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towards a subject-specific device by means of musculoskeletal modelling

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TOWARDS A SUBJECT-SPECIFIC DEVICE BY MEANS OF MUSCULOSKELETAL MODELLING

BY
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2. Wee J, Shank TM, **Castro MN**, Ryan LE, Costa J, Rahman T (2019) Elbow Flexion Assist Orthosis for Arthrogryposis. In: *16th IEEE/RAS-EMBS International Conference on Rehabilitation Robotics (ICORR)*, Toronto, Canada.

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This thesis has been submitted for assessment in partial fulfilment of the Ph.D. degree. The thesis is based on submitted and published scientific manuscripts, which are listed above. Parts of the manuscripts are used directly or indirectly in the extended summary of the thesis. As part of the assessment, co-author statements have been made available to the assessment committee and are also available at the Faculty of Engineering and Science.

CV

Miguel Nobre Castro graduated in Biomedical Engineering from Instituto Superior Técnico – University of Lisbon, Portugal, December 2013. He started his research career as Research Assistant in an equine biomechanics project in Lisbon for six months. Right after that, he decided to pursue a Ph.D. degree at Aalborg University and moved to Denmark in August 2014. His passion for biomechanics had started earlier during his Master's when he first studied the mathematical formulations that allowed describing human movement and mechanics. That sparked the idea to do research on the applicability of musculoskeletal modelling to design assistive robotic technology and to investigate how to solve current challenges within this subfield of Biomechanical Engineering.

ENGLISH SUMMARY

Neuromuscular impairment caused by disorders or injuries reduces the quality of life of those that, in the absence of a healthy motor function, have trouble living independently. This physical limitation prevents these patients from performing simple activities of the daily living, such as feeding and toileting. Even though the patients may undergo physical rehabilitation starting from a young age, it is not guaranteed that their motor function is restored. For that reason, the continuous rehabilitation process typically involves the use of arm assistive technologies, which can exploit their residual motor function. Among these devices, active and passive devices can be recommended depending on the severity of the impairment and how much residual motor function the patient has retained. Even though the arm assistive devices have shown effectiveness in enabling independent living, designing a lightweight, compact, and inconspicuous wearable device still remains a challenge. This is mostly due to the design volume and design constraints imposed by necessary assistive torque providers, i.e. by motors and/or elastic energy storing elements such as springs. Therefore, since cumbersome devices are hardly wearable and stigmatizing, new design approaches that enhance treatment and do not compromise the assistive requirements must be investigated.

In this PhD study, a passive upper extremity orthosis is designed for patients with neuromuscular disorders using prior knowledge obtained from subject-specific musculoskeletal modelling and simulation. To that end, the assessment of the motor performance of the upper extremity is initially studied by means of estimating the reachable 3-D workspace. A new experimental protocol is proposed for reconstructing both close to - and far from the body regions of the entire reachable volume. Subsequently, the varying volume and shape changes of this quantity are observed for a small cohort of ten healthy test-subjects using four different hand-payload cases and correlated with measurements of their anthropometry and individual strength capabilities.

In the light of the kinetic nature of the reachable 3-D workspace, musculoskeletal models are built, scaled and validated for each test-subject using the reachable 3-D workspace, since it holds as a good performance metric. In order to investigate motor function in real patients, the same workflow is replicated on two young patients with neuromuscular impairment. Additional data such as electromyography and articular ranges of motion are also collected for modelling assumption purposes. Patient-specific models are optimised and evaluated by comparing simulated reaching capabilities of the patients against their experimental counterparts.

Finally, a novel compact shoulder mechanism with three degrees-of-freedom is created for exoskeleton and orthotic applications. This new spherical scissors mechanism fits close to the body, being able to fit underneath clothing, and perfectly

matches the kinematics of the anatomical shoulder joint. The mechanism is, then, used on a passive feeding-assistive orthosis prototype that is designed for partial balancing of the upper extremity. In exchange for the full gravity balancing capabilities, this passive orthosis uses a different spring configuration that brings some spring attachment points closer to the body in a compact manner, and allows the user to body-power the device with residual muscle function of their antagonistic musculature that works with gravity. The results show that the impaired patient is able to reach the frontal region of the reachable 3-D workspace and able to reach her mouth independently. When combined with musculoskeletal simulation, such design approach may be able, in the future, to enhance treatment by targeting the rehabilitation of specific muscles.

DANSK RESUME

Neuromuskulær svækkelse forårsaget af sygdomme eller ulykker reducerer livskvaliteten for patieter, der i mangel af en sund motorisk funktion, har problemer med at leve uafhængigt. Den fysiske begrænsning forhindrer de ramte i at udføre simple dagligdags aktiviteter, såsom spisning og personlig hygiejne. På trods af tidlig fysisk rehabilitering er det ikke garanteret, at den motoriske funktion gendannes. Af den grund involverer den kontinuerlige rehabiliteringsproces typisk brug af hjælpemidler til armene, som kan udnytte den restmotoriske funktion. Blandt disse enheder anbefales aktive og passive løsninger, afhængigt af sværhedsgraden og den resterende førlighed. Selvom hjælpemidlerne har vist sig effektive til forbedring af det uafhængige liv, er det stadig en udfordring at designe lette, kompakte enheder, der ikke vækker opsigt. Dette skyldes for det meste konstruktionsvolumen og designbegrænsninger, stammende fra nødvendige elementer såsom motorer og/eller elastiske elementer, såsom fjedre, til lagring af energi. Eftersom klodsede og iøjnefaldende anordninger kan være stigmatiserende for brugeren, skal nye designs, der forbedrer behandlingen og ikke kompromitterer de funktionsmæssige krav, undersøges.

I dette ph.d.-studie er en passiv ortose til overekstremiteten designet til patienter med neuromuskulære forstyrrelser ved hjælp af forkendskab opnået fra individ-specifik muskuloskeletal modellering og simulering. Med henblik herpå klassificeres først overekstremitetens motoriske funktion ved estimering af den tredimensionale rækkevidde. Der foreslås en ny eksperimentel protokol til rekonstruktion af både nære og fjerne arbejdsområder i hele det tilgængelige volumen. Derefter observeres variation og formændring af arbejdsvolumen for en lille kohorte af ti raske testpersoner i fire forskellige lasttilfælde i hånden, og disse korreleres med målinger af antropometri og individuel styrke.

Idet den tredimensionale rækkevidde er kinetisk bestemt, bygges muskel- og skeletmodeller, som skaleres og valideres for hvert testperson ved hjælp af den målte rækkevidde. For at undersøge motorisk funktion af funktionshæmmede gentages den samme arbejdsgang på to unge patienter med neuromuskulær svækkelse. Yderligere data, såsom elektromyografi og artikulære bevægelsesområder, indsamles også til undersøgelse af modellens antagelser. Patientspecifikke modeller optimeres og evalueres ved at sammenligne simulerede rækevidder hos patienterne med deres eksperimentelle resultater.

Endelig opfindes en ny og kompakt mekanisme til skulderleddet med tre frihedsgrader til anvendelse i exoskeletter og ortoser. Denne nye, sfæriske saksemekanisme ligger tæt på kroppen, kan skjules under tøjet og passer perfekt til kinematikken i det anatomiske skulderled. Mekanismen anvendes herefter på en passiv ortose til spisning, der er designet til delvis afbalancering af oveekstremiteten. I modsætning til

perfekt tyngdekraftkompensation bruger denne passive ortose en anden fjederkonfiguration, der anbringer fjederfastgørelsespunkterne tættere på kroppen og giver brugeren mulighed for at bevæge enheden med den residuale funktion af den antagonistiske muskulatur i samarbejde med tyngdekraften. Resultaterne viser, at den funktionsnedsatte patient er i stand til at nå det frontale område af det tredimensionale arbejdsområde og er i stand til at nå mund uden yderligere assistance. I kombination med muskuloskeletal simulering kan en sådan fremgangsmåde i fremtiden være i stand til at forbedre behandlingen ved at målrette rehabiliteringen mod specifikke muskler.

PREFACE

This thesis has been submitted to the Faculty of Engineering and Science at Aalborg University in partial fulfilment of the requirements for the degree of Doctor of Philosophy in Mechanical Engineering. The work has been carried out at the Department of Materials and Production, Aalborg University, in the period from August 2014 to May 2019. The present work is part of a strategic platform for research and innovation called "Patient@Home" which targets the development of technological solutions to improve independence of subjects with physical impairments. This platform is funded by The Danish Agency for Science, Technology and Innovation. This work was supervised by Associate Professor Michael Skipper Andersen and co-supervised by Associate Professor Shaoping Bai and Professor John Rasmussen.

I would like to thank my supervisors, Associate Professor Michael Skipper Anderson, Professor John Rasmussen, and Associate Professor Shaoping Bai, for allowing me to join their research team and work with the AnyBody Modeling System as part of my Ph.D. study. This had been a dream since I started working on my Master Thesis back in Portugal! I would also like to thank them for the guidance, support and for turning me, hopefully soon, into a real Scientist. It was both a pleasure and a challenge to work with and be surround by such world-class experts in the biomechanics research field.

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Last but not least, I would like to thank my family, especially my better half. Thank you for everything.

To Ana,

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CHAPTER 1. INTRODUCTION

1.1. BACKGROUND AND MOTIVATION

This research project is part of a strategic platform for research and innovation called Patient@Home, which intends to enable patients with motor disabilities such that they can live independently. Most of these patients totally lost their motor function or are partially paralysed due to neuromuscular diseases, disorders or accidents. Such conditions either affect the neural pathways, i.e. the central nervous system, or the muscles directly, leaving the patients without the necessary strength to perform simple tasks of the daily living, for instance eating or toileting. Consequently, they rely on a family member or on a caregiver to provide them assistance most of the time. Naturally, this has both negative psychological and negative economic impact in the lives of the patients, resulting also in a heavy burden on those who provide them help. Moreover, millions are spent by the national healthcare systems on rehabilitating such patients and further expenses arise from work compensations paid to those who are still within active labour age.

Living with a disability nowadays does not have to mean that one cannot live independently. Assistance and rehabilitation can be provided by robotic technology, which may be passive/body-powered, where the patient's motion is enabled by the robot, or active, where the patient’s intentions to move are perceived and executed by the robot itself (Rahman, Basante, & Alexander, 2014). What distinguishes these two main types of assistive devices from one another is whether the mechanical energy is stored in the form of potential energy or whether it is directly converted from electricity, i.e. electromechanical energy. Both types of devices benefit from not requiring a health professional for enabling the patients to engage into continuous rehabilitation therapy and treatment for longer periods of time, while also providing motion assistance (Dunning & Herder, 2013; Gopura, Kiguchi, & Bandara, 2011; Lo & Xie, 2012). Still, the devices are not widely accepted by the patients. In most cases, they are not only expensive but also heavy and bulky. This implies that they are hardly wearable and stick out from the body, resulting in conspicuous solutions that stigmatize the user. Up to this point, a fully inconspicuous wearable assistive device is yet to be created.

The main advantages of the passive assistive devices over the active ones are their non-requirement of an electrical power source and their strength augmentation function as a body-powered device. The first advantage is accomplished by relying on mechanical elements that can store potential energy, e.g. springs, while the latter gives full control to the user, thus allowing a rehabilitation interface this way. Since the amount of assistance can vary in accordance to the choice of stiffness of all springs used, the passive device can allow for different postures to be more or less attainable by exploiting more of less the patient’s residual muscular strength. Recent advancements in musculoskeletal modelling may be used to perform virtual prototyping and design optimisation using biomechanical models of each user along with a computational model of the assistive device itself. This may allow design simulations targeting specific muscle groups while constraining the solution towards a more compact and wearable orthosis. To this end, it is, however, important that the musculoskeletal model accurately represents the capabilities of the patient.

Hence, the specific goals of this PhD project are: 1) to understand what the patient-specific assistance requirements are, 2) to understand the underlying properties of an orthoses for upper extremity assistance of impaired users, and 3) to investigate new ways to design a lightweight, wearable and inconspicuous device capable to restore upper limb function.

1.2. ARM ASSISTIVE DEVICES

Arm assistive devices provide assistance and rehabilitate people who live with reduced motor function. These include not only disabled people, but also the elderly. Moreover, the increasing use of this type of devices nowadays by healthy individuals for augmented strength capabilities should also be highlighted (Herr, 2009). The targets are the automotive and construction industries where these wearable devices are used to assist workers, typically during repetitive tasks (de Looze, Krause, & O'Sullivan, 2017). Given that the devices provide external torques to the upper extremity, they can balance the weight of the arm segments and/or balance the weight of some hand payload. So, arm assistive devices are said to partially or fully cancel the effect of gravity, thereby diminishing the amount of required effort to perform a given task, and thus help to reduce fatigue and the risk for work-related musculoskeletal injuries.

For designing an ergonomic and well-performing assistive device, it is necessary to take into consideration the upper extremity kinematics and kinetics. The first requirement they must fulfil is to be compatible and compliant with a minimum number of the degrees-of-freedom (DOFs) of the upper limbs. Such devices are worn externally attached to the arm segments. Therefore, they must not interfere with the natural anatomical joint motion, while they operate in parallel with the upper extremity. This means that these mechanisms also behave as open kinematic chains just like the human limbs. In regards to the DOFs present in the upper extremity, there are nine main DOFs in total, in case the joints between the fingers' bones are not taken into account, as shown in Figure 1-1. These are the five DOFs in the shoulder joint (three-DOFs glenohumeral, and two-DOFs sternoclavicular joints), two DOFs at the elbow joint and two DOF at the wrist joint (Tondu, 2007). Still, this number of DOFs may vary depending on the kinematic model that is chosen to study upper extremity motion (Sonia Duprey, Naaim, Moissenet, Begon, & Chèze, 2017). Yet, an arm assistive device can be functional even without spanning all those DOFs as long as it complies with the anatomical joints of the user in order to avoid discomfort. Such discomfort is usually caused by undesired residual internal forces that can arise from mechanical-to-anatomical joint axis misalignment (Schiele & van der Helm, 2006).

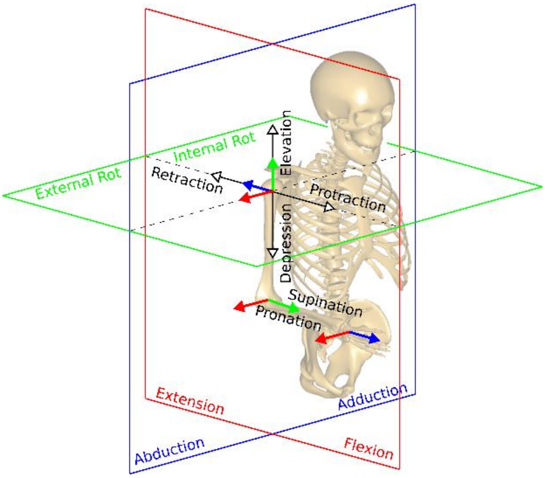

Figure 1-1. The degrees-of-freedom present in the upper extremity.

On top of what was mentioned above, the external torque provider elements of the device are the components that influence the wearability of the device the most. Either passive or active design approaches resort to mechanical springs or electromechanical actuators (and respective power source), without which the device cannot provide the required assistive torques. These often lead to heavy and bulky apparatuses that compromise wearability. Such types of assistive devices will be introduced in the next section and their specific advantages and disadvantages will be presented. The reader should, however, bear in mind that the aim of this project is to develop a passive arm assistive device, therefore active devices will not be discussed in extended detail.

1.2.1. TYPES OF ASSISTIVE DEVICES

Two main categories are frequently used to classify the different types of arm assistive devices (Van der Heide et al., 2014). One group is that of the active devices, also called externally-powered, which drive the upper extremity by means of actuators that are controlled by the user. These devices are capable of sensing the user’s intentions to move the arm in a given direction and are usually based on myocontrol (Kiguchi & Hayashi, 2012; Rosen, Brand, Fuchs, & Arcan, 2001). The second group is that of the passive devices, also called body-powered, which rely the residual muscle function of the user (Dunning & Herder, 2013). Energy exchanges between elastic and gravitational potential energy in the human-orthosis system allow the user to perceive the arm moving in partial or full zero gravity effect. Among these two groups of devices, some are compatible with just a couple of DOFs, while others cover almost all anatomical DOFs of the upper extremity. Major characteristics and examples of these devices will be presented in the following sections.

1.2.1.1 Active devices

Active devices are characterized by their motor power, which drives the joints of the exoskeleton mechanism. That occurs either distally, at the joint level, or proximally, by means of cables. When the actuators are placed at the joint level, it implies that the mass of the distal motors has to be carried by the precedent/proximal motors. As a consequence, these proximal actuators must have high torque generation capacity – a phenomenon called the pyramidal effect (Siciliano, Sciavicco, Villani, & Oriolo, 2009). Moreover, with regards to wearability, the design of cable-driven solutions enable placement of all actuators proximally, potentially leading to an opportunity to hide these components at the level of the device's torso attachment.

In general, these actuators also require their respective controllers and an external power source. To that end, there are different control strategies that enable sensing of the user's intention to move and converting that intention into motion (Proietti, Crocher, Roby-Brami, & Jarrasse, 2016). Such strategies, which are also used to drive prosthetics, rely on angular position, velocity and acceleration tracking and are usually accomplished through myocontrol (Kiguchi & Hayashi, 2012; Rosen et al., 2001) or force control (Islam, Xu, & Bai, 2019). Both control strategies use continuous recording of surface electro-myography signals (sEMG) or force myography signals (FMG) resulting from muscular bulging during muscular contraction, respectively. While sEMG-based control is versatile to even work with neuromuscular impaired patients, the FMG-based control requires a healthy muscle contraction, since bulging is necessary.

According to Gopura et al. (2011), the active devices can be divided in three types depending on the type of actuator: 1) electrically actuated, 2) pneumatic actuated and 3) hydraulically actuated:

- The electrically actuated devices represent the majority of active devices due to their high speed, high accuracy and advanced motion control provided by electric motors. The ARMin III (Nef, Guidali, & Riener, 2009) and the back-mounted MGA (Carignan & Liszka, 2005) are examples, both having six DOFs. The CAREX (Mao & Agrawal, 2012) is an example of a five-DOFs cable-driven exoskeleton. And the four-DOFs AXO-SUIT's (Bai, Christensen, & Islam, 2017) upper extremity exoskeleton is another case.
- The pneumatically actuated devices have lower accuracy and lower precision on velocity control, but have been used in research for developing soft exo-suits given their capacity to bio-mimic real muscles. The lightweight seven-DOFs exoskeleton developed by Caldwell et al. (2007), the five-DOFs RUPERT IV (Balasubramanian, Perez, Shepard, Koeneman, & Koeneman,

2008) and four-DOFs BONES (Klein et al., 2008) are examples of such type of active devices.

- Finally, the hydraulically actuated devices are few due to their apparatus and potential oil leakage, despite their high precision and velocity. Two examples include the four-DOFs NEUROexos with muscle-like hydraulic actuators (Lenzi et al., 2011) and the Sarcos Master Arm (Mistry, Mohajerian, & Schaal, 2005).

Recent developments have also been made towards achieving a soft-coupling in arm assistive devices, so that these rely only on the anatomical joints. These are also called as soft exo-suits. A Harvard team has recently proved that building such bio-inspired technology is possible for the lower-limbs during walking (Ding, Kim, Kuindersma, & Walsh, 2018). A similar approach was shown for the upper extremity for assisting the shoulder and elbow movements (Xiloyannis, Chiaradia, Frisoli, & Masia, 2019) and for hand grasping (Xiloyannis, Cappello, Binh, Antuvan, & Masia, 2017). And another exo-suit was developed by NASA, the Soft Wearable Upper Extremity Garment or “Armstrong”, which uses a Bowden cable transmission system for controlling the shoulder and elbow joints (Kadivar, Beck, Rovekamp, O’Malley, & Joyce, 2017).

1.2.1.2 Passive devices

Passive arm assistive devices are body-powered apparatuses that can augment the strength of its users by means of mechanical components, which store potential energy. In general, these types of systems are designed based on energy methods that rely on the static balancing principle. This principle states that a mechanical system is capable of attaining static equilibrium for every position of its configuration space (Walsh, Streit, & Gilmore, 1991). This is possible through exchanges between elastic and gravitational potential energies, with conservation of the total energy in the system. Therefore, these systems are said to be energy-free (Just L. Herder, 2001). An intuitive and simple example of such kind of system is that of an equipoise desk-lamp (Carwardine, 1935). In the case of a human-orthosis system, it results in a weightless feeling across all attainable upper extremity postures. In the absence of need to work against gravity, the residual muscle function of a large group of muscles would suffice for moving the arm from one posture to another.

The effect of a gravitational force acting on a rotating body is nonlinear, but it can be counteracted by linear or non-linear force elements placed on the device. This equilibrium can be achieved using counterweights or mechanically elastic elements such as springs. The former option has always been disregarded as the counterweights add rotational inertia and volume to the device, thus compromising its compactness and/or wearability. The latter strategy is widely used and the respective designs may include the addition of auxiliary parallelogram structures to the device’s mechanism. However, while adding parallelogram structures still contributes to a bulky design, the strategic placement of the spring attachment points can itself compromise the compactness of the device. Dunning and Herder (2013), who carried a comprehensive investigation on passive devices, stated that "*only 4 out of 23 devices are wearable and have a relatively small amount of volume, which is enclosed by 20 mm from the arm and trunk*". Additionally, Dunning and Herder (2013) referred to the Wilmington Robotic Exoskeleton, or the WREX (Rahman et al., 2006), as the "*only wearable passive orthosis presented in the literature that can perform within the entire natural workspace of the human arm*", referring also to the others mounted to wheelchairs as "*rather bulky, and not inconspicuous*".

Hence, two main sub-types of passive devices can described in detail as follow:

- The devices with auxiliary parallelogram structures may 1) enable location of the centre-of-mass of the mechanical system such that it can be directly supported by a mass or a spring (Agrawal & Fattah, 2003), or 2) add support for the strategic placement of the mechanical elastic elements (Rahman, Ramanathan, Seliktar, & Harwin, 1995). Nonetheless, the parallelograms add extra inertia and mass to the system, making it bulky and difficult to wear. In some cases, they are wheelchair-mounted and the end-link connected to the forearm cuff (Cardoso, Tomázio, & Herder, 2002; Just L Herder, Vrijlandt, Antonides, Cloosterman, & Mastenbroek, 2006). Examples of these devices are the four-DOFs WREX (Rahman et al., 2006), which is still one of the most robust passive devices, and the ARMON (J.L. Herder, 2005), which is a single point support three-DOFs passive orthosis with an electronically load-adjustment mechanism. Another case is that of the Dynamic Arm Support (DAS) (Kramer, Romer, & Stuyt, 2007), which consists of a three-DOFs device of modular parts that allows the arm to move freely in a horizontal plane using a spring-based parallelogram link.
- The devices that are solely composed of an open chain of linkages with elastic elements attached, such as extension springs, are the most promising with respect to being lightweight and wearable. As zero-free-length (ZFL) springs are required to achieve full balance, these can also be cable-driven to distally transfer forces if conventional helical springs are used instead and friction is very low. Examples of these devices are the basic Wilmer orthosis (Plettenburg, 2007), the mobile arm support (MAS) (Lin, Shieh, & Chen, 2013) and the four-DOFs A-Gear (Dunning, Janssen, Kooren, & Herder, 2016; Kooren et al., 2015).

The idea of using bending beams to partially balance the upper extremity, instead of extension springs, was presented (Dunning, Stroo, Radaelli, & Herder, 2015).This has also been accomplished in passive orthosis for back support (Näf et al., 2018). Other partial passive assistance design has been reported by resorting to optimization (Veer & Sujatha, 2015), musculoskeletal modelling (Agarwal, Neptune, & Deshpande, 2016; Lelai Zhou, Bai, Andersen, & Rasmussen, 2015; Lelai Zhou, Li, & Bai, 2017), and sliding spring mechanism design (Wee et al., 2019).

1.2.2. DESIGN LIMITATIONS AND USER REQUIREMENTS

1.2.2.1 Mechanism kinematics, assistance and comfort/safety

While passive assistive devices are intrinsically more limited in terms of the number of DOFs about which they can provide assistance, the active devices can provide "unlimited" assistance. They only depend on actuation torque specifications that span a given DOFs (Gopura & Kiguchi, 2009). Thus, they are widely used for rehabilitation purposes (Maciejasz, Eschweiler, Gerlach-Hahn, Jansen-Troy, & Leonhardt, 2014), and even enable to assist fully impaired users. The available torque can also be useful to provide additional weight lifting assistance for picking up objects. This is a feature that is difficult to implement on a passive device due to specific placement of spring attachment points that aim at gravity balancing only the arm segments. However, surveys have shown that patients still prefer to use passive devices, since these are safer and cheaper than the active ones (Prior, 1990; Rahman et al., 1996; Stanger, Anglin, Harwin, & Romilly, 1994). Hence, there are strong reasons for developing a well-performing body-powered device that can assist patients with neuromuscular impairment.

A key design aspect to take in consideration is that such a device has to be lightweight so that it can attach close to the body and be wearable (Herr, 2009). In contrast, some devices are anchored to the ground (immovable) or mounted on a wheelchair. This also implies that mechanical parts of the rigid device must connect to arm and forearm segments. Since the devices operate in parallel with the upper extremity and are typically made of interconnected rigid segments, it is mandatory that the mechanical joints align with the anatomical ones (Schiele & van der Helm, 2006). Otherwise, misalignments will produce extra torques that may trigger pain in the joints and in the surrounding soft tissues. So far, only self-aligning mechanisms have been attempted for designing active devices (Stienen, Hekman, van der Helm, & van der Kooij, 2009), while other authors even suggested only using the anatomical joints, if they are still functional (Ammar, Kaddouh, Mohanna, & Elhajj, 2010). The latter approach is called as soft-coupling, and may imply cable-driven strategies using Bowden cables, which can add friction to the system. Yet, this soft-coupling approach may also contribute to an increase in the internal reactions at the anatomical joint level.

Another kinematic limitation of most arm assistive devices arises from their shoulder component. The mechanism surrounding the shoulder joint and its structures (bones, muscles and skin) must be designed such that it mimics the anatomical shoulder kinematics, lest pain will be triggered due to misalignment (Schiele & van der Helm, 2006). Simultaneously, this type of mechanism has to behave as a hollow ball-and-socket joint with a remote centre-of-motion matching that of the anatomical joint. The most adequate type of mechanism that satisfies these criteria is a spherical mechanism (Chiang, 1988). Spherical mechanisms are normally composed of a series of curved linkages or of parallel linkages (Bai, Li, & Angeles, 2019). This usually leads to three main perpendicular axes of rotation (3R), so they behave like gimbal mechanisms (Ball, Brown, & Scott, 2007; Carignan, Tang, & Roderick, 2009; Perry, Rosen, & Burns, 2007). However, a gimbal has singular configurations, where the mechanism locks due to the alignment of two axes of rotation. So, different workarounds have been proposed to avoid the singularity problem, such as: 1) configuring the mechanism such that the singularities only occur in shoulder postures that are not reached very often (Ball et al., 2007; Carignan et al., 2009; Perry et al., 2007); 2) using redundant linkages, i.e. designing a 4R spherical mechanism (Lo & Xie, 2013); or 3) optimizing the length of the linkages that compose the spherical shoulder mechanism (Lum, Rosen, Sinanan, & Hannaford B, 2004). Only recently, this problem was solved by Christensen and Bai (2018), who proposed a double parallelogram spherical mechanism able to produce singularity-free rotations in the anatomical shoulder joint workspace. Nonetheless, the mechanism is too bulky, protruding out of the shoulder region and compromising the wearability of the device. Therefore, the creation of a similar but compact singularity-free spherical shoulder mechanism is yet to be accomplished.

1.2.2.2 Overcoming stigmatization by achieving compactness

From the perspective of a user of an arm assistive device, the above-mentioned lightweight and compactness are as important as the performance of the device. This is due the fact that disabled patients do not want to appear disabled after all. Hence, patients have preference for inconspicuous designs (Dunning & Herder, 2013; Gunn, Shank, Eppes, Hossain, & Rahman, 2016; Rahman et al., 2006). This means that, in the case of a passive orthosis, it should be designed such that it sits close to the body, without interfering with soft tissues and causing discomfort, and fit underneath clothing.

Dunning and Herder (2013) performed a survey on the state-of-the-art passive assistive devices available, where they evaluated which devices were wearable and which could fit underneath clothing. They reported that, at the time of publication, only the Wilmington Robotic Exoskeleton (WREX) (Rahman et al., 2006), from Nemours/Alfred I. DuPont Hospital for Children, could be worn and attached to the torso and arms. Still, no device could potentially be hidden under clothing. A few years later, the A-Gear assistive device appeared (Kooren et al., 2015). This one can potentially be worn at the torso, but still fails the requirements for fitting underneath clothing. Both devices can fully gravity balance the upper extremity. However, while the WREX lacks of compactness because of its parallelogram configuration, the A-Gear lacks of compactness because of the spring attachment points and placement required to fulfil the gravity-balancing effect. This suggests that it might difficult to design fully gravity-balanced devices that can fit underneath clothing. However, this problem may also be tackled by potentially designing a partially balanced device that can be hidden. This would be in line with designing task-specific devices for these patients, e.g. a device that provides feeding assistance (Rahman et al., 2006, 1996).

1.2.2.3 Custom-fitting the orthosis to the physiognomy of the user

A possibility to solve the problem above is to reduce the volume of the device's parts in its interfaces with the body, namely its torso- and arm-cuff attachments. Close-fitting of the orthosis parts to the user can minimize the displacements caused by the inherent flexibility of the skin as well as enable a compact design that can be hidden underneath clothing. New CAD workflows involving 3-D scanning, 3-D modelling and 3-D printing technologies that allow collecting and working on physiognomic data can be used to achieve custom-fitted parts. Figure 1-2 shows an example of such a workflow that was attempted in this project. The bare-chested torso of a user was targeted to design a custom-fitted torso brace. The workflow consisted of: 1) reconstruction of a 3-D point cloud using the non-commercial version of the ReconstructMe software (Heindl, Bauer, Ankerl, & Pichler, 2015) (PROFACTOR, Steyr-Glein, Austria) to process the data collected from a Kinect™ v.1.0 infrared laser sensor (Microsoft®, New Mexico, USA), 2) meshing and 3-D clay-like sculpting using Sculptris Alpha 6 (ZBrush, Pixologic Inc, CA USA) CAD modelling tool, which allowed to smooth the surface of the mesh, 3) solid modelling and pre-print slicing of the mesh using SolidWorks. This brace example was later 3-D printed in ABS plastic.

Figure 1-2. Workflow for design custom-fitted orthosis parts. From a 3-D point cloud of a scanned shoulder region to a comfortable fitting cuff.

1.2.3. STATE-OF-THE-ART PASSIVE DESIGN APPROACHES

1.2.3.1 Energy-based methods

As previously mentioned, the use of parallelogram mechanisms for constructing arm assistive devices (Rahman et al., 1995) may still compromise the desire for a compact solution (Dunning & Herder, 2013). Using the same underlying principle of conservation of potential energy, a more promising planar energy method called the stiffness matrix approach enables the design of more compact gravity-balanced devices (Lin, Shieh, & Chen, 2010). The new method is based on vector algebra and involves state vectors, which correspond to the planar orientations of each linkage in an open chain. Stiffness block matrices that relate the stiffness of the system, about a single or a group of joints, can be constructed such that the global stiffness matrix is configuration independent, i.e. state independent. This can be accomplished by forcing all of its off-diagonal elements to be zero. Furthermore, it was later possible to directly assess which DOFs of the system need to be balanced for each particular mechanism (Y. Y. Lee & Chen, 2014). The stiffness matrix approach was originally formulated in polar coordinates, and later in Cartesian coordinates by Lustig et al. (2015).

Similar to the design of a parallelogram mechanism, this method makes use of ZFL extension springs. In order to achieve a ZFL behaviour with a regular extension spring connected to a cable, the undeformed spring length is hidden behind a pulley, about which the cable wraps without friction (Rahman et al., 1995). As this pulley works as the origin point from which the spring elongation is measured, the force generated by the ZFL is only zero when the distance between the two spring attachment points is also zero. Despite presenting a nonlinear behaviour outside their usual working domain, some rubber-like materials, e.g. rubber bands, can also be used as ZFL (Smith, Lobo-Prat, van der Kooij, & Stienen, 2013). These can help achieve a more compact design since no undeformed spring length has to be hidden. Furthermore, these rubber bands require less initial force and can also stretch more than extension springs (Rahman et al., 2006).

The Mobile Arm Support (Lin et al., 2013) was designed using the stiffness matrix approach and, for the first time, multi-articular ZFL springs were used with success on an arm assistive device. In more detail, a bi-articular flexion ZFL spring, spanning the shoulder and elbow joints, and a mono-articular extension ZFL spring, spanning the elbow joint, were used to balance the arm in the entire 3-D space. The A-Gear (Kooren et al., 2015) proposed a reconfigured positioning of the mono-articular ZFL spring. Since these devices were still not inconspicuous enough, another design was presented by Dunning and Herder (2015) to minimize the design volume by using an additional mono-articular extension ZFL spring spanning the shoulder joint.

1.2.3.2 Virtual prototyping using musculoskeletal modelling

Virtual prototyping is simulation-based development that allows reduction of the number of design iterations and to reduce the costs of physical prototyping. This allows the engineers to reach a more finalized version of the product at the time of testing the first prototypes. With regards to the testing of arm assistive devices, it always requires a human subject at some phase of the development. But, as these devices are meant to aid people with disabilities, it turns out to be troublesome and complicated to test the device on a patient every time a new design iteration is needed. The inconvenience of bringing a patient to a testing facility or lab, on top of regulatory testing constraints before having a final product, makes this task nearly impossible.

Musculoskeletal modelling is a viable solution that allows having a virtual human in the loop of development without actually requiring the person to physically be there (Agarwal, Narayanan, Lee, Mendel, & Krovi, 2010). These virtual human models (**Error! Reference source not found.**) are embedded with the mechanical properties of the human body segments, joints and muscles, thus enable kinematic and dynamic analyses of the human-machine system (Bai & Rasmussen, 2011). Moreover, this type of simulation-based design allows to predict muscle activations and respective loading in the muscles, which can be suitable for design upper extremity assistive devices (Agarwal et al., 2010). This led to studies of metabolic costs of specific energy-efficient upper extremity movements (L. Zhou, Bai, Hansen, & Rasmussen, 2011; Lelai Zhou, Bai, & Li, 2017), of gravity assistance requirements for arm supports (Essers, Meijer, Murgia, Bergsma, & Verstegen, 2013), of drafting of potential rehabilitation programs (L. F. Lee, Narayanan, Kannan, Mendel, & Krovi, 2009), and testing performance of pre-existing arm assistive devices (Tröster, Schneider, Bauernhansl, & Rasmussen, 2018).

Concerning actual arm assistive devices that were entirely designed using musculoskeletal modelling, there are two major examples of two passive prototypes, one cable-driven and another using a parallelogram configuration. The first prototype created by Zhou et al. (2015) is a soft-coupled spring-loaded cable-driven wearable device with four DOFs. It is composed of three rigid components (a torso cuff, an upper and forearm braces) and a five springs array box, which enables the storage of elastic potential energy to compensate for gravity. Three springs were connected to upper brace in order to assist the shoulder joint, and two other connected between the upper and lower cuffs (assisting the elbow joint). The second prototype created by Zhou et al. (2017b) is a wearable device similar to the WREX with four DOFs, which consists of a two parallelograms (four-bar mechanisms) connected in series. Each of the parallelograms has a spring to provide assistance throughout its vertical DOF. In both simulation studies, the stiffness of all springs were optimized by reducing the required muscle activation to accomplish a specific motion that was prescribed to the model. The simulation results showed that it is possible to assist an idealized patient by means of exploiting their residual muscle function.

Figure 1-3. Musculoskeletal simulation-based design of an arm assistive device.

These results show that musculoskeletal simulation-based prototyping may enable designing personalized solutions for each individual patient. It also means that the amount of assistance provided can be tuned, such that the residual muscle function exploitation can be adjusted to each neuromuscular disability case. That is convenient for tackling edge cases and potentially improve rehabilitation treatment (Bergsma, Lobo-Prat, Vroom, Furlong, & Herder, 2016). Still, this will only be possible when these virtual human models can truly represent the strength characteristics of the patients being modelled. More details on musculoskeletal modelling and on ideas on how this subject-specificity can eventually be achieved will be presented in the following section.

1.3. MUSCULOSKELETAL MODELLING

Musculoskeletal modelling software is an important tool for advanced biomechanical research and development. The AnyBody Modeling System (Damsgaard, Rasmussen, Christensen, Surma, & de Zee, 2006), OpenSIM (Delp et al., 2007) and SIMM (Motion Analysis, CA, USA) are some examples of the available frameworks that include full body models. These have been used to:

- perform treatment and rehabilitation studies (Dzialo et al., 2018; Fregly, Boninger, & Reinkensmeyer, 2012; Halonen et al., 2017; Sartori, Gizzi, Lloyd, & Farina, 2013),
- orthopaedics (Fregly, Besier, et al., 2012; Marra et al., 2015; C Quental, Folgado, Ambrósio, & Monteiro, 2013)
- design, test and evaluate performance of assistive (Agarwal et al., 2016; Tröster et al., 2018; Lelai Zhou et al., 2015; Lelai Zhou, Li, et al., 2017) and of prosthetic (Sartori, Llyod, & Farina, 2016) devices,

- develop more ergonomic workstations/occupational (Davoudabadi Farahani, Svinin, Andersen, de Zee, & Rasmussen, 2016; Pontonnier, de Zee, Samani, Dumont, & Madeleine, 2014; Wu, Chiou, & Pan, 2009),
- design better sports equipment (H. Lee, Jung, Lee, & Lee, 2017; J. Rasmussen et al., 2012).

In detail, musculoskeletal modelling is a tool that allows study of the physics of the human body by means of simulation. It enables the *in-silico* estimation of biomechanical variables of interest, e.g. muscle loading and internal joint reaction loads, which are otherwise immeasurable *in-vivo* or require invasive experiments. Such biomechanical variables provide highly valuable insight in disease triggering mechanisms and progression, and potentially improve treatment (Winter, 1990). To that end, equations of motion are formulated for analysing the human body as a mechanical system (de Jalón & Bayo, 1994; Nikravesh, 1988; Shabana, 1998). This is accomplished by considering the different body segments as interconnected rigid bodies, which are actuated by muscles (Nigg & Herzog, 2007). A multibody mechanical system consists, therefore, of some idealized anthropometric attributes, such as body segment length and mass, bone geometries, mechanical joints, muscle insertion points, muscle parameters, among other relevant data.

These attributes used are obtained from anatomy studies performed on cadaveric data. Examples of musculoskeletal models of the upper extremity that were built this way are the Delft Shoulder Group's (Van der Helm, Veeger, Pronk, Van der Woude, & Rozendal, 1992; Veeger, Van Der Helm, Van Der Woude, Pronk, & Rozendal, 1991; Veeger, Yu, An, & Rozendal, 1997) and the Visible Human Project's (B a Garner & Pandy, 2001; Brian a. Garner & Pandy, 1999), among others (de Zee, Hansen, Wong, Rasmussen, & Simonsen, 2007; C. Quental, Folgado, Ambrósio, & Monteiro, 2016). Since these cadaveric data will not fit the population, these pre-built models are initially geometrically (Andersen, Damsgaard, MacWilliams, & Rasmussen, 2010; Lund, Andersen, Zee, & Rasmussen, 2015) and strength (John Rasmussen et al., 2005) scaled to the physiognomy of the test subject of interest. Scaling laws can also be used to infer the strength capabilities of the musculoskeletal models from a test-subject's anthropometrics. The way this strength scaling is performed is by adjusting the parameters of the muscle sub-models, which are embedded on the major musculoskeletal model, as it will be discussed in the next section. Lastly, human motion is prescribed to the musculoskeletal model (Andersen, Damsgaard, & Rasmussen, 2009) and an inverse dynamic analysis of the system behaviour allows estimation of internal joint reactions and muscle forces generated by the system (Damsgaard et al., 2006).

1.3.1. MUSCLE-TEDON UNIT MODEL

The muscle elements present inside a musculoskeletal model are sub-models of the bigger model that simulate the contraction dynamics of muscle tissue (Nigg & Herzog, 2007). The three-elements muscle-tendon unit model, as described by Zajac (1989), is the most commonly used mathematical formulation often used to replicate the force-length and force-velocity relationships of muscles according to the findings of Hill (1938). This Hill-type model comprises a contractile element that works as an actuator of the mechanical system and is connected to a parallel-elastic element and a serial-elastic element. These two elastic elements account for the elasticity of the tissues surrounding the muscle fibres, namely connective tissue and tendon tissue. Consequently, the behaviour of these mechanical elements is a function of a set of parameters such as nominal isometric strength, physiological cross-section area (PCSA), optimal fibre length, pennation angle, absolute contraction velocity, and tendon slack length. Unfortunately, the force estimations obtained from the musculoskeletal models tend to be highly sensitive to these parameters, especially to tendon slack length (Ackland, Lin, & Pandy, 2012; Carbone, van der Krogt, Koopman, & Verdonschot, 2016; De Groote, Van Campen, Jonkers, & De Schutter, 2010; Redl, Gfoehler, & Pandy, 2007). In order to attenuate this effect, these values are often calibrated to joint positions that correspond to optimal fibre lengths (Heinen, Lund, Rasmussen, & de Zee, 2016).

The study of the dynamics of a multibody musculoskeletal system can be formulated by two different simulation approaches, namely forward and inverse dynamics. In a forward dynamics-based formulation, muscle and external forces acting on the system are known *a priori* and the aim of the simulation is to calculate the output kinematics. This formulation is sometimes also referred to as dynamic optimization (Anderson & Pandy, 2001) or optimal control (Ackermann & van den Bogert, 2010). On the other hand, the inverse dynamics formulation requires prior knowledge of the model's joint kinematics and external forces to output the internal reactions and muscles forces (Silva & Ambrósio, 2002, 2004). In this latter approach, since there are usually more unknown muscle forces than then the total number of equations that describe the dynamic equilibrium of the system, the system is said to be statically indeterminate. In order to mimic the same biological muscle recruitment efficiency used by the human brain, i.e. by the central nervous system, different recruitment criteria have been proposed to computationally simulate muscle synergy (Crowninshield, 1978; Crowninshield & Brand, 1981). In the scope of investigating the strength capabilities of disabled people for designing assistive devices, it is necessary to simulate maximal voluntary contractions. This implies that at least one synergetic muscle-tendon unit is fully activated in the musculoskeletal model (see Figure 1-4). This can be achieved by using a min/max muscle recruitment criterion (John Rasmussen, Damsgaard, & Voigt, 2001). Its corresponding activation function a is formulated as:

$$
\begin{aligned}
& a = \min_{\mathbf{f}\in\mathbb{R}} \max\left(\frac{f_i^{(\mathrm{M})}}{N_i}\right), \qquad i = 1, \dots, n^{(\mathrm{M})} \\
& \textit{subject to} \qquad\qquad\qquad\qquad\qquad\qquad (2) \\
& \mathbf{Cf} = \mathbf{r}
\end{aligned}
$$

$$f_i^{(\mathrm{M})} \geq 0, \qquad i = 1, \ldots, n^{(\mathrm{M})}$$

where $f_i^{(\mathrm{M})}$ is the force generated by the i^{th} muscle, N_i is the instantaneous strength. As constraints, $\mathbf{C}$=[$\mathbf{C}^{(\mathrm{M})}$ $\mathbf{C}^{(\mathrm{R})}$] is a matrix of coefficients depending on the current global position of the model segments, $\mathbf{f}$=[$\mathbf{f}^{(\mathrm{M})\mathrm{T}}$ $\mathbf{f}^{(\mathrm{R})\mathrm{T}}$]$^{\mathrm{T}}$ is a vector of unknown muscle and reaction forces, respectively. **r** is a right-hand side vector composed of external and inertial forces. Finally, the end goal of performing the inverse dynamic analysis is to obtain the vector **f** of all forces.

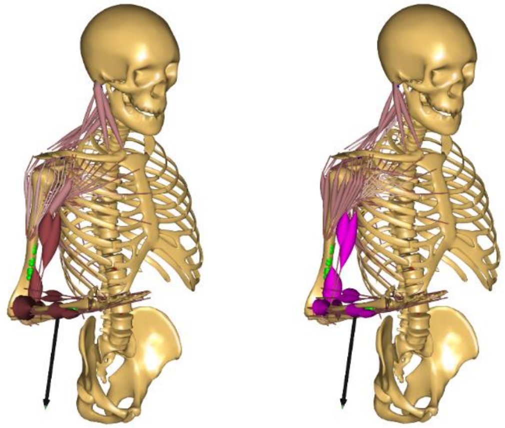

Figure 1-4. Muscle-tendon models being maximally activated beyond the nominal strength limits of the model.

1.3.2. ADVANCEMENTS IN MODEL VALIDATION

1.3.2.1 Subject-specific Modelling

Generic, linearly scaled musculoskeletal models created from cadaveric data might not truly represent a given subject or patient being modelled. From time to time, a higher level of detail might be a requisite for answering a specific research hypothesis, and the use of these models in clinical applications for the upper extremity is increasing (Bolsterlee, Veeger, & Chadwick, 2013). Thus, if such models are not able to reflect the strength capabilities of a patient with a neuromuscular disability, they stop being useful (Giuffre et al., 2010). The degree of model complexity can also impact the outcomes obtained (Lenaerts et al., 2009; Carlos Quental, Folgado, Ambrósio, & Monteiro, 2015; Valente, Martelli, Taddei, Farinella, & Viceconti, 2012; Wagner et al., 2013). Hence, there will always be a trade-off between choosing a detailed model under some idealized assumptions (Van Der Valk, Van Driel, & De Vos, 2007).

In recent years, subject-specific modelling has increased. As models get more personalized, the required data collection approaches become more complex, and the respective processing time increases. Accordingly, constraints on the different types of data that can be collected from a target group of test-subjects/patients will also influence the degree of subject-specificity that can be used. One of the simplest approaches consists of collecting individual isometric and isokinetic strength data to re-adjust/re-scale the parameters of the muscle-tendon units in the generic linearly scaled model (B. A. Garner & Pandy, 2003; Heinen, Rasmussen, & de Zee, 2019; Lloyd & Besier, 2003; Winby, Lloyd, & Kirk, 2008). This includes optimising the nominal isometric strength, muscle fibre length and tendon slack length, which requires very expensive dynamometric equipment and computationally expensive optimization procedures. Sometimes, the PSCA is also used as force normalization factor, and it can be estimated from time-consuming segmentation of muscle volume (Bolsterlee, Vardy, van der Helm, & (DirkJan) Veeger, 2015; Holzbaur, Delp, Gold, & Murray, 2007; Holzbaur, Murray, Gold, & Delp, 2007).

Other more advanced approaches imply the segmentation of bone, muscle and tendon tissues from medical imaging data, namely medical resonance imaging (MRI) data, sometimes called MRI-based musculoskeletal modelling. This approach mitigates the problems of using the previous approach. It enables acquisition of the correct individual segment lengths, reconstruction of individual joint geometry and kinematics, geometrical transformation of the geometry of the generic muscle attachment points by performing bone registration (Carbone et al., 2015; Dzialo et al., 2019; Halonen et al., 2017; Marra et al., 2015), and adjustment of muscle-tendon unit parameters from the volumetrically reconstructed muscle tissues (Bolsterlee et al., 2015; Modenese, Ceseracciu, Reggiani, & Lloyd, 2016; Valente, Crimi, Vanella, Schileo, & Taddei, 2017; Valente et al., 2014).

1.3.2.2 Validation Metrics and the Reachable 3-D Workspace

Some verification and validation standards have been proposed (Hicks, Uchida, Seth, Rajagopal, & Delp, 2015; Lund et al., 2012). In regards to the biomechanical variables typically output by the musculoskeletal models, it is important to highlight the following validating counterparts: (1) joint reaction forces can be validated against data measured by force sensors embedded on joint implants (Bergmann, Deuretzbacher, Heller, Graichen, & Rohlmann, 2001; Marra et al., 2015; Westerhoff, Graichen, Bender, Rohlmann, & Bergmann, 2009), (2) muscle forces against tendon buckle gages (Fleming & Beynnon, 2004) or optical fiber cables (Komi, 1990), (3) muscle activations against surface or needle electromyography data (S. Duprey, Savonnet, Black, & Wang, 2015), (4) predicted ground reaction forces against force plates data (Fluit, Andersen, Kolk, Verdonschot, & Koopman, 2014; Skals, Jung, Damsgaard, & Andersen, 2016). The major problem is that, with exception of force plate data, all other validation data may only be obtained by means on invasive methods. Moreover, when working with patients, there will always be constraints imposed on what data can be collected and the time that it takes to collect. Thus, musculoskeletal models have to be validated in order to be useful for musculoskeletal-based virtual prototyping. At the same time, it is also important to explore new metrics that can fulfil the requirements for verification of model performance.

Many studies have shown the reachable 3-D workspace of healthy and disabled individuals can provide an insight on upper extremity function (Han et al., 2016; Han, Kurillo, Abresch, de Bie, et al., 2015; Klopčar, Tomšič, & Lenarčič, 2007; Matthew, Kurillo, Han, & Bajcsy, 2015; Ngan et al., 2019; Oskarsson et al., 2015). This approach is likewise suitable for designing ergonomic equipment for specific working environments (A. K. Sengupta & Das, 2000, 2004) or even for designing and testing performance of arm assistive devices (Dunning et al., 2016; Schiele & van der Helm, 2006). Lastly, it has a kinetic nature as it depends on strength (Han, de Bie, et al., 2015; Park, 2007) and hand-payload (Johnston, Dewis, & Kozey, 2015; Park, 2007).

In biomechanics, by definition, the reachable 3-D workspace is described as the region/volume that a point located in the wrist or hand can reach with at least one orientation (Lenarcic & Umek, 1994). Such metric derives from the research field of robotics where the workspace volume spanned by the end-effector of a manipulator is usually used as a performance metric (Siciliano et al., 2009). Moreover, this metric helps mapping and reducing the dimension space spanned by the joints of a given manipulator, typical greater than 3-DOFs, and enables visualizing and interpreting performance in the 3-D space. Simultaneously, the reachable 3-D workspace overcomes kinematic redundancy. In layman’s terms, this means that a given point in the 3-D space can be reached by multiple different arm postures.

Two different methods have been proposed to estimate the reachable 3-D workspace. The first one finds the envelope by fitting a spherical surface to the experimental data directly obtained from all points attainable by the wrist/hand or hand effector (Kurillo et al., 2012; A. Sengupta & Das, 1998). This can be accomplished either with a camera-based sensor such as the Microsoft’s Kinect™ (Han et al., 2016; Han, Kurillo, Abresch, de Bie, et al., 2015; Han, Kurillo, Abresch, De Bie, et al., 2015; Kurillo, Chen, Bajcsy, & Han, 2013; Kurillo, Han, et al., 2013; Oskarsson et al., 2015) or with a computerized potentiometric measurement system (A. K. Sengupta & Das, 2000). The second method consists of using pure kinematic models of the upper extremity (Klopčar et al., 2007; Lenarcic & Umek, 1994; Matthew et al., 2015; Schiele & van der Helm, 2006; Yang, Abdel-Malek, & Nebel, 2005). While some models allow the direct mathematical derivation of the reachable workspace and its respective volume (Yang et al., 2005), the other models require inputs such as the ROM of each human joint that needs to be sampled. In order to overcome the fact that the anatomical shoulder joint does not behave as a pure spherical joint, coupled motions generated from the sternoclavicular, acromioclavicular and scapulothoracic joints are also considered in the most advanced models (Klopčar et al., 2007).

In the context of musculoskeletal modelling, the reachable 3-D workspace can be a potential direct validation metric of subject-specific models because it can be measured *in-vivo* (Lund et al., 2012). Besides, if a model is able to reliably replicate the strength capabilities of a given individual, it should theoretically be able to accurately predict the reachable 3-D workspace of that individual, and the same should hold for impaired patients. Consequently, as the reachable 3-D workspace volume covers many of the activities of daily living of interest in studies targeting the assessment of impaired patients and in studies targeting the design of assistive devices for these patients (Rahman et al., 1996; Rosen, Perry, Manning, Burns, & Hannaford, 2005), its use can improve virtual prototyping (Figure 1-5), eventually allowing it to become the golden standard for designing assistive devices.

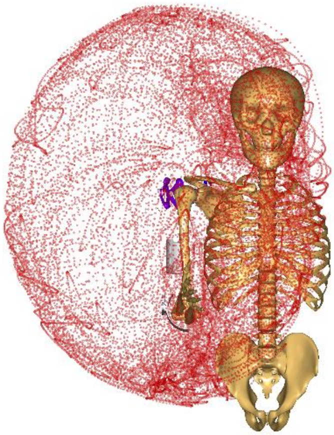

Figure 1-5. A point cloud corresponding to an experimental upper extremity reachable 3-D workspace mocap data acquisition.

1.4. AIMS AND OUTLINE OF THE DISSERTATION

In the light of the state-of-the-art presented above, the design of passive arm assistive devices may benefit from musculoskeletal modelling and help designing tailor-made rehabilitating devices. In order to investigate this opportunity, it is necessary to understand the underlying biomechanics of the patients and how well the musculoskeletal models can replicate these subjects. Accordingly, it is one of the aims of this thesis to investigate how patient-specific models can be built and evaluated such that they can be valuable for simulation-based design approaches. At the same time, the mechanical properties and the design approaches of the current state-of-the-art passive assistive devices should be investigated in order to pursue new ways of designing more compact assistive devices. This will ensure that the patients receive the desired amount of assistance, and that they are satisfied wearing devices that do not compromise their self-esteem.

Hence, the objectives of this Ph.D. project include the following points:

- Investigate experimental assessment protocols that can be used for estimating upper extremity performance.
- Define upper extremity metrics that relate to individual strength and can be simultaneously measured *in-vivo* and *in-silico*.
- Validate upper extremity musculoskeletal models scaled from subject-specific strength data on healthy individuals.
- Evaluate the performance of strength-scaled musculoskeletal models on real patients with neuromuscular impairment.
- Identify the design details of passive arm assistive devices that can potentially be made more compact.
- Design a light-weight wearable orthosis capable to assist the user in a compact manner.
- Test the upper extremity passive orthosis on real patients with neuromuscular impairment.

While the present chapter introduces the background and motivation of this study, a literature overview and the current state-of-the-art of both arm assistive devices and musculoskeletal modelling, the results from the objectives presented above are organized as a collection of five scientific journal articles in this thesis. Each chapter is described as follow:

Chapter 2 proposes a new experimental kinematic and kinetic assessment protocol for estimating the reachable 3-d workspace on ten healthy individuals. This protocol was designed to reach volumes close to the body that are important for daily life activities but were not considered in previous experimental assessments. Moreover, this upper extremity performance metric was also chosen for investigating the change of volume and shape as a function of different hand-payloads carried by the test-subjects. The intention was to observe changes in the full reachable 3-d workspace volume that would eventually be present in real patients with neuromuscular impairment. In parallel, dynamometric unidirectional strength measurements were collected in order to investigate the dependency of the reachable 3-d workspace volume on individual strength.

In **Chapter 3**, the same data were used for building and validating musculoskeletal models of the ten healthy individuals. In this work, the models were kinematically scaled to the motion-captured data and strength-scaled using the dynamometric strength measurements. An optimisation routine was formulated to use the latter data for enhancing the subject-specificity of the models, this way enabling them to better replicate the strength capabilities of the test-subjects. Afterwards, the reachable 3-d workspaces for the different hand-payload cases were simulated using the models and validated against those measured experimentally for each test-subject.

The same subject-specific modelling approach was attempted in **Chapter 4** on two young patients with neuromuscular impairment. This work resulted from the direct collaboration between the Department of Materials and Production and the Pediatric Engineering Research Laboratory (PERL) at Nemours/Alfred I. DuPont – Hospital for Children (Wilmington, Delaware) where the PhD student did his 4 months study abroad period in March 2016, under the supervision of Tariq Rahman, PhD, Lab Head and Senior Research Scientist. Two young patients with Arthrogryposis, who were born without biceps brachii muscles and weakened musculature, were recruited. Kinematic, dynamometric and electromyography data were collected from them, patient-specific models were built and strength scaled/optimised. The reachable 3-d workspace volumes were simulated and compared against the experimental ones to evaluate the performance of the musculoskeletal models.

Chapter 5 presents a novel and compact shoulder mechanism (also known as CXD – short for Compact X-scissors Device) for exoskeleton applications. This innovative mechanism was designed to overcome the usual bulky and kinematically limited shoulder mechanisms used in these devices. Most shoulder mechanisms have three-DOF, protrude away from the body and suffer from singular points in which the mechanisms lock and cannot further move. Consequently, the exoskeleton users experience limitation in the ROM of the shoulder and these components cannot be hidden underneath clothing. The new CXD has three-DOF and curves and works on an imaginary spherical surface that sits very close to the skin of the user. Moreover, the mechanism is singularity-free within the ROM of the anatomical shoulder joint. Thus, it can fit underneath clothing. It is also important to highlight that this invention resulted in a patent application and it was the winning entry of the 2018 Wearable Robotics Association's Innovation Challenge (Scottsdale, AZ). Subsequently, AAU Innovation also awarded a 9-months Proof-of-Concept Grant for future maturation of the product.

Chapter 6 concerns the final paper in which a feeding-assistive passive orthosis prototype was designed and manufactured. The device proposed in this work included the new spherical scissors mechanism described in **Chapter 5** and a new spring configuration with pulleys that allowed to switch on and off the moment arms provided by the springs, thus enabling to passively control the amount of assistance provided. In this part of the dissertation, the orthosis prototype was tested on one of the young patients modelled in **Chapter 4**, and the model helped to gain some insight for developing an assistive device that could be body-powered using antagonist shoulder and elbow muscles, such as the triceps brachii muscle, and achieve slightly more compactness.

The last **Chapter 7** summarizes results by individually analysing the outcomes of the five studies performed, evaluates the contributions and impact of the work as an effort to advance the current state-of-the-art, and proposes ideas for future research directions.

CHAPTER 2. PAPER I

The reachable 3-D workspace volume is a measure of payload and strength: a quasi-static kinetic assessment

Castro, M. N., Rasmussen, J., Bai, S., & Andersen, M. S. (2019). The reachable 3-D workspace volume is a measure of payload and body-mass-index: a quasi-static kinetic assessment. *Applied Ergonomics*, 75, 108–119. https://doi.org/10.1016/j.apergo.2018.09.010

CHAPTER 3. PAPER II

Validation of subject-specific musculoskeletal models using the anatomical reachable 3-D workspace

Castro, M. N., Rasmussen, J., Bai, S., & Andersen, M. S. (2019). Validation of subject-specific musculoskeletal models using the anatomical reachable 3-D workspace. *Journal of Biomechanics*, 90, 92–102. https://doi.org/10.1016/j.jbiomech.2019.04.037

CHAPTER 4. PAPER III

Evaluation of upper extremity musculoskeletal models for young patients with arthrogryposis

Castro, M. N., Rahman, T., Oliveira, A. S., Shank, T., Wee, J., Nicholson, K. F., Bai, S., Rasmussen, J., & Andersen, M. S.

Submitted to *IEEE Transactions on Biomedical Engineering*

CHAPTER 5. PAPER IV

A compact 3-DOF shoulder mechanism constructed with scissors linkages for exoskeleton applications

Castro, M. N., Rasmussen, J., Andersen, M. S., & Bai, S. (2019). A compact 3-DOF shoulder mechanism constructed with scissors linkages for exoskeleton applications. *Mechanism and Machine Theory*, 132, 264–278. https://doi.org/10.1016/j.mechmachtheory.2018.11.007

CHAPTER 6. PAPER V

A case study on designing a passive feeding-assistive orthosis for arthrogryposis

Castro, M. N., Rahman, T., Nicholson, K. F., Rasmussen, J., Bai, S., & Andersen, M. S.

Submitted to *Journal of Medical Devices*

CHAPTER 7. DISCUSSION

7.1. SUMMARY OF RESULTS

This last chapter offers an overall and individual summary of the results obtained from the five articles comprised in the dissertation. Paper I proposes a new experimental protocol for measuring the reachable 3-d workspace that is essential for deriving the results of the following papers. The correlation between individual strength and the reachable 3-d workspace is also assessed. Paper II and III use the reachable workspace as a validation metric for musculoskeletal modelling, first on healthy test-subjects and then on young patients with neuromuscular impairment. Dynamometric data is also acquired for subject-specific model scaling/optimisation purposes. Paper IV investigates a solution of the common problem of bulkiness that affects all arm assistive devices and proposes a new compact shoulder mechanism that sits close to the body and is singularity-free within the range-of-motion of the anatomical shoulder joint. The last Paper V attempts to design a more inconspicuous body-powered arm orthosis for feeding assistive purposes (Paper IV). The device includes the new mechanism plus a new spring configuration that allows the patients to body-control shoulder and elbow flexion by means of their functional antagonistic muscles. Finally, the contribution, impact and limitations of this project are discussed, and suggestions for future work are made, aimed at building more robust rehabilitation devices by means of musculoskeletal simulation-based design.

Paper I: The reachable 3-D workspace volume is a measure of payload and body-mass-index: a quasi-static kinetic assessment

The first Paper I focuses on the creation of a new experimental protocol that allows to better capture both kinematic and kinetic natures of the reachable 3-D workspace. This new protocol enables the assessment of close-to-torso as well as far-from-torso regions of the reachable volume, which are of great importance especially in clinical settings. The reachable 3-D workspace is measured for ten test-subjects for four distinct hand-payload cases and reveals a statistically significant correlation between volume reduction and increasing hand-payloads. Additional surrogates of individual strength, namely measurements of maximal force generation capability in the direction of shoulder flexion, shoulder abduction and elbow flexion are also found to be correlated with the reachable 3-D workspace volume. Consequently, a multivariate linear regression model is defined. This statistical model that depends on both hand-payload and body-mass-index is capable of explaining 73% of the variation in the reachable 3-D workspace volume data. That finding represents an increase of 10% when comparing to a statistical model only depending on hand-payload alone. Moreover, the processing of the 3-D point cloud data into a volumetric mesh, allows retrieval of the non-convex shape of the reachable 3-D workspace using the alpha-shapes algorithm by introducing an alpha-radius with a dimension of the order of the actual torso/waist dimensions of the respective test-subject.

Paper II: Validation of subject-specific musculoskeletal models using the anatomical reachable 3-D workspace

In the light of the findings from the previous paper, the reachable 3-D workspace is used in Paper II for model validation. Musculoskeletal models require validation to be trustworthy. Since the reachable 3-D workspace can be used as a performance metric, models should be able to replicate the reaching capabilities of the real subject by simulation if properly calibrated. A total of 36 strength measurements are used to strength-scale a subject-specific musculoskeletal model for ten healthy individuals. The performance of such a model was compared against a default model that was only geometrically and length-mass-fat scaled. The 140 hill-type muscle-tendon units present in the upper extremity model are grouped into 16 groups, each with joint strength factors assigned to it that are used as design variables for pre-multiplying the nominal strength of each muscle-tendon unit. A one-step calibration method is used to adjust the tendon slack length of the muscle models to known optimal lengths, and an optimization routine is defined such that the joint strength factors can be adjusted until the overall muscle activation attains a full activation state, i.e. 100% activation, during the simulation of the strength measurements. The performance of strength-scaled models is compared against that of the same models before optimisation by generating the reachable 3-D workspace through simulation for different hand payload cases, and by comparing it to the experimentally measured reachable workspaces. It is found that the strength-scaled model can predict the reachable workspace better than the default calibrated model. However, the joint strength factors reach high values suggesting that the antagonist muscles generate high passive forces that need to be counteracted by the nominal strength of agonist muscles. These are most likely resultant from the poor tendon slack length one-step calibration method. Yet, models are, in general, weaker than the test-subjects that are being modelled.

Paper III: Evaluation of upper extremity musculoskeletal models of young patients with arthrogryposis

Paper III applies the same modelling workflow and experimental methodology described in Paper II in a clinical setting for patient-specific modelling purposes. In this particular work, two young patients with arthrogryposis are enrolled as test-subjects given their particular neuromuscular impairment pattern. Patients with arthrogryposis usually present amyoplasia of the biceps brachii muscles, i.e. congenitally under-developed or absent muscle tissue, accompanied by general weakness of the upper extremity muscles that work against gravity (mainly flexors and abductors). On top of that, the patients present shoulder joint deformity (caused by decreased fetal movement during pregnancy – fetal akinesia) with internally rotated and ulnarly deviated forearms. Different types of data are collected from the two patients: active and passive joint ROM, active reachable 3-d workspace, electromyography and force generating capacity in the direction of canonical DOF, i.e. surrogates of individual strength that are measured for maximal isometric voluntary contractions (MVC) against a hand-held dynamometer. The experimental results show that these patients present a reduced active range of motion, and a small and shrunk reachable 3-d workspace that spans the inferior-lateral and inferior-medial far-from-torso aspects of its volume. The electromyography studies do not show any signs of myopathy in the remaining muscles, apart from the bicep brachii muscle that is known to be wasted. The strength-scaled models show a better approximation to the strength measurements after being optimised, namely predicting maximal muscle MMACT values in the interval of [0.5,1.50] for the MVC cases (where MMACT=1 is expected), whereas values of MMACT between [0.0,0.75] were previously being predicted. This proves that the models tend to be initially stronger than the patients for some DOFs as they do not account for the patient's weakness pattern, e.g. shoulder and elbow flexor muscles, but are still weaker (Paper II) for the DOF about which the patient's musculature is not compromised, e.g. shoulder and elbow extensors. With respect to the prediction of the active reachable 3-D workspace by means of simulation, the strength-scaled models were able to capture the patients' inability to reach the anterior-medial aspect of both close-to-torso and far-from-torso regions of the reachable 3-d workspace. This part of the reachable 3-D workspace volume directly depends on shoulder and elbow flexion. However, the models fail to match the patients' abduction strength capabilities, thus predicting exaggerated lateral to medial far-from-torso reaching capabilities.

Paper IV: A compact 3-DOF shoulder mechanism constructed with scissor linkages for exoskeleton applications

A very compact 3-DOF shoulder joint for exoskeletons is conceptualized in Paper IV, using a novel spherical scissors mechanism. This spatial mechanism has a remote centre-of-motion that coincides with the same rotation centre of the anatomical shoulder joint without interfering with the natural joint motion and neither with the surrounding soft tissues. The forward and inverse kinematics of this mechanism are derived theoretically. A manipulability analysis confirms that the mechanism is singularity-free within the range-of-motion of the anatomical shoulder joint. A prototype of the mechanism is built with 3-D printed steel and assembled on an upper extremity exoskeleton. Then, the five-task protocol described in Paper I for the estimation of the reachable 3-D workspace is used to show the reaching function differences for a test-subject wearing and not wearing that exoskeleton. The results show the reachable workspace volume while wearing the exoskeleton nearly matches the one corresponding to free motion. The subtle volume differences do not arise from the mechanism itself, but from an inherent design constraint of the exoskeleton, namely the missing shoulder elevation DOF. In sum, the novel spherical scissors mechanism represents an advancement on this type of shoulder joint mechanisms concerning upper extremity assistive devices and can fit underneath clothing.

Paper V: A case study on designing a passive feeding-assisitive orthosis for arthrogryposis

To design a more compact passive feeding-assistive device, Paper V proposes a new orthosis design that is characterized by its alternative spring attachment configuration. This device was designed while accounting for the residual strength capabilities of the patient group presented in Paper III. Furthermore, the orthosis prototype includes the above-mentioned spherical scissors mechanism as its shoulder component (Paper IV). Since there is a trade-off between the balancing capabilities of passive devices and their compactness, the feeding-assistive device relies on a partial gravity balancing strategy rather than on a fully balanced one. Therefore, two ZFL springs are used: one said to be bi-articular, spanning both the shoulder and elbow joints, and a second one said to be mono-articular, spanning the elbow joint only. The difference between this new configuration and the one presented by the A-gear device (Kooren et al., 2015) is the integration of a small pulley system for each spring that allows to alter the pass of the spring to reduce its moment arm about the elbow joint towards zero for elbow joint flexion ranges below 30º. This subtle change allows the patient to perform the beginning of the elbow flexion without any assistance and to control the orthosis afterwards using their elbow extensor musculature. Moreover, this partial assistance strategy allows bringing the insertion points of both springs more closely to the elbow joints. A prototype of the orthotic device is built and tested on a patient with arthrogryposis who could only initially perform a 90° elbow flexion. Afterwards, the patient was not only able to reach the mouth but also to reach the anterior close-to-body aspect of the reachable 3-d workspace volume.

7.2. CONTRIBUTIONS AND IMPACT

The proposed experimental five-task protocol used to measure the reachable 3-D workspace is capable of capturing the kinematic as well as kinetic natures of this quantity. Therefore, it contributes mainly for the ergonomics field as a valuable metric for motor performance that can be used to design equipment/devices for humans, such as assistive devices. Moreover, the results obtained also allow estimation of the volume of this metric as a function of hand-payload and body-mass-index. It should also be highlighted that previous protocols for the estimation of the reachable workspace were either only capable of collecting spherical surface data spanning the far-from-torso region or estimating the whole reachable 3-d workspace volume and shape from prior measurements of the active anatomical joint ROM. Furthermore, this new protocol allows retrieval of the true non-convex shape of the reachable 3-d workspace, which is shaped by the intersecting human torso.

The reachable workspace metric can equally be used as a validation metric for musculoskeletal modelling of the upper extremity. Other validation metrics typically include the measurement of ground reaction forces, force sensors embedded in implants, tendon strain using invasive sensors or electromyography, but with the exception of the latter, none of these are favourable for validating upper extremity models. A workflow including a minimal and inexpensive data setup is also presented, which is later proved to nearly mimic the data setup acquisition allowed in a clinical setting.

The compactness of the new spherical scissors mechanism allows a tighter fitting closer to the body without interfering with the natural shoulder motion, which enables designing inconspicuous wearable devices that can fit underneath clothing. This shoulder mechanism is a game changer, capable of establishing itself as the standard for the next generations of lightweight rigid exoskeletons, both the passive and the active ones.

More compact passive orthoses can be achieved by allowing the balancing capabilities of the devices to be uneven such that a partial balancing device exploits and rehabilitates the patient's residual musculature. This opens an opportunity for musculoskeletal simulation-based design development workflows given that specific muscles can be targeted directly for body-powering the orthotic device after performing a detailed biomechanical assessment of the user, and using a trustworthy validated musculoskeletal model for design optimisation. In parallel, further investigation can be facilitated by the musculoskeletal models for developing a treatment/rehabilitation plan based on the effects of wearing the optimised device.

7.3. LIMITATIONS AND RECOMMENDATIONS FOR FUTURE RESEARCH

Different contributions were made to advance the current state-of-the-art in the fields of assistive technology and biomechanics, some limitations were found during this project. Thus, some key aspects of the research are yet to be solved and worth of discussion and improvement.

The reachable 3-d workspace can experimentally be assessed using a five-task protocol (Paper I). This protocol shows that a set of arm motions is able to capture both close-to-torso and far-from-torso regions of the target volume. Despite measuring this quantity for different hand-payload conditions across ten different test-subjects,

- The reliability of this metric has to be studied in more detail. This includes a bigger a cohort of test-subjects, the analysis of the intra-subject variability and evaluation of how fatigue can affect such variability due to the movement repetition during and between each of the five-task protocol.
- Additionally, it is worth investigating how well this quantity matches with the reachable workspace volumes shapes obtained from potentiometric measurement systems (A. K. Sengupta & Das, 2000) and from methods involving the estimation of the reachable workspace from the active ROM

using kinematic models of the upper extremity (Klopčar et al., 2007; Lenarcic & Umek, 1994; Matthew et al., 2015; Schiele & van der Helm, 2006; Yang et al., 2005).

- The use of dumbbells as hand-payloads can also potentially be substituted by heavy wrist/forearm-adjustable straps or braces to allow the test-subjects to feel more comfortable during the assessment and to avoid the dumbbells interfering with the torso, thus resulting in an underestimation of the real volume.
- Finally, the statistical modelling shows that, besides hand-payload weight and body-mass index (Johnston et al., 2015; Park, 2007), the reachable workspace volume can be derived from net joint strength. Park (2007) demonstrated this using a simplified planar biomechanical model to generate the reachable 3-d workspace as function of the input joint strength, body weight and hand-payload weight. Eventually, a radial-basis-function can also be used to obtain the final shape as function of these inputs.

Subject- and patient-specific modelling can be accomplished fairly using low-cost dynamometric devices such as unidirectional force sensors (Paper II) or hand-held dynamometers (Papers III). The measurements obtained from these devices help to strength-scale/optimise the muscle tendon properties of the parameters that govern the muscle-tendon units present in the bigger musculoskeletal model. As in most state-of-the-art literature, this study used Hill-type muscle models, which can accurately define the force-length and force-velocity relationships of muscular contraction. However, each of these non-linear muscle-tendon unit models require input in terms of nominal strength, tendon slack length, fibre length, fibre pennation angle, among other parameters. To that end, most studies rely on more advanced Isokinetic equipment (e.g. the Biodex measuring system). Even though simple (non-Hill-type) muscle models with a constant force-length relationship can be used, they will always overestimate the strength capabilities of the test-subject. This would occur since these simplified muscle models have nominal strength independently of the joint angles, i.e. independently of the elongation of the muscle element. Thus, in order to keep using Hill-type models with lower quality and quantity of data it might be necessary to

- Investigate how muscle grouping affects the matching between experimental and simulated strength measurements.
- Directly compare the influence and effects of strength-scaling musculoskeletal models with two distinct types of devices and try to quantify a minimum data threshold from which the model calibration starts to disagree.
- Search for new ways to strength-scale musculoskeletal models that do not directly require any specific machinery or devices.

This last bullet point is also in line with new improvements that may result in more accurate matching between the experimental strength measurements and their simulated counterparts. Ideally, future works may be able to understand the kinetic aspect of the reachable workspace and use some of these data points for strength-scaling the models. In the long run, optimisation problems may be formulated such that the unknown muscle-tendon unit parameters can be directly obtained from the shape of the reachable workspace volume under specific hand-payload conditions. Longitudinal studies of patients with neuromuscular impairment that present irregular active reachable workspace shapes may also be valuable for understanding disease progression and for assisting modelling. Last but not least, it is also worth attempting to validate lower extremity models using this workflow by defining hypothetical lower extremity reaching capabilities.

Even though the results positively showed that a partial gravity balanced device can assist a patient on feeding tasks, the reader should note that such unbalanced devices assume that the patients retain a residual/considerable amount of antagonist muscle extension capabilities to body-power the device against the increased shoulder and elbow flexion moments produced by the spring imbalance. This area is exactly where musculoskeletal simulation-based design may be useful. With trustworthy musculoskeletal models it will be possible to accelerate the virtual prototyping process by testing the devices in-silico and to target and control the specific biomechanical effects that may result from continuously wearing the arm assistive device for a long term.

7.4. CONCLUDING REMARKS

The main goal of this dissertation was to develop a more robust and compact orthosis for patients with neuromuscular disorders. Since bulkiness in passive arm assistive devices depends on the theoretical formulations behind a given spring configuration design, e.g. a full gravity balancing strategy, it is difficult to achieve a very compact device by analytical methods. The introduction of numerical musculoskeletal modelling in the device development workflow may improve the design if patient-specific model validity can be obtained. To that end, a common metric between musculoskeletal models and arm assistive devices that can help to evaluate motor performance was investigated, namely the reachable 3-D workspace (Paper I). After assessing the correlation between this volumetric quantity and both hand-payload carrying capacity limits and individual strength, musculoskeletal models of healthy subjects (Paper II) and of young patients (Paper III) were built for understanding the potential of these models for simulating the real reaching capabilities of their human counterparts. Afterwards, an arm assistive device was designed using a new shoulder mechanism with improved compactness capable of replicating the kinematic properties of the human shoulder (Paper IV), and a different spring configuration of a passive orthosis was proposed to allow patients with neuromuscular disorders, such as arthrogryposis, to body-power the device with their gravity antagonistic musculature (Paper V). Even though it was not possible to combine the findings of Paper III into Paper V, and prove the advantages of musculoskeletal simulation-based design, the modelling workflow and the partial gravity balancing design can be used in future research for designing better devices. This will not only help to rehabilitate the patients in a compact and non-stigmatizing manner, but also enable the clinicians and therapists to target muscle-specific motor function improvement.

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