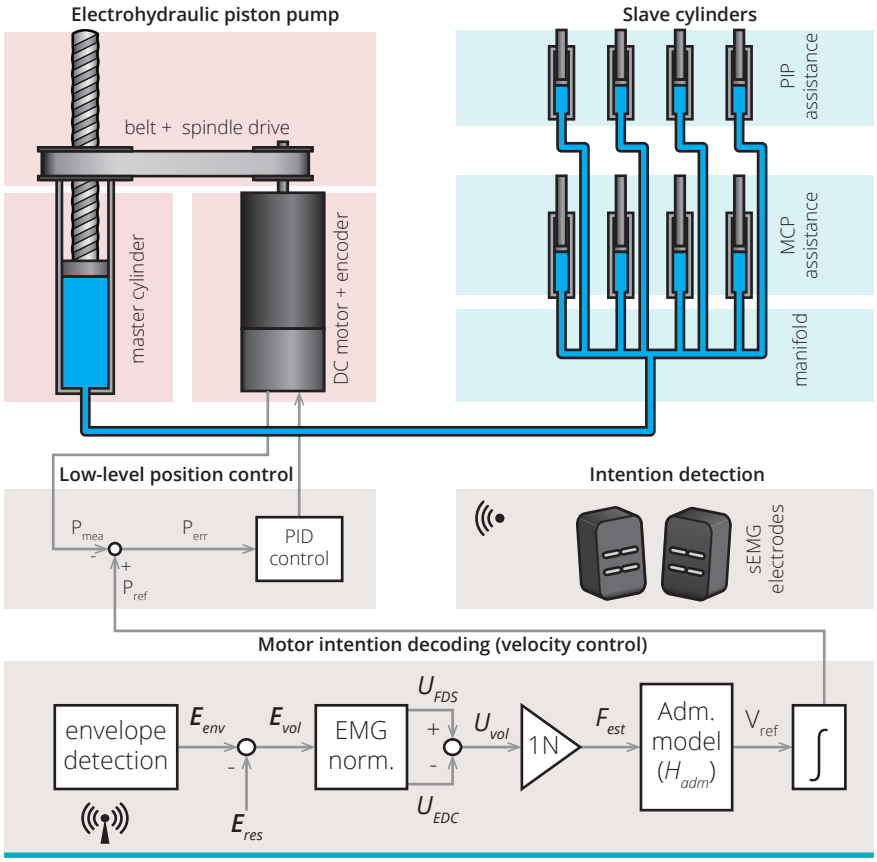

Figure 7.3 Detailed overview of the system, illustrating overall working principle and key components.

Mechanical domain - Mechanical work was transmitted using a hydraulic master-slave system [59]. The master cylinder was integrated in the electrohydraulic piston pump, dividing its pressure among all slave cylinders that were fixed on the finger modules, creating an underactuated system with an adaptive grasp. Figure 7.3 shows how the slave cylinders were connected. Each finger module was equipped with two slave cylinders that acted on the metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joint. The distal interphalangeal (DIP) joint was not actuated but was protected from overextension using passive structures. Valves can be used to selectively move one or multiple finger modules, allowing for individual finger movements or movement patterns [59]. In this study, in the interest of a simple control method, only a single DOF was controlled, and the use of valves was therefore omitted.

The slave cylinders were custom-made single-acting hydraulic cylinders, with an active protraction and passive retraction using return springs. The return springs were fixed on the outside of the cylinder and could easily be interchanged with springs with a higher or lower stiffness, allowing for adjustments towards the preferences and conditions of an individual. In this study, all cylinders were equipped with stainless steel springs with a stiffness of 0.01 N/mm (T40740E, Tevema Technical Supply BV, Almere, Netherlands). Water was used as the hydraulic fluid, which was degassed before filling the hydraulic circuit. A 3 mm tubing material (Legris 1025P03 00 18, Parker Hannifin Corporation, Cleveland, OH, USA) was used to connect all slave cylinders to a manifold, which was connected to the piston pump using a single tube.

The finger modules served as the interface between the slave actuators and each finger, where the size was adjusted to the measurements of the participant's fingers. For a more detailed description of these modules, we refer to our previous work [59]. In addition, the wrist and thumb were fixed in a functional position using a thermoplastic splint (Rolyan PAT-081572429, Performance Health, Warrenville, IL, USA). The wrist was slightly extended with the thumb in opposition, such that the tip of the thumb could oppose the tip of the index and middle fingers to allow for a three-jaw chuck grasp. Similar to all other fingers, the thumb's most distal joint (interphalangeal (IP) joint) was only protected against overextension, leaving the palmar area and as much as possible of the lateral side available for tactile feedback.

The orthosis could be donned by first securing the wrist and thumb splint using Velcro straps. Each finger module could then be slid on the fingers one by one, attaching them to a snap-fit mechanism on the dorsal side of the splint. These snap-fit mechanisms were attached to the splint using Velcro, allowing for corrections in the distal or proximal direction.

Experimental protocol

The participant took part in two sessions, the first of which included the construction of the thermoplastic hand splint with an occupational therapist and the measurement of the fingers for customizing SymbiHand. During the second session, and in order to assess whether SymbiHand could potentially provide assistance during activities of daily living, the participant was asked to perform a force-tracking task using the grasping force as input. For this purpose, an open-fist cylindrical grasp [249] was carried out on a sensorized cylindrical object, without and with the hand orthosis.

At the start of the second session, the participant was asked to grasp the object as hard as possible, simultaneously giving an MVF measured with the sensorized object and an MVC measured with both sEMG signals. Both MVF and MVC were acquired as the mean signal over a period of three seconds of active grasping. During the force-tracking task, the participant was asked to grasp the same object, while also tracking a reference force that ramped up to a specific percentage of the MVF for 3 s, remained there for 1.5 s, and then ramped down to zero again for 3 s. These percentages were varied between 10, 20, and 30% of the MVF. Each force level was repeated three times per group of nine trials, and each group was repeated twice, resulting in a total of 18 trials. After every nine trials, a resting period of at least two minutes was given to the participant to avoid the effects of fatigue in our data. All trials were executed in a randomized order in order to avoid order effects on our data. A questionnaire was filled in after the completion of all trials to assess overall task load.

Then, the participant was fitted with SymbiHand. At first, the participant was allowed to familiarize himself with the device and its control for 10 minutes. This was followed by the same task as described previously, including a new measurement of the maximum attainable grasping force, only now with SymbiHand. The same questionnaire was filled in afterwards. To conclude the experiment, any additional informal feedback was registered.

Data analysis

Muscular activation & grasping force - Muscular activation and grasping force were taken as the main outcome measures in this study. The raw force signal was low-pass filtered (2nd order Butterworth filter, $f_{c,lp}$=20Hz),

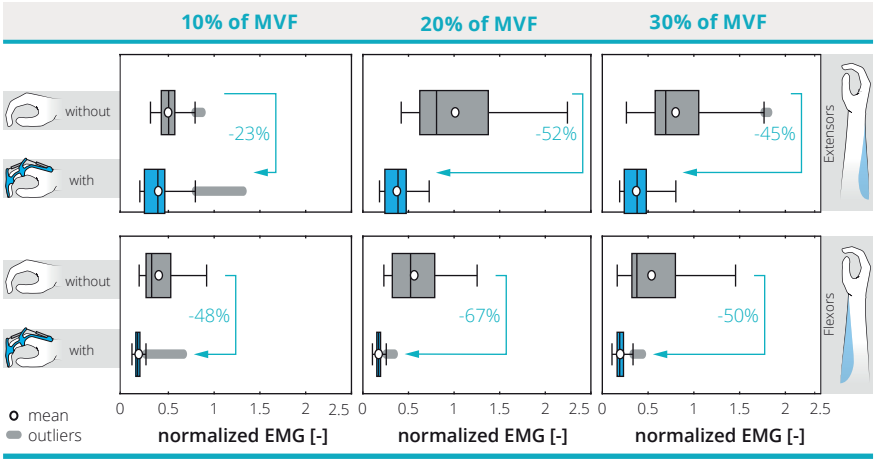

Figure 7.4 Muscular activation of the extensor and flexor muscles during the task at 10%, 20%, and 30% of the MVF, without and with SymbiHand. For each level of MVF, the muscular activation was averaged over the 6 trials, corresponding to that level. Percentages indicate drops of the median value. EMG was normalized according to the MVC without SymbiHand.

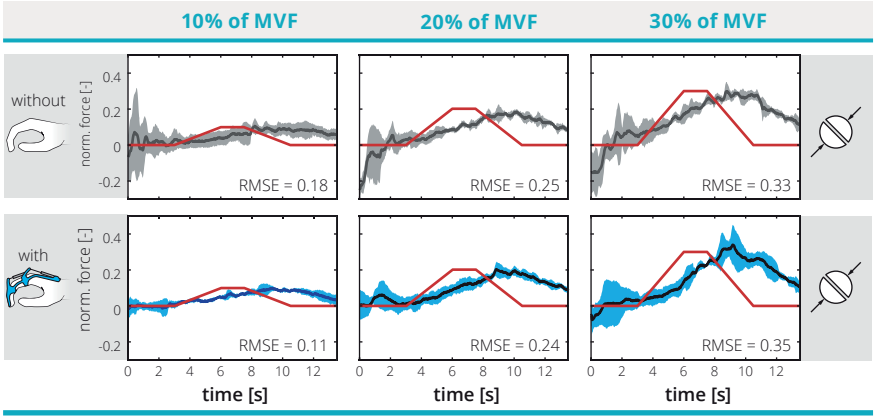

Figure 7.5 Force-tracking performance while performing the task at 10%, 20%, and 30% of the participant's MVF, without and with SymbiHand. Force was normalized according to the MVF without SymbiHand and averaged across the 6 trials per MVF level.

before the analysis. The grasping force was used to determine force-tracking performance, defined as the root mean squared error (RMSE) between the imposed force trajectory and the grasping force exerted by the participant. MVC and MVF measurements were taken as a measure of the participant's maximum capacities and used to normalize force and sEMG. All data was recorded both without and with SymbiHand. The datasets generated for this study can be found in the IEEEDataPort repository and are available online (DOI: 110.21227/gerz-8s29).

Range of motion - Range of motion of the fingers was assessed by photogrammetry [250]. Photographic images (EOS 70D, EF-S 18–135mm, Canon Inc, Tokyo, Japan) were taken from the radial side of the participant's hand and analyzed in image processing software to quantify the angle between the phalanges. This was done both without and with the hand orthosis to evaluate any differences that the orthosis may impose.

Task load - The NASA-Task Load Index (NASA-TLX) was used as a measure of task cognitive load. Only the individual unweighted subscales were used (raw TLX) [251]. The results were then compared between the conditions without and with the hand orthosis, allowing for a qualitative comparison of task cognitive load for this participant using the subscales.

7.3 RESULTS

Muscular activation & grasping force

Muscular activation from the extensors and flexors for all repetitions at every force level are shown in boxplots in Figure 7.4. The average and minimum/maximum values of the force-tracking tasks for every force level are shown in Figure 7.5. Additionally, MVF and MVC values are shown in Figure 7.6. SymbiHand was able to increase the participant's grasping force of the cylindrical object from 2.5 to 8 N, with a slight increase in muscular activation (+12%). Moreover, without compromising force-tracking performance, extensor muscular activation was reduced by an average of 40% and flexor by an average of 55%. The participant exhibited a similar delay in the onset of tracking both with and without the orthosis during the force-tracking task (Figure 7.5).

Range of motion

Range of motion was limited to the participant's comfortable limits. Taking the index finger as an illustrative example, maximum flexion angles without/with the hand orthosis were approximately 46, 91 and 39 for the MCP, PIP, and DIP joint, respectively. The hand orthosis therefore barely limited the active range of motion.

Participant feedback

The NASA-TLX scores on each subscale are shown in Table 7.2 (scores between 1–21, where high scores indicating high perceived cognitive load). These results show that mental demand increased while wearing SymbiHand, in addition to slight increases in physical and temporal demand. Performance and frustration scores decreased, indicating that the participant felt that he was doing better at the task while wearing the orthosis, and doing so with less frustration. Effort was not affected.

The participant indicated that the finger modules did not feel comfortable. Despite a polished finish, the 3D-printed material felt rough and had a few ragged edges. Because the participant's fingers and skin were much more sensitive than that of a healthy individual, a cutting feeling was experienced at the skin creases on the palmar side of the finger joints. The wrist and thumb splint were quite comfortable for the

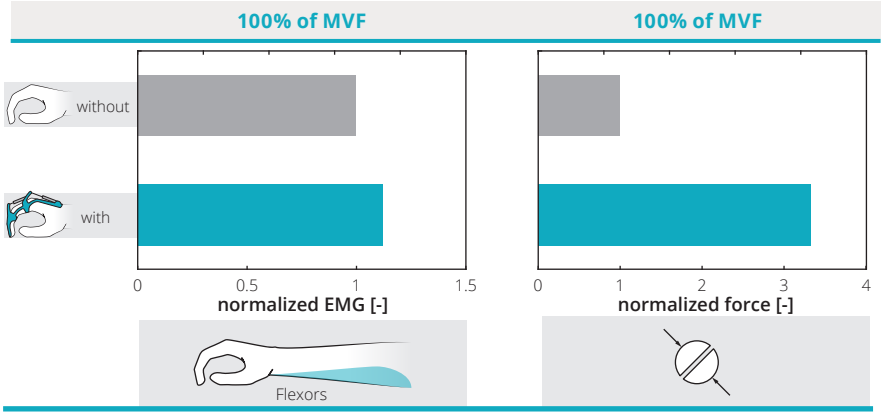

Figure 7.6 Maximum muscular activation and maximum grasping force recorded during the MVF measurements, without and with SymbiHand. EMG and force were normalized according the value without SymbiHand.

participant while he was wearing it, and it provided sufficient support. However, donning the splint was quite cumbersome; in particular, when the MCP knuckles had to be slid through an opening that was a little bit too small, the participant indicated that it was unpleasant.

Table 7.2 **NASA-TLX scores on the subscales, as indicated by participant after completion of the tasks, without and with SymbiHand.**

Subscale	Without	With
Mental demand	6	16
Physical demand	11	13
Temporal demand	4	6
Performance	15	11
Effort	11	11
Frustration	7	5

7.4 DISCUSSION

Motor intention decoding

The combination of direct sEMG control with a first-order admittance model enabled the participant to control the SymbiHand. Results showed a decrease in muscular activation while wearing the orthosis, without the loss of similar tracking performance. This is supporting evidence for the intuitiveness of the proposed motor intention decoding method. The participant adapted with 10 minutes of training, showing a strong training effect, as already suggested in previous studies with individuals with DMD [54]. Direct control was robust to the arm movements of the participant. Additionally, combination with an admittance model allowed for the further customization of the control, thus making it effortless for the participant.

Being able to open and close the hand allows for a large variety of power grasps frequently used during household activities [252], such as medium wrap and power sphere. Our choice for direct sEMG was largely motivated by the fact that only a single DOF needed to be controlled. For more DOF, however, direct sEMG control requires the generation of

independent sEMG signals and the identification of independent sites for their acquisition, which can be cumbersome for the user and results in a limited number of simultaneously controlled DOF [253]. In order to increase the range of assistance provided by SymbiHand (e.g., with an active thumb), in addition to enabling the control of more grasps used during ADL [123] (e.g., by adding valves), different sEMG-based motor decoding approaches should be explored. Future work will investigate the possibility of employing regression [254], pattern recognition [253], or EMG-driven model-based techniques [186], [255]. Nevertheless, such approaches are still not broadly applied in clinical practice for hand orthoses, mainly due to the challenges they present for daily use in a home environment compared to direct sEMG control, which include the larger number of electrodes, longer and more frequent training and calibration, and a lack of robustness to electrode shift due to limb movements (e.g., pronation/supination).

In addition to intuitive intention detection, it was essential that the participant could use his own intrinsic physiological feedback mechanisms (e.g., tactile and auditory feedback, proprioception, and vision) during the experiment. Hence, no explicit forms of augmented feedback were applied, resulting in a simple and easy-to-use approach. Implicitly, aside from the interaction force between the orthosis and the participant, motor noise could also be used as additional auditory information on the orthosis' operating conditions. The delay in tracking onset that the participant exhibited during the force-tracking task was similar both with and without the orthosis and cannot be attributed to the motor intention decoding.

Mechanical design

The hardware components of SymbiHand were well able to provide the assistance to improve the participant's grasping performance. The flexure elements proved to be very effective in aligning the orthosis' rotational centers with those of the anatomical joints. To mitigate the cutting feeling felt by the participant in the palmar creases, the finger modules were relocated to a slightly more distal position. This barely affected the quality of the fit of the orthosis, as the bending shape of the flexure elements was still able to self-align to the location of the anatomical joints. The use of standard hand sizes (e.g., small, medium, and large) are therefore possible, avoiding the need to manufacture bespoke parts. The retraction springs on the slave

cylinders were strong enough to extend the fingers back to a slightly flexed resting position. These factors indicate that the overall design of the hand orthosis works as intended and has the potential to help increase the hand functionality of an individual with a muscular weakness.

Donning the different parts of the hand orthosis was difficult and uncomfortable for the participant. First, the tight fit of the wrist and thumb splint made it unpleasant to put on. Second, because the fingers were so sensitive, sliding the finger modules on the fingers was not very comfortable. As a result, the finger modules could not be donned easily one by one because the stiffness of the hydraulic hoses would add additional forces to the fingers. We believe that a modular or hinged splint with additional straps could help to reduce these problems, as well as finger modules that allow for quick and easy donning from the dorsal side of the hand. Third, positioning the thumb in opposition to the volar pads of the index and middle finger put it in an awkward resting position. This means that an additional thumb mechanism that is able to switch between a resting and functional position is necessary.

Despite the low mass of the hand orthosis, it was still an issue for the participant. The arm support could help with lifting the arm, but the high concentration of mass on the dorsal side of the hand made it impossible to pronate/supinate. A more strategic distribution of mass could be used to reduce the moment of inertia around the center of rotation of this particular movement. Additionally, overall mass reductions are possible, e.g., by making the hydraulic parts more lightweight. We also believe that the little finger does not need active support because the corresponding finger module only seemed to get in the way while grasping an object or while orienting the hand along the wheelchair tray. The ring finger can possibly be omitted as well, but further research is required with regard to how this reduction in mass and complexity affects the attainable grasping performance.

Relevance

As this paper presents a case study, we cannot generalize the results to a large group of individuals with DMD that might benefit from SymbiHand. Future work will test a broader range of individuals to make stronger conclusions. However, our results show that the participant was able to preserve task performance and reduce muscular activation while wearing

the hand orthosis. This implies that, while wearing SymbiHand, the same task could be performed with lower neuromuscular effort than when not using the orthosis. This can reduce the burden on the muscles, delay the onset of fatigue, and lengthen the time span in which the user can use his own hand while performing ADL. Additionally, the increase in available grip strength can broaden the range of objects that the user can interact with. The applied current limit to the motor, however, implies that the device was over-dimensioned for this particular participant. The main reason for this added limit was to prevent exerting excessively high forces and flexion velocities on the sensitive fingers and skin of an individual that is not used to being assisted by a dynamic hand orthosis. It is possible that the motor's capacities can be further utilized as the participant gets more used to the device, or that other participants prefer higher levels of assistance.

The increased muscular activation observed during the tracking task without the orthosis—especially in the extensor muscles, which were not expected to be that active during a grasping task—can be partially attributed to the effort of the participant to stabilize his wrist without the orthosis. While wearing SymbiHand, the wrist was supported by a thermoplastic splint, which may have contributed to the large reduction in muscular activation. This may be a strong indication of the importance of supporting the wrist. However, further research is needed to investigate the effect of passively supporting the wrist on the reduction of muscular activation during functional hand use.

The fact that the participant was able to control the hand orthosis without any artificial sensors at the end-effector (i.e., strain gauges and potentiometers placed on the hand) tells us that the hydraulic transmission provided a predictable link between muscular activation and the speed of the orthosis. This makes the use of miniature hydraulic technology very interesting in the field of assistive devices controlled by the means of human intention detection schemes. In the presented hand orthosis, however, pressures are still quite low for a hydraulic system (<1.5 MPa). Even smaller hydraulic cylinders can be used to further improve efficiency, and a smarter way of integrating the hydraulic circuit within the mechanism can result in a more inconspicuous design. The hydraulic hoses in the presented prototype, for example, decrease overall cosmesis and will get in the way in a daily environment.

The combination of SymbiHand with arm [54] and trunk [53] orthoses

for individuals with DMD can complement the increase of the reachable workspace the latter aim to provide by allowing individuals with DMD to functionally interact with their environment. Furthermore, we believe that the use of SymbiHand can be extended to more pathologies, e.g., the daily assistance of elderly individuals with weakened muscles due to sarcopenia or individuals with stroke that have reduced hand strength. Another interesting application is a combination with augmented reality for a broad range of physical therapy exercises. This may further enable the multi-disciplinary rehabilitation of the hand for individuals with DMD, as proposed by Bushby et al. [30], [31].

7.5 CONCLUSION

This case study has shown that an individual with DMD underwent an amplification of grip strength, with no loss of tracking performance, when wearing the SymbiHand. The results have shown that, along with grip strength amplification, the SymbiHand enabled reduction in muscular activation during a force-tracking task. This was realized using a direct sEMG control approach with a tuned admittance model, in combination with a hydraulic transmission and differential mechanism. This has never been demonstrated before for individuals with Duchenne muscular dystrophy, highlighting the potential of this approach to enhance hand function and reduce fatigue while performing ADLs. For use in a daily setting, however, adjustments need to be made to facilitate more comfortable donning of the device and reduce unfavorable effects due to its total mass and mass distribution. These adjustments can assist the development of SymbiHand towards a larger-scale study and broaden its use for a larger group of potential users and applications.

CHAPTER 8

DISCUSSION

8

This dissertation presented several studies aiming at "**the characterization of the neuro-motor function of the hand, the decoding of hand motor intention decoding and the implementation of this in an active hand support for individuals with DMD.**"

The following questions were answered during the research phase of Symbionics 1.3 project:

Research Questions	
I.	Can we characterize the neuro-motor hand function of individuals with DMD? Part I (Chapters 2-4)
II.	Can we identify a feasible way to decode hand motor intention in real-time in order to control an active hand orthosis for individuals with DMD? Part II (Chapters 5-7)

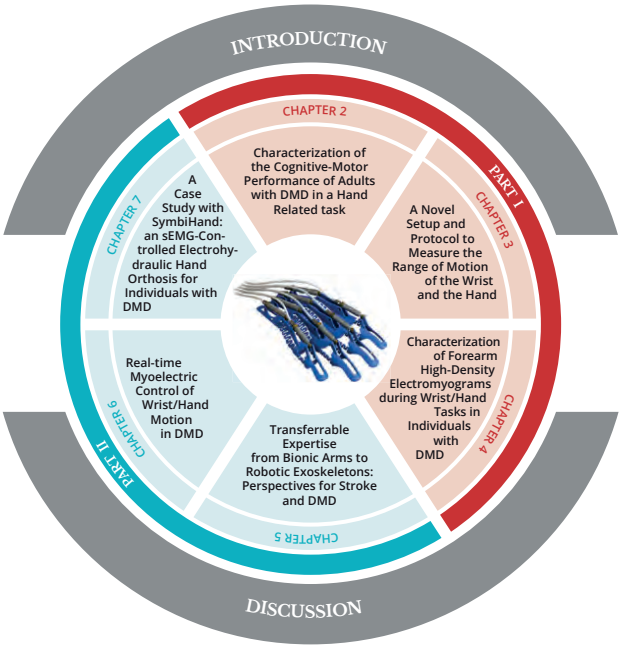

Figure 8.1 Overview of the parts corresponding to the research questions and the chapters of this dissertation

8.1 SUMMARY OF RESULTS AND CONCLUSIONS

Individuals with DMD can benefit from the use of assistive devices for hand/wrist supports. Such devices will enhance the independence and improve the quality of life of individuals with DMD. However, since the disease affects first the proximal upper extremity muscles, characterization and treatment of the hand function of individuals with DMD has not yet received much attention. Individuals with DMD currently substitute this function, when impaired, by using external robotic manipulators that are wheelchair mounted, hence disusing their own limb. In our effort to develop an active hand orthosis for individuals with DMD, we first identified surface electromyography (sEMG) combined with admittance for an additional level of customization, as a promising way of decoding hand motor intention. Subsequently, due to the scarce evidence regarding the systematic characterization of the neuro-motor hand function of individuals with DMD, we performed several studies towards this goal and developed a novel protocol for kinematic characterization of the hand and wrist. Individuals with DMD have significantly lower hand motor-cognitive performance compared to healthy controls and especially for multi-finger movements, and similarly distinct differences in forearm electromyograms.

However, we were still able to identify the potential for myocontrol, which led us to the development of real-time methods to decode hand motor intention from sEMG. Our first attempt to decode simple movements in real-time in combination with an admittance model from an individual with DMD, indicated the feasibility of this method. Lastly, we applied sEMG hand motor intention decoding with an admittance model, in real-time for the control of an active hand orthosis by an individual with DMD. This was demonstrated for the first time and the results showed a decrease in muscular activation accompanied by a threefold increase in grasping force.

To conclude, the characterization of the neuro-motor hand function of individuals with DMD in terms of motor performance, kinematics and forearm electromyography, together with the development and application of robust and successful hand motor intention decoding for the control of an active hand orthosis, present significant steps towards more complete and effective hand treatment and support for this population. We hope that our studies will create the basis for the multi-level and multi-disciplinary hand treatment of individuals with DMD

and other patient groups with similar diagnosis and help them to regain independence and control over their immediate environment.

PART I

HAND NEURO-MOTOR CHARACTERIZATION IN DUCHENNE MUSCULAR DYSTROPHY

I. Can we characterize the hand neuro-motor function of individuals with DMD? *(Chapters 2-4)*

Part I of this dissertation described the studies we performed, to gain insights into the hand neuro-motor function of individuals with DMD. This analysis was performed in three levels (Chapters 2-4). The first level focused on cognitive-motor performance characterization (Chapter 2). The second level focused on the creation of a reliable tool for measuring hand kinematics to characterize the hand ROM in DMD (Chapter 3). Lastly, the third level focused on the characterization of forearm electromyograms of individuals with DMD (Chapter 4). The combination of these three studies helps to create a neuro-motor profile for individuals with DMD.

In Chapter 2, we presented the systematic characterization of the hand cognitive-motor performance of individuals with DMD and comparison to healthy individuals during a hand related task. Our results showed, that individuals with DMD performed significantly worse than the healthy controls, during the hand related visuo-motor task. This study indicates that there is indeed a difference in hand motor-cognitive performance between healthy individuals and individuals with DMD. This suggests the need for an active hand support to offset this difference and provide multi-finger support, which we developed [59] and evaluated as described in Chapter 7.

In Chapter 3, we described the development of a reliable protocol for measuring hand and wrist range-of-motion (ROM. The results suggest low agreement between the goniometer (current golden standard) and the

leap motion sensor, yet showing a large decrease in measurement time and high reliability when using the later. Despite the low accuracy, the Leap motion sensor offers a reliable and fast way of driving subject specific hand and wrist rehabilitation in a clinical setting.

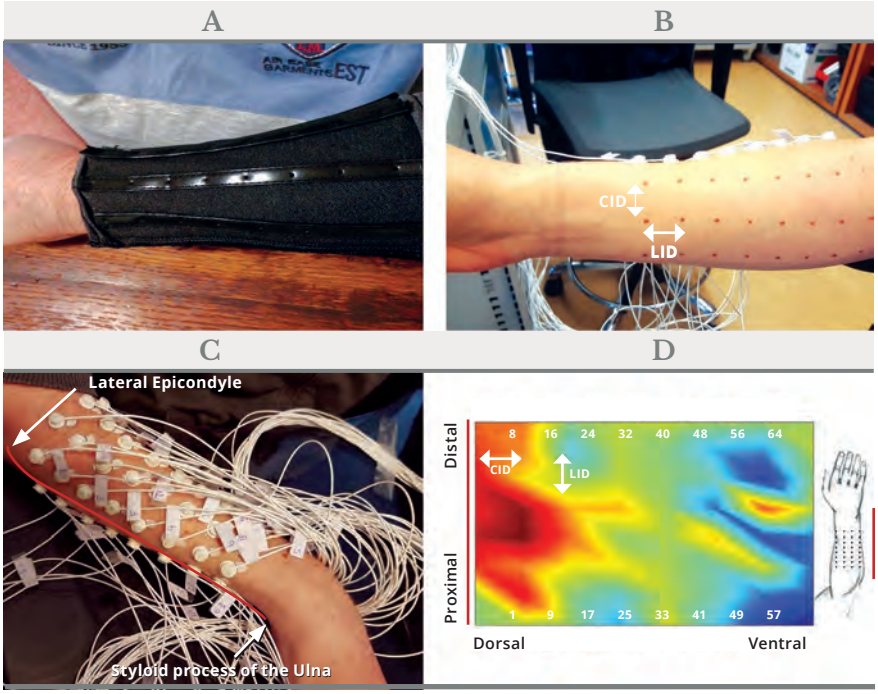

Figure 8.2 The figure shows the process of the electrode placement. A) The flexible custom-made sleeve that was used for marking the skin of the participant. The sleeve is flexible only around the circumferal direction and stiff along the longitudinal direction of the arm. B) The marked skin of the participant. The longitudinal inter-electrode distance (LID) is fixed at 2cm (L), while the circumferal inter-electrode distance (CID) depends on the forearm width of each participant. C) The participant with all the 64 electrodes placed. The virtual line that connects the lateral epicondyle and the styloid process of the ulna was used as the border between the dorsal and ventral side of the forearm. The placement of the electrodes starts right above this line, with electrode number 1 placed proximally (at 20% of forearm length from the elbow) and 8 distally. The rest of the electrode rows are placed counter-clockwise as someone is looking at his right arm. D) This way electrodes 1-32 were placed over the dorsal side (sketch) and 33-64 over the ventral side of the forearm.

In Chapter 4, inspired by the promise sEMG showed as a way to decode arm motor intention in DMD [8]; we characterized for the first time the forearm electromyograms of three individuals with DMD and compared them to eight healthy individuals. We found that the participants with DMD, exhibit lower dimensionality (decreased repertoire of spatially distinct activations) and an increase in overall activation effort compared to the healthy participants. However, they were able to repeatedly perform the same activation pattern. Additionally, when using pattern recognition algorithm, the offline performance of the DMD individuals while lower than the healthy participants, was still more than 80% for the classification of seven different gestures and more than 90% for four gestures (Figure 8.3). This indicates that sEMG based hand motor intention decoding is feasible for individuals with DMD, despite the progressive muscle tissue degeneration, and deserves further investigation (Chapter 6).

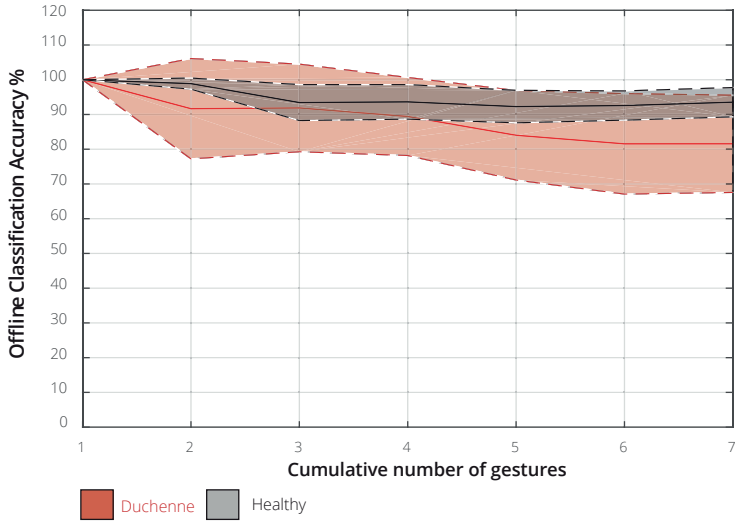

Figure 8.3 ***The difference in average offline classification accuracy for healthy and DMD participants, as a function of the gestures needed to be identified by the LDA classifier. The full lines represent the mean and the dashed the standard deviation.***

PART II

HAND MOTOR INTENTION DECODING IN DUCHENNE MUSCULAR DYSTROPHY

II. Can we identify a feasible way to decode hand motor intention in real-time in order to control an active hand orthosis for individuals with DMD? *(Chapters 5-7)*

Part II of this dissertation described the exploration of various motor intention detection approaches (Chapter 5) and the application of the knowledge gained in chapter 4, for the real-time hand/wrist motor intention decoding in individuals with DMD, using myocontrol. First, we applied two commonly used myocontrol methods in order to assess the feasibility of real-time myocontrol in DMD and compare to healthy individuals during a computer-based task (Chapter 6). Subsequently, we used the findings described in Chapter 6, in order to develop the myocontrol method for the real-time control of an active hand orthosis by an individual with DMD (see Chapter 7).

In Chapter 5, we presented a focused perspective on how knowledge from bionic research can help address the challenges related to motor intention decoding, that currently limit the systematic adoption of robotic exoskeletons. This perspective was with regard to upper extremity function. The knowledge gained from the design and implementation of human-machine interfaces for bionic arms can benefit the field of robotic exoskeletons, given the close relation and overlap between them regarding HMIs. Three broadly used motor intention decoding approaches in bionic arms were investigated in Chapter 5, including surface electromyography [113], [114], [181]–[186], [255] impedance [193]–[197] and body-powered control [200]–[203], [206]**.** We propose the use of sEMG combined with impedance/admittance model in order to compensate for disease specific abnormalities and offer an additional level of control customization for individuals with DMD (Figure 8.4). These conclusions were inspired by the results described in Chapter 4 and led to the development of the motor intention decoding approaches implemented in Chapters 6 and 7.

In Chapter 6, we tested in practice how feasible sEMG [113] is for the real-time control of hand and wrist motion with an individual with DMD during a target-reaching task. We compared two broadly used approaches for myoelectric control, namely sequential direct control (DC) [112], [240] and pattern recognition (PR) control [199]. Results show that despite the progression of muscular degeneration in the DMD participant, myoelectric control performance is comparable to that of the healthy participants (Figure 8.5). Both approaches were combined with an admittance model

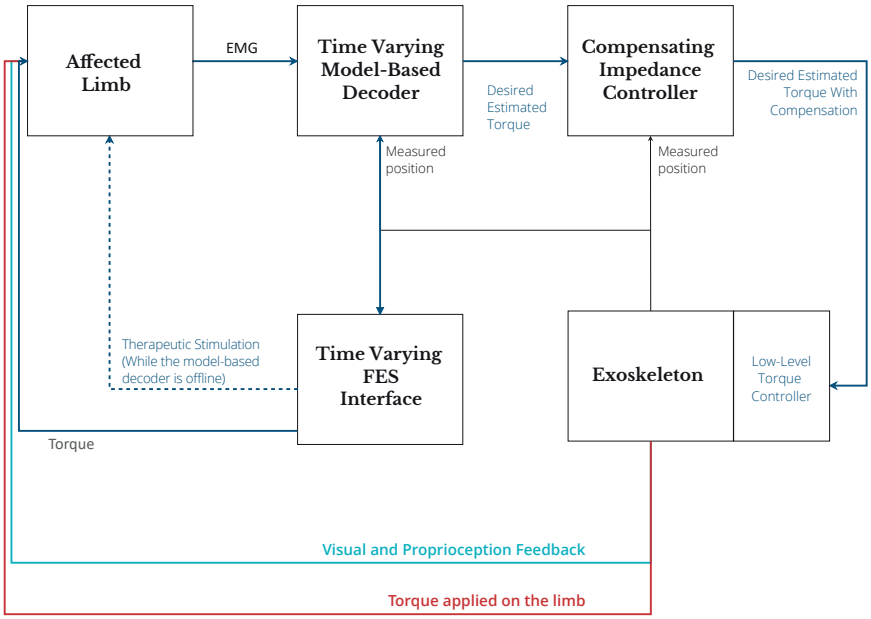

Figure 8.4 *This figure illustrates the proposed motor intention decoding diagram for DMD. In this case we combine sEMG with a time-varying biomechanical model (due to the progressive nature of the disease) and impedance control. The impedance controller aims to compensate for abnormal synergies and stiffness of the limb. The estimated torque from the biomechanical model based on the sEMG measured, will be driven through compensating impedance, which will adjust the torque according to subject specific abnormalities. The final torque with compensation, will be driven to a low-level torque controller and then to the robotic exoskeleton. We also aim to use electrical stimulation (influenced by the biomechanical model and integrated in the robotic exoskeleton), when the controller is offline, in order to keep the quality of the muscles higher and slow the progress of the disease.*

to allow for further customization of the control and we found that the participant with DMD needed a different admittance model than the healthy participants.

In Chapter 7, we described the case study of the SymbiHand (second prototype developed within our project [59]) with an individual with DMD (Figure 8.6). The SymbiHand is a dynamic, underactuated, wearable myoelectric hand orthosis for individuals with DMD. sEMG signals control an electrohydraulic pump by decoding the users hand motor intention, in real-time, using DC control [112] as described in Chapter 6. The SymbiHand increased the participants grip strength by threefold, while preserving tracking performance during a force tracking task. Additionally, the participant was able to open and close his hand with lower effort, indicated by a large decrease in sEMG activation. Individuals with DMD experience high normalized muscle activations, during performing hand related tasks and this can lead to early fatigue onset (see Chapter 4). Therefore, this was an important result of this case study, which demonstrated that the SymbiHand combined with sEMG and an admittance model, is able to provide active hand assistance to an individual with DMD. Lastly, due to its design, the SymbiHand is able to provide multi-finger training and support, which is declining in individuals with DMD (see Chapter 2) and is crucial for the preservation of hand functionality.

In conclusion, by characterizing the neuro-motor hand function of individuals with DMD, exploring the feasibility of electromyography as a motor intention decoding method together with the development and application of robust and successful hand motor intention decoding for the control of SymbiHand, we made significant forward steps towards a more complete and effective hand/wrist function support for individuals with DMD. We hope that our efforts will create the basis for the multi-level and multi-disciplinary hand treatment of individuals with DMD and help them to regain independence and control over their immediate environment.

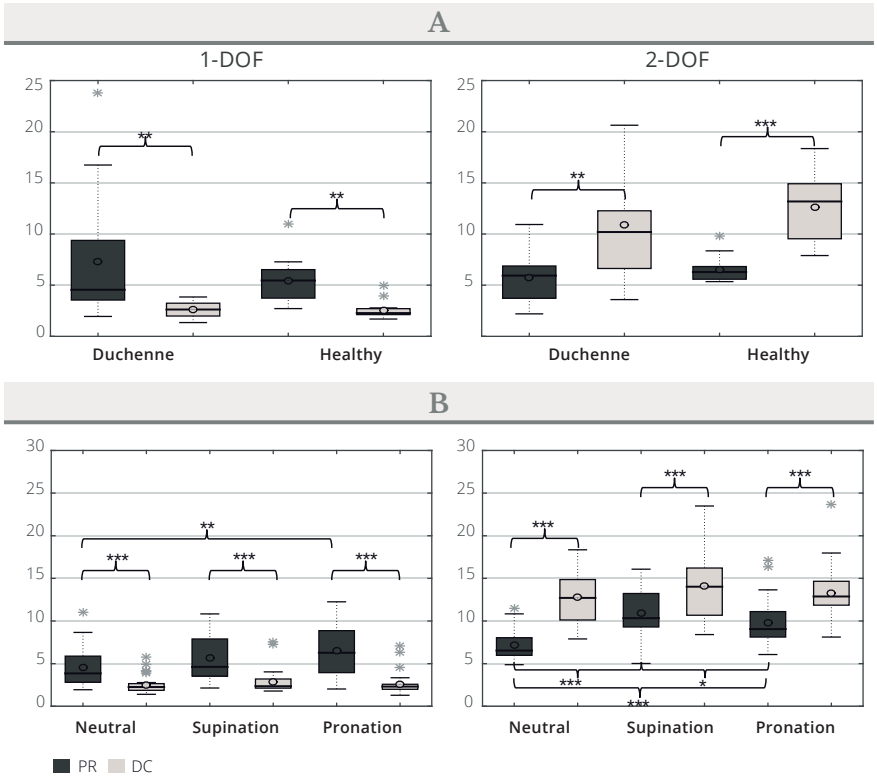

Figure 8.5 ***Boxplots and non-parametric Wilcoxon tests of the reaching time for all participants. 1-DOF and 2-DOF tasks were compared separately. Each forearm orientation was plotted with both PR and DC method.*** *A)* ***Since the participant with DMD performed half of the targets, we compared his data with a subset of the healthy data and the samples per boxplot number 16.*** *B)* ***The boxplots consist of the average reaching time of the ten healthy participants. Since every DOF includes four targets and each target was performed eight times, we have 32 samples per boxplot. A line represents the mean value and a circle the median. Significant differences are marked with stars: *P < 0.05, **P < 0.01, ***P < 0.001.***

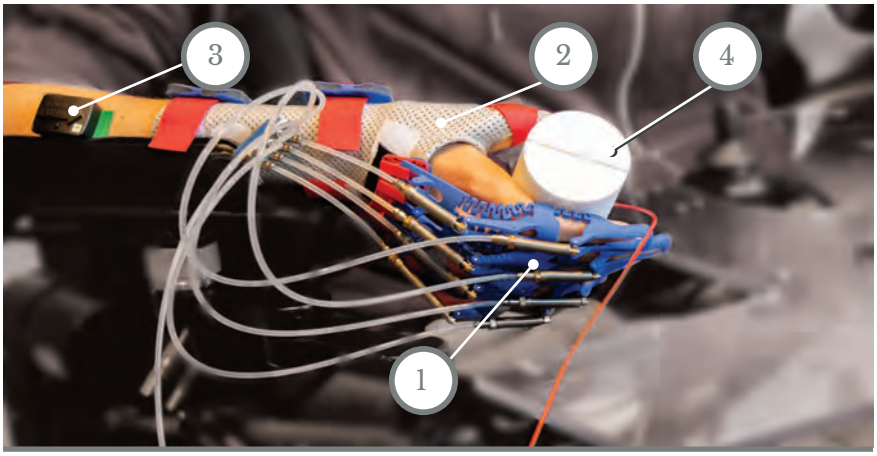

Figure 8.6 ***The participant with DMD grasping the sensorized object while wearing the SymbiHand orthosis.*** *1)* ***SymbiHand, consisting of four finger modules.*** *2)* ***The thermoplastic hand splint, used to stabilize the wrist and the thumb while providing an anchoring surface for the four finger modules.*** *3)* ***Wireless sEMG sensor, placed on the extensor digitorum communis muscle.*** *4)* ***The cylindrical sensorized object, used for measuring grasping force.***

8.2 FUTURE CONSIDERATIONS AND GENERAL CONCLUSIONS

This section offers a brief overview of the limitations in our approaches to answer the research questions and offers suggestions on how to tackle them. Additionally, it offers directions for future steps towards the realization of the development of an active hand orthosis for individuals with DMD. It also presents the author's view on the general lessons learned during the process of the Symbionics 1.3 project and conclusions made on less technical albeit, important considerations, for the better utilization of the results described in this dissertation, in line with the multi-disciplinary approach in treating DMD as suggested by Bushby et al. [30], [31].

Research Limitations

Number of participants - The studies described in this dissertation and include participants with DMD, are limited by the low number of participants. This is a common characteristic of such studies and it is mainly attributed to the low population density and the fact that many individuals with DMD are active participants in various ongoing research projects [8]. Due to our

steadfast commitment towards causing the least inconvenience possible to the participants and keep high ethical standards during performing high-level research, we performed our studies with a limited number of participants. Hence, our conclusions must be regarded with caution as a higher number of participants would be required to ensure they are appropriately robust and generalizable over the whole population.

Despite any limitations however, our studies provided enough evidence of the feasibility of our methods and answered our research questions. We chose to develop and test a complete characterization framework and several myocontrol methods with a low number of participants, instead of conducting full-scale studies with a large number of participants, over fewer concepts. After this initial exploratory phase and keeping in mind the outcomes, the investigated protocols can now be optimized and applied to a larger number of participants and allow for a more generalized set of conclusions.

Simplified protocols - As the disease progresses, individuals with DMD consistently experience early fatigue onset. In our comparative studies with participants with DMD, we modified and simplified our protocols. Additionally, the experimental tasks were related to functional tasks that involve the hand and the wrist, however they were also simplified (i.e. mouse clicking in Chapter 2, hand/wrist related gestures in Chapter 4, hand open/close in Chapters 6 and 7). Nevertheless, the modifications in our protocols ensured that enough trials were performed with the appropriate variability for extracting useful insights, while ensuring any ethical requirements were met, and the participants did not get fatigued.

The goal of Symbionics 1.3 is the development of a hand orthosis for daily home use. In line with this, we tried to evaluate myocontrol outside of the lab (Chapter 6). However, more studies are needed in a home setting, involving daily tasks of high functional value. Such studies, will give very important insights regarding the robustness of myocontrol methods in realistic scenarios and in the long term (to observe the effects of learning, fatigue, skin changes etc.). Additionally, the effect of forearm orientation and how the dynamic use of the arm affects hand/wrist motor intention decoding, should be further explored in DMD. Initiatives like the Eurobench project [256] aiming for a common framework and various testbeds for robotic devices and facilities such as the usability

lab in the Roessingh Research and Development [257], can be of great assistance in the performance of future studies that will focus testing a greater variety of motor skills.

Heterogeneity in DMD - DMD is a disease with many specificities related to hand function, which we explored systematically (Chapters 2-4), addressed regarding motor intention decoding (Chapter 5), and finally developed and successfully tested customized hand/wrist motor intention decoding paradigms (Chapters 6 and 7). Additionally, there is evidence of great functional heterogeneity among individuals with DMD [26]. This heterogeneity is induced by the disease progression pattern (Chapter 1), different treatment approaches dependent on the country of origin, the caregiver or the financial and social status of the patient [17] and different sub-phenotypes [26].

In the studies described in Chapters 2 and 4, the participants with DMD (three in each study) were chosen to have different levels of residual hand function and therefore induce a high functional variability in the characterization phase. In Chapter 5, we describe a personalized human machine interface scheme for individuals with DMD (Figure 8.2). This takes into account the progression of the disease by including a time-varying intention decoding approach and the various specificities of the user by a compensating impedance controller. Later, in Chapters 6 and 7, we developed personalized approaches in hand/wrist motor intention decoding for each of the two participants, as Lobo Prat recommends for testing active assistive devices for individuals with DMD [8]. However, due to time constraints we were not able to test our protocols in large heterogeneous groups of individuals with DMD, and explore all the space of possibilities discussed in Chapter 5.

Future studies should investigate further, how this inherent heterogeneity plays a role in motor intention decoding in DMD. Additionally, EMG-driven model-based techniques [186], [255], have the potential explore the change in muscle properties over the progression of the disease, and combined with more traditional approaches, provide an adaptive and personalized motor intention decoder for individuals with DMD. Lastly, the recent work from Keemink et al. [258] provides a comprehensive and complete admittance controller framework, that can be used for physical human-robot interaction and enhance user tailored control.

Developed Prototypes - In the Symbionics 1.3 project two active hand orthosis prototypes [58], [59] were developed (Figure 8.7). However, we only have tested the second prototype with one individual with DMD. Due to time constraints, we did not have the chance to re-test the second prototype and also test the first prototype with one or more individuals with DMD. Nevertheless, the case study with the SymbiHand (Chapter 7) has already revealed some aspects that need to be improved and future work should focus in improving and testing both prototypes with a larger number of participants.

One such aspect is the addition of an active thumb module. Ongoing work is focusing on upgrading both prototypes with an active thumb module. Additionally, according to research [1], in the majority of the currently developed hand orthoses, the wrist is often supported, albeit locked or assisted. However, the wrist is considered to be a crucial element in supporting hand function, and especially in the case of DMD, supporting the combination of wrist and grasping functions can be essential. Such additions though, will increase the total mass of our orthoses and will also create the need for a more sophisticated hand/wrist motor intention decoding approach than the one described in Chapter 7.

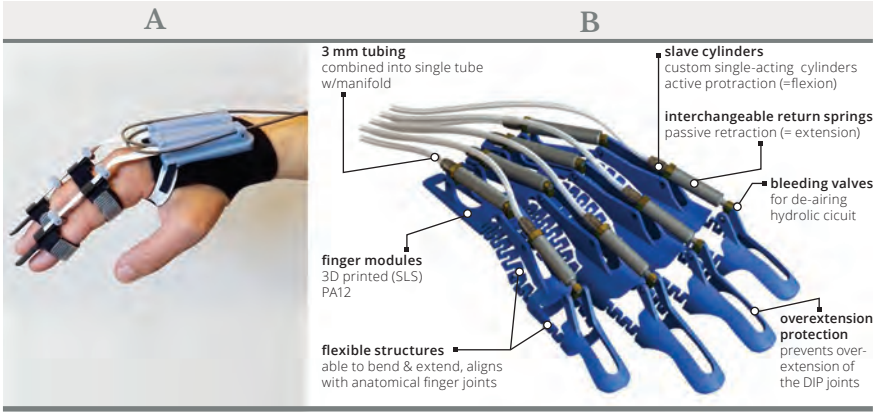

Figure 8.7 A) The first prototype developed in the Symbionics 1.3 project. Its design is based on a novel tape spring mechanism. B) The second prototype (SymbiHand). This design is based on the concept of miniature hydraulics

Despite the low mass of the SymbiHand, weight was still an issue for the participant with DMD. The integration with an arm support could help with lifting the arm, but the high concentration of mass on the dorsal side of the hand made it impossible to pronate/supinate. This calls for a more strategic distribution of mass, which can be used to reduce the moment of inertia around the center of rotation of this particular movement. This interesting result of the study described in Chapter 7, needs to be carefully considered, before adding more modules to the hand orthosis. However, overall mass reductions are possible, for example by making the hydraulic parts more light-weight. We also believe that the little finger does not need active support, because the corresponding finger module only seemed to get in the way while grasping an object or while orienting the hand along the wheelchair tray. The ring finger can possibly be omitted as well (similar to what we did for the first prototype [58]), but further research is required how this reduction in mass and complexity affects the attainable grasping performance. Additionally, the prototype was able to support successfully an individual with DMD and increase grasping force by threefold, only at the 30% of its capabilities. This indicates that the prototype might be overpowered and the overall mass and complexity of it could potentially be further decreased while retaining a good performance.

Another point of interest that emerged from the case study of the SymbiHand was that donning the different parts of the SymbiHand was difficult and uncomfortable for the participant. Firstly, the tight fit of the wrist and thumb splint made it unpleasant to put on. Secondly, because the fingers were so sensitive, sliding the finger modules on the fingers was not very comfortable. As a result, the finger modules could not be donned easily one by one because the stiffness of the hydraulic hoses would add additional forces to the fingers. We believe that a modular or hinged splint with additional straps can help to reduce these problems, as well as finger modules that allow for quick and easy donning from the dorsal side of the hand. Thirdly, positioning the thumb in opposition to the volar pads of the index and middle finger put it in an awkward resting position. This means that an additional thumb mechanism is necessary that is able to switch between a resting and functional position.

All the characterization studies and protocols described in Chapters 2-4, can be used in the future to evaluate the performance of both

prototypes. The novel tool for the fast measurement of hand kinematics (Chapter 3), can potentially display improvements in the active ROM of individuals with DMD, while wearing the orthosis. Additionally, in the future the protocol described in Chapter 2, could be applied while an individual is actively controlling the SymbiHand, and show the degree of support in a quantitative way. Lastly, it would be interesting in the future to characterize the forearm electromyograms of an individual with DMD (Chapter 4), after wearing the orthosis for a long time and identify, changes in motor control due to adaptation effects, emerging from the symbiotic relationship between the user and the device.

Future Steps and Recommendations

Importance of Effective Hand Rehabilitation - At the beginning of the design process of both prototypes, we held focus groups together with patients, occupational therapists and clinicians, to ensure that we will address the specificities and needs of individuals with DMD appropriately. It became quickly apparent that due to extensive contracture of the long finger flexors, individuals with DMD need a modular hand orthosis that will enable comfortable donning and doffing. If the individual's fingers are stiff and experience contractures (Figure 8.8) the passive ROM is minimal and a hand orthosis might not be able to deliver any functional benefit. Therefore, effective hand wrist rehabilitation is a necessary first step before a functional active hand orthosis can help in daily living. In that sense, the SymbiHand could serve as an early rehabilitation tool, before transitioning into a more functional support in later stages of the disease. This way an early symbiotic relationship can be built between the user and the device, that may lead in retention of finger flexibility for a longer time

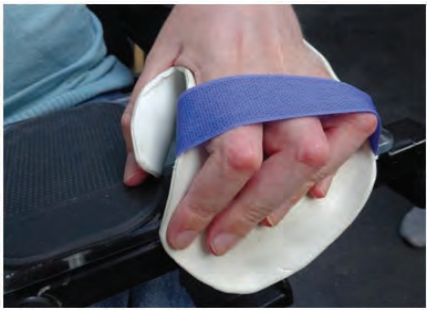

Figure 8.8 ***The fingers of an individual with DMD, while wearing a resting splint. There are visible contractures in the proximal interphalangeal joint of the fingers.***

and progressively into daily support when that is no longer feasible for the user.

The results described in Chapter 2 indicate the need for multi-finger rehabilitation. Optical sensors such as the one described in Chapter 3 can be used in combination with virtual/augmented reality, in order to deliver effective hand rehabilitation and at the same time perform real-time measurements of the users' active ROM and performance. Furthermore, a protocol as the one described in Chapter 4, can provide real-time high-density electromyographic feedback during VR rehabilitation, and serve as an outcome measure. Moreover, a large amount of active hand orthoses are already combined with virtual reality in order to enhance hand rehabilitation [1]. Although the SymbiHand orthosis was developed for daily assistance, an interesting application would be the combination of the SymbiHand with virtual/augmented reality for a broad range of physical therapy exercises. This may further enable the multi-disciplinary rehabilitation of the hand for individuals with DMD as proposed by Bushby et al. [30], [31].

Integration of Assistive Technologies for Individuals with DMD and the Concept of Simplicity - DMD is characterized by progressive loss of muscle strength, and bodily functions. There are various ongoing projects that explore the active assistance of the trunk and neck [52], [53], the arm [8] and the hand functions [10], [58], [59] of individuals with DMD (see Chapter 1). Each of these investigated functions is complimentary to one another and all together present a complete system that aims in the daily support of individuals with DMD. A functional active hand orthosis cannot achieve much as a standalone application, if the active ROM of the arm and the trunk is minimal. Therefore, it becomes apparent, that the integration of all these technologies will be a challenge that deserves future focus and cannot be overlooked. Such a system will have serious demands in energy, space, number of sensors used and will create challenges on user comfort, training of using all the separate modules, high cognitive load, fitting and cost [17]. It will also vastly delay the translation of such technologies from research to market and subsequently the user.

This calls for simplicity in the design of assistive technologies for DMD. In Symbionics 1.3 we strived for a minimalistic and underactuated design, combined with a simple hand motor intention detection approach (see

Chapter 7). We used a small amount of sensors, straightforward intention decoding and made choices for the support of two digits [58] in our first prototype and four in our second [59] combined with a modular design that allow us to increase or decrease the complexity of the SymbiHand at will. Research has shown that being able to perform a power grasp improves the amount of manipulation that can be achieved for ADLs [123] and finger independence studies indicate that supporting fewer fingers may not result in decreased functionality [72]. Moreover, simpler approaches may reduce the already high costs of DMD rehabilitation [17]. We believe that integration of assistive technologies for DMD, out of the lab testing, translation to the market and user satisfaction will greatly benefit by a careful compromise between functionality and simplicity.

Integration of Assistive Technologies and Virtual/Augmented Reality for Individuals with DMD - Late technological developments, like the hololens 1 and 2 [259], the magic leap one [260], the leap motion sensor [261] and the oculus [262], provided a boost to AR/VR technologies. Such technologies are increasingly used for marketing, training, social interaction and gaming. Currently physical therapy is the most commonly prescribed hand rehabilitation intervention. VR/AR [263], [264] and serious gaming [265] however, are increasingly used in combination with rehabilitation robotics for stroke [211], [266], [267], and for DMD [41] in order to provide motivation for the users and targeted specific muscle groups, with reportedly promising results [268], [269]. Its added value though, is still unclear compared to conventional therapy [111], [266], [268]. Nevertheless, literature suggests that VR has potential and can add benefits combined with conventional therapy [268] in order to increase the amount of rehabilitation time [266] and help patients who are unable to visit the clinic regularly [111], such as individuals with DMD. Additionally, it can be integrated together with the SymbiHand, in order to provide an immersive rehabilitation experience, in combination with an active hand orthosis. The potential benefits of VR/AR technologies for the engaging rehabilitation of individuals with DMD, present an interesting future research avenue (briefly discussed in Chapter 3).

Hand/Wrist Workspace Characterization - The pioneering work from J.J. Han

et al. [270]–[272] in the field of reachable upper extremity workspace in DMD, indicated the value of optical sensors as a reliable, fast and fun clinical outcome. The Kinect sensor was evaluated as a reliable and quantitative assessment tool of the upper extremity capabilities of individuals with DMD. Additionally, it was demonstrated that optical reachable workspace assessment has concurrent validity [271] with a DMD specific upper extremity function outcome measure (PUL [247]). Our work with the LEAP motion sensor presented in Chapter 3, could be further extended in order to characterize the reachable workspace of the hand/wrist, similar to the work done by Han et al [270]–[272]. We briefly assessed the reliability of the LEAP motion sensor via a test re-test approach with healthy participants. However, more studies should investigate the sensitivity, validity and the potential link between an optical assessment of the hand/wrist with the LEAP motion sensor and currently used outcome measures for individuals with DMD, such as the PUL. A combination of the Kinect and the LEAP motion sensor can create a unified framework for the complete assessment of the upper limb function of individuals with DMD, in a non-contact, reliable, quick and motivating way.

Wrist Motor Intention Decoding - Achieving higher standards of rehabilitation may increase the hand/wrist capabilities of individuals with DMD. This in turn will require a more complex orthosis to support the full range of the users' capabilities, including more active modules (i.e. wrist and thumb) as previously discussed. Subsequently, more sophisticated motor intention decoding approaches will be necessary for the intuitive and robust control of these additional DOFs. Some of the aforementioned approaches were briefly explored in Chapters 4 (offline pattern recognition [198]) and 6 (online pattern recognition [243]). However due to the simple protocol of direct myocontrol [112], [240] applied in the control of SymbiHand (see Chapter 7), such approaches were not tested in combination with the orthosis and may compromise both comfort and integration by violating the concept of simplicity.

There is a lot of knowledge coming from the field of bionic arms and hands regarding motor intention detection that can directly be translated to robotic orthoses (see Chapter 5). Future work should focus on the exploration of motor intention decoding approaches such as regression [188] (continuous mapping of sEMG signals to kinematic

variables). However, training in a specific spatiotemporal condition using machine learning does not necessarily translate into another [189]. The combination of such approaches with biomechanical models can overcome this limitation [184], as recently demonstrated [185], [186]. Additionally, HD-sEMG grids combined with regression can successfully decode motor intention in real-time over multiple DOFs as it was illustrated in the case of individuals that underwent targeted muscle re-innervation (TMR) [273]. However, the combination of sEMG electrodes with wearable robotics can be challenging since sEMG signals are highly sensitive to movement artefacts and collisions [168]. Textile integrated sEMG sensors [274] could possibly improve the usability (i.e. donning) and robustness of sEMG based motor intention decoding.

In addition to motor intention decoding, there are several issues already addressed in bionics, which can enhance the adoption of orthotic technologies. Effortless donning and doffing of an external device can have a positive effect on a user's satisfaction and presents an aspect already well-studied for bionic arms. Orthoses can benefit from the successful examples already set for bionic arms. The fact that amputees may have specific surgeries performed to improve fit (like osseointegration) or bionic arm control (like TMR) suggests that surgical procedures could become available for individuals using orthoses.

In the same sense invasive technologies for motor intention decoding can provide a future focus for individuals with DMD. Thanks to the ongoing development of implantable myoelectric systems [275] and neural electrodes [276] for invasive recordings and stable motor intention decoders that do not need daily training, invasive technologies, could become a way to increase the performance of the current motor intention decoders. DMD, in contrast to other disorders, does not affect the neural pathways and therefore the control commands can also be decoded from invasive nerve or muscle implantable electrodes. Such signals may be more specific and have a high signal to noise ratio and allow for the better quality bio-signals for longer time, in individuals with DMD.

Implications for Other Pathologies - Although the neuro-motor characterization approach and the assistive technology described in this dissertation were developed for individuals with DMD and were highly tailored to the specificities of this disease, individuals with other neuromuscular diseases

may also benefit from our findings. In Chapter 5, we make an initial proposal for the use of DMD as a representative case study for similar diagnoses. Additionally, we offer our view on how individuals with stroke that have reduced hand strength can benefit from similar intention decoding approaches combined with active robotic orthoses. Furthermore, we believe that the use of SymbiHand can be extended the daily assistance of elderly individuals with weakened muscles due to sarcopenia.

Ethical Considerations and User Involvement

Ethics in Engineering - Until the mid-eighties, ethics was thought as impeding the creativity of engineers, and not given much attention until 1986 and the challenger disaster [277], [278]. However, finding innovative solutions within ethical boundaries and user consideration requires significant creativity. The importance of ethics for engineering has been increasingly recognized, leading to the funding of respective research projects by the EU (e.g. COST Action CA16116 [279] and INBOTS project [280]) and ethics classes in engineering education [281], [282]. Additionally, initiatives like the Foundation for Responsible Robotics (FRR) [283] and the work from Fosch Villaronga et al. [284] have started to create a robust legal and ethical framework for the development and use of robotic technologies. The integration of ethics into research has been fueled by the concept of responsible research and innovation (RRI), which has been highlighted by the European Commission in their Horizon 2020 funding scheme [285]. Responsible research is "a transparent, interactive process by which societal actors and innovators become mutually responsive to each other with a view to the (ethical) acceptability, sustainability, and societal desirability of the innovation process and its marketable products (in order to allow a proper embedding of scientific and technological advances in our society)" [286].

With biological robots taking over crucial parts of human daily living and being an integral part of our future, RRI is very important in the field of robotics. Subsequently, engineers are required to develop a keen sense of ethical conduct and integrate ethics into the design process and understand their professional role in society. Instead of looking at ethics as an obstacle, it may be time to consider it as a meaningful addition that can protect the developer and the user from the consequences of rush decisions [278] and make the difference between socially barren and socially impactful research. According to Nisselbaum et al.

[287], the set of criteria that engineers are using to evaluate systems should incorporate social, ethical and political criteria. RRI does not only concern the evaluation of developed technologies but also highlights the importance of ethical considerations during their development. For not only robotics but technologies in general, Friedman et al. developed the so-called value sensitive design (VSD) approach, which aims at incorporating ethical considerations into the design process from its very beginning [288], in a three-step investigation process:

- Conceptual: identifying relevant values and who might be relevant stakeholders and using philosophical and social science theory.
- Empirical: actively engaging stakeholders' perspectives to identify variation and commonalities, by observation, surveys, interviews and focus groups.
- Technical: Proactive designs to support values identified in the conceptual and empirical investigation and identify how existing technological properties support or hinder realization of these values.

Ethics in Symbionics 1.3 - In order to relate ethics to our research, collaboration with the philosophy department of the University of Twente was initiated. This collaboration took the form of Symbionics 1.3 being a case study in the MSc. project of Alexandra Kapeller [289]. Her thesis researched enabling technologies in general, introducing the 'dilemma of assistance and acceptance', which describes the potential stigmatization and discrimination of disabled individuals through enabling technologies parallel to their need for assistance. The recommendations for ethically acceptable enabling technologies she developed were applied to the SymbiHand.

A main result of Kapeller's research is that enabling technologies should avoid medical paternalism, i.e. doctors and technologies aiming for 'fixing bodies', thereby re-enforcing the medical model of disability. To avoid such paternalism, it is important to know whether a specific technology is actually desired by its potential users and not merely assumed to be useful based on literature gaps. In the case of Symbionics, this interest is manifested in the request of and financial participation in the development of the technology.

Furthermore, although enabling technologies should be universal if possible, i.e. usable by everyone, many assistive technologies, such

as the SymbiHand, cater for specific needs and cannot be designed universally. As a result, they risk contributing to the stigmatization of disabled individuals. However, they can also – if designed in a proper way – contribute to a more positive view on disability by expressing disability pride. To not make disabled individuals 'frontiers of justice' and to avoid paternalism, they need to be given a choice between a noticeable or inconspicuous design – depending on whether the users want to show their disability or hide it. Other meaningful choices in the design and use of the technology available to the users would understand the users as autonomous persons instead of dependent patients.

In our design, we strived for a highly modular approach in order to allow for as many configurations and user choices as possible, involving the users in the thinking process. Considering the integration with other devices (see Section **Future Steps and Recommendations**), we kept in mind the possible need for compatibility with other technologies for active support of individuals with DMD. Lastly, both prototypes address specific user demographics as they were specifically developed for individuals with DMD and offer the choice for different design options. However, opposed to similar projects that aim for an inconspicuous design [9], [121], we propose a different perspective. We would like our users to be proud of their active support and not try to hide it under clothing instead. This is partially in conflict with the need for user choices (i.e. a user may want a minimal, inconspicuous hand orthosis), but our first prototype is in accordance with the wish for an inconspicuous design. Unfortunately, due to time constraints, we mainly focused on the control and did not sufficiently address the topics of user comfort and the cosmesis of the SymbiHand [290]. The hydraulic hoses in the presented prototype, for example, decrease overall cosmesis and will get in the way get in the way in a daily environment (see Chapter 7).

In Section Future Steps and Recommendations, simplicity was discussed with respect to control and integration of multiple technologies for individuals with DMD. However, simplicity has also clear ethical and psychological impacts on the user. It has been suggested that individuals with DMD experience a progressive loss of control over what happens to them [15]. This loss of control can be alleviated by experiencing an immediate positive impact, such as a functional hand orthosis. However, we need to carefully study the long-term effect of such an intervention

and technology-user adaptation and try to avoid offering technologies with an expiration date as this will lead to further experiencing of loss of control (i.e. when due to progression of the disease, the technology cannot adapt and it is not usable any more). Simple motor intention approaches as the one described in Chapter 7 (direct control [112]), may be able to offer long-term usability. However, more longitudinal studies are necessary to address this important topic of adaptation in time. Technology is important and can prove beneficial for individuals with neuromuscular disorders. Nevertheless, we should carefully consider the benefits of our proposed technology with regard to existing interventions, as we do not want to create independency from caregivers and at the same time create dependency on engineers and technicians.

User Participation in Research - Our efforts focus on helping individuals with DMD, but we should not forget that this relationship is bidirectional. Inspired from previous endeavors [6], instead of merely assuming our users wishes and characteristics, the Symbionics 1.3 team aimed for genuine user involvement. We held focus groups and meetings with experts, occupational therapists, doctors, engineers and individuals with DMD, in order to discuss our design process. These focus groups were an important first step towards user participation. Nevertheless, active user participation in the design process together with the fact that individuals with DMD are already investing time and effort by their participation in multiple research projects means more user burden. Despite this effort though, individuals with DMD still have minimal access on the data from this research. To tackle the latter issue, Elizabeth Vroom, founder and president of the Duchenne Parent Project in The Netherlands [49], has recently commenced the creation of a unified platform with research data [291], where individuals with DMD will have access to the data derived from or provided by them. Such initiatives will enhance user participation and keep them and their families up to speed with the current research efforts. Additionally, it will create a structured platform for researchers to responsibly access a vast amount of data, thus preventing data underutilization and fast-tracking adoption of innovative technologies by health providers. Therefore, a unified data platform will benefit both individuals with DMD and researchers at the same time. Additionally, it may mitigate limitation of number of available research participants (see

Section Research Limitations), by providing an extra incentive to potential participants.

A Different Approach for the Support of Individuals with DMD

A recent study suggests that motor learning rehabilitation combined with an Internet of Things (IoT) strategy can be developed for an improved and engaging rehabilitation of both the upper and the lower extremities [292]. This can help achieving a unified "electronic home rehabilitation gym" [293] and improve the effectiveness of tele-rehabilitation [294], by monitoring physical activity [295]. System integration of all the developed active supports for individuals with DMD can benefit from such paradigms. Additionally, in a highly computerized and interconnected world, individual independence and social participation may stop relying on physical manipulation of the environment, but rather on the ability to interface with smart devices. In line with this, it may be proved substantially more important to decode user intention for interfacing with such devices. This way, individuals with DMD may be able in the future to manipulate their entire "smart" environment, by transmitting their intention to various interconnected devices and being professionally active.

B

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All my years in Greece, I managed to make a lot of friends and over the last few years, despite most of us migrating, we managed to always meet 2-3 times a year. I want to thank all of them.

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than family!

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Special thanks to my girlfriend Nikola! I love my life since I met you and thank you for all of your incredible support. Nickaki, miluji tě a nemůžu bez tebe žít.

To all of you people that brought me a step closer to the conclusion of this work, thank you from my heart!

Kostas Nizamis
Enschede, March 2019

BIOGRAPHY

Kostas (Konstantinos) Nizamis was born on May 15th of 1988 in Kavala, Greece. He studied Electrical and Computer Engineering at the Democritus University of Thrace (DUTh) and receive his Master of Engineering degree in Electronics. The title of his Master project is "Study and development of an electronic system for creating an adaptive railroad network using methods inspired by nature". After graduating, he decided to continue by pursuing another MSc. degree in Biomedical Engineering at the University of Twente in The Netherlands. There he worked with Dr. Joan Lobo-Prat, Dr. Arno Stienen and Professor Bart F.J.M. Koopman, towards the "Switching Proportional EMG Control of a 3D Endpoint Arm Support for People with Duchenne Muscular Dystrophy", as part of the Flextension A-Gear Project. At the end of the study program, he was offered the opportunity to work in the Symbionics project, as a PhD candidate at the Department of Biomechanical Engineering of the University of Twente, and continue his research towards the active upper extremity support of individuals with Duchenne muscular dystrophy. This dissertation on ***Hand Neuro-Motor Characterization and Motor Intention Decoding in Duchenne Muscular Dystrophy*** is the result of his work in the Symbionics project. During his PhD project he presented his work in various national and international conferences and chaired two international symposia. Additionally, since 2017 he is a member of the European COST action on Wearable Robots, and more specifically of the group dealing with the ethical, legal and societal aspects of wearable robotics. Since March 2019, he is working as an Assistant Professor at the Department of Design, Production and Management at the University of Twente. His current work focusses on user-centered, multi-disciplinary design and systems engineering, with an interest in rehabilitation technology.

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SCIENTIFIC CONTRIBUTIONS

Journal publications

1. **K. Nizamis**, N.H.M. Rijken, R van Midelaar, J. Neto, H.F.J.M. Koopman and M. Sartori "*Characterization of Forearm High-Density Electromyograms during Wrist-Hand Tasks Individuals with Duchenne Muscular Dystrophy*", June 2019 (under review)

2. **K. Nizamis**, A.H.A. Stienen, D.G. Kamper, T. Keller, D.H. Plettenburg, E.J. Rouse, D. Farina, H.F.J.M. Koopman and M. Sartori "*Transferrable Expertise from Bionic Arms to Robotic Exoskeletons: Perspectives for Stroke and Duchenne Muscular Dystrophy"*, ", IEEE Trans. Med. Robot. Bionics, April 2019

3. R.A. Bos*, **K. Nizamis***, H.F.J.M. Koopman, J.L. Herder, M. Sartori and D.H. Plettenburg *"A Case Study with Symbihand: An sEMG-Controlled Electrohydraulic Hand Orthosis for Individuals with Duchenne Muscular Dystrophy*", March 2019 (under review)

4. **K. Nizamis**, A. Ayvaz. N.H.M. Rijken, H.F.J.M. Koopman and M. Sartori "*Real-Time Myoelectric Control of Wrist/Hand Motion in Duchenne Muscular Dystrophy*", February 2019 (under review)

5. **K. Nizamis**, W. Schutte, J.J. Grutter, J. Goseling, N.H. M. Rijken and H.F.J.M. Koopman "*Characterization of the Cognitive-Motor Performance of Adults with Duchenne Muscular Dystrophy in a Hand-Related Task*", November 2018 (under review)

6. **K. Nizamis**, N.H.M. Rijken, A. Mendes, M.M.H.P. Janssen, A. Bergsma and H.F.J.M. Koopman *"A Novel Setup and Protocol to Measure the Range of Motion of the Wrist and the Hand*", MDPI - Sensors, vol. 18, no. 10, p. 3230, September 2018.

7. J. Lobo-Prat, **K. Nizamis**, M.M.H.P. Janssen, A.Q.L. Keemink, P.H. Veltink, H.F.J.M. Koopman and A.H.A. Stienen "*Comparison between sEMG and force as control interfaces to support planar arm movements in adults with Duchenne: A feasibility study*", Journal of NeuroEngineering and Rehabilitation, vol. 14, no.1, p.14:73, July 2017

8. R.A. Bos, C.J.W. Haarman, T. Stortelder, **K. Nizamis**, J.L. Herder, A.H.A. Stienen, and D.H. Plettenburg *"A structured overview of trends and technologies used in dynamic hand orthoses*", Journal of NeuroEngineering and Rehabilitation, vol 13, no. 1, p 13:62, June 2016

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* *Indicates equal contribution*

International peer-reviewed conference publications

9. R.A. Bos, **K. Nizamis**, D.H. Plettenburg and J.L. Herder "*Design of an Electrohydraulic Hand Orthosis for People with Duchenne Muscular Dystrophy Using Commercially Available Components*", IEEE BioRob 2018, August 26-29, 2018, Enschede, NL

10. **K. Nizamis**, W. Schutte, J. Goseling and H.F.J.M. Koopman "*Quantification of Information Transfer Rate of the Human Hand during a Mouse Clicking Task with Healthy Adults and One Adult with Duchenne Muscular Dystrophy*", IEEE ICORR 2017, July 18-21, 2017, London, UK

11. **K. Nizamis**, J. Lobo-Prat, A.Q.L. Keemink, R. Carloni, A.H.A. Stienen and H.F.J.M. Koopman "*Switching Proportional EMG control of a 3D Endpoint Arm Support for People with Duchenne Muscular Dystrophy*", IEEE ICORR 2015, August 11-14, 2015, Singapore

Chairing international symposia

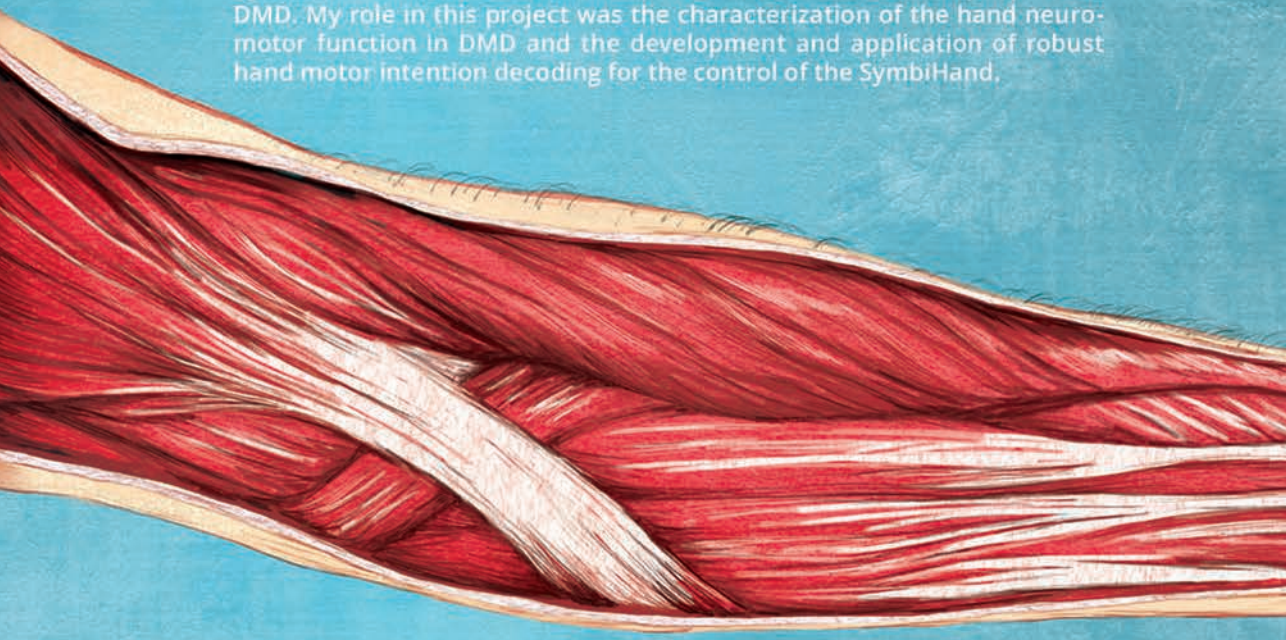
12. Title: *Prosthetics to Orthotics: Transferable Expertise?* ISEK 2016, July 5-8, 2016, Chicago, USA

    Participant List:
    - Derek Kamper, Ilinois Institute of Technology
    - Thierry Keller, Tecnalia Research and Innovation
    - Dick Plettenburg, Delft University of Technology
    - Dario Farina, University Medical Center Goettingen
    - Elliott Rouse, RIC / Northwestern University
    - Arno Stienen, University of Twente (*https://isek.org/wp-content/uploads/2016/04/ISEK-2016-Detailed-program_April20.pdf)3*

13. Title: *Use it or Lose it: Improving Robotics-Assisted Stroke Rehabilitation* IEEE BioRob 2018, August 26-29, 2018, Enschede, NL

    Participant List:
    - Geert Verheyden, KU Leuven
    - Arno Stienen, MotekForce Link
    - Lena Ting, Emory University
    - Heike Schmidt-Felzmann, NUI Galway
    - Agnès Roby-Brami, Pierre and Marie Curie University
    - Jaap Buurke, University of Twente (*https://ctw-bw124.ctw.utwente.nl/roborehab/*)

The hand is a complex and versatile tool, which allows humans to interact with their immediate environment, engage in daily life activities and socialize. Individuals with Duchenne muscular dystrophy (DMD), experience years of deteriorated hand function, leading to severe dependence on caregivers. Robotic exoskeletons can provide a feasible solution for the active hand support of individuals with DMD. The work presented in this book describes the development of a hand exoskeleton that meets the specific needs of individuals with DMD, in order to raise their quality of life and social participation and acceptance. In the Symbionics project, we developed the SymbiHand orthosis; an active wearable hand exoskeleton for people with DMD. My role in this project was the characterization of the hand neuromotor function in DMD and the development and application of robust hand motor intention decoding for the control of the SymbiHand.



Kostas Nizamis was born in Kavala (Greece) in 1988. He acquired his M.Eng. degree in Electrical and Computer Engineering at the Democritus University of Thrace, Greece in 2012 and subsequently his MSc. Degree in Biomedical Engineering, at the University of Twente, The Netherlands in 2015. There, he continued with his Ph.D. at the Department of Biomechanical Engineering (2014-2018) and since March 2019, he is working as an Assistant Professor in multidisciplinary design at the Department of Design, Production and Management.