Analysis of kinematic and muscular synergies as assessment tools during rehabilitative robotic training

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SINGAPORE

**ANALYSIS OF KINEMATIC AND MUSCULAR
SYNERGIES AS ASSESSMENT TOOLS DURING
REHABILITATIVE ROBOTIC TRAINING**

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(HEALTHTECH NTU)**

2018

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REHABILITATIVE ROBOTIC TRAINING**

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IN MEMORY OF MY LOVING GRANDFATHER **SRIRAMULU GADDAMADUGU**, WHO INSPIRED MY QUEST FOR KNOWLEDGE AND ZEAL FOR CONTRIBUTING TO SCIENCE IN HELPING HUMANITY

Abstract

Cerebrovascular accident (commonly referred as Stroke) is the leading cause of disability worldwide [1]. Depending on the location and severity of the lesion, it results in different neurological deficits in motion, sensation, cognition, and emotion affecting their activities of daily living (ADL). Hemiparesis (paralysis on one side of the body) that affects 80% stroke survivors is the major post-stroke motor deficit. The motor damage can be recovered by rehabilitation therapy and exercises. In recent years, to meet the growth in size of the stroke population coupled with the limited availability of trained therapists and financial resources robotic devices have been introduced as a potential solution. The motor recovery depends on many factors :intensity, frequency of robotic therapy and mainly 'control strategy' adopted in the specific robot. Also, the heterogeneity in stroke location and its effects provides an impetus to develop and validate user-specific adaptive rehabilitation control strategies for faster recovery post-stroke by minimizing the motor-coordination difficulty. This thesis aims to **augment the recovery process** in stroke subjects via **rehabilitation robotics** as an **optimal assessment** tool by validating and assessing novel control algorithms based on motor control principles. Specifically, I address the following:

1) Validate the efficacy of the novel robotic control strategies that adapt haptic force from assistance to disturbance based on user performance to provide optimal training. The boost in development and utilization of robotic devices in clinical settings suggest that intense neuro-rehabilitative treatments can significantly improve the functional recovery in post-stroke. However, the choice of control strategy that provides optimal motor recovery is still an open question. H-MAN, a novel upper limb rehabilitation planar robot designed by our team at Nanyang Technological University is employed

in a longitudinal study. A novel control strategy with underlying principles of 'Challenge Point Framework', that transits haptic forces from guidance to disturbance based on user's movement smoothness is implemented. The motor performance of the post-stroke subjects undergoing therapy (with robot vs conventional) is assessed. The results indicate that a performance based adaptive controller (with both assistive and disturbing feedback forces) produces significant gains in motor functions.

2) Promote the adaptation of technology-aided tool for sensorimotor assessment

In addition to designing better control algorithms, an arguably important factor is the 'lack of clear understating of the level of sensorimotor deficits'. Rehabilitation robotic devices has the potential to provide objective, high resolution, subject-independent sensorimotor assessments. However, their adaptability in clinical setting is yet to be established. With results from two clinical studies, I propose few recommendations to develop standardized robotic tasks and performance metrics similar to clinical scales. Integrating physiological (EMG) measures with task metrics (from robotic tasks) during specific motor task resulted in the superior level of assessment.

3) Investigate the feasibility of muscle synergies to evaluate the task relevance

Muscle synergies are believed to be basic building blocks of Central Nervous System (CNS) for motor control and are proposed as a solution for 'Degrees of Freedom' problem in the literature. Through 'Augmented Synergies' proposed in this thesis, I aim to explain their task relevance with results from an isometric shoulder task in control healthy population. Relating muscle synergies with action enable us to identify the compensatory strategies subjects. This will in-turn aid in developing a subject-specific training paradigms with muscle synergies as feedback to augment the recovery process.

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“Whether I shall turn out to be the hero of my own life, or whether that station will be held by anybody else, these pages must show.” ✎ Charles Dickens, *David Copperfield*

1

Introduction

“We have a brain for one reason and one reason only – that’s *to produce adaptable and complex movements*. Movement is the only way we have (been) affecting the world around us. ...I believe that to understand movement is to understand the whole brain. And therefore it’s important to remember when you are studying memory, cognition, sensory processing, they’re there for a reason, and that reason is ***action ...through contractions of muscles***.” - an excerpt from **TED** talk by David Wolpert, a neuro-scientist and engineer who pioneered in computational biology.

A neurological injury such as **stroke** [2] results in different **movement disorders** affecting the survivors activities of daily living [ADL] and may have severe clinical implications. Owing to neuro-plasticity, brain has the capacity to re-learn; post-stroke rehabilitative treatment is practiced to improve their motor functions. The past three decades witnessed a growth in the development and deployment of the technology assisted systems for rehabilitation. This thesis aims to **augment the recovery process** in stroke subjects via rehabilitation robotics as an **optimal training and assessment** tool by validating and assessing novel control algorithms based on **motor control** principles.

1.1 MOTIVATION- INVESTIGATING MOTOR CONTROL PRINCIPLES FOR EFFECTIVE REHABILITATION IN STROKE

Stroke is the leading cause of disability [1] with 33 million stroke survivors worldwide [3]. With increasing aging population and life expectancy, stroke is estimated to be the fourth leading cause of disability-adjusted life-years (DALY) in developed countries by 2030 [4]. It results in neurological impairment in motion, sensation, cognition, and emotion. Hemiparesis that affects 80% of stroke survivors is the major post-stroke motor deficit. With this condition, patients experience a full/partial paralysis on one side of the body losing sensorimotor control, face trouble in moving his/her limbs and maintaining balance affecting their activities of daily living (ADL). Although most subjects regain their gait ability, 30% to 66% of the survivors cannot use their affected arm limiting their independence [5]. Studies have shown that post-stroke rehabilitative treatment induces plasticity, thereby improving motor control and their quality of life [6–8].

Several robotic devices have been introduced over the years to address the rehabilitation needs and have been proved to augment the recovery process [9–11]. To meet the demands of the increasing aging population coupled with the limited availability of trained therapists and financial resources, an **intervention of robotic devices** for therapy is seen as a potential solution. The present state of art rehabilitation robots are shown to induce **moderate gains in motor functions** when compared to the conventional therapy [12]. These robotic devices are aimed at different upper limb joints - hand, wrist, elbow, and shoulder etc., [13] and are equipped with different interaction modalities - passive, active, assistive, resistive, passive-mirrored, corrective, and path-guidance [14]. Many control algorithms are available in the literature to achieve learning through different strategies such as assistive, error amplification, and haptic- simulation etc., reviewed in [15]. However, the

In addition to designing better control algorithms, an arguably important factor is the 'lack of clear understating of the level of sensorimotor deficits'. Most of the studies present only changes in standard clinical scores as outcome measures to track subject's progress during therapy. Conventional clinical measures are ordinal and are therapist dependent. Also, clinical assessments are usually repeated only at a few stages to monitor the patient's progress and they are time consuming. Quantitative measures derived from the motor performances of participants during the robotic tasks might

overcome these limitations [16, 17]. Quantitative robotic scales are shown to provide more reliable, objective, and accurate quantification of sensorimotor state during the training task itself without the need for any additional assessment phase. However, their use in clinical settings is scarce. There are many metrics adapted in various studies to assess a same measure [18–20]. For example to assess smoothness of a movement: different metrics such as SPARC [21], spectral arc length (SAL) [22], log jerk [23], number of peak velocities and MAPR [24] etc., are employed. This limits the generalization of a task measure and comparison across different studies, unlike the standard clinical studies. Moreover, some quantitative measures are defined for specific robotic setup and assessment task. Variations of robotic tasks (protocol/definition) can affect the reliability and sensitivity of derived measures and associated metrics [20]. Hence, there is a significant need to understand the task dependency of these measures with an aim to develop standard, reliable, valid, and clinically relevant quantitative metrics for tracking the neuro-motor recovery process.

A clearer knowledge of the motor control mechanisms from **neuro-muscular** perspective will provide an understanding of how Central Nervous System (CNS) executes coordinated and skilled movements to design better training paradigms [25, 26]. In the stroke, movements are characterized by *reduced speed, high variability in movement smoothness, and limited range of motion* [8]. Upper arm impaired stroke survivors exhibit **compensatory strategies** such as co-contraction of agonist-antagonist muscle pairs, excessive use of trunk movement, reduced degree of freedom to complete a required task. A short term gain in task performance can be improved by using these compensatory actions. So, to identify if the improvement in the motor task is achieved by true functional recovery or by undesired compensatory movements simply analyzing kinematic/kinetic task measures is not suffice. Since the muscles are the actuators of the movement (that reflect the related motoneuronal activity), examining the muscular activity (collected from surface electromyography (SEMG)) would present a better assessment of motor functions. Monitoring and analyzing the alterations in EMG patterns during a specified task in healthy-control and post-stroke subjects enables us to associate the cause and result of impaired movements [27]. This would give better insight into the movement strategy. However, EMG signal is highly variable as the measured signal activity depends on many anatomical, physiological and technical factors detailed in [28]. Owing to its dependence on many factors, the consistency in measuring EMG becomes a daunting task making this

analysis sometimes unreliable. Also, only the superficial muscles can be measured, and the discharge of adjacent muscles cannot be distinguished. Moreover, the data to be analyzed when we are collecting from multiple muscles for long duration is exhaustive and redundant at times. Hence, the practical difficulties in relying on the EMG data limits its use in some conditions. To overcome this, different computational techniques such as **feature extraction and dimension reduction** are used to identify the useful information. Among these, muscle synergies is the most common method.

Muscle synergy hypothesis is extensively studied and validated in understanding the motor control. Proposed by Bernstein in 1967 [29], synergies are **group of muscles that act together** to simplify a motor task. It is believed to be the basic building blocks of CNS that execute movement by solving the '**Degrees of Freedom**' (redundancy) problem [30, 31]. Recent studies on the muscle synergy analysis with **post-stroke** subjects hint that stereotyped compensatory movements observed in impaired subjects might be due the **alteration** in the synergy patterns, their activation profiles or reduced number of synergies [32–35]. Further, in Roh et al. [36] showed that the amount of alterations in synergy structure depends on the level of impairment. Nevertheless, the **task-relevance of these synergies is yet to be answered** i.e., how does this muscle synergy activation translate into movement and how the alteration in synergy post-stroke effects the movement. Understanding this would provide an insight into the association of muscle synergy activation with endpoint force production resulting in a movement. I expect that integrating this muscle synergy at muscular level to the force production at task level would aid in identifying how CNS controls movements at task-level. Relating muscle synergies with action enable us to identify the compensatory strategies in stroke that are necessary from erroneous ones. This will in-turn aid in developing a **subject-specific training** paradigms with muscle synergies as feedback to augment the recovery process.

1.2 OBJECTIVES

Based on the above discussion, this thesis aims to enhance the benefits of rehabilitation therapy in stroke for **efficient motor learning**. The two main components of therapy are **training and assessment** of motor functions. I propose novel approaches to improve both these aspects by validating and developing different control strategies and assessment methodologies based on motor control principles. The objectives of the thesis are outlined below:

- **Validating the efficacy of a novel control algorithm with underlying principle based on 'Challenge Point Framework' for optimal motor training and improved learning:**

The control strategy that adapts the haptic forces from a guidance (assistance) to a disturbance (distraction) in the movement based on participants motor performance can provide optimal challenge to the stroke subject and hence an improved motor learning. I plan to validate this by assessing the learning and retainment of the therapy benefits in stroke subjects that underwent robotic therapy (with the proposed control strategy) in comparison with the subjects that did conventional therapy alone.

- **Investigation of task variation effects and complementary measures for accurate sensorimotor assessment:**

For a reliable, objective, and accurate quantitative assessment, the effects of task variation on robotic measures and associated metrics is to be studied. This could provide us with guidelines to establish standardized robotic tasks similar to clinical scales for detailed sensorimotor assessment. Adopting physiological measures such as EMG complementary to the commonly used end-effector measures is hypothesized to provide a deeper level of assessment individually.

- **Estimation of the task-relevance of muscle synergies for better understanding of motor control:**

A profound knowledge on the muscular organization and how CNS control movements is critical in understating the movement (and is related disorders). I attempt to realize this by estimating muscle synergies along with task forces from an isometric task with novel methodologies (in healthy control subjects).

1.3 ORGANIZATION OF THE THESIS

The organization of thesis is as follows and is summarized in figure 1.1

- **Chapter 2** presents a literature review on the current robotic devices (features and control strategies) and relevant clinical studies in neuro-rehabilitation. The potential of these devices for assessment of motor functionality along with the limitations is discussed. This chapter also introduces the concept of muscle synergies, their alteration in neuro-pathologies, and motivation on how we can use

them to design a control strategy for effective and subject-specific rehabilitative treatment.

- In **Chapter 3**, materials and methods used in the thesis are explained. The mathematical formulation of different kinematic and physiological signal measures are explained. Also, the formulation of muscle synergies; a step-by-step guide to extract synergies from Electromyography signals using Non-negative matrix factorization algorithm (NNMF) and a modified algorithm proposed in this thesis is presented.
- In **Chapter 4**, I investigate the motor learning benefits of a robotic therapy employing a novel control algorithm that adapts based on the smoothness of subjects movements. Results from a randomized clinical trial (RCT) in stroke subjects with upper limb impairment divided into Robot assisted therapy (RT) and Conventional therapy (CT) groups is presented. The motor performance during the training and follow-up assessments are evaluated with clinical and robotic quantitative measures. The estimation of clinical scales from robotic measures is validated to adopt the later for sensorimotor assessment for tracking the recovery process.
- In **Chapter 5**, the relationship between robotic tasks and their effect on respective quantitative measures is studied. Also, the effect of variation within task definition (in here direction of assessed task) on the subject performance is investigated. I explore the limitations in the translation of robot aided measures as assessment markers for neurological impairment in clinical setting. Based, on these results I propose some recommendations to follow for a more reliable, sensitive and accurate sensorimotor assessment.
- **Chapter 6**, the feasibility of using electromyography (EMG) signal based measure as a complementary assessment metric to generally used end-effector kinematic task metrics is evaluated. Based on the results and discussion from above chapters, we adapt the use of EMG to study muscle synergies in better understanding of basic mechanisms underlying motor control in healthy and impairments in stroke.
- In **Chapter 7** the muscular synergies from an upper-limb isometric task with traditional and modified NNMF algorithm proposed in this thesis is presented. The data is collected from healthy control subjects population. A novel method

to extract synergies called 'Augmented Synergies' is introduced to estimate their influence on task-space forces. The results highlight the potential of employing these synergies in post-stroke to administer subject-specific rehabilitation for maximum therapy benefits.

- In **Chapter 8**, I conclude the thesis summarizing results from the previous chapters and their implications to the research field. I propose future research work that can be carried in the development and refinement of control strategies in addition to the plausible clinical applications.

Figure 1.1: The overview of different studies presented in this thesis summarized

"Nothing in life is to be feared, it is only to be understood. Now is the time to understand more, so that we may fear less. "

Marie Curie

Nobel Prize in Physics and Chemistry (1903 and 1911).

2

Literature Review

This chapter presents a review of the state of art rehabilitation robotics and control strategies employed in such devices. The need for technology-assisted rehabilitation with more sophisticated and reliable control design and assessment methods is thoroughly explored. Muscle synergy hypothesis as a motor control strategy and assessment marker is discussed along with its clinical significance and limitations.

2.1 STROKE: CAUSES AND ITS CONSEQUENCES

Stroke, also called cerebral vascular accident (CVA), is a neurological disorder resulting due to a sudden interruption of blood supply to the brain. According to the World Stroke Organization (WSO) annual report in 2016, it affects 17 million people worldwide annually, resulting in 6.5 million deaths (a second leading cause of death) with more than 33 million stroke survivors. It is the major cause of long-term disability in adults [1] with most of the burden in low-income and middle-income countries [3]. In the USA alone, nearly 7.9 million people experience a new or recurrent stroke annually [37]. High blood pressure, Diabetes Mellitus, disorders of heart rhythm, high blood cholesterol and other lipids, physical inactivity, unhealthy diet, harmful use of alcohol,

hypertension, atrial fibrillation, raised blood lipid levels, obesity, male gender, genetic disposition, and psychological factors are the major risk factors [37, 38]. A stroke causes partial destruction of cortical tissue and results in disturbed generation and integration of neural commands. The interrupted generation and integration of neural commands from the sensorimotor areas of the cortex results in a reduced or even absent ability to selectively activate muscle tissue, which affects motor- task performance. A consequence of disturbed neural command generation in the sensorimotor cortex is impaired arm and hand motor function. Almost 80% of the affected subjects survive, but depending on the location and severity of the lesion, they suffer from different neurological deficits, such as hemiparesis, double vision, numbness, apraxia (altered voluntary movements), post-depression, cognitive deficits, and dysarthria (slurred speech) [39, 40]. Hemiparesis is a full/partial paralysis on one side of the body where the patient loses motor control and faces trouble in moving his/her limbs, and maintaining balance affecting the activities of daily living (ADL) [8]. The ability to perform basic activities of daily living initially is reduced in three out of four patients with stroke. After the acute phase, although most subjects regain their gait ability, 30% to 66% of the survivors cannot use their affected hand limiting their independence [5, 41]. This effects their reaching and grasping movements characterized by decreased muscle activation and weakness [42], disrupted inter-joint coordination [43], decreased smoothness of movement [19]. Stroke rehabilitation is the restoration of patients to their physical, mental and social capability. The motor functions can be restored with rehabilitation and physical therapy [9, 44–47]. Receptivity to therapeutic interventions such as physio therapy and occupational therapy training is shown to aid in the recovery process during the acute phase of stroke [9, 48, 49] and also in chronic subjects [50–52]. Neuro-rehabilitative treatment based on motor control principles promote faster motor recovery in movement coordination and improved motor learning by reducing abnormal synergies to enhance the quality of life of stroke affected subject [53, 54].

Although mortality rate due to stroke has declined worldwide in the past two decades [37], the incidence of stroke, the number of impaired stroke survivors, and the overall global burden of stroke (DALY's lost) continues to rise [3]. It is estimated that the stroke affected population will increase further by 30% between 2000 and 2025 [55]. This growth in the size of the stroke population in developed and developing countries worldwide, coupled with the limited availability of trained therapists and financial re-

sources, means that patients don't always get the required amount of therapy. This limitation is reflected in the progressive reduction of In-hospital rehabilitation during the acute stages of stroke [38, 56], and the rising trend towards delivering therapy in the community through stroke follow-up clinics. In [57], showed that increased medical costs resulted in reduced medication access to stroke survivors raised significantly from 8.1% to 12.7% overall in the USA from 1997 to 2004. This can lead to a recurrent stroke incidence potentially. To meet the demands of increase in aging population, higher life expectancy, and limited availability of therapists; robotic devices for therapy are introduced as a potential solution for effective and subject specific rehabilitative treatment. Hence there is both a need and an opportunity to deploy technologies such as robotics to assist in the recovery process. The paradigm shift for rehabilitation robotics to enhance clinician productivity is explored in [9] and discussed briefly in the next section.

2.2 ROBOT-AIDED REHABILITATION: DEVELOPMENT AND OUTLOOK

Beginning in the late 1980s, intervention of robotic devices for therapy is seen as a potential solution for effective and subject-specific rehabilitative treatment and led to development of "Rehabilitation Robotics" [9, 43]. Rehabilitation Robotics has been defined as a special branch of robotics which focuses on machines that can be used to help people recover from severe physical trauma or assist them in activities of daily living [58].

Using robotic assisted therapy offer following advantages:

- Robot-assisted movements can be performed with minimal or no supervision from therapists. This could provide therapists sufficient time in treating more number of subjects or for devising training regimes that robot alone could not provide.
- The nature of exercises (and difficulty) in robotic therapy can be tailored to each subject based on their ability. Sensory feed-backs integrated to such robotic devices motivate the subject to perform tasks.
- The patients assume a central role in their rehabilitative training as they have the control and the perception of task performance and improvements.
- The robots provide a real-time, objective, continuous, and quantitative sensorimotor assessment of the subject during the training, based on the task execution. This gives the therapist more reliable information on devising an efficient training paradigm relieving him from performing additional assessment tests.

Table 2.1: Advantages of Robot-assisted Therapy in comparison with Conventional Therapy

Robotic Therapy	Conventional therapy
1. Supports therapist to reduce workload	1. Limited by manpower
2. High reliability	2. Poor repeat-ability of movements
3. High amounts of repetitions / intensity	3. Limited number of repetitions
4. Adaptive assistance or resistance forces can be implemented	4. Difficult for severely affected patients
5. Quantifiable and objective assessments	5. Ordinal or therapist dependent
6. Highly motivating for some with interesting visual games	6. Motivation dependent on patient-therapist relationship
7. Detailed timed sensory feedback comparable across sessions and subjects	7. Subjective feedback
8. Scope for new and better interventions	8. Limited progress in new therapy

The advantages and limitations of robotic therapy over conventional therapy is summarized in the following tables 2.1 and 2.2

The upper extremity rehabilitation device MIT-MANUS developed by Krebs and Hogan at MIT is one of the earliest rehabilitative device aimed at improving the range of motion, co-ordination, smoothness of the movement and strength of muscles [9].

Table 2.2: Limitations of Robot-assisted Therapy in comparison with Conventional Therapy

Robot-assisted Therapy	Conventional Therapy
1. Costly (short-term)	1. Less costly (short-term)
2. Space consuming	2. No big space requirements
3. Risk of obsolescence	3. No risk of obsolescence
4. Devices specific for individual limbs	4. Treatment of any body part
5. Lacks degree of feedback or flexibility	5. High degree of feedback or flexibility
6. Limited communication and feedback	6. Communication dependent on therapist

Figure 2.1: Few rehabilitation robotics developed in past decades that are currently in the market [9]

The MIT-Manus, one of the pioneer UE robot (commercially available as InMotion2 Shoulder-Elbow Robot) has been tested in more than 250 patients and results suggested a 30% improvement within 6 weeks into therapy [59, 60] for simple point to point reaching tasks, refer figure 2.1. This is followed by the development of many such devices for hand [61–63], wrist [64–66], upper arm (elbow and shoulder) [59, 67–70]. An extensive review by Maciejasz et al. [13] with over 120 upper limb robotics and another study by [71] on assistive devices for lower extremities manifest the growth in the development the technology assisted systems for rehabilitation. Although, the robot assisted rehabilitation is in practise since 30 years, it is not widely used due to the high cost and maintenance, lack of resources, and more research needs to be carried to understand what is the best robotic paradigm and protocol for optimal recovery. Also, the transfer of these learning benefits through robotic training to activities of daily living and hand capacity functions appears to be limited [72, 73].

2.3 HOW DO THESE ROBOTS PROMOTE MOTOR LEARNING ? - A BRIEF REVIEW ON CONTROL STRATEGIES

In the following section, an overview of the current control approaches in rehabilitation robotic devices to optimize recovery is discussed with respective studies and their findings. Thereby, the selection of the studies is not constrained to stroke patients as well as studies with healthy participants. Over the last years, along with the development of technology based devices for rehabilitation, equal efforts were put into the research of control strategies and interactions between these robots and the patients [74].

The first and most common training paradigms for motor rehabilitation used an assistive controller following a guidance. Generally speaking, the guidance approach aims to reduce the severity of errors or even prevent the patient from making errors.

In this scheme, performance of the patients is enhanced by (haptically) assisting the patient in the supposed movement or limiting a free movement by e. g. barriers, thereby the assistance can range from only supporting the patient in the movements, to fully moving the patient's limb while the patient could remain passive [75, 76]. The rationale behind this approach is still applied in research are manifold [7, 77]. By moving the limb of a patient in a way that the patient would not be able to move independently, it is hypothesized the training provokes new somatosensory stimulation and initiates brain plasticity [78, 79]. Additionally, muscles and tissue might get stretched which leads to a reduction in spasticity [80] and by demonstrating a movement pattern, the patient gets helped in learning this movement [81].

Although providing too much assistance might have a bad influence of the motor learning improvements of patients and causes slacking [82], the paradigm “**assist-as-needed**” emerged [83–85]. The basis of this philosophy is from “**Challenge Point Framework**”, developed by [86], which states that *‘subjects learn better when they are optimally challenged’*. In such a scheme, the assistance controller adapts the interaction forces in a way such that the robot assists only as much as it is necessary for the patient to fulfill the task. The adaptation criteria can be based on muscular activity (EMG), e. g. [87], impedance (e. g. assistance kicks in once a certain error threshold is reached [88]) or a performance metric [81]. Out of these, the adaptation based on a performance metric was shown to be more feasible with better learning results. Marchal-Crespo and Reinkensmeyer proposed in their study with a steering task in a virtual environment a ‘guidance-as-needed’ control algorithm that adapts the force applied to the user’s hands depending on the tracking error between the real position on the virtual path and the desired position [81]. Thereby, it aims to increase the guidance with large errors and to decrease the guidance with the user making fewer errors. Therefore, the guidance force is dependent on the tracking error as well as an adaptive control gain.

Apart from the ‘**assist-as-needed**’ approach, several studies have shown that a degradation of the performance might help patients in motor learning or recovery, what seems initially contradictory to the formerly established approach. In [75], a study with healthy subjects was conducted that compared the learning results of an error-amplification and a haptic-guidance algorithm based on a time-based task with a 1DOF device. Indeed, It is found that skilled subjects benefited significantly more from

error-amplification training than haptic guidance, while haptic guidance helped less skilled subjects relatively. Few studies have validated this method in control subjects. For example, in [89], applied the performance degradation not by enlarging the healthy user's performance error but by disturbing the user in the movements. Out of the four different conditions tested in the tracking experiment (only vision/no haptics, progressive haptic guidance, haptic disturbance with a) repulsive force, b) noise-like force), the noise disturbance achieved the best performance in the retention test, whereas during the training phase the guidance group performed best. As the repulsive force is directly related to the tracking error, it can be understood as error dependent disturbance in contrast to the random noise disturbance. This study provides an important insight into different performance degradation methods and compares them with the conventional guidance paradigm. Recently in 2017, Crespo et al. [90], studied how the nature of task effects the motor learning by comparing different interaction strategies in discrete and continuous tasks (based on task duration). It is shown that for a discrete movement training, the subjects' performance improved with haptic guidance, whereas the error amplification strategy had better motor learning and retainment results.

Among the above discussed control approaches for rehabilitation devices, the 'assist-as-needed' approach revolutionized the motor learning guidance approach, and the new contra-intuitive ideas that performance degradation might augment the learning have a very high potential. The field lacks a further evolution. It has been shown that the learning outcome can be improved by adapting the assistance depending on the individual subject and the subject's daily condition. In addition to that, there is evidence that the motor performance of presumably less impaired subjects might be even further promoted by disturbing the subjects in their movements rather than supporting them. Nonetheless, no study so far has combined these two approaches by adapting assistance and disturbance. Closing this gap, might adjust more specifically to the patients' performance alterations and potentially reach a larger patient group. This remains to be tested in a clinical setting with neurologically impaired subjects in a longitudinal study. To our understanding, no study so far has employed challenge point frameworks based controller to offer an optimal level of challenge for training in stroke subjects. Hence, it is necessary to investigate the efficacy of this new approach towards a subject specific neuro-motor recovery.

2.4 POTENTIAL OF REHABILITATION ROBOTIC DEVICES AS SENSORIMOTOR ASSESSMENT TOOL IN A CLINICAL SETTING

Robotic rehabilitation in upper limb impairment is shown to have modest gains in reducing motor impairments in comparison with the conventional rehabilitation therapy. Duncan et al. [91] reported that only 33% to 70% of the stroke patients regain useful arm ability post-therapy. The limited recovery and retainment might be due to the limited amount of training offered to the affected population which can be improved by providing an optimal intensity of training. However, an arguably if not more important factor contributing to this limited improvement can be attributed to the partial understanding and incomplete assessment of the disability itself. Technology aided measures can offer a promising solution to overcome these limitations and yet they have been explored less thoroughly.

2.4.1 TOWARDS TECHNOLOGY-AIDED QUANTITATIVE (KINEMATIC) ASSESSMENT FROM CONVENTIONAL CLINICAL OUTCOME MEASURES : OPPORTUNITIES AND SCOPE

The conventional approach to assess sensorimotor control is through standard clinical procedures that most often utilize ordinal measurement scales where therapist assigns a score after observation of patient's movements in different predefined tasks - some gold-standard examples include Fugl-Meyer [92] and Action Research Arm Test (ARAT) [93] are estimated by physical observation of therapist, while performing standard set of defined tasks. Although these measures are easy to use and are widely accepted, standardized, and validated they are still subjective and suffer from low resolution (insensitive to small but significant changes) which is typical of ordinal scales [17, 94]. Also, clinical assessments are usually repeated only at a few stages to monitor the patient's status and progress. It also does not provide sufficient details and insight into the nature of the disability. Furthermore, the time required to perform manual assessment discourages their regular administration to track and understand motor recovery in continuous terms in affected population.

Technology aided measures can offer a promising solution to overcome these limitations. The information from the robotic sensors such as their kinematic profile, applied forces, joint movements can be used in providing the feedback to users/therapists, in quantitatively assessing the impairment to keep progress of the recovery process,

and in designing better rehabilitation paradigms. Robot-aided assessment using integrated sensors offers the possibility to have more continuous (high resolution measures) and this does not require additional setup and time because sensory information can be collected simultaneously during regular therapy from inbuilt sensors. Functional abilities while performing various tasks on robotic setup can be derived from raw sensor data and parameters or from feature extracted with processed data. Being (semi-)autonomous, technology based solution are potentially more objective (therapist independent), sensitive (able to detect changes) and less prone to human error/subjectivity [17, 20, 95]. However, the lack of evidence in terms of reliability and efficacy limits the use of such technology based measures as an objective assessment tool for sensory motor impairment. Multiple studies have adapted these measures to track and assess the recovery process. Moreover, few studies attempted at identifying the relation between robotic scales and the clinical scales [96, 97] with an aim to predict later from sensory based tasks. Further, data analysis techniques such as principal components analysis (PCA) have been applied to identify clinically relevant robotic metrics [98]. A detailed review of robotic metric employed for upper-limb assessment and hand function are presented in [22, 99, 100]. However, this form of assessment has yet to be fully established and validated when compared to the gold standards, for use in standard clinical practice.

The main challenge is in identifying and evaluating the robotic metrics that are valid, clinically relevant, reliable, robust and sensitive to changes from the robotic tasks independent of robotic setup. To date, due to multiple variations of assessment tasks (point-point, shape drawing, shape tracking, isometric assessment etc.,) and varying outcomes of quantitative measures as a consequence. The use of technology based assessment of upper limb motor function is still limited [101]. Understanding how variations of task can affect the reliability and sensitivity of a measure and vice-versa is critical for devising and integrating objective assessments in clinical settings. Ambiguity in generalizing these task measures in different studies is arguably one of the major reasons hindering the widespread use of such measures. For example, it is not clear if a (metric/measure) used in one task will be reliable for another task or conversely a measure considered reliable for one task will be equally useful for another task. Moreover, there are many metrics (methods developed) to assess one measure and different studies use different methods various studies [20, 22]. This limits the comparison of the robotic measures across different studies unlike the standard clinical studies. Further, it hinders the trans-

lation of robotic scales for clinical use. So, it is highly desirable to investigate the effects of task variations on robotic measures and associated metrics.

2.4.2 ELECTROMYOGRAPHIC SIGNALS COMPLEMENTARY TO TASK METRICS IN ASSESSING MOTOR FUNCTIONS TO DETECT COMPENSATORY ACTIONS

In stroke, movements are characterized by reduced speed, high variability in smoothness of movement, and limited range of motion [8] that can be identified by evaluating the kinematic task performance. Additionally, in case of upper extremities, the most commonly observed stereotyped patterns are: flexor synergy (simultaneous shoulder abduction and flexion of the elbow), and the extensor synergy (simultaneous shoulder adduction and elbow extension) (Radomski and Latham 2008). In addition to stereotyped movements, post-stroke subjects also exhibit abnormal joint coupling in the upper and lower limbs and non-typical trunk movement used as a compensatory strategy in reaching tasks [8], loss of coordination among agonist and antagonist muscles [102] in both affected and unaffected side reduction in maximum voluntary strength [103], altered muscle activity patterns in spatial and temporal domains. A short term gain in task performance can also be improved by using these compensatory actions. So, to identify if the improvement in the motor task performance or learning is achieved by true functional recovery or by undesired compensatory movements simply analyzing kinematic/kinetic task measures is not suffice. Since the muscles are the actuators of the movement (that reflect the related motoneuronal activity), examining the muscular activity (collected from surface electromyography (SEMG)) would present a better assessment of motor functionality. The main advantage of measuring electromyographic(EMG) is that the linear envelope of the EMG gives an appropriate estimate of the torque(force/tension) generated at the joint. Different features from electromyography(EMG) signals are extracted to predict the movement and to understand motor control strategies [104, 105]. Hence it is strongly recommended to assess muscular activity in combination with task-space kinematic measures for developing more effective and subject-specific neuro-rehabilitation paradigms along with conventional clinical scales.

However, EMG signal is highly variable as the measured value depends on many anatomical, physiological and technical factors. Owing to EMG dependence on many factors, the consistency in measuring EMG becomes a daunting task making this analysis sometimes unreliable. The summary of all the factors categorized as causative,

intermediate and deterministic are presented in [28] and unfortunately at the present state of the art not all factors can be properly regulated. Hence it is necessary to understand the source and influence of the factors and aim to collect a consistent and well defined EMG signal. The choice of electrodes (diameter, size and shape) and amplifiers (gain, impedance, and filters), external noise, difference in location of muscle belly and placement of electrode site, cross talk due to the nearby muscles and tissue thickness, physiological changes and temperature are some of the main factors that influence the EMG signal. Also, the data to be analyzed when we are collecting from multiple muscles for long duration is exhaustive and redundant at times. To address this, different computational methods to extract useful information from EMG signals have been developed in recent times [106]. 'Muscle synergy' analysis is the most common one aimed at describing the muscular organization at motor control level. This is further discussed in the below section.

2.5 MUSCLE SYNERGIES HYPOTHESIS IN MOTOR CONTROL STUDIES

'It takes 12 facial muscles to smile' - the simple daily activity of smiling involves a control of 12 muscles; This makes us wonder how the central nervous system(CNS) performs different complex actions involving multi-joint movement, numerous muscles etc., with such ease, flexibility and perfection in very little amount of time. Motor control is the active co-ordination of muscles and limbs to perform a task guided by neuro-muscular system.

The translation of sensory information and motion planning to execute a desired task by activation and co-ordination of various muscles along with perception and sensory feedback requires the interaction between Central Nervous System (CNS) and musculoskeletal system. Hence motor co-ordination, being one of the fundamental and intricate aspects of control is the optimal combinations of kinematic (direction, trajectory, joint angles) and kinetic (forces, joint torques) body movements such that the required task is achieved in a smooth, efficient, and in timely manner. This involves the integration of proprioceptive information detailing the position and movement of the musculoskeletal system with the neural processes in the brain and spinal cord which control, plan, and relay motor commands to the muscles. But the fundamental problem or complexity of motor control paradigm lies in the very well known **"Degrees of Freedom (DOF)"** problem, which states that there are many solutions to achieve a single task

and how the CNS '**selects**' a subset of these near-infinite DOF's. One of the proposed solution by Bernstein is "**Muscle Synergy**" hypothesis [107]. A hierarchical control is proposed where the higher levels (cortical level) activate the lower levels i.e. 'synergies', a group of muscles that are constrained to act together. Muscle synergies are low-level description of neurally encoded muscle patterns. According to this, the computational complexity of motor co-ordination is simplified by activating few groups of co-activated muscles, called synergies instead of individual muscles. This theory could also explain the elimination of un-coordinated movements as the group of muscles act as a single unit, and synergy tries to eliminate some muscle activation patterns that might give rise to uncoordinated movements [108]. In Independent control of each muscle, a slight change in one muscle activity demands fine tuning of all other muscles to avoid the occurrence of uncoordinated actions and if they are grouped together, like a synergy the co-activations changes would compensate or assist to execute a controlled movement even in case of a perturbation [108]. Electromyogram (EMG) signals are believed to provide the evidence to this hypothesis, many muscles during natural behaviors can be reconstructed by linearly combining a few synergies, identified by dimension reduction algorithms. The details of such techniques (formulation and analysis), validation of this theory in different species and their clinical significance is discussed below.

2.5.1 EXTRACTION OF MUSCLE SYNERGY USING DIMENSION REDUCTION ALGORITHMS

A muscle synergy is defined as the coordinated recruitment of a group of muscles with specific activation waveform [30] to perform a desired task. Synergies can be observed by decomposing the pre-processed Electromyogram (EMG) signals. Followed by pre-processing steps: i.e rectification, low-pass filtering, the muscular activity is decomposed to synergy and their co-activation patterns. time-invariant muscle synergy (w_j) is an M-dimensional vector capturing the specific activation balance of all the muscle activation during the task. The muscle activation vector $m(t)$ is decomposed to a linear combination of N synergies ($w_j, j = 1 \dots N, N \leq M$) and their corresponding activation profile $c_j(t)$. The muscle components of w_j are fixed, hence we refer to w_j as time -invariant synergies. The dimension is reduced from M (number of muscles) to N (synergies) and the synergies are activated by their respective time-varying coefficients. The time invariant

muscle synergy can be formulated as:

$$m(t) = \sum_{j=1}^N c_j(t) * w_j \quad (2.1)$$

where,

- $\mathbf{m}(\mathbf{t})$: M-dimensional vector of muscle activation, a time profile of pre-processed EMG across all M muscles.
- $\mathbf{c}_j(\mathbf{t})$: the time-varying temporal coefficient for the j-th synergy
- $\mathbf{w}_j$: time-invariant synergy specifying the balance between the muscle activations.

In the above example, $m(t)$ a five dimensional muscle vector is decomposed to three time- invariant synergies(w_j)[$j=1,2,3$], and their corresponding time activation profiles $c_j(t)$ reducing the dimension by two. From the above figure, it can be observed that, one muscle can be recruited in multiple synergies, corresponding to the fact that the motoneuronal pool of every muscle is activated by many inter neuronal groups. In other words, time invariant synergies (w_j) are activated by CNS through time varying activation commands $c_j(t)$ resulting in the corresponding muscle activity.

Dimension reduction algorithms are adapted in extracting synchronous synergies from multi-channel EMG data. The commonly used techniques are principal component analysis (PCA) [109, 110], independent component analysis (ICA) [111–113], Factor analysis [25], and Non-negative matrix factorization (NNMF) [114–116]. PCA and ICA do not impose non negativity on the synergy components because of which the positive and negative muscle components of synergy arise and they could be interpreted as the excitatory (positive components) and inhibitory (negative components) synapses between the synergy coding inter neurons and the motor neurons. PCA algorithm extracts synergy vector such that they are orthogonal and the first component called principal synergy is chosen in the direction with maximum variance described by the EMG signals. ICA algorithm imposes the statistically independence condition on the synergies. Non-negative matrix factorization (NMF) enforces the synergies and their activation patterns to be non-negative. Factor analysis (FA) seeks the smallest set of synergies that account for the common variance in a set of muscles. Tresch et al. [117] tested the performance of these algorithms to extract the appropriate number of muscle synergies in simulated data sets and suggested that, PCA is generally poorer than other algorithms. In data which is mixed signal-dependent

noise, ICA's performance was also impaired significantly. The synergies extracted by PCA or ICA tend to be holistic (i.e. non-zero activation components are present in most of the recorded muscles) and thus less physiologically interpretable. NNMf does not have independence' or 'orthogonality' condition, thus supports that activations of multiple synergies are correlated [118]. As a result of the non-negativity constraints, the extracted synergies tend to be sparse (i.e. only a few of all muscles have non-trivial activation components in a synergy) rather than holistic. From physiological approach, muscle are modelled as a springs that can only be pulled or have positive amplitude, hence the non-negativity constrain aids in reliable understanding of the muscle synergies. Hence in muscle synergy analysis, **negative matrix factorization** is most popular algorithm in deriving the muscle synergy owing to its sparse representation and part-by-part decomposition.

2.5.2 INVESTIGATING MUSCLE SYNERGIES AND THEIR IMPLICATIONS

A significant amount of experiments validating muscle synergy hypothesis has been conducted in frogs and rats [118–120], cats [121–123], primates [124–126]. In humans, its has been extensively investigated during dynamic reaching tasks [116, 127, 128], isometric force matching tasks [129, 130], locomotion [7, 131–133], posture control and maintenance of balance [26, 134]. Few studies have investigated synergy organization of the CNS during onto-genetic development [135] and observed that the two temporal synergies identified in stepping neonates are retained through development, added by two new synergy patterns in toddlers. The effect of aging has been studied by studying the muscle activity in young and elderly people, where no significant effect of aging on synergy compositions and activation is found [136] This section provides a brief review on the existing state of art in muscle synergy studies and its implications

- **Robustness of muscle synergies: similarity across subjects and tasks**

In a study by Tresch et al. [120] a small set of synchronous muscle synergies were used to generate large number of reflexive motor patterns in cutaneous stimulation of the frog hind limb; Moreover, micro-stimulations of the spinal cord produced similar muscle synergies to natural movements reflecting a consistent modular organization. The experiments by D'Avella et.al [137] revealed that a few time-varying synergies explain the muscle patterns required for a frog kicking task in different directions. The synergy identification is generalized to a wide range of natural tasks such as jumping, swimming and walking in frogs. It is observed that

some synergies are shared across these (jumping, swimming, and walking) tasks along with behavior specific synergies [138]. The muscle synergies are identified in human reaching tasks by observing muscle activation patterns during natural reaching movements in different directions [106] and speed [139]. The synergies are observed to be similar across subjects and the difference in speed and direction did not have any significant variation. Another series of experiments in isometric reaching tasks, by Roh et al. [129] showed that a set of synergies could reconstruct the average patterns of muscle activation observed during isometric forces production across different healthy control subjects. Hence a similarity in synergies irrespective of direction, speed and subject is observed in reaching tasks. This shared and task specific synergies is also observed in human locomotion [131], balance control [134]. The synergy composition might slightly with subject and the subject specific synergies might be accounted to differences in limbs bio mechanics of individuals. appropriate modulation of the synergy activation.

- **Effect of sensory feedback on muscle synergy** The effect of sensory feedback in the muscle synergy organization is examined by Cheung et al. [140] where synergies are extracted from loco-motor behaviors of bullfrog before and interrupting its sensory pathways (i.e. deafferentation). Synergies are conserved in both the cases, and when sensory feedback is removed, an additional synergy was required to explain the muscle activation pattern. These results support the existence of synergies as centrally organized structures modulated by sensory inflow.

2.5.3 LIMITATIONS IN VALIDATION OF MUSCLE SYNERGY HYPOTHESIS

Given the current scenario, it is a difficult task to prove if synergies are centrally organized structures or phenomenological output of motor coordination required for the task due to biomechanical constraints. Kutch et al. [141, 142] designed carefully thought experiments and simulations to show that muscle synergies can be rather flexible and exist even when nervous system does not have direct control. Similar result were also found in [143]. The neural origin of these synergies is investigated in few studies [144, 145], although their existence is still an open question [146].

Also, it is equally important to understand how muscle synergies manifest onto task forces at end-effector. Ting and colleagues introduced the concept of 'functional syner-

gies' to study the relation between the activation of muscle synergies and endpoint task forces by applying dimensions reduction on the change in forces similar to EMG [121]. High correlation between the synergies activation and force basis vector indicated that each synergy resulted in a unique endpoint force vector. In another study, to investigate this muscle synergy association with the task performance and force control, Berger et al. [147] compared trajectory paths and other kinematic parameters in an isometric force reaching task, in a virtual environment where the animated cursor movement is manipulated according to the a) kinetic force for the end-effector, b) force estimated from EMG (by regression), and c) the last case with force estimated by reconstructed EMG using synergy control. Results indicated no significant difference in joint angles, end point errors, etc., in all the cases, implying the lower dimension of force control by muscle synergies. However, this still do not provide any neural relation to the synergies and force at task space. According to Signal Dependent Noise (SDN) principle by [148], a motor output is composed of desired endpoint force and fluctuations. It is hypothesized that if motor output is corrupted by neuronal noise, it manifests as fluctuations at motor level and is scaled with respect to the magnitude of the desired force/motor activity. Hence these fluctuations could reflect the lower level neural activity and might constitute the underlying the muscle properties such as mechanical muscle action direction or the evidence for the neural existence of muscle synergies. Hagio et al. [149] through an isometric force matching task around the ankle, obtained a the correlation between the variability in task space forces to sum of synergy activation and also between the time sequence of synergy activation and task force traces. All such studies attempt to establish relation to the forces and muscle synergy either by correlation or regression analysis after processing them as separate entities. Nevertheless, this is not suffice to how to explain the task relevance of these muscle synergies, i.e., to directly correspond the task force to the estimated synergies. Moreover, in calculation of synergies, most of the studies normalized the input muscle activity to have unit variance, to prevent any bias towards highly-variance muscle; but, according to SDN and other minimum-variance hypothesis of motor control, "variance" in a signal might consist of vital information and normalizing the signals to have unit variance might devoid us from analyzing critical information. In summary, muscle synergies can be considered as feasible physiological mechanisms for the implementation of near-optimal motor behaviors. However, further research needs to be carried in developing better algorithms that can explain the task association, and also account for the variance in a task [150].

2.5.4 CLINICAL SIGNIFICANCE OF MUSCLE SYNERGIES IN NEURO-PATHOLOGY

Muscle synergies analysis is considered as helpful tool in interpreting the onset of altered movements and their influence on the muscle activity and functional abilities during motor tasks. The post-stroke alterations in different motor tasks have been studied in human upper arm [32, 36, 151, 152] and in lower extremity [131, 153–155]. The initial studies with mildly affected stroke subjects showed that the muscle synergies were preserved with most of the synergies remaining similar to that of healthy subjects strengthening the low dimensional modular organization of muscle coordination approach. The change in the performance or disturbance in the smooth performance of the task may be attributed to the abnormal recruitment of muscle synergies.

In Cheung et al. [32] the muscle synergies were identified from 12–16 upper limb muscle activity during different motions involving single and multi-joint movements of elbow and shoulder joints. The analysis was performed on both unaffected and the stroke-affected arms of subjects with hemiparesis, with mild to severe lesions. Despite heterogeneity in cerebral lesion location and size, the muscle synergies were comparable to that observed in healthy group inferring movement impairment is due to the interference in the neural activation pattern that recruit synergies. This study was extended to find the differences in mildly to moderately impaired stroke survivors with lesions in the motor cortical areas. Although, task performance difference is observed in both the cases muscle synergies from the stroke-affected arm were similar to those of the unaffected arm [32]. This observation is congruence with the hypothesis that muscle synergies are encoded in the brain stem or spinal cord and after a stroke, altered commands from the supra-spinal areas might result in abnormal motor behavior due to altered activation of the spinal modules [144, 155]. However, in contrast the same study when extended to severely impaired stroke patients [32, 33] showed that fewer synergies were sufficient to explain the variance of EMGs recorded from stroke subject in the affected limb during reaching motion. The new/altered synergies were identified to be a merging or fractioning of multiple healthy muscle synergies. This explains the existence of ‘**stereotyped movements**’ where the number of degrees of freedom post-stroke is reduced, impeding the motor performance developing abnormal synergies.

Similar post stroke synergy analysis was carried out by Roh et al. [35, 36] from an upper limb 3-D isometric force target matching task in reaching different directions

among chronic and moderately impaired subjects. Four synergies were able to reconstruct the EMG signal in both healthy and impaired subjects efficiently. Synergies were divided into elbow (extension and flexion synergies) and shoulder synergies (adduction and abduction) and it was observed that the elbow synergies are mostly preserved in both the groups, but the shoulder-related synergies were altered in all three impaired groups (mild, moderate and severely) of stroke survivors compared with that of control group.

In conclusion, there is no consensus regarding the alterations of stroke w.r.t to muscle synergies and their activation patterns that hinder the motor efficiency and more studies are required to validate any of these facts, based on more varied tasks and conditions. Muscle synergy analysis can be taken as a measure to identify abnormalities in muscle coordination in terms of an altered number, structure, and activation of muscle synergies. This provides a basis for a neuro-rehabilitation study for stroke patients to design protocols that focus on reducing the abnormal activation patterns [156–158].

An expert is a person who has found out by his own painful experience all the mistakes that one can make in a very narrow field.

Niels Bohr

1992 Nobel prize in physics for quantum theory

3

Materials and Methods

This chapter presents the methodology of different analysis and materials used in this thesis. For the first part with clinical studies, the apparatus and data analysis techniques described in chapter 4, 5, 6 are presented. This is followed by the definition, formulation, and various steps involved in muscle synergy extraction from surface electromyography (SEMG) signals. A novel methodology of synergy extraction adapted in chapter 7 is discussed in detail.

3.1 APPARATUS AND EXPERIMENT SETUP

3.1.1 H-MAN ROBOT- AN UPPER LIMB REHABILITATION ROBOT

The experimental apparatus used for our study is the 'H-Man' robot shown in Figure 3.1. It is a compact, planar two degree of freedom robot designed by Campolo and colleagues [70] at Nanyang Technological University. Characterized by a simple mechanical design and a H-shape cabled differential transmission, it was employed in post-stroke rehabilitation therapy for rehabilitation of sensorimotor functions [159] and for human motor control experiments in healthy participants [27, 159]. The unique features of H-man are its low cost, ease of control owing to its homogenous workspace, lightweight (about

Figure 3.1: A) Current version of 'H-man', a compact robot designed for the training and assessment of upper-limb impaired stroke population B) A stroke subject using H-MAN embedded with visual feedback developed in UNITY for therapy at Tan Tock Seng Hospital, Singapore

7kg), and intrinsic safety. Planar H-shapedS cable-driven differential mechanism transmits motion from motors to a handle, allowing for free and safe movements in the horizontal (XY) plane. By using mechanical stoppers, motion can be restricted to a particular direction (i.e., X, Y, XY diagonal). The system can be used in passive mode (motors off) for simple assessment tasks and in active mode (motors on) for training motor functions. During training, assistance (through haptic interface) during reaching movements can be provided by a virtual (damped) spring exerted at the handle, that can pull a subject's hand towards a desired target or in a desired path. System parameters like stiffness (K) and the damping factor (B) of the virtual spring can be modulated online, giving the opportunity to the therapist to provide training to the participant according to the need/ progress. A visual environment that is developed using any game engine, (here UNITY) provides the patient with different gaming environments to perform goal directed reaching tasks correlated with the H-man manipulandum movements, refer Figure 3.1. In case, the participant is unable to reach the specified target, assistance is provided to complete the task by increasing the stiffness (k) that acts as attractive elastic force. Both assistive and resistive forces can be given as feedback to the user based on the control strategy employed in the training paradigm. The progress can be tracked by analyzing the various performance metrics from the user's kinematic profile. From a rehabilitation perspective, this device can be employed in decentralized settings, to participants with less access to therapists and clinical assistance. With validated assessment protocols [160], it can provide continuous updates about motor progress to the patient, their caregivers, and the therapist. The clinical feasibility of this device was val-

idated with 12 stroke patients and 20 control subjects in [94].

3.1.2 ELECTROMYOPGRAPHY DATA ACQUISITION SYSTEM

The muscle activity is measured by the surface Electromyopgraphy (sEMG) signals acquired through Biopac MP150 module (flow Monitor) which contains an inbuilt differential amplifier and band-pass filter as shown in. The MP150 is a high-speed data acquisition system from Biopac, embedded with the Universal Interface Module, UIM100C. It acquires and amplifies muscle potential collected from the electrodes placed on the interested muscles. Each EMG 100C module is employed for single muscle and it acts as a channel connected to the acquisition device MP150. For all the experiments in this thesis, amplifier settings of gain (k) =500 and band-pass filter specifications of 10-500Hz cutoff frequencies, i.e., 500 Hz cutoff frequency in LPF (low-pass filter) and 10 Hz cutoff frequencies in HPF (high-pass filter) respectively are adapted in a differential mode. So the SEMG signal is pre-amplified and is devoid of the high frequency noise.

Data Collection Protocol and Electrode Specification: EMG collection procedure is standardized in order to make the results more comparable and encourage the creation of large knowledge base on the use of EMG for various functions [28]. The data collected in the experiments is reported according to ISEK standards [161] and the Surface EMG for NonInvasive Assessment of Muscles -SENIAM [162] standards are followed in the electrode placement on the muscles. The first step is skin preparation: i.e abasing followed by cleaning the skin with alcohol. After adequate skin preparation, Meditrace 200 monitoring electrodes are used in SEMG recordings and their specifications are reported according to The International Society of Electrophysiology and Kinesiology (ISEK) in reporting the EMG data The specifications of Meditrace 200 monitoring electrodes used for the experiments presented in this thesis are:

- Electrode material: AgCl
- Electrode size: 30mm diameter (disc shaped)
- Inter-electrode distance: 10-20 mm depending on the length and type of muscle
- Gel type: Solid Gel Electrode
- Electrode Dimension: 20 mm

3.2 FORMULATION OF KINEMATIC TASK PERFORMANCE METRICS FOR SELF-PACED REACHING AND TRACING TASKS

To assess the task performance of participants from robotic task during reaching or tracing tasks studied in chapter 4 metrics/features were derived from the kinematic data collected from the integrated sensors. The raw kinematic data (position and velocity) during a reaching motion was filtered using a low pass filter (Butterworth: 6th order, cut-off frequency F_c : 20Hz, sampling rate, F_s : 1000Hz).

Overall, 30 quantitative performance indices (metrics) from literature [17, 20, 98, 163] were analyzed to assess the participants sensorimotor functionality. Out of these, few metrics describing the smoothness, temporal efficiency and task deviation error constructs were identified based on reliability and sensitivity analysis. For example, to assess the smoothness, different metrics such as SPARC [164], spectral arc length (SAL) [165], log jerk [23], number of peak velocities and MAPR [24] were evaluated and high correlation was observed between them, thus analyzing one metric was adequate to remove any redundancy in the information. A similar procedure was followed for the temporal efficiency: velocity related metrics such as Time to peak velocity, peak velocity, etc., were evaluated. To measure task deviation error: length of curves ratio [8], RMSE error [166], axis ratio [167], deviation angle [20], area between curves etc., were calculated. Among these, few of the measures used in this thesis are presented below:

3.2.1 QUANTITATIVE MEASURES OR TASK PERFORMANCE INDICES

1) SPECTRAL ARC LENGTH:

Smooth movements is a characteristic feature of healthy and well-trained motor behaviour and are believed to be a fundamental property of motor control principles. Spectral Arc Length (SAL) [19] is a dimensionless smoothness measure derived from negative arc length of the amplitude and frequency-normalized Fourier magnitude spectrum of the velocity profile over the applicable bandwidth for human actions.

$$SAL = - \int_0^{\omega_c} \sqrt{\left(\frac{1}{\omega_c}\right)^2 + \left(\frac{d\hat{V}(\omega)}{d\omega}\right)^2} d\omega \quad (3.1)$$

Where $[0, \omega_c]$ is the frequency band of interest (typically ω_c is 20 Hz for normal human movements).

Figure 3.2: Speed profile and its respective Fourier magnitude spectrum. Figure is adapted for illustration from [22]. A) A smooth movement (top row) is characterized by a less no. of peak velocities and hence a simpler Fourier spectrum. B) An unsmooth movement (bottom) is characterized by large sub movements and a complex Fourier spectrum

The Fourier magnitude spectrum of the velocity signal $v(t)$ is given by $V(w)$ and is normalized to :

$$\hat{V}(w) = \frac{V(w)}{V(0)} \quad (3.2)$$

A higher SAL value indicates a better smoothness i.e., less number of sub-movements.

2) SPECTRAL ARC (SPARC)

SPARC (Spectral ARC) developed in [164] is the modified version of SAL. In contrast to SAL, SPARC is independent of temporal movement scaling, and retains the good sensitivity and reliability of the SAL. The difference in SPARC from SAL is the selection of **cutoff frequency** ω_c ; The SPARC extends SAL in that ω_c is adaptively selected based on a given *threshold* $\bar{V}$ and is *upper-bound* by ω_c^{max}

$$\omega_c \triangleq \min \left\{ \omega_c^{max}, \min \left\{ \omega, \widehat{V(r)} < \bar{V} \quad \forall \quad r > \omega \right\} \right\} \quad (3.3)$$

3) TIME TO PEAK VELOCITY:

The temporal measures provide an understanding of the adapted motion planning strategy as described in [18, 168]. A typical healthy subject movement is characterized by

Figure 3.3: A typical bell shaped velocity profile in a reaching task. The onset time is the time instant when the tangential velocity exceeds the 5% of the maximum velocity (V_{peak}) and offset time (V_{offset}) is the time velocity drops below the threshold of 5% of the maximum velocity (V_{peak}).

a symmetric bell-shaped velocity profile. As the planar reaching task or tracing tasks carried out in experiments conducted across this thesis impose no constraints on the velocity range, time to complete the task as well as the maximum distance, a normalization of temporal measures to assess and compare across the subjects is required. The onset time is the time instant when the tangential velocity exceeds the 5% of the maximum velocity (V_{peak}) and offset time (V_{offset}) is the time velocity drops below the threshold of 5% of the maximum velocity (V_{peak}) as shown in Figure 3.3.

Time to Peak Velocity:

$$T_{peak} = T_{(peak)} - T_{(onset)} \quad (3.4)$$

$$Movement\ time = T_{offset} - T_{onset} \quad (3.5)$$

Time to Peak Velocity Normalized (by time):

$$T_{peakN} = \frac{T_{peak}}{Movement\ time} \quad (3.6)$$

4) SKEWNESS IN VELOCITY PEAK (SVP)

The temporal efficiency is also the ability the ability to perform a task with a symmetrical and bell shaped velocity profile [169, 170]. As the current tasks were not restricted in time and the distance travelled, the time to peak normalized to the total time was considered as suitable metric as shown above. Hence, the range of value lies in the range 0 to 1. In an ideal case, time to peak velocity (T_{peak}) occurs during the mid of the trial (50% movement time) according to dynamic dominance hypothesis for a dominant hand performance [170, 171]. For further comparison across subjects with high variability and to test the nature of symmetricity of velocity profiles, we removed the bias of 0.5. Any deviation thereof was estimated as a disability in temporal efficiency and is calculated by:

Skewness in Velocity Peak:

$$SVP = |(T_{peakN} - 0.5)| \quad (3.7)$$

5) ROOT MEAN SQUARE ERROR (RMSE):

For line tracing task, the RMSE assesses the deviation of the subject's observed path from the straight regression line fitted between the starting point and final position of the handle, and is given by:

$$RMSE = \sqrt{\frac{\sum_{i=1}^n (\hat{y}_i - y_i)^2}{n}} \quad (3.8)$$

where y and $\hat{y}$ denote the observed and the predicted data points (obtained from linear regression), respectively.

6) LENGTH OF CURVES RATIO (LOC-A):

The deviation from the desired path was considered as task error, measured by the length of curves ratio metric. A curve [here, a line for line tracing or an ellipse for circle tracing task depending on the nature of the task] was fitted from the subject's trajectory. The ratio of length of this fitted curve to the original trajectory curve gave the task deviation error. The length of the curve is calculated by cubic spline interpolation of the kinematic metrics. In the ideal case, where there is no error, the length of the curve ratio is 1, so

Figure 3.4: Task error is the deviation from the desired trajectory/path. A curve (line or ellipse based on the task) is fitted from the observed trajectory of the participant using liner regression model and the difference between these two (in terms of shape, length etc.,) are used in error calculation

to remove any bias towards overshooting and undershooting, we remove the bias 1 and calculated task error as follows:

$$LOC - A = |(\frac{length(y)}{length(\hat{y})} - 1)| \quad (3.9)$$

3.3 PRE-PROCESSING AND FORMULATION OF PHYSIOLOGICAL ELECTROMYOPGRAPHY (EMG) METRICS

The EMG signal is typically in the range of -5 to 5 mV and a frequency range of 6-500Hz. The base line noise should be limited to 3-5 μ V. The raw EMG itself does not reveal much information, so there is a need to preprocess the original signal to extract useful information. The following steps were applied in the

- **Rectification:** taking the absolute of the EMG raw i.e., $|emg_i(t)|$ enables us to assess the phasic activity of muscle groups. The visual representation of a rectified signal gives more insight into contraction and relaxation cycles of the muscle.
- **Filtering:** The full-wave rectified signal is passed through a low-pass filter to form the linear envelope of the signal. In [172], it is shown that the filtered signal resembles the shape of the muscle tension. Hence, the low pass filter for a muscle EMG has to be designed in order to match its impulse response. A fourth order low pass Butterworth filter of with a cutoff frequency of f_c at 20 Hz is recommended for upper limb muscles [28]

The filtered EMG data can be used to estimate different time domain features such as Integrated Average Value, Number of zero crossings, wavelet functions; frequency domain features such as mean frequency, median frequency, Signal-to-Motion artifact Ratio [173]. In this thesis since we were only interested in the relative amplitude across muscles, we measured only time domain features such as IAV discussed below.

INTEGRATED ABSOLUTE VALUE:

The time domain EMG feature - called IAV (Integral of Absolute Value) [174] measure describes the strength of the muscle activation during the trial and represents the weight of its contribution to the task. The IAV of a signal x of segment length N is given by:

$$IAV = \frac{1}{N} \sum_{i=1}^N |x_i| \quad (3.10)$$

3.3.1 DEFINITION AND FORMULATION OF MUSCULAR SYNERGIES

A muscle synergy is defined as the coordinated recruitment of a group of muscles with specific activation waveform to perform an action in a simple manner [30, 118]. Synergies can be observed by decomposing the pre-processed Electromyogram (EMG) signals. It is a low-dimensional representation of muscle activity. Different factorization algorithms are used to identify muscle synergies and their activation coefficients underlying a set of muscle activation patterns.

For each muscle i , raw EMG, $emg_i(t)$ is collected, rectified, and low-pass filtered to muscle activation $m_i(t)$. Mathematically, the pre-processing is given by:

$$m_i(t) = LP_{20Hz}[|emg_i(t)|] \quad (3.11)$$

where $LP[.]$ denotes the low-pass filtering operation.

When dealing with multiple muscles, it is convenient to define the muscle activation vector as a collection of muscle activation of all M -muscles measured given by:

$$\mathbf{m}(t) = [m_1(t) \ m_2(t) \ \dots m_M(t)]' \quad (3.12)$$

A time-invariant muscle synergy ($\mathbf{w}_j$) is an M -dimensional vector capturing the specific activation balance of all the muscle activation during the task. The muscle activation vector $m(t)$ is decomposed to a linear combination of N synergies $\mathbf{w}_j$, ($j = 1 \dots N, N \leq M$) and their corresponding activation profile $c_j(t)$. The muscle components of w_j are

fixed, hence we refer to w_j as time-invariant synergies. The dimension is reduced from M (number of muscles) to N (synergies) and the synergies are activated by their respective time-varying coefficients. The time invariant muscle synergy can be formulated as:

$$\mathbf{m}(t) = \sum_{j=1}^N \mathbf{c}_j(t) \times \mathbf{w}_j \quad (3.13)$$

where,

- $\mathbf{m}(t)$: M -dimensional vector of muscle activation, a time profile of pre-processed EMG across all M muscles.
- $\mathbf{c}_j(t)$: the time-varying temporal coefficient for the j -th synergy
- $\mathbf{w}_j$: time-invariant synergy specifying the balance between the muscle activations.

which is expanded to:

$$M = \begin{bmatrix} \mathbf{m}_1(t) \\ \mathbf{m}_2(t) \\ \vdots \\ \mathbf{m}_M(t) \end{bmatrix} = \begin{bmatrix} m_1(t_1) & m_1(t_2) & m_1(t_3) & \dots & \dots & m_1(t_t) \\ m_2(t_1) & m_2(t_2) & m_2(t_3) & \dots & \dots & m_2(t_t) \\ \vdots & \vdots & \vdots & \dots & \dots & \vdots \\ m_M(t_1) & m_M(t_2) & m_M(t_3) & \dots & \dots & m_M(t_t) \end{bmatrix} \quad (3.14)$$

$$\approx \begin{bmatrix} w_{11} & w_{12} & \dots & w_{1N} \\ w_{21} & w_{22} & \dots & w_{2N} \\ \vdots & \vdots & \ddots & \vdots \\ w_{MN} & w_{1N} & \dots & w_{MN} \end{bmatrix} \times \begin{bmatrix} c_1(t_1) & c_1(t_2) & \dots & \dots & c_1(t_t) \\ c_2(t_1) & c_2(t_2) & \dots & \dots & c_2(t_t) \\ \vdots & \vdots & \dots & \dots & \vdots \\ c_N(t_1) & c_N(t_2) & \dots & \dots & c_N(t_t) \end{bmatrix}$$

$$\mathbf{M}_{(M \times T)} = \mathbf{W}_{(M \times N)} \times \mathbf{C}_{(N \times T)} + RES \quad (3.15)$$

The above equation gives the matrix representation of muscle synergies. A muscle activity matrix M is decomposed into a lower dimension time invariant synergy matrix W and its corresponding activation matrix C . Here T is the a function of time. For dynamic task it is the measure of time while performing a task. For an isometric task, the number of trials are considered as time samples. In case of repetitive tasks, the EMG across same movements is either averaged or concatenated. To model the modular organization of muscle patterns, synergies are extracted from the pre-processed EMG by using

the appropriate matrix factorization algorithms.

The muscle activity can be reconstructed from the synergies based on the above mentioned formula as:

$$\begin{aligned}
m_1^*(t) &= w_{11} \cdot c_1(t) + w_{12} \cdot c_2(t) + w_{13} \cdot c_3(t) + \dots + w_{1N} \cdot c_N(t) \\
m_2^*(t) &= w_{21} \cdot c_1(t) + w_{22} \cdot c_2(t) + w_{23} \cdot c_3(t) + \dots + w_{2N} \cdot c_N(t) \\
&\vdots \\
m_M^*(t) &= w_{M1} \cdot c_1(t) + w_{M2} \cdot c_2(t) + w_{M3} \cdot c_3(t) + \dots + w_{MN} \cdot c_N(t)
\end{aligned} \tag{3.16}$$

i.e., the reconstructed matrix M^* is given by

$$M_{(M \times T)}^* = W_{(M \times N)} \times C_{(N \times T)} \tag{3.17}$$

OPTIMAL NUMBER OF SYNERGIES (N):

To assess the quality of the synergies, the VAF (Variance Accounted For) metric is typically used. VAF quantifies the percentage of variability in the EMG dataset that is attributed by the extracted synergies. A high value of VAF indicates good reconstruction of the recorded EMGs, and explains a large part of the EMG variance. For the muscle activity vector $\mathbf{m}(t)$, the estimated muscle activation vector reconstructed from $\mathbf{w}$ and $\mathbf{c}$ is $\mathbf{m}^* = \mathbf{w} \times \mathbf{c}$. The VAF to assess the muscle synergy quality is given by:

$$VAF = 1 - \left(\frac{SS_E}{SS_T} \right) = 1 - \left(\frac{\|\mathbf{m} - \mathbf{m}^*\|^2}{\|\mathbf{m}\|^2} \right) \tag{3.18}$$

This metric is also used in **selecting the number of synergies to be retained** i.e., the synergy space. We calculate muscle synergies for $N=1$ to Number of Muscles (Input Space: M) and estimate VAF in each case. The number of optimal synergies is defined either by the point where the VAF-graph (i.e., the curve of VAF vs number of synergies) reaches a threshold level (e.g., 90%) [175] or by its flattening point, where an increase in the synergy number does not increase the VAF anymore. In addition to the VAF metric, other metrics such as log-likelihood function [117] have been proposed to evaluate the effectiveness of extracted synergies.

3.3.2 STEPS TO CALCULATE MUSCLE SYNERGIES USING TRADITIONAL NNMF

Non negative matrix factorization is the most popular algorithm in deriving muscle synergies [26, 106, 176, 177] owing to its sparse representation and part-by-part decom-

position [114]. Also, it is likely to have physiological relevance since the algorithm is in accordance with the intuitive notion of additive combining parts to form a whole [178]. This section describes the step by step process to estimate muscular synergies from pre-processed muscular activity (EMG signals) using traditional NNMF adapted in literature [35, 179, 180].

1. The pre-processed EMG collected into data matrix (A) is organized as $M \times T$ matrix, where M is the number of muscles. T is the measured time stamps (in a dynamic task) or number of trials (in an isometric task). The input muscle activity is normalized the to have unit variance;
2. For a pre-defined N, compute the non-negative factors W (synergies) and C (respective co-activation signal) in an iterative process to minimize $F(A, WC)$, where $F(X, Y)$: **cost function** that defines the “distance” between X and Y;
The matrix factorization is formulated as:

$$(A)_{M \times T} = (W)_{M \times N} \times (C)_{N \times T} + \text{error} \quad (3.19)$$

and the cost function is given by

$$F(A, WC) = \frac{1}{2} \|A - WC\|^2 := \frac{1}{2} \sum_{ij} [A - WC]_{ij}^2 \quad (3.20)$$

3. The choice of distance metric (in solving the gradient-descent cost function) effects the outcome factors. Most commonly used distance metric is the **Euclidean Distance**, also called the Frobenius norm. In [181, 182] Lee and Seung in their seminal work proposed **two simple and elegant update** rules to solve this cost function given by:

$$C \leftarrow C \circ \frac{[W^T A]}{[W^T WC] + \varepsilon} \quad (3.21)$$

$$W \leftarrow W \circ \frac{[A C^T]}{[W C C^T] + \varepsilon} \quad (3.22)$$

where $X \circ Y$ is the **dot product** of X and Y matrices.

ε is introduced in the denominator to remove any division by zero condition;

In the standard NMF algorithm, W and C are initialized with random values, and updated with above rules. In order to speed up the convergence of the solution

reliable estimation of W and C , the process is repeated for 50-100 times in MATLAB initial values for W and C obtained from previous repetition.

4. Repeat this process for $N= 1$ to M (input matrix dimension) and calculate Optimal (minimal) number of synergies to retain based on the selected VAF criteria.

FORMULATION AND EXTRACTION OF AUGMENTED MUSCLE SYNERGIES: PROPOSED NOVEL METHOD

In literature, most of the studies normalized the input muscle activity to have unit variance, to prevent any bias towards highly-variance muscle. According minimum-variance hypothesis of motor control [183–185] and synergy studies performed by Kutch et al. [141, 186], '**variance**' in a signal might consist of vital information and normalizing the signals to have unit variance might devoid us from analyzing critical information. Hence, we add the variance as "weight" of each signal. To evaluate how muscle synergies manifest to end-effector task, we attempt to append these forces with the EMG activity. Also the distance metric used in standard procedure is the Euclidean distance metric that does not work in the case where inputs are of different units and scales. Since we propose to include forces and EMG, that are of different units, we adopt Mahalanobis distance, a widely used measure in Statistics and Pattern Recognition to treat mixed data. [187]. Mahalanobis distance has the advantage of being unit-less, scale-invariant, and takes into account the correlations of the data set.

Considering these factors, I modified the traditional NNMF to account for the above limitations. Firstly, the variance of the each signal is organized into a **kernel matrix 'K'** (an $M \times T$ matrix). The distance metric is chosen to be the **weighted-euclidean** distance whose cost function is given by :

$$F(A, WC)_K = \frac{1}{2}(\|A - WC\|_K)^2 := \frac{1}{2} \sum_{ij} [K \circ (A - WC) \circ (A - WC)]_{ij} \quad (3.23)$$

- Here K : Variance matrix of A , i.e σ_A^2 .
- If K : Unitary matrix, this is equivalent to traditional NNMF algorithm with euclidean distance and equation 3.23 reduces to equation 3.20

The update rules in step 3 of section 3.3.2 are modified to :

$$C \leftarrow C \circ \frac{[W^T(K \circ A)]}{[W^T(K \circ (WC))]} \quad (3.24)$$

$$W \leftarrow W \circ \frac{[(K \circ A)C^T]}{[(K \circ (WC))C^T]} \quad (3.25)$$

Hence with these modifications, the input signal matrix A is not limited to input signals with same units/scales (i.e. EMG alone). We can add different task-space measurements (kinematics, dynamics) to investigate the inter-relation.

3.4 CONCLUSION

This chapter 3 provides the details of the different data analysis and materials used in this thesis.

- The experimental apparatus, data collection procedures and protocols followed in the thesis are discussed.
- The **mathematical formulation** of kinematic task metrics used to assess motor performance, pre-processing of muscular activity is explained to carry out data-analysis in the future chapters.
- A step by step procedure to extract and analyze muscle synergies using a Non negative Matrix Factorization (**NNMF**) dimension reduction algorithm from muscular activity is presented. NNMF is select method owing to *sparse representation and part-by-part decomposition techniques*. All the elements the NNMF are positive, which has **physiological relevance** as the muscle activity can only be positive and is in accordance with the intuitive notion of additive combining parts to form a whole [178].
- To extract muscle synergies, I adapt the simplified **update rules** popularized by Lee and Seung [181, 182], that are widely used in dimension reduction studies.
- A novel approach with modified NNMF with **weighted-euclidean** distance metrics for better approximation of muscle synergies is proposed and update rules are discussed.

"Ideas do not always come in a flash, but by diligent trial and error experiments that take time and thought. "

CHARLES K. KAO

2009 Nobel Prize in Physics for Optical communication

4

Assessment and modelling of motor learning effects from novel control algorithm design in post-stroke subjects: a randomized control study

HOW DOES ROBOT THERAPY IMPROVE MOTOR FUNCTIONS? This chapter presents the results from a randomized control trial, that was conducted to test the efficacy of a control strategy with underlying principles from 'challenge point framework' in rehabilitation post-stroke. The data collected from 26 stroke subjects (divided into robotic and conventional therapy groups) is presented. My contributions to this work were the development of study protocol, data collection from control and stroke individuals, formulating the performance indices, analysis, and interpretation of the results.¹

¹This work is under preparation for submission at Journal of NeuroEngineering and Rehabilitation (JNER). Aamani Budhota, Asif Hussain, ... Etienne Burdet and Domenico Campolo et al. **Robot assisted upper-limb training post stroke : Randomized control trial towards increasing productivity in rehabilitation.** Preliminary Results with few stroke subjects are published in ICORR 2017, Hussain,

4.1 INTRODUCTION

The recent extensive studies on the effects of upper limb robotic therapy by with 38 randomized clinical trials (RCT's) shows that technology based interventions have significant but only modest gain in functional abilities when compared to the conventional therapy [11]. However, the improvements are small with no clinical significance and are not reflected in upper limb capacity. Also, in [73] only 18 out of 34 RCT studies had follow-up assessments with limited improvement in activities of daily living and showed a retainment or decrease in robotic therapy benefits [49, 188]. The plausible reason for **limited gains might be the absence of optimally challenged tasks** during training. We hypothesize that introducing robotic training regime where the task difficulty can transit from guidance mode to disturbance mode can adapt the task more aptly with patient's recovery. Also, most of the studies present only changes in clinical scores that are ordinal and therapist dependent; but incorporating quantitative measures (that can be derived from robot itself) will provide insight on how exactly people learn and in more reliable and accurate quantification of the motor recovery process.

In this study, I investigate the efficacy of a hybrid robot control strategy in a randomized clinical trial (RCT) in sub-acute to chronic stroke subjects with upper limb impairment. The subjects are divided into two groups (intensity matched): Robot Assisted Therapy (RT) and Conventional Therapy (CT) in a study that lasted for six months. The RT group trained on H-Man and received 60 minute robotic and 30 minute conventional therapy where-as CT group received time-matched 90 minute conventional therapy alone for 18 sessions in 6 weeks. The **longitudinal change** in both the clinical outcomes and the quantitative metrics (derived from two robotic tasks) from assessment of the subject's performance at four-time points (base-line(week 0), mid-training (week 3), post-training (week 6) and follow-up (week 12)) is presented. The results showed RT group had better improvements in functional abilities compared to the CT group post training. This promotes the employment of 'Challenge Point Framework' in robotic rehabilitation complementary to regular therapy. From the results, we also aim to address the following: a) to investigate if therapy benefits retained in the follow up periods; b) to analyze the correlation between the functional impairment scales and the

A., Budhota, A., Contu, S., Kager, S., Vishwanath, D. A., Kuah, C. W., ... & Campolo, D. (2017, July). **Quantitative assessment of motor functions post-stroke: Responsiveness of upper-extremity robotic measures and its task dependence.** In Rehabilitation Robotics (ICORR), 2017 International Conference on (pp. 1037-1042). IEEE.

quantitative kinematic metrics and estimate clinical outcome from kinematics to characterize the sensorimotor impairment status of the participant. It is shown that H-man provides **optimal intensive training** and can also be used as an assessment tool to provide continuous, objective, and **quantitative assessment feedback**.

4.2 METHODS

4.2.1 PARTICIPANTS

Twenty-Six subjects were recruited from the NRH stroke database and the study was conducted at the Centre for Advanced Rehabilitation Therapeutics (CART), **Tan Tock Seng Hospital**, Singapore. The demographic and clinical information of the 26 stroke participants, divided into two groups (13 each) is provided in Table 4.1. Prior to subject recruitment, ethical approvals were obtained from the Domain Specific Institutional Review Board (IRB) of the National Healthcare Group (NHG), Singapore. All subjects gave written informed consent to screening procedures and recruitment (clinical-trial ID: NCT02188628 - clinicaltrials.gov)

INCLUSION CRITERIA AND DIVISION OF SUBJECTS

Inclusion criteria for stroke participants in the study were first ever clinical stroke (ischaemic or haemorrhagic) confirmed by brain imaging, post-stroke duration of 3 to 24 months (sub-acute to chronic group), with shoulder abduction and elbow flexion greater or equal to 3/5 on the Medical Research Council scale for muscle strength, and a Fugl-Meyer Upper Extremity Motor Assessment (**FMA**) **score of 20-50** or predominant motor ataxia or in-coordination ($FMA > 50$). Participants were excluded if they had any non-stroke related arm impairment, moderate arm spasticity as indicated by the Modified Ashworth Scale (> 2), moderate shoulder pain ($VAS > 5/10$), visual impairment (hemianopia), visual spatial neglect, and/or cognitive impairments (Mini Mental State Exam (MMSE) $< 26/28$).

Furthermore, the stroke subjects are divided into two groups (13 subjects each), in a **randomized control** manner to conventional and robotic therapy groups. Randomisation was performed by computer selection using a block of 4 and participants were informed of their assignments after recruitment.

Table 4.1: The demographic details and clinical characteristics of the subjects participated in the randomized control trial divided into robotic and conventional therapy groups. No significant difference between the groups was observed at the baseline assessments

Characteristic	Robotic Therapy (RT)	Conventional Therapy (CT)
Age- year		
Mean	56.36	51.46
Range	31-67	34-72
Sex- No (%)		
Male	7 (53.84)	8 (61.53)
Female	6 (46.15)	5 (38.46)
Ethnic Group- No (%)		
Chinese	11	10
Malay	1	1
Indian	1	0
Other	0	1
Handedness-No (%)		
Right	12 (92.31)	12 (92.31)
Left	1 (7.69)	1 (7.69)
Side of Stroke-No (%)		
Left	8 (61.53)	10 (76.92)
Right	5 (38.46)	3 (23.07)
Time Since Stroke-Months		
Mean	13.3	13.8
Range	3 - 23	5 - 24
Type of Stroke-No (%)		
Haemorrhagic	5 (38.46)	10 (76.92)
Ischemic	8 (61.53)	3 (23.07)
Clinical Outcomes - Mean (sterr)		
Fugl-Meyer Assessment (FMA)	40.08 (0.78)	36.76 (1.09)
Action Research Arm Test (ARAT)	27.15 (1.31)	20.61 (1.52)
Grip Strength (GS)	7.66 (0.25)	6.83 (0.37)

4.2.2 TRAINING PROTOCOL

Both the groups received a intensity matched training of 90 minutes for 18 sessions (3 times a week) over a span of 6 weeks. The Robotic Therapy (RT) patients underwent a 60 minutes robotic therapy session with point-to-point reaching task (in different shape patterns exploring their range of motion) followed by a 30 minuets conventional training session. Conventional Therapy (CT) group received 90 minutes of conventional training alone by a trained occupational therapist (OT).

CONVENTIONAL TRAINING

The conventional therapy included passive mobilization and active-assisted approaches based on neurodevelopmental techniques to enhance normal movement patterns, repetitive task specific training for functional reach training [189] and use of upper limb inclined board and motorized arm bike.

ROBOTIC TRAINING

In robotic Therapy (RT), the subjects trained on H-Man 3.1.1, a novel upper limb rehabilitation robot provided with a performance based adaptive controller. The controller adjusts the interaction dynamics trial-by-trial according to the smoothness during a point to point reaching task ranging from performance enhancement to performance degradation. The performance enhancement scheme is realized by assistance and the performance degradation by disturbance in the movements.

CONTROL ALGORITHM DESIGN: An **adaptive controller** that adapts haptic forces at the end user based on **previous trial** performance is proposed for impedance controlled point-to-point reaching tasks. The trial-by-trial adaptation is based on the user's performance in previous completed trials (a set of 5 trials) and compared to a reference performance, derived in this case from healthy participants. The deviation between the participant's performance and the reference performance determines the interaction dynamics of the subsequent trial. Thereby, the performance evaluation criterion takes the natural variability in movements into account and is not restricted to a specific metric. Moreover, the proposed adaptive algorithm is applied to a two-stages interaction scheme, ranging from **performance enhancement to performance**

degradation.

The adaptation of the **interaction dynamics** is conducted after each completed trial k and applied onto the subsequent trial $k+1$. During the execution of a movement, no update of the adaptation occurs. The user's whole-trial performance error e of a completed trial is determined by equation 4.1:

$$e^k = \frac{\bar{\mu}^k - \mu^*}{\delta \sigma^*} - 1 \quad (4.1)$$

with

$$\bar{\mu}^k = \frac{1}{n} \sum_{i=k-n}^k P^i \quad (4.2)$$

where $\bar{\mu}$ describes the **(moving) averaged performance** defined by the performance metric P of the user's last n trials with P being defined positive with a larger value indicating a worse performance. μ^* and σ^* are the average and standard deviation of the reference performance, and δ describes a tuning factor. The difference in the user's and the reference performances is set into relation with the weighted variability of the reference performance metric. This weighted variability accounts for the sensitivity of the metric and the associated variability in reference performance. As a result, the task performance of a whole trial is evaluated by comparing the **deviation from a desired/reference performance** with a **tuned natural movement variability** in the respective metric. The tuning factor δ ($0 < \delta < \infty$) allows to accommodate the maximal deviation from the reference performance that is considered as comparable to the reference performance. If $\delta=1$, the user's performance is evaluated strictly (with)in the natural variability of the reference performance, if $\delta>1$, the user can deviate more than/from the reference performance and is still considered as comparable thereto, and if $\delta<1$, the user is pushed to achieve a performance better than one deviation from the reference's performance. Further, the error evaluation is centred around zero for easier processing: an error greater than 0 ($e^k > 0$) demands for less challenging interaction dynamics in the next trial, while an error smaller than 0 i.e., ($e^k < 0$) is followed by more challenging interaction dynamics in the next trial Figure xx. Besides, the normalization with the natural variability makes the error criterion applicable to any arbitrary performance metric. Based on the whole-trial error e , the impedance controlled interaction dynamics in equation 4.3 between the user and the device for the next trial are adapted:

$$F^{k+1} = K^{k+1} \Delta x + B^{k+1} \dot{x}; \Delta x = x - x_{Haptic\ Target} \quad (4.3)$$

where $\mathbf{K}$ and $\mathbf{B}$ describe the stiffness and the damping, Δx the distance between the current position and the haptic target and $\dot{x}$ the velocity. Thereby, either one or both, the stiffness and the damping, can be defined as **adaptation parameter(s)** κ and be updated according to:

$$\kappa^{k+1} = (1 - \gamma)\kappa^k + \alpha e^k + \beta \Delta e \quad (4.4)$$

where α and β are **weighting factors** ($\alpha, \beta \leq 0$) tuning the error e of the last trial k and the change in the error Δe between the error of the last k and the previous trial $k-1$, respectively. γ is a slacking factor ($\gamma \leq 0$). It hinders users from fully relying onto the support of the device and thus not putting effort into the completion of the task by simulating a ‘lazy robot’. This adaptive controller covers the full spectrum of training starting from performance enhancement and moving towards performance degradation as the patient improves, hence incorporating the optimal challenge point framework [86]. In the following, we describe one approach for implementing the controller. However, the approach can be applied in multiple different forms. In this case, stiffness K is chosen as the adaptation parameter κ while the damping B is kept constant during the adaptation process given by equation below. So, the lower the adaptation parameter κ , the more challenging the interaction dynamics.

$$K^{k+1} = |\kappa^{k+1}| \quad (4.5)$$

Each interaction starts in the performance enhancement stage with a fixed initial κ^0 for the first n trials to familiarize the participant.

Performance Enhancement Stage ($\kappa^{(k+1)} \leq 0$): Also referred to as assistance phase, in this, a non-negative adaptation parameter κ defines the performance enhancement stage. The user is assisted in the movements via a virtual spring as in 4.3, where the haptic and visual targets coincide as shown in Figure 4.1. An increase in challenge ($e^k < 0$) in this stage corresponds to a decrease in stiffness, i.e. less assistance, a decrease in challenge ($e^k > 0$) equals a higher stiffness, i.e. more assistance in the next trial. This stage follows the well-studied assistance paradigms that were found to be especially beneficial for more impaired users. To avoid the need to classify users before the commencement of the training, each user starts the training in this assistive stage. If the assistance provided is not sufficient to fulfill the movement within a certain time threshold, the assistance will be automatically increased.

Figure 4.1: Robotic Training Algorithm Adaptation Scheme: Assistance is provided during the performance enhancement stage) and disturbance in performance degradation stage mode. The interaction dynamics are adapted based on the previous trial performance during the impedance controlled point-to-point reaching tasks. In the present training protocol, movement smoothness, measured by SPARC [164] is chosen as performance metric.)

Performance Degradation Stage ($\kappa^{(k+1)} < 0$) : Less impaired participants show a performance comparable or better than the reference performance combined with the tuning factor and might reach an adaptation parameter κ equal to zero, i.e. no assistance, at some point in training. To keep those users engaged and challenged, the task difficulty is increased by providing disturbance related forces. In this case, the haptic target no longer concurs with the visual target but is located on varying positions outside the optimal movement path. Here, an increase in challenge ($e^k < 0$) results in a higher stiffness of the distractive force and analogously, a decrease in challenge ($e^k > 0$) in a lower distractive force. This is also referred to the disturbance mode

Robotic Training Session Protocol:

Each robotic training session consisted of three units of a haptic feedback game (HF), each for 15 minutes, alternated by two units of each 5 minutes with a different simple reaching game without haptics (nHF) and an optional three minutes break after the second HF unit (HF – nHF – HF – break – nHF – HF). The nHF gaming units served as breaks and intermediate assessment units, and are not further discussed

here. The HF game comprises simple point-to-point reaching tasks, whereby the target positions form three different shapes: a square, an upright triangle, and an upside-down triangle with side lengths within the range of 15 to 18cm. One trial was defined by the connection of two corner points of the shapes, whereby only those two points were displayed to not constrain the movements to a desired trajectory. The graphical background of the interface (adapted based on the user's liking for the interface), the shape and the movement direction (clockwise and counter-clockwise) were alternated after 12 trials (3 repetitions for the square, 4 for the triangles).

Smoothness is seen as a crucial marker for motor recovery of stroke patients [23] as reaching movements get smoother with motor learning and motor recovery after a stroke [9]. Hence, we here evaluate the movements according to the smoothness metric SPARC [164] (For eases of computation, the negative form of SPARC was used as performance metric.). After the completion of each trial, SPARC was computed of all data points between the first initialization of the movement from the user and the point when the visual target point was first reached. The reference performance values were extracted from 9 healthy control subjects from a previous study with H-Man ($\mu^* = 1.65, \sigma^* = 0.20$). The window-size of the moving average, and the constant tuning and weighting factors were experimentally determined to: $n=4, \delta=1.5, \alpha=1.5, \beta=1$. The slacking factor γ was set to 0.05 (constant) in the performance enhancement stage ($\kappa^{(k+1)} \leq 0$), and removed in the performance degradation stage ($\kappa^{(k+1)} < 0$) since the user is not relying on the robot's assistance in that stage, thus is gratuitous. Each first unit of the HF game in each training session started with the performance enhancement stage with the fixed stiffness initial adaptation parameter κ^0 ($K_0 = 50N/m, B = 20Ns/m$) that was not sufficiently high as that the robot could perform the movement without additional force input from the user. The following two units of the HF game within a session continued with the adaptation parameter of the last trial of the previous unit. The maximal value for the stiffness was set to $K_{max} = 120N/m$.

Additionally, a transition phase between the two stages was implemented: As soon as ($\kappa^{(k+1)} < 0$) occurs for the first time, the stiffness was set to zero ($K=0$) for 10 trials to avoid sudden changes in the interaction dynamics for the user. Besides, these trials could be used as assessment of a user's autonomous movements during the training. The stiffness in the first trial in the performance degradation stage after the transition phase,

Figure 4.2: Cohort diagram of the study: The enrollment, division of subjects, and the study outcome measures are summarized here

was set to $K=30 \text{ N/m}$. The haptic target positions in this stage varied over two positions on the perpendicular through the middle point of the desired movement path in a distance of 10 cm in a pseudo-random manner. For the case that a subject could not complete the movement within 10 seconds, the subject was asked to return to the previous target (home position) and the stiffness was increased by 15 N/m for the performance enhancement stage and decreased by 10 N/m for the performance degradation stage. The subject repeated the trial with less challenge interaction dynamics.

4.2.3 ASSESSMENT PROTOCOL

The performance of the participants from both the groups were assessed five times over a period of 6 months at baseline (week 0), mid-training (week 3), post training (week 6) and two follow-ups (at 12 and 24 weeks) to assess the sensorimotor performance over time. Since this is an ongoing study, sub-sample interim analysis from baseline to first follow-up at week 12 is presented in this chapter. The enrollment, division of subjects, and the study outcome measures are summarized in the Figure 4.2

CONVENTIONAL ASSESSMENT PROCEDURE

Clinical outcome measures included the FMA (Fugl-Meyer et al. 1974), Action Research Arm Test (ARAT), French Army Test (FAT) and Grip Strength (GS- Kilograms of Force: KgF) assessed via digital dynamometer. Adverse events such as increased pain (visual analog scale 0–100), increased arm spasticity (Modified Ashworth Scale (0–4)), and dropout rate were also measured. All clinical assessments were performed by qualified occupational therapists not involved in the training of subjects.

ROBOTIC ASSESSMENT PROCEDURE

In the robotic assessment, the subjects performed two tasks i.e., a line tracing and a circle tracing tasks, inherently different from the training task (the point-to-point reaching) as described in the procedure below with H-Man described in 3.1.1. The choice of tasks was based on their wide use and adaptability in literature, for example, a non-constrained reaching task [24, 190, 191], and circle drawing [167] have been employed for assessing sensorimotor impairment in stroke participants for robotic assessment. In here, circle drawing was chosen as one of the task as it required the coordination of multiple joints and represented a complex functional movement.

Participants were seated on a chair with a back support and H-Man was placed in front of the subject on a fixed table. A flat screen (32 inch) monitor was placed in front of the H-Man device and delivered visual feedback throughout the experiment as shown in Figure 4.4. The Visual stimuli developed in UNITY(v.5.0.2) consisted of a required movement path and the task instructions. The starting posture was adjusted with respect to the subject such that the sternum was aligned with the handle of the H-Man robot, and the elbow bent at 90°. The initial position of the handle of the robot was set at approximately 25 cm from the sternum. Physical trunk restraint was used during the experiment to limit trunk movements during task executions. A wrist grip using a strap is provided if the subject has severe impairment in grasping and high tone. Subjects were asked to perform assessment tasks using both paretic and non-paretic arm with natural movement at their own speed following the instructions displayed on the screen. Prior to this, a demo session is conducted (if required/requested) that lasted for few trials to familiarize the subject with the task.

Line tracing:

Participants were asked to move along a straight line and reach as far as possible within their Range of Motion (RoM). The straight line was pseudo-randomly chosen among three directions (i. e. -45° , 0° and $+45^{\circ}$ from the vertical axis) and was displayed on the screen during the whole duration of each trial as shown in Figure 4.4 . At the beginning of each trial, the target movement direction was presented, and participants were asked to initiate their outward reaching movement. Participants were instructed to reach their maximum range of motion and then hold on to that position for 3 seconds. This is followed by an instruction to go to the home position to initiate inward reaching movement. Six trials were carried out in each of the three directions (i.e., 18 trials in total).

Circle tracing:

The subjects were asked to trace the circle with radius of 20 cm corresponding to work space with the corresponding hand directed by the visual feedback as in 4.3. Like line tracing, subjects were asked to complete the task without any time constraints. The trial finished when the participant had reached back to the initial position. Subjects repeated the task 6 times in both counter and clockwise directions in randomized order (i.e., 12 trails in total). The subjects had to cover at least half the radius (ROM: 10 cm) of the given circle to be able to perform the task. Only 22 subjects were able to finish the circle tracing task, as high tone and limited ROM restricted the other four participants' in performing this slightly complex task.

4.3 DATA ANALYSIS

4.3.1 PRE-PROCESSING OF KINEMATIC DATA

The raw kinematic data (position and velocity) during a reaching motion was filtered using a low pass filter (Butterworth: 6th order, cut-off frequency F_c : 20Hz, sampling rate, F_s : 1000Hz). The filtered data was used in offline data processing to calculate task performance indices detailed in Chapter 3 for each task.

For the line tracing task, the movement was divided into outward and inward movement segments based on the maximum distance and the peak velocity was divided into an outward and inward movement segment by analysing the filtered distance and

Figure 4.3: Robotic assessment setup with participant seated approximately 25 cm from of the handle of the robot. The visual feedback of line/circle tracing task with instructions is provided continuously.

Figure 4.4: A) CAD model of 'H-Man', a novel, compact novel upper-limb rehabilitation robot. B) Representation of assessment task protocols for subjects with left and right hand use with direction notation. C) Representation of visual stimuli used for the line tracing task. D) Visual stimuli in form of a planet orbiting the sun is shown for a circle tracing task

velocity profile along with the state of the task defined by the game (visual display). The outward movement segment was defined as movement from the instant the distance crosses the base position (2 cm) and ends at 95% of the maximum distance reached. It was followed by the rest phase where the distance covered is above 95%. The inward movement is the return phase of the movement, starting from instant when the distance to the base station is below 95% of the maximum distance, to the instant the subject reaches the base station. The segmented movement is further refined (to remove any abnormalities) by analysing the velocity profile. For both outbound and inbound movements, the onset time is the time instant when the tangential velocity exceeds the 5% of the maximum velocity (V_{peak}) and offset time (V_{offset}) is the time velocity drops below the threshold of 5% of the maximum velocity (V_{peak}). Similar procedure was followed for circle tracing task and only outbound movements are discussed in the methods chapter 3.

Given that some participants performed the task with the left hand (affected hand for stroke participants), while others performed the task with the right hand, the independent variable movement direction was coded with respect to an egocentric frame of reference. As such, when movements were performed with the left hand, ipsilateral refers to the -45° movement direction, contralateral refers to the 45° movement direction, and front refers to the 0° movement direction. When movements were performed with the right hand, ipsilateral, front and contralateral correspond to the $+45^\circ$, 0° , and -45° movement directions, respectively. For the remainder of this chapter, in the line tracing task, movement direction will refer to one of the three directions: contralateral, ipsilateral, and frontal; Similarly, for the circle tracing task, the movement directions in the participants performing with the left hand are mirrored so that they are comparable with others. This is because performing in clockwise with right hand (movement passing through the body plane) is similar to counter clockwise movement with left hand w. r. t to body plane. To maintain consistency, we refer to clockwise (CW) as movement direction initialized towards the contralateral direction and counter-clockwise (CCW) clockwise as direction initialized towards the ipsilateral direction irrespective of hand.

The task performance of the subjects are measured in three aspects: Smoothness by SPARC formulated in section 3.2.1, Temporal efficiency by Skewness to peak velocity from 3.2.1 and Task error by Length of Curve Ratio from section 3.2.1

4.3.2 STATISTICAL ANALYSIS

INTRA-GROUP CLINICAL OUTCOME MEASURES OVER TIME

A t-test was performed to verify that there is no significant difference ($p < 0.001$) between the RT and CT groups at baseline to ensure unbiased division of subjects. The change in the clinical outcome measures in both the robotic (RT) and conventional Therapy (CT) groups across the four assessments points (baseline, mid-training, post-training, and follow-up at 12 weeks), were analyzed with a mixed design ANOVA with group as the between factor and session as the within factor. Since normality condition was satisfied for the clinical outcome measures cases (Kolmogorov-Smirnov (K-S) test) we adapt parametric ANOVA test for further analysis. Pairwise comparisons between baseline assessment with the subsequent sessions were run to identify significant changes across sessions (Bonferroni corrected $p < 0.017$) separately in the two groups. Pairwise comparison between week 6 (post-training) and week 12 (follow-up) outcome measures is investigated to see if the functional gains are retained in the follow up period. Gain analysis investigated the change in clinical measures (from baseline to consecutive assessments) between-groups i.e., RT vs CT.

QUANTITATIVE ROBOTIC MEASURES OVER TIME ACROSS GROUPS AND DIRECTIONS

A mixed design ANOVA was used to investigate the effect of the between factor Group (RT and CT) across the four assessment points over 3 months (within factor Session: baseline assessment, mid-training, post-training and follow-up) and across the direction of task i.e., Contralateral, Frontal, Ipsilateral directions for line tracing and Clockwise and Counterclockwise directions for circle tracing tasks (within factor as Direction). Significant main effects and interactions were compared using Bonferroni post-hoc analysis. The median value of (each session and direction) is taken as representative performance of each subject for respective session and direction and the trend of these metrics across the RT and CT group are analyzed. The above analysis gives a detailed analysis about the effect of Time (training intensity), Group (robotic vs conventional) and Direction (task variation in robotic assessment) on the impairment status of the stroke patients. Also, similar analysis was carried out for the variability in the robotic task metrics across subjects (in each session and direction), to measure the reliability and repeatability of the performance in the robotic assessment task.

CORRELATION OF CLINICAL AND QUANTITATIVE MEASURES

Correlation within clinical scores for the stroke subjects (in both RT and CT group combined) is investigated to identify dependent scales. A poor correlation between 2 or more clinical scales would emphasize the need for each of the test as they measure different functional aspects and a good correlation indicates the redundancy, allowing the evaluation of just one of the correlated scales to save time of assessment. The correlation and their significance values are evaluated using Pearson correlation. Correlation within quantitative measures from the robotic assessment task for the stroke subjects (in both RT and CT group combined) is also investigated to ensure independent task metrics are being evaluated. Three Linear regression models were employed to estimate the clinical scores such as the FMA, the ARAT, and the Grip Strength from robotic quantitative metrics. One model is based on metrics from line tracing, one from circle tracing and a third one called mixed model is based on the combination of metrics from both the circle and line tracing task. The independence between robotic metrics avoids the interaction factor between the variables during the regression and is not affected by multicollinearity. Because the metrics had different units, normalization was performed to scale the data such that each metric had 0 mean and standard deviation of 1. The data is randomly divided into 75% of the data to train the regression model and 25% to test the model derived from the training set. No significant difference (t-test, $p > 0.4$) between the datasets showed that the training and validation data sets were from similar distribution. Regression performance was measured by the correlation (R) the between the clinical scores and estimated scores from the robotics metrics model. The process is repeated 5 times to verify the model for reliable results with cross validation (k-fold) method and the weights that yielded minimal error are chosen. A Mann–Whitney U test was performed on the predicted and actual clinical scales revealed no significant difference. Clinical scores = $f(\text{quantitative measures}) + \text{error}$ Results are presented as least-squares means with standard errors or 95% confidence limits. All statistical analyses were performed in SPSS software and MATLAB for regression

4.4 RESULTS

The reaching trajectories and the velocity profile of a representative stroke participant for both line tracing and circle tracing task is shown in Figure 4.5. A significant difference

in performance across both task is observed from the kinematic profile. Relative to the line, for circle tracing trials subjects took longer time, exhibited lowered average velocity, and unsmooth movements, irregular velocity profile, and large path errors.

4.4.1 LONGITUDINAL CHANGES IN CLINICAL OUTCOME MEASURES

The changes in the clinical outcome measure compared to the baseline are presented in Figure 4.6. Data shown are least-squares median and standard error at each assessment point. Higher scores indicate better functioning for the FMA, ARAT, GS clinical outcomes. Pairwise comparisons of clinical scores showed that compared to baseline at week 0, FMA gains were significant only in the follow-up at week 12 for the CT group, whereas they were significant in all subsequent sessions for the RT group ($p < 0.01$). No significant gains were noted in the ARAT score in the CT group; while in the RT group improvements from week 0 were significant at post training (week 6) and maintained in the follow-up (week 12) session ($p < 0.01$). A similar trend was observed for the GS scale: no differences between sessions were observed for the CT group, but changes were significant in the RT group because of therapy (mid and post training assessments $p < 0.01$), although this was not retained in the follow-up session (week 12, $p = 0.14$). The gains analysis in clinical scales, showed significant differences between-groups at post training assessment, i.e., RT vs CT ($p = 0.03$). This shows that RT group achieved significant gains compared to CT indicating the efficiency of robotic therapy and its potential for rehabilitation. However, no such superiority of RT over CT was found at follow-up period. Post-hoc analysis across week 6 and week 12 revealed no significant differences between them FMA ($p > 0.4$), ARAT ($p > 0.4$) and GS ($p > 0.1$) in both RT and CT groups indicating that the therapy benefits retained in the follow up periods. In general, no increases in pain, spasticity or other adverse events were reported by participants.

4.4.2 DISTRIBUTION OF QUANTITATIVE MEASURES ACROSS SESSIONS IN LINE TRACING ASSESSMENT TASKS (LTA)

SMOOTHNESS

It is observed that the SPARC values showed an increasing trend in most of the subjects indicating an improvement in movement smoothness. The statistical analysis verified this, wherein both RT and CT groups the smoothness was significantly different at post-

Figure 4.5: Representative kinematic trajectories of a stroke subject for A) line tracing and B) circle tracing task (bottom).

Figure 4.6: Changes in clinical measures (A.FMA, B.ARAT, and C.GS) during the longitudinal study over 12 weeks in comparison with Baseline assessment (at Week 0) is presented. Mean and Standard Error of the change in the clinical outcomes for the Robotic therapy(RT) and Conventional Therapy (CT) across 4 sessions is shown. The patients receiving training with robotic intervention showed significant functional recovery in comparison with participants undergoing the conventional therapy alone. * signifies $p < 0.05$

training (week 6) at follow up (week 12) assessment when compared to baseline (all directions and combined; p 's < 0.01) see Figure 4.7 with SPARC values of RT group at Wko: -5.66 ± 2.37 ; Wk6: -4.61 ± 0.95 ; Wk12: -4.52 ± 1.01 ; and CT group at Wko: -5.71 ± 1.38 ; Wk6: -6.05 ± 1.42 ; Wk12: -5.01 ± 1.48 respectively. During training sessions for both groups, the results showed gradual improvement over time, however this was not translated into significant effects (no significant difference between week 3 and week 6; $p > 0.022$). Further, at week 12 both groups retained the training effects; no significant difference was observed between week 6 (post training) and week 12 (follow-up) (both $p > 0.05$). Variability analysis as shown in 4.7 also showed similar trends as median i.e., decrease in variability (improvement in task performance) with training over sessions, however was not statistically significant in both groups (p 's > 0.6).

TEMPORAL EFFICIENCY

Comparing the two groups, Normalized Time to Peak Velocity revealed that although robotic group performed better at post training, it was not significant (RT vs CT) in terms of improvement of symmetric velocity profile ($p = 0.84$) and the variability of measure ($p = 0.91$).

TASK ERROR

The distribution of task deviation error measured by length of curve ratio and its variability within subjects across the four sessions is presented in Figure 4.7. Like smooth-

Figure 4.7: A) Median and B) Variability of robotic task metrics in the line tracing task : smoothness measured by SPARC; temporal efficiency measured by normalized time to peak velocity(TpeakN); and task deviation error measured by Length of Curves (LOC). across four sessions is shown. The * signifies $p < 0.05$

ness and temporal measures, error median and variability decreased with training in both groups compared to baseline (RT- Wko: 0.10 ± 0.05 , Wk6: 0.055 ± 0.035 ; CT - Wko : 0.11 ± 0.06 , Wk6 : 0.09 ± 0.05), however this difference unlike other measures could not reach any statistical significance in both groups due to the inherent nature of error measure ($p > 0.05$) When comparing the two groups i.e., RT vs CT, at post training, no significant differences were observed for median ($p = 0.71$) and in variability ($p = 0.27$), although lower error values for the RT group compared to CT group was observed.

4.4.3 DISTRIBUTION OF QUANTITATIVE MEASURES ACROSS SESSIONS IN CIRCLE TRACING TASKS

SMOOTHNESS

The distribution in smoothness measure across the four assessment points is presented for all the subjects participated in the study is presented in 4.8. In demanding circle drawing task, the smoothness measured by SPARC improved in both groups over sessions compared to baseline (at Wko, RT: -10.73 ± 5.97 , CT: -13.09 ± 3.97) as shown in figure 4.4.3, however was only significant at follow up in both RT (-7.9 ± 3.44) and

CT (-9.75 ± 20.26) group (p 's < 0.03). Also, no significant difference between training sessions (i.e., mid training and post training) was identified in both groups ($p > 0.63$). This was also true for variability analysis, but only for robotic group ($p = 0.03$). No significant difference was observed from baseline at the follow-up in CT group for variability analysis ($p = 0.74$). In both groups, the patients progress continued post training (RT: -9.16 ± 3.05 and CT: 12.59 ± 3.51) at follow-up (RT: -7.9 ± 3.44 and CT: -9.75 ± 20.26) assessment, but statistical significant differences were only found in RT ($p = 0.004$) but not in CT group ($p = 0.83$). The RT group showed better performance in the follow-up indicating that the robotic therapy group improved significantly even after the training. In variability of the measure, no significant difference was observed across these two sessions (both $p > 0.7$). Overall, circle tracing tasks, changes in smoothness, measured by SPARC was not significantly different in Group (RT vs CT) ($p = 0.23$) and this was also reflected in the variability of the measure, with no statistical significant difference between groups ($p = 0.2$).

TEMPORAL EFFICIENCY

The temporal efficiency in the circle tracing task measured as function of time to peak velocity across time is shown in Figure 4.4.3. Significant improvement in time to peak velocity performance from baseline (RT: 0.38 ± 0.09 ; CT: 0.37 ± 0.07) was significant only in the RT group at post-training (0.32 ± 0.06) with $p = 0.02$ (with all other session, $p > 0.3$); No significant difference with baseline to any subsequent sessions was observed in CT group (all p 's > 0.1). Also, the variability of the measures showed no significant difference from baseline to any later session in both the groups ($p > 0.6$). The learning effects were found to be retained with no significant difference between the post-training and the follow-up in both the groups median (all $p > 0.3$ in RT and $p > 0.8$ in CT) and its variability (all $p = 1.0$ in both groups). When comparing the two groups i.e., RT (0.32 ± 0.06) vs CT (0.30 ± 0.08) at post training, no significant difference in groups ($p = 0.86$) is observed. Likewise, the variability of the measures is not significantly affected by group ($p = 0.36$). No directional difference in performance was observed in Normalized Time to Peak Velocity was observed in both the groups (both $p > 0.3$) and its variability (both $p > 0.1$).

Figure 4.8: Distribution of smoothness measured by SPARC across four sessions in a circle tracing task. Out of the 26 participants only 22 subjects were able to perform this task during the baseline (Week 0) assessment indicated by the subject ID in the title of each sub-figure. High tone and limited ROM restricted the other four participants in completing this task.

Figure 4.9: A) Median and B) Variability of robotic task metrics in circle tracing task: smoothness measured by SPARC; temporal efficiency measured by normalized time to peak velocity(TpeakN); and task deviation error measured by Length of Curves (LOC). across four sessions is shown. The * signifies $p < 0.05$

TASK ERROR

The analysis of task error, showed significant differences in performance from baseline (RT: 0.07 ± 0.09 CT: 0.13 ± 0.33) with all the consecutive sessions (all $p < 0.03$) in RT group. In CT group, although error seems to diminish with training, no statistical significant changes (gains) from baseline were identified with any of the later session (all $p > 0.6$), refer figure. The variability of the measure appears to be decreasing with training as shown in figure, nevertheless no statistical significance over session from baseline was observed (all $p > 0.1$). The therapy effect is shown to retain in both the groups as no significant difference in the post-training and the -follow-up was observed in the measure (both $p > 0.3$). This is also similar in variability of the measure ($p = 1.0$ in both RT and CT). Comparison of groups revealed, the error reduced significantly in RT group compared to CT group by post training. Although, no significant difference between them (RT: 0.03 ± 0.04 vs CT: 0.11 ± 0.14) in the error metric ($p = 0.05$) and its variability ($p = 0.72$) was noted. Within direction, no significant difference in performance with direction was observed in the task error measure ($p > 0.3$) and its variability ($p > 0.2$) in both the groups.

4.4.4 CORRELATION OF CLINICAL OUTCOME MEASURES AND QUANTITATIVE ROBOTIC MEASURES

Correlation within clinical scales as shown in in Table 2 revealed high correlation between the FMA, and ARAT measures ($r=0.93$, $p < 0.0001$) as both these measure functional activity and ability move isolated joints. A poor correlation of both FMA and ARAT scales with Grip Strength (($r_{FMA-GS} : 0.41$, $r_{ARAT-GS} : 0.44$ with $p < 0.01$) was observed. This is expected as recovery in the ability to move isolated joints and grip strength are independent constructs and may not be correlated. Also, correlation within quantitative metrics is performed to investigate the independence of measures presented in Table 4.2.

4.4.5 DERIVING CLINICAL SCALES FROM THE TASK PERFORMANCE INDICES BY MULTIPLE LINEAR REGRESSION MODEL AND ITS VALIDATION

The weights of the linear regression model to derive the clinical measures from the kinematic metrics for three different cases (line tracing, circle tracing, and mixed model) with their significance values are presented in Table 4.3. No model reached significance for GS estimation (all p 's > 0.3). In both FMA and ARAT, the results showed positive weighting towards smoothness metrics and a negative contribution from the error measure as expected for all the three models. Although FMA, is highly correlated to ARAT they exhibit different weight distribution in task models. The model efficiency given by the correlation value of predicted (from model) and measured clinical scores for the training and validation results are shown in Table 4. It is observed that model with line tracing metrics showed significant correlation between predicted and measured FMA for training ($r= 0.53$, $p = 0.04$); and model with circle tracing has significant correlation for ARAT measure in both training ($r= 0.53$, $p = 0.04$) and validation ($r= 0.53$, $p = 0.04$). Also, the mixed model gave better results in training (FMA ($r=0.68$), ARAT ($r=0.61$)) and validation (FMA ($r=0.73$), ARAT ($r= 0.62$)) comparatively for both FMA and ARAT scales (see Table 4.4). Poor correlation with GS scale for training and validation observed in all the models (all p 's > 0.1).

Table 4.2: Correlation of clinical outcome measures and quantitative robotic measures from Line Tracing Assessment task (LTA) and Circle Tracing Assessment task (CTA) . The * signifies $p < 0.05$

R-value	FMA	ARAT	GS	LTA_SPARC	LTA_T2PK	LTA_LOC	CTA_SPARC	CTA_T2PK	CTA_LOC
FMA	1.000	0.930*	0.475*	0.468*	-0.459*	-0.420*	0.436*	-0.170	-0.620*
ARAT	0.930*	1.000	0.611*	0.448*	-0.382	-0.0271	0.562*	-0.0256	-0.608*
GS	0.475*	0.611*	1.000	0.328	-0.0243	-0.038	0.0286	-0.320	-0.416*
LTA_SPARC	0.468*	0.448*	0.328	1.000	-0.391	0.060	0.455*	-0.034	-0.0260
LTA_T2PK	-0.459	-0.382	-0.0243	-0.391	1.000	-0.046	-0.0222	0.363	0.398
LTA_LOC	-0.420	-0.0271	-0.038	0.060	-0.046	1.000	0.130	-0.0235	0.023
CTA_SPARC	0.436*	0.562	0.0286	0.455*	-0.0222	0.130	1.000	-0.0253	-0.498*
CTA_T2PK	-0.170	-0.0256	-0.320	-0.034	0.363	-0.0235	-0.0253	1.000	0.411*
CTA_LOC	-0.620*	-0.608*	-0.416	-0.0260	0.398	0.023	-0.498*	0.411*	1.000

Table 4.3: The weights of robotic task metrics of the linear regression model from Line Tracing (LTA), Circle Tracing(CTA), and Mixed Model (combined from both tasks) is presented.

	Line Tracing (LTA)			Circle Tracing(CTA)			Mixed Model			
	FMA	ARAT	GS	FMA	ARAT	GS	FMA	ARAT	GS	
Constant	20.251	1.976	1.029	0.510	1.712	1.835	LTA	CTA	LTA	CTA
	0.114	0.113	0.091	0.031	0.090	0.032	2.526	0.028	30.297	2.772
SPARCin XY										
T2PK	-4.649	-4.432	-1.718	0.897	-0.925	-3.757	0.104	0.028	0.099	0.082
LOC	-20.238	-0.967	0.004	-1.659	-1.168	-0.826	-2.516	-0.706	-1.944	-20.232
ANOVA results for										
each model:										
F-STAT	3.95	2.08	0.392	2.11	2.83	1.17	30.28	2.41	0.942	
P-Value	0.03	0.156	0.761	0.152	0.083	0.361	0.05	0.114	0.511	

Table 4.4: R Values measuring similarity between the actual clinical scores and scores predicted from the linear regression models. Results for line tracing, circle tracing and the mixed model are presented The * signifies $p < 0.05$

	Line tracing		Circle tracing		Mixed model	
	<i>Training</i>	<i>Validation</i>	<i>Training</i>	<i>Validation</i>	<i>Training</i>	<i>Validation</i>
FMA	0.533*	0.6826	0.346	0.5250*	0.686*	0.7374*
ARAT	0.342	0.4587	0.414*	0.5126	0.616	0.6172*
GS	0.09	0.3444	0.227	0.0186	0.386	0.0041

4.5 DISCUSSION

This chapter discusses the results from an on-going randomized control trial with stroke subjects to improve motor functions using the planar two degrees of freedom robot H-Man. The aim is to investigate the efficacy of a combinatory training scheme with robotic and conventional therapy in comparison with conventional therapy alone. The robotic therapy was provided by a 'H-Man' robot that adapts the haptic interaction dynamics of a point-to-point reaching task based on the smoothness performance, thereby ranging from performance enhancement (assistance) to performance degradation (disturbance). Overall, by the end of the therapy and in the follow-up assessments it is shown that the subjects performed and retained smoother movements with better temporal efficiency and reduced task deviation errors compared to their baseline performances which is also reflected in their respective clinical outcomes. Furthermore, regression models were used to describe the relative contributions of each of the quantitative metrics to the three clinical measures and their validation results promote the idea of employing robotic measures for objective and reliable sensorimotor assessment. In the remaining section, we discuss in detail the main findings of the study.

4.5.1 SIGNIFICANT IMPROVEMENT IN MOTOR CONTROL OVER TIME WITH ROBOTIC THERAPY - AN ALTERNATIVE TO REDUCE THERAPIST WORKLOAD AND ENHANCE PRODUCTIVITY IN REHABILITATION SETTING

In clinical scales, overall significant gains at post-training and follow-up assessments compared to baseline were observed for the RT group but not in the CT group (except in FMA at the week-12 follow-up). The performance at the end of the training period (week 6) compared to the follow-up assessment (at week 12) showed no significant difference in FMA and ARAT indicating that therapy benefits (learning) retained in the

stroke subjects. However, there is a drop in the GS during the follow-up; this could be because the subjects were only trained in reaching movements at proximal joints with their hands strapped to the robot handle, this did not aid in improving the grip strength performance.

Majority of rehabilitation studies report only changes in clinical outcome measures [67, 72], here we also report on quantitative metrics derived from robotic assessment tasks in both RT and CT groups. In the quantitative metrics for both robotic assessment tasks, within session analysis, revealed significant improvement in smoothness, temporal abilities, and reduced task error (only in circle tracing task for error) performance from baseline to post training in RT group. Moderate improvements in task metrics are also noted in the CT group which the clinical scales were unable to detect. The gains analysis in clinical scales, showed significant differences between-groups post training, i.e., RT vs CT ($p=0.03$) in FMA, with robotic group having higher gain than the conventional group (see Figure 2a). However, this was not translated to ARAT and GS measures.

The results promote the use of this performance based adaptive hybrid controller in rehabilitation robots (in H-man here) where, the therapists can share their workload with the robot (to administer high intensity repetitive tasks) requiring minimum supervision. This could allow therapists sufficient time in treating more number of subjects or for devising training regimes that robot alone could not provide. This can also be seen as prospective solution to participants with limited access to a therapist, to account for rise in aging population and transport cost factors by adapting them in decentralized rehabilitation settings [80, 192, 193].

4.5.2 “MORE TASKS ASSESS BETTER”: – A POTENTIAL FOR H-MAN AS A TOOL FOR SENSORIMOTOR ASSESSMENT FOR TRACKING CHANGES IN PERFORMANCE

In conventional therapy (CT) group, although the clinical assessment indicated no significant changes across sessions, the kinematic metrics showed significant changes in smoothness and error measures indicating the sensitivity of H-Man and promoting its use in qualitative assessment to track progress. The communication gap between the clinicians and researchers, and usage of many different measures that are robot or task specific impedes the translation to clinical practice. Hence, [17, 98] address the need to develop more valid, reliable and clinically relevant robotic metrics for an accurate knowledge of subject status. Also, in [191], robotic metrics are shown to be task dependent. This rises a major argument on how robotic tasks and metrics can be employed for accurate and objective assessment. To address this, we used linear regression models to

estimate and validate the gold standard clinical outcome measure such as FMA, ARAT, and GS from the task performance indices in robotic assessment tasks (individual and combined) similar to [194].

The analysis of weights from each model investigated the effect of each task construct to the clinical scales. Smoothness showed a positive weight for all clinical scales but only significant for FMA and ARAT. As expected the task error has a negative weighting (i.e., less error implies better clinical score/motor ability) but only showed significant effect for estimation of FMA. For training in individual task models, correlations of the FMA was higher with line tracing model; ARAT had better correlations with circle tracing task. This might be because the circle tracing is more complex task that requires joint co-ordination; ARAT test, a measure of activity according to ICF classification [195] constitutes various sub tasks that require coordination and fine control. This signifies that both tasks are different highlighting unique knowledge on motor impairment status of individual.

From the correlation and regression models results, it is shown that the mixed model that is based on metrics from both tasks outperformed the individual task model. This holds true for both training and validation data set. However, a poor regression and low correlation values (non-significant) is noted for the grip strength (GS) in all the models. This is understandable, as grip strength is a dynamic measure and the robotic tasks here are limited to metrics derived from kinematic performance. Hence, embedding varied kinetic or force related tasks would aid in better approximation of impairment scale such as GS. The results promote the need for varied standard tasks to obtain superior level of assessment. Also, the potential for H-Man as a tool for upper-limb assessment in tracking recovery process is validated.

LIMITATIONS

It is important to highlight that this study was limited to chronic stroke participants, a higher degree of improvement is expected for acute and sub-acute population but needs further validation. Also, the results presented here are from a sub-sample interim analysis of an on-going study with 44 subjects (all subjects have been recruited). The younger age of few stroke subjects due to sampling error and short-term follow-up might be a limitation to generalize the findings. Future studies with complete cohort of subjects will further aid in understanding the benefits of robotic therapy clearly. This also applies to regression models where different populations can have varied weighting. Better results with the mixed model that contains information from two unique tasks and a poor

estimation of Grip Strength (GS) strongly recommends the need for adapting diverse robotic tasks that can assess different range of motor behaviours (such as functionality, strength, co-ordination). This would enable both clinicians and researchers with more reliable, accurate and relevant estimation of sensorimotor state of the stroke subjects. This knowledge will aid in designing better and effective subject-specific therapy regimes to improve their motor function recovery.

4.6 CONCLUSION

In this chapter, results from a randomized control trial validating the efficacy of a controller with the underlying principle based on challenge point framework is presented. The longitudinal changes in the clinical outcomes and the quantitative metrics (derived from two robotic tasks) from assessment of the subject's performance at four-time points is presented. The results showed RT group had better improvements in functional abilities compared to the CT group.

- The efficiency of a robotic controller that adapts depending on the individual subject's movement smoothness is validated. A **novel interaction** approach of the haptic forces via a virtual spring transition from assistance (performance enhancement mode that assist the subject movement towards the target) to disturbance (performance degradation that creates a pull away from the target) is implemented.
- The robot-assisted rehabilitative therapy with H-Man (60 minute) combined with conventional therapy (30 minute) that lasted for 18 sessions, showed significant improvement in motor function from baseline in clinical and robotic tasks. Furthermore, these **motor benefits were retained** in the follow-up assessment, indicating long term learning in both the groups.
- The results from this chapter promote robotic therapy in rehabilitation in addition to regular therapy to provide optimal intensive training. This in-turn could decrease the workload of a therapist, while producing relatively better outcome measures than conventional therapy alone .
- Clinical scales were derived from **regression models** with robotic scales indicating that 'H-man' robot can also be used to provide continuous, objective, and quantitative feedback to keep track of the progress. Mixed model with quantitative metrics from **two tasks** had better results compared to individual task signify

that inclusion of more diverse tasks will provide a better understanding of sensorimotor state.

"Discovery consists of looking at the same thing as everyone else and thinking something different." ☒

Albert Szent-Györgyi,
1937 Nobel Prize in Physiology for discovering vitamin C
and the components and reactions of the citric acid cycle.

5

Relationship between upper-extremity robotic tasks measures and associated metrics- A novel study to improve robotic assessment

HOW CAN WE BETTER ASSESS THE SENSORIMOTOR SKILLS OF PARTICIPANTS AND THE EFFECTS OF THERAPY USING TECHNOLOGY AIDED SYSTEMS?

This chapter presents the results from data collected from two clinical studies. The quantitative scales derived from robotic tasks provide objective assessment and are shown to have advantages over conventionally used clinical scales. However, their use is limited as further research to identify optimal, reliable and easy to use robotic tasks and performance metrics is required. The objective of this chapter is to investigate the task dependency of performance measures in upper-limb robotic tasks from two clinical studies. Based on the results, I derive few recommendations to choose optimal robotic tasks and task metrics depending on the skills and impairment level of the participant. My contri-

butions to this work were the development of study protocol, data collection from the healthy control and stroke individuals, analysis, and interpretation of the results. ¹

5.1 INTRODUCTION

Rehabilitation from robotic devices or physical therapy showed only modest or limited improvements in the hand capacity and functional abilities of the stroke survivors [72, 196]. Duncan et al. reported that only 33% to 70% of the stroke patients recover useful arm ability, and initial paresis severity still remains the best predictor of arm function recovery over 6 months [103, 197]. It is possible that the limited recovery success for UE dysfunction after stroke is hampered by the **limited amount of training** offered to the affected population. Increasing intensity of training along with the development of better therapy regimes that can achieve better learning effects could significantly improve performance. However, an arguably equal, if not more important factor contributing to this limited improvement can be attributed to the **partial understanding and incomplete assessment** of the disability itself, which in technology intervention systems has been explored less thoroughly [94]. For developing efficient training, a detailed sensorimotor state of the subject is essential. This can be obtained by assessing the performance of the subject while doing some motor tasks. Although clinical measures are widely accepted, standardized and validated, they are still subjective and suffer from low resolution (insensitive to small but significant changes) which is typical of ordinal scales [163, 198]. Clear knowledge of the level of sensorimotor deficits is required for devising a comprehensive and efficient training regime. **Technology-aided measures** can offer a promising solution to overcome these limitations of conventional scales. The information from the robotic sensors such as their kinematics, applied forces, joint movements etc., can be used in providing the feedback to users/therapists, in quantitatively assessing the impairment to keep progress of the recovery process. This would aid in designing **better subjective** therapy regimes to improve their motor skills while reducing the disability itself.

Multiple studies have previously addressed variations in performance metrics in robotic work-space [17, 18, 199] as markers for assessing the functional abilities in impaired subjects. Being (semi-)autonomous, technology-based solution is potentially

¹A part of this chapter is published in Hussain, Asif, Aamani Budhota et al. **Self-paced reaching after stroke: A quantitative assessment of longitudinal and directional sensitivity using the H-man planar robot for upper limb neurorehabilitation**, Frontiers in neuroscience 10 (2016).

more objective (therapist independent), sensitive (able to detect changes) and less prone to human error/subjectivity. However, their use in assessment of impairment and recovery process is still limited and needs innovation. The main **challenge** is in identifying and evaluating the robotic metrics that are **valid, clinically relevant, reliable, robust and sensitive** to changes from the robotic tasks independent of robotic setup. Also, due to variations in protocols/task definitions (for example point to point vs. path reaching, free reaching vs. supported movements) and varying outcomes, ambiguity in task measures, the reliability and validity of reaching movements as measures of upper limb motor functionality is still limited [17, 189, 200]. In here, I would like to make clear distinctions between metrics, measure, and tasks.

Task: An action user is required to perform to complete the assessment. Example: in upper limb, point to point to reaching task, path tracing (line, square), force manipulation tasks etc.

Measure: Measure is the category in which the specific aspect of the subject task performance is assessed, as in temporal efficiency (movement time or any velocity related measures), active range of motion, smoothness, task error etc., or any other factor a clinician is interested in to understand improvement in performance.

Metric: The particular equation or method used for calculating a specified measure. For example, smoothness measure can be calculated using different metrics such as SPARC, SAL, log jerk, no of peak velocities, MAPR ratio etc.

Ambiguity in differentiating between these factors is arguably one of the major reasons hindering for widespread use of such measures for-example, it is not clear if a (metric/measure) used in one task will be reliable for another task or conversely a measure considered reliable for one task will be equally useful for another task. Some evidence in support of this argument exist on ad-hoc basis if we assess different articles [20, 163, 199]. Moreover, there are *many metrics to assess a similar measure* that have been adapted in various studies [20, 80]. Some quantitative measures are defined for specific robotic setup and task. This limits the generalization of a task measure and comparison of the robotic measures across different studies unlike the standard clinical studies. This develops an impetus to investigate the relation between performance measure and task itself.

To address the above issues, in this chapter results from two experiments are presented. In the first study, I investigated the feasibility of the **H-Man robot** as a **sensori-motor assessment** tool for evaluating subjects' impairment status and tracking recovery process. The control (healthy aged population) and chronic stroke subjects task perfor-

mance during a line reaching task is evaluated. The aim is to detect differences in planar self-paced reaching task performance as a function of neurological status (stroke, age-matched healthy control), direction (frontal, ipsilateral, contralateral), and movement segment (outbound, inbound). Subsequently, in the second experiment, I investigate the effects of task variations on robotic measures and associated metrics. Results from 32 stroke subjects performance in two robotic task as described in section 4.2.3 is presented. Depending on the task, the meaning and significance of measure can greatly vary. I also analyze how the impairment level of subject effects the sensitivity of the robotic tasks. The results offer an urging need for standardized robotic tasks and performance measures (and metrics) based on the subject's skill and impairment level.

5.2 EXPERIMENT 1: QUANTITATIVE ASSESSMENT OF SELF-PACED REACHING REACHING TASK IN CONTROL AND STROKE SUBJECTS

PARTICIPANTS

Twelve stroke participants (mean age: 55, SD = 10.0 yrs., 7 male, mean time since stroke = 11.2 months, SD = 6.0) were recruited for the study. Seven patients had an intracerebral haemorrhage (mean age: 49.3, SD = 4.3, mean time since stroke = 9.6 months, SD = 2.6), and five patients had an infarct (ischaemic stroke, mean age= 58.0, SD = 11.3, mean time since stroke = 12.3 months, SD = 7.0). Seven patients had hemiplegia of the right arm, and five patients had hemiplegia of the left arm. Nine neurologically healthy individuals served as aged matched control participants (mean age: 53 ± 4.3 yrs., 4 male). The inclusion criteria of stroke subjects is presented in 4.2.1.

5.2.1 PROTOCOL AND DATA ANALYSIS

The experimental apparatus and setup is similar to the previous chapter and is described 3.1.1. The participants performed the self paced reaching task (with no constraints on maximum distance or average velocity) on a similar to the procedure detailed in section 4.2.3. The kinematic data from each reaching trial is processed and segmented into outward, rest, and inward movements as described in section 4.3.1. The quantitative measures are derived from the assessed task to provide overall information about the subject's motor performance and co-ordination. The following metrics: Spectral Arc Length to assess smoothness [3.2.1], Normalised time to peak velocity [3.2.1] for temporal efficiency and RMSE error [3.2.1] for task error are evaluated.

5.2.2 STATISTICAL ANALYSIS

The specific aims of the study were to examine differences in planar reaching as a function of 1) neurological status (stroke patient, age-matched controls), 2) direction (contralateral, ipsilateral, and frontal), and movement segment (inbound or outbound). Given that some participants performed the task with the left hand (dominant hand for control and or affected hand for stroke participants), while others performed the task with the right hand, the independent variable movement direction was coded with respect to an egocentric frame of reference as in 4.3.1.

- **Intra-group: Directional difference within control and within stroke participants for a non-constrained reaching task:**

The one-way ANOVA was used on the data of healthy (control) participants to investigate the difference between the three different directions. The analysis was carried out for both inbound and outbound segments of movement's separately. Significant main effects were compared using Tukey's honest significant difference test (HSD) to understand differences between directions. Further, the two-sample t-test was employed to compare inbound vs. outbound movement segments (for each direction individually). Similar statistical analyses were carried out on stroke participants to see the directional difference within impaired participants.

- **Inter-group: Directional difference between control and stroke participants:**

A two-sample t-test was used for comparing directional differences between control and stroke participants, i.e. front direction of all control participants was compared with that of all stroke participants (combined). The procedure was followed separately for both inwards and outwards movement segments.

5.2.3 RESULTS

The kinematic (distance and velocity) profile of a representative control and stroke participant for a line tracing task in frontal direction is presented in Figure 5.1. The task performance in stroke subjects is characterized by **shorter range of motion, longer task duration, lowered average velocity, and highly variable velocity profile** compared to age matched healthy control participants. The control subjects exhibited smoother

Figure 5.1: A) Kinematic profile (distance and velocity with time) of representative age matched healthy control and B) a stroke subject for a reaching task in frontal direction. The stroke subject exhibited shorter range of motion, longer task duration, lowered average velocity, and highly variable velocity profile compared to age matched healthy control participants

and straight line movements. Below section presents the distribution of selected across directions, movement segments and experiment groups (control and stroke).

DIFFERENCES IN REACHING MOVEMENTS OF HEALTHY (CONTROL) PARTICIPANTS

a) Spectral Arc Length (SAL):

Overall, outbound segment of movements (-2.27 ± 0.23) for all directions were significantly smoother when compared to inbound segments (-2.42 ± 0.38) of movements (all p 's < 0.001 , t-test) (see Figure 5.2). Within each segment of movement (inbound/outbound) for the three directions, SAL was found to be significantly different for outbound movement ($p < 0.001$) but was not significantly different within directions for inbound segment of movement ($p < 0.053$). For outbound segment of movements, smoother movements were observed in the front direction (-2.208 ± 0.1908) compared to both contralateral (-2.265 ± 0.285) and ipsilateral (-2.348 ± 0.213) directions, while post-hoc Tukey's HSD test showed a statistically significant difference between the front and contralateral directions only.

b) Normalized time to peak velocity:

Times to peak velocity were significantly different between the outbound and inbound

segments of movement for all directions (all p 's < 0.001), with a shorter inbound movement (3.88 ± 2.94) compared to outbound movements (5.26 ± 3.31). Like SAL among the three directions (for inbound/outbound movement segments), time to peak velocity had a significant difference when moving outwards ($p < 0.002$), but was not significant for inbound movements (See Figure 3); Tuckey HSD testing on outbound movements further showed significantly lower time to peak velocity for the front direction compared to the contralateral direction. However, in terms of mean difference, the front direction had a higher mean time (4.56 ± 2.16) than both contralateral (6.12 ± 4.91) and ipsilateral (5.11 ± 2.867) directions.

c) Root Mean Square Error:

The comparison between RMSE inbound and outbound for corresponding directions were significantly different (all p 's < 0.0001) for all the three directions 5.2. For both outbound and inbound movements, a significant difference was observed between directions ($p < 0.0001$) for each movement segment (outbound/inbound). The front direction (inbound 1.29 ± 0.715 , outbound: 1.56 ± 0.80) demonstrated significantly higher root mean square error and variability compared to contralateral (inbound: 0.3752 ± 0.20 , outbound: 0.2318 ± 0.1475) and ipsilateral (inbound: 0.31 ± 0.1153 , outbound: 0.21 ± 0.09) directions, as verified by the Tuckey HSD test.

DIFFERENCE IN REACHING MOVEMENTS WITHIN STROKE PARTICIPANTS:

a) Spectral Arc Length (SAL):

Similar to control participants, outbound vs. inbound movement segments for corresponding directions were significantly different (all p 's < 0.05, t -test), though the combined directional average was not different between the two segments (inbound: -4.124 ± 2.261 , outbound: -4.19 ± 2.21). Within each movement segment (outbound/Inbound) significant directional differences were observed for both inbound and outbound (p 's < 0.008). Further post hoc Tuckey's HSD test showed significant differences between direction 1 (front) and direction 3 (ipsilateral) for outbound movements, and direction 1 (front) and direction 2 (contralateral) for inbound movements. Overall, in both movement segments the front direction (inbound: -3.64 ± 1.71 , outbound -3.72 ± 1.83) demonstrated higher smoothness and relatively low variability compared to other contralateral (inbound: -4.48 ± 2.66 , outbound: -4.33 ± 2.18) and ipsilateral directions (inbound: -4.2491 ± 2.4123 , outbound: -4.52 ± 2.618).

Figure 5.2: Distribution of smoothness measure SAL for Control and Stroke participants in three directions for outbound and inbound movements

b) Normalized time to peak velocity:

Unlike control participants and the SAL measure, no significant difference (all p 's > 0.05 , t-test) was observed between corresponding directions for outbound and inbound movement segments (inbound: 15.934 ± 21.98 , outbound: 14.11 ± 24.88). Within movement segments, directional difference was not significantly different (p 's > 0.05) for both inbound and outbound movement segments (See Figure 5.3).

c) Root Mean Square Error:

A significant difference was only observed for the front direction when comparing the outbound movement segment with the inbound ($p < 0.001$) movement, with 1.72 ± 1.32 overall inbound mean compared to 1.52 ± 0.962 for the outbound mean in Figure 5.4. Within movement segments, a significant difference was observed between directions ($p < 0.001$) for both inward and outward movements. Further, post hoc Tuckey's HSD

test showed significant difference between the front direction (inbound: 3.17 ± 2.23 outbound: 2.73 ± 1.64) when compared with contralateral (inbound: 1.04 ± 1.01 , outbound: 0.96 ± 0.60) and ipsilateral (inbound: 0.94 ± 0.74 , outbound: 0.86 ± 0.63) directions, with higher variability in the front direction when compared to other directions.

Figure 5.3: Distribution of time to peak velocity measure distance normalized for Control and Stroke participants in three directions for outbound and inbound movements.

DIRECTIONAL DIFFERENCE BETWEEN CONTROL AND STROKE PARTICIPANTS:

Comparison between stroke and control participants for corresponding directions showed significant difference (all p 's < 0.001) for both inbound and outbound movement segments. As expected, control participants showed significantly smooth movements, better temporal efficiency with small RMSE error compared to stroke participants for all directions and segmented movements.

5.2.4 DISCUSSION

PLANAR REACHING TASKS FOR ASSESSMENT- H-MAN BASED REACHING PROTOCOL CAN BE USED TO DIFFERENTIATE BETWEEN STROKE AND CONTROL PARTICIPANTS

The results demonstrated that movements performed by stroke patients were less smooth (and more variable), featured longer normalized time to peak velocities, and larger RMSE errors, compared to their age-matched neurologically healthy counterparts. Similarly, within each population group significant differences in performance were observed within directions for both control and stroke populations. The results indicate that the assessment performed by the H-Man robotic device was sensitive to kinematic differences due to movement segment and direction.

DIRECTION AFFECTS PERFORMANCE SIGNIFICANTLY FOR SELF-PACED REACHING-A POTENTIAL INDICATOR FOR DIRECTION SPECIFIC TRAINING

Overall, control participant performed smoother movements compared to stroke participants. Within the control group the outbound reaching movements were generally smoother and featured shorter average normalized time to peak velocity values when compared to inbound movements. In contrast, the kinematics of stroke participants were generally similar for outbound and inbound segments of movements. However, in both groups significant directional differences (contralateral, front, and ipsilateral) were observed for Spectral Arc Length and Time to Peak Velocity, except deviation fit RMSE. In general for both cases less variability and higher performance was observed for the front direction compared to ipsilateral and contralateral directions, implying ease in performing tasks in the front direction. This also gives an indication that performing the task in the ipsilateral and contralateral directions might be more useful compared to front direction (for self-paced tasks) when training due to relative difficulty in performing smooth tasks in those directions.

5.3 EXPERIMENT 2: TASK DEPENDENCY OF ROBOTIC METRICS - A NOVEL STUDY TO IDENTIFY THE RELATION BETWEEN PERFORMANCE MEASURE AND TASK

5.3.1 METHODS AND DATA ANALYSIS

Results from data analyzed with 32 sub-acute to chronic stroke subjects recruited for the study similar to section 4.2.3 are presented. The participants performed two planar tasks- line tracing and circle tracing with H-MAN robot similar to Chapter 4 4.2.3. The motor performance of the stroke patients from their kinematic profiles was assessed in three aspects in both tasks: Smoothness using SPARC, temporal efficiency using Skewness in Velocity profile, and task error by the amount of deviation from the desired trajectory.

STATISTICAL ANALYSIS

Different statistical tests are performed in sequential to address the following questions:

- **How to select what we measure?** At first, we attempted to identify the independent metrics (both clinical and quantitative) to assess various sensorimotor aspects from correlation analysis. This aids us to remove any redundancy in measurements. The r value determines if the two tasks are related and its p -value that shows if the correlation coefficient is significantly different (statistically) from 0.
- **How does the performance vary across tasks, does a selection of task affect what we measure?** To investigate how task variation effects the metrics, we performed correlation of respective quantitative task performance metrics. Assuming limited learning of assessment tasks, each session was considered as an independent data sample as they were conducted on different days. This is an ongoing study, so the data from 27 subjects (only 27 out of 32 could finish the circle tracing task) with number of sessions varying from one (baseline) to five (till second follow-up at week 24) was used to compare across the tasks.
- **Does variation within task effect one's performance?** The effects of variation within the task was examined by a Kruskal-Wallis (KW) analysis, a rank-based non-parametric test. This test investigated if there was any difference in performance between the three directions in line tracing task and similarly across the

two directions for circle tracing task. Significant main effects were compared using Tukey's honest significant difference test. (HSD) post-hoc analysis. Further, the Mann-Whitney U-test (also referred to as Wilcoxon rank-sum test- RS test) was employed to compare directional difference for each subject separately.

- **How do we select the right set of tasks based on the impairment leve?** To investigate how the nature of impairment is related to the assessed task or measure, the stroke subjects were divided into three groups based on their FMA scores: severe (FMA: 20-35, n=11), moderate (FMA: 36-50, n=11), and mild (FMA > 50, n=5) groups. The variability of the metrics across the two tasks and the three groups is assessed by Friedman's test, a non-parametric equivalent of 2- way ANOVA test. Tukey's honest significant difference test (HSD) was employed as a post-hoc test to detect specific differences among the groups with significant main effect.

5.3.2 RESULTS

The reaching trajectory of representative stroke subject (FMA at Week 0 = 47) during line tracing (in 3 directions) and circle tracing (clockwise) task is presented in Figure 5.5. Relative to the line, circle tracing movements are less smooth characterized by longer time duration, irregular velocity profile, and large path errors.

The distribution (median and standard deviation) of a SPARC in line tracing and circle racing task across directions as a representative measure is presented in Figure 5.6. From the figure it can be seen that the subject exhibited very less smoothness and had high variability in the circle tracing task in comparison to the line tracing task. Within the line tracing task, frontal direction showed significant smoother and reliable movements compared to contralateral and ipsilateral directions. Similar to the result from experiment 1. the movements in ipsilateral direction had high variability owing to the relative difficulty of the task. In circle tracing task, the clockwise direction had smooth (but highly variable) movements significantly different from counter-clockwise direction smoothness were observed.

INTER-TASK VARIATION ON THE TASK PERFORMANCE:

The similarity/ disparity in the performance of subjects across different tasks was computed by correlating the task metrics. The results are presented in the Table 5.1.

Smoothness measured by SPARC showed moderate correlation across task with $r = 0.56$ ($p < 0.001$). Although, a poor correlation was observed in both temporal and task error metrics (both $r < 0.3$). This shows that metrics (that measure a particular measures) associated with one task cannot be translated to other tasks.

Table 5.1: Correlation of the task performance metrics across line tracing and circle tracing tasks

Measure	Metric	r	p
Smoothness	SPARC	0.5600	1.3650e-10 **
Temporal Efficiency	Skewness in Peak Velocity	0.146	0.1231
Error	Length of Curves Ratio	0.2571	0.0062 **

5.3.3 INTRA-TASK VARIABILITY: MOVEMENT DIRECTIONAL DIFFERENCE ON TASK PERFORMANCE IN STROKE SUBJECTS.

SPARC

Line tracing task: For smoothness measure in the line tracing task, Rank Sum-test (RS-test) used to compare differences between directions for each subject individually revealed significant difference across directions in 14 out of 32 subjects. The frontal direction exhibited significantly smoother movements compared to ipsilateral ($p < 0.02$) and contralateral direction ($p < 0.04$) respectively. However, the correlation of smoothness metric in all the subjects across the directions was high and significant (all r 's > 0.76 for all directions, all p 's < 0.0001) indicating that results from one direction can be used in estimating performance in other direction for a reaching task.

Circle tracing task: Similar to line tracing, Rank Sum-test (RS-test) showed significant effect of direction in 12 out of 27 subjects direction is noted. Smoothness in CW direction was characterized by high SPARC values and less variability. variability of performance across subjects in the counter-clockwise directions is observed. Since variability in the task performance can be associated impairment it indicates task performance in counter clock-wise direction is difficult compared to clockwise. A high correlation in SPARC across CW and CCW directions values was noted ($r = 0.77$, $p < 0.001$).

SKEWNESS IN PEAK VELOCITY

Line tracing task: Similar to smoothness, with Rank Sum-test (RS-test), SVP metric showed significant effect of direction in only 8 out of 32 subjects. Furthermore, the performance across the directions showed high correlation only between frontal and contralateral direction ($r=0.48$, $p=0.05$) and poor, non significant correlation between other direction pairs (all $r<0.3$, $p>0.05$).

Circle tracing task: RS test showed directional difference in temporal efficiency measured by normalized time to peak velocity in 10 out of 27 subjects. A moderate and significant correlation of clockwise performance with counter-clockwise direction ($r=0.44$, $p=0.02$) is observed.

LENGTH OF CURVES RATIO

Line tracing task: Individually, the RS test results showed directional differences in 24 out of 32 subjects (most of the subjects). Also, a poor correlation of LOC ratio within directions (all $r<0.1$, $p>0.4$) was observed. Unlike smoothness and temporal efficiency, the task deviation error showed significant difference in performance across directions overall ($p \ll 0.001$) in KW-test. Post-hoc Tukey's HSD test showed significantly high error values in contralateral (0.26 ± 0.16) compared to frontal (0.07 ± 0.04) and ipsilateral (0.10 ± 0.13) directions (both $p<0.02$).

Circle tracing task: RS test showed directional difference in 14 out of 27 subjects. Although lower error in CW direction (0.07 ± 0.24) compared to CCW (0.12 ± 0.21), and a strong correlation between them was observed ($r=0.8$, $p<0.001$). Unlike line tracing task, LOC ratio was not significantly different across directions ($p=0.33$) in circle tracing task.

5.3.4 EFFECTS OF IMPAIRMENT LEVEL ON THE RELIABILITY AND SENSITIVITY OF ROBOTIC ASSESSMENT TASKS:

SPARC:

The distribution of the variability of smoothness in the three impairment groups across line and circle tracing task is presented in Figure 5.7 A. Overall the circle tracing task showed significant high variability in smoothness compared to a line tracing task in the mild and moderate groups ($p<0.05$); Although, no significant difference in the severe

impaired group ($p=0.0341$) was noted. This might be due to the difficulty in repeating the movements in similar patterns across time in severely impaired subjects. Within groups, significant difference in the variability was observed in both line ($p=0.045$) and circle tracing ($p=0.035$) tasks. In post-hoc analysis, line tracing detected significant difference only across severe and mild impairment ($p=0.03$) groups. Whereas, circle tracing could detect difference from severe group with both moderate ($p=0.02$) and mild impairment ($p=0.009$) respectively. No difference in moderate group variability with mild group was detected in both the tasks ($p>0.6$).

SKEWNESS IN VELOCITY PEAK:

The Skewness in Velocity Peak, a measure for temporal efficiency showed no significant difference in the variability of circle vs line tracing in all the three groups all $p's > 0.09$). Also unlike smoothness, no significant difference was observed within groups in both line ($p=0.52$) and circle ($p=0.80$) tracing task. This might also be due to the nature of the metric, since it is a measure of strategy of how subject plans a task, it could be similar across tasks and groups.

LENGTH OF CURVES RATIO:

From the error measure showed in Figure 5.7 significant difference in tasks (Circle vs task) only in the severe impaired group ($p=0.007$) and no differences in moderate and mild groups (both $p>0.9$). Like smoothness, the within group analysis showed group as significant factor in both line tracing ($p=0.001$) and circle tracing ($p=0.04$). Post-hoc analysis showed significant difference of variability in severely impaired with mild ($p=0.005$), but not with moderate ($p=0.33$) in line tracing task. Circle tracing task, showed significant difference of severe group with both moderate ($p=0.01$) and mild group ($p=0.03$). No difference within moderate and mild group was detected in both the tasks ($p>0.4$).

5.3.5 DISCUSSION

The aim of this experiment is to investigate the how the nature of tasks affect patients' assessment. The motivation was to bridge the gap in using different outcome measures across numerous studies and for approaching a systematic mechanism for employing robotic measures for widespread use of sensorimotor assessment post neurological injuries. The results from sub-acute to chronic stroke participant's performance during a

line and a circle tracing task using a planar two degrees of freedom robot, H-Man, are presented. The results discuss on how tasks effect the selected outcome measure and their inter-relation. Furthermore, the effect of impairment levels on the sensitivity of robotic metrics and tasks is investigated by the variability analysis. It is essential to classify and adapt different robotic assessment tasks based on the type and level of impairment. In the remaining section, we discuss in detail the main findings of the study.

LIMITED CORRELATION OF ROBOTIC METRICS ACROSS TASKS

How the choice of tasks affects the understanding of motor performance is still an area to be explored. Hence, we analysed the relation between similar task metrics across two different robotic assessment tasks. The robotic metrics derived from the line and circle tracing task showed moderate to low correlation with each other. The results show how variation in tasks offer a completely different interpretation of the measure itself. A clear review of tasks itself makes it a bit more obvious. Smoothness when defined in terms of line tracing task is relatively simpler task of coordination between shoulder and elbow joint, while a circular motion requires significant multi-joint coordination and motor control. Hence smoothness assessed in one task may not be easily translatable to the other. This was particularly true for other metrics that assess temporal or task error measures. Hence a simpler (such as line tracing) task might be employed to provide a surface level estimation of sensorimotor skills and a complex (circle tracing) task for a detailed assessment.

Furthermore, we examined how variations within the task effects the participant's performance. In Hussain et al 2016 [101], it is shown that direction affects performance for self-paced reaching. Also in this study, significant difference across directions (between the three directions in line tracing task and across the two directions for circle tracing task) was observed. In the line tracing task, frontal direction had smoother and less errored movements compared to ipsilateral and contralateral directions. Also, for the circle tracing task, the clockwise (CW) direction movements were characterized by high SPARC values and in the metrics compared to the CCW direction performance. We also observed, a high correlation across direction is observed in these metrics implying that results from one direction can be used in estimating performance in other direction. This indicates that even a small variation within the task (the task direction here) can play a significant role.

RELIABILITY AND SENSITIVITY OF A ROBOTIC METRICS DEPEND ON THE TASK AND IMPAIRMENT LEVEL

The selection of an optimal sensorimotor robotic task from the large number of tasks available in literature is challenging. The impairment status might limit the ability to perform the task in a reliable manner. This was observed by looking at variability of task performance over trials. Highly impaired subjects showed higher variability across session in performing the task. The LT task showed lower variability across all impairment groups compared to the CT task in smoothness (SPARC) and task error (LOC) indicating higher repeatability and hence reliability in the assessed metrics. However, with LT one could only differentiate between the two extreme ends (severely and mildly impaired) subjects due to limited sensitivity. In this study, both tasks failed to differentiate between the moderately and mildly impaired group possibly because of small sample size of mild group.

While it is necessary to refine the tasks further, it is also crucial that we have a series of tasks (with increasing level of difficulty based on the nature and level of impairment) to have a more detailed picture of patient's performance. For a reliable and accurate sensorimotor assessment, we recommend the following systematic approach: Identify task assessment metrics that are robust, easy to measure, and are invariant to robotic setups. Regarding the tasks, for the initial assessment the subjects could be assessed by simpler tasks (with low variability i.e., high repeatability) to reliably grade overall category of the patient's impairment status. Example: self-paced reaching task, line tracing etc. This could be followed by another task (with high sensitivity) which requires greater level of skills for improved resolution. Example: Circle drawing, shape-shifting etc. Also, embedding tasks with different factors such as task dynamics kinetic measurements such as force, torque, etc., would provide a better understanding of the subject's motor condition in cases with spasticity, ataxia, etc. Clear knowledge of sensorimotor deficits will further aid in designing efficient training regime for improved benefits with rehabilitation robotic therapy.

5.4 CONCLUSION

This chapter presents the results from two clinical studies analyzing how technology aided measures can be improved to provide a better estimate of sensorimotor impairment. The results promote the use of technology aided assessment task complementary to the the conventional clinical tests to evaluate the impairment status more reliably and

accurately.

- In the first experiment with healthy control and stroke subjects in a self-paced reaching task, significant difference in the control and stroke subjects performance was noted.
- The effect of task movement (outbound vs inbound) was significant in healthy control. In healthy control, the **outbound** bound movements were **smoother with better temporal efficiency** compared to inbound movements. However, no such difference in task metrics were observed in the stroke subjects due to reduced sensitivity. Functional ability (measured by task performance) altered with **task direction**.
- In the second series of experiments with sub-acute to chronic stroke subjects, significant differences between the two tasks (circle tracing and line tracing task) with **limited to no correlation** was noted. This indicates that findings from one task cannot be transferred to the other tasks. This has implications in comparing different studies which use different assessment tasks and outcome measures. It is important to constitute different assessment tasks that could measure various constructs such as: *strength, co-ordination, functionality with increasing level of difficulty*.
- The reliability and sensibility of task measures are investigated by measuring the variability of task performance over trials across task based on the impairment status. The results demonstrate the need for developing a normative set of robotic tasks and metrics based on the nature and the level of impairment independent of the robotic/ sensory device employed.
- As more data is collected from standard robotic tasks, a database of normative motor function specific to the H-Man assessment can be formed. This would provide clinicians with the opportunity to compare a patient's performance against the reference values and make appropriate treatment decisions based on that data.
- This chapter highlights the gaps in translation of robotic assessment metric to clinical settings. The results illustrated the task dependency of these metrics and their limitation in reliable assessment of subjects. Based on these results, in the next chapter, we test the usefulness of physiological measures (Surface Electromyography activity) as a bio-marker for impairment.

Figure 5.4: Distribution of RMSE for Control and Stroke participants in three directions for outbound and inbound movements in a self paced reaching task

Figure 5.5: Representative kinematic movement profile of a stroke subject (FMA at Week 0 = 47) during A) line tracing and B) circle tracing (clockwise) task is presented.

Figure 5.6: The distribution (median and error bar) of a SPARC metric (a measure of movement smoothness) of a stroke subject (with FMA at Week 0 = 47) during A) line tracing (in 3 directions) and B) circle tracing (clockwise) task is presented.

Figure 5.7: Distribution of the variability of task performance metrics in the three impairment groups (severe, mild, and moderate) across line and circle tracing task is presented in the order. A) smoothness measured by SPARC; B) Temporal efficiency measured by normalized time to peak velocity(TpeakN); C) Task deviation error measured by Length of Curves (LOC).

Our virtues and our failings are inseparable, like force and matter. When they separate, man is no more.

Nikola Tesla
Inventor and Futurist

6

Role of EMG as a complementary tool for assessment of motor impairment and performance marker

In this chapter, the feasibility of employing Electromyography (EMG) signal measure as a complementary assessment metric to kinematic metrics is evaluated. The results from a case-study on five healthy adult, five healthy aged, and two stroke subjects is presented. My contributions to this work were the development of protocol and GUI interface, data collection from healthy (adult & aged) and stroke individuals, and their performance evaluation. ¹

The previous chapters discussed how kinematic task information from the H-MAN sensors can be potentially used as a tool for an accurate and objective sensorimotor assessment. Nevertheless, the task dependency and unavailability of standardized robotic task and performance metrics drive us to explore for more valid and reliable bio-markers.

¹The results from this chapter are from published work. Budhota, A., Hussain, A., Hughes, C., Hansen, C., Kager, S., Vishwanath, D. A., ... & Campolo, D. (2016, June). Role of EMG as a complementary tool for assessment of motor impairment. In Biomedical Robotics and Biomechatronics (BioRob), 2016 6th IEEE International Conference on (pp. 692-697). IEEE.

Physiological signals such as Electromyography(EMG) have been used to predict the movement and to understand motor control deficits [174, 201, 202]. In the present study the assessment of performance during a planar reaching task was made through kinematic task parameters (smoothness of movement and time to peak velocity) and EMG signal measure (Integrated Average Value) from the upper limb muscles. The results indicated the potential use of EMG-based metric as a complementary measure to generally-used end effector robotic metrics to assess and track the recovery process of sensorimotor impairments.

6.1 INTRODUCTION

The robotic controllers used in rehabilitation settings in general adapt based on the task performance of the participant. Most standard approaches for designing such controllers rely on kinematic parameters collected from robotic sensors [82, 203, 204]. These parameters are used to derive information about the subject's performance and adaption to the robotic feedback and training. The objective of robotic control algorithms is to provoke motor plasticity, and hence augment motor recovery. However, no optimal control strategy is defined yet, as each stroke individual is unique in their performance/impairment owing to the heterogeneity in stroke and its effects.

In the past few decades, EMG signals are used in motor control studies [143, 205], to control prosthetic devices [206–209] in gait and posture analysis [210]. Different features extracted from the EMG signals are used as feedback signals in rehabilitation robots for active therapy [104, 211] and for predicting the movement in control of exo-skeletons [174, 212] and telerobots etc [213]. Muscles are the actuators of the movement, and analyzing how the ability to activate muscles is altered post-stroke is important. This could provide a basis to understand how robotic controllers could be improved [82, 214]. Analyzing EMG aids in better understanding of the reasons behind motor in-coordination in stroke individual.

In stroke, movements are characterized by reduced speed, high variability in movement smoothness, and limited range of motion [8]. Upper arm impaired stroke survivors exhibit compensatory strategies such as co-contraction of agonist-antagonist muscle pairs, excessive use of trunk movement, reduced degree of freedom to complete a required task. A short term gain in task performance can be improved by using

these compensatory actions. So, to identify if the improvement in the motor task is achieved by true functional recovery or by undesired compensatory movements simply analyzing kinematic/kinetic task measures is not suffice. Since the muscles are the actuators of the movement (that reflect the related motoneuronal activity), examining the muscular activity (collected from surface electromyography (SEMG)) would present a better assessment of motor functions. Monitoring and analyzing the alterations in EMG patterns during a specified task in healthy-control and post-stroke subjects enables us to associate the cause and result of impaired movements [27].

The limited studies on the effects of stroke on motor control and muscle synergy organization in the human upper extremity suggest that stroke alters the normal muscle patterns [151, 215]. Surface Electromyography (SEMG) provides an estimate of muscle activation of nearby electrodes. In general, the analysis of muscle activation in stroke subjects compared to healthy control in upper extremity studies revealed longer (delayed) onset periods, lower modulation strategies, and higher muscle activation in stroke subjects [216]. Also, co-contraction of agonist-antagonist pair [207] and trunk movement [217] are common compensatory strategies noted in stroke subjects resulting in abnormal synergistic patterns and altered movements. But there are very limited studies that studies how alteration in the EMG activity are reflected in task space parameters. This limitation strongly suggest the need for an assessment of muscular activity in combination with task-space kinematic measures for developing subject-specific neuro-rehabilitation paradigms.

This study is aimed at verifying whether muscle signal information can aid in better assessment of impairment and recovery process in stroke. In this case study, we also investigated how aging (by comparison of performance in healthy adult and aged group) and neurological impairment (stroke) affect the motor performance metrics of a subject during an upper limb planar reaching task. We hypothesized that since EMG could provide additional information about the muscular co-ordination, this will provide insight about the subject's motor control strategies and compensatory movements. Furthermore, this information can be used to model an adaptive controller for maximum therapeutic benefits.

6.2 METHODS

6.2.1 PARTICIPANTS

Ten healthy control subjects divided into young adults and age matched groups and two chronic stroke patients with upper limb motor impairment participated in the study. The demographic details of the control participants and the two stroke patients are provided in Table 6.1. All the control participants had corrected to normal vision, and had no known neuromuscular disorders.

Table 6.1: Demographic and clinical information of participants

	Control Adult	Control Aged	Patient 1	Patient 2
Age	26.4 (3.78)	54.9 (4.1)	56	67
Gender	3M, 2F	2M,3F	F	M
Type of lesion	-	-	Infarct	Ischemic
Side of lesion	-	-	Right	Right
Time since onset (months)	-	-	12	20
Fugl-Meyer Score	-	-	43	20

- Patient 1 is a 56-year-old right-handed female who had suffered a lacunar infarct to the right hemisphere 12 months earlier. The patient had a total Fugl-Meyer Assessment (FMA) score of 43/66 with signs of motor incoordination (i.e. motor ataxia), dysmetria and intentional tremor that impaired upper extremity movements, as observed by an occupational therapist.
- Patient 2 is a 67-year-old right-handed male who suffered a right hemisphere ischemic stroke 20 months prior to the baseline assessment. Clinical assessment scales showed an FMA score of 20/66. The patient did not present any associated motor incoordination or motor ataxia.

6.2.2 APPARATUS

The robotic platform used for this study is the H-Man device detailed in section 3.1.1 and muscular activity is measured using BIOPAC as described in 3.1.2 .

Figure 6.1: (Top) Subject using H-Man robot for assessment task. (Bottom) Visual stimuli used for the assessment with the directions explained.

ELECTROMYOGRAPHY:

The EMG activity of the following upper limb muscles: Brachioradialis (BRAC), Biceps Brachii (BICP), Triceps lateral head (TRIC), Deltoid Medial (DMID), Deltoid Anterior (DANT), Deltoid Posterior (DPOS) and Trapezius Superior (TRAP) was collected. Muscle selection is based on the task requirement and adapted from similar studies [25, 151, 152]. The EMG data is synchronized with the kinematic data from the H-MAN controller that contains information about velocity and position relevant to the task conditions.

6.2.3 PROCEDURE

For robotic assessment, the subjects were asked to perform a planar reaching movement in three directions (-45° , 0° and $+45^\circ$) to understand their natural motor performance (see Figure 6.1). The procedure is similar to the previous chapters described in section 5.2.1. The entire testing session (including the placement of the EMG electrodes) took approximately 45 minutes.

6.2.4 DATA ANALYSIS

The raw kinematic data of the velocity and distance profile obtained from the robot controller was low pass filtered (Butterworth: 6th order, cut off F_c : 20Hz, F_s : 1000Hz) for further analysis. The movement is segmented and processed similar to 4.3.1 to derive Spectral Arc Length 3.2.1, Normalised time to peak velocity 3.2.1 measures. The raw EMG data acquired from the NI CARD processed offline to a rectified and low pass filtered signal (Butterworth: 4th order, cut off F_c : 20Hz) to estimate the IAV measure defined in section 3.3.

6.2.5 STATISTICAL ANALYSIS

To identify the intra subject variability across different directions [45° , 0° , and $+45^\circ$], a non-parametric Kruskal Wallis (K-W) test [218] was performed on each measure for the respective groups. The statistical significant difference among the three groups [control adult, aged, and stroke] was tested by a Wilcoxon rank sum (RS) test for all the directions and the respective measures. The critical p-value of 0.05 was selected for rejecting the null hypothesis unless stated otherwise.

6.3 RESULTS

The reaching trajectory of the selected control subjects and the stroke participants is presented in Figure 6.2. Similar behavior among the control groups (Adult and Aged) and a significant difference in performance with stroke subjects is observed from the kinematic XY profile. In stroke subjects reduced performance is noted to be correlated with the level of impairment.

6.3.1 SMOOTHNESS OF MOTION

In general, both aged and adult control participants made smoother reaching movements compared to stroke patients, irrespective of directions (see Figure 6.3). This was verified by a RS test (control adults vs stroke, all directions: $p < 0.001$ in control aged vs stroke, all directions: $p < 0.001$). Comparison between the control adults and aged was only significant for the middle direction (control adults vs. aged, sagittal frontal direction $p < 0.004$) with a relatively smoother movement as observed by spectral arc length measure for adults compared to aged participants. Directional difference within each

Figure 6.2: Reaching trajectories (XY-profile) during the planar reaching task of subjects - control adult, control aged, and two stroke participants respectively.

group (adult, aged, patient 1 and 2) using K-W test showed significant differences for the adult and aged healthy participants (both cases: $p < 0.0001$). However for the two stroke participants no significant difference was found across directions (potentially due to the lower number of trials and thus increased variability).

6.3.2 TEMPORAL EFFICIENCY

Similar to the smoothness metric, significant difference was observed between the aged vs. stroke participants (all directions: $p < 0.0001$) and adults vs. stroke participants ($p < 0.001$ – except direction 3: $p > 0.05$) in normalised time to peak velocity measure. The K-W test across directions in each individual group showed significant difference for control aged, adults ($p < 0.001$) and stroke participant 1 ($p < 0.04$) but was not significant for participant 2 (Figure 6.4)).

Figure 6.3: Spectral Arc Length distribution for all directions for combined control (adult and aged) and two stroke participants. Red crosses and green squares represent mean and median respectively.

Figure 6.4: Temporal measure distribution for all directions for combined control (adult and aged) and two stroke participants. Red crosses and green squares represent mean and median respectively.

6.3.3 EMG MEASURE

The Integral of Absolute Value (IAV) values of the EMG of the collected upper limb muscles are presented in Figure 6.5. The activation pattern across the control groups and stroke subjects can be observed from the IAV amplitude values of the measured EMG signals. From the figure and the statistical test results performed to compare across different groups (aged, adult and stroke), a high similarity in muscle recruitment in adult and aged (control group) is observed except for the case of the BIC, TRIC, DMID muscles ($p > 0.1$). The RS test showed significant differences among the control group and both the stroke participants with in the corresponding muscles for all the cases ($p < 0.05$) except for the DANT muscle ($p > 0.2$). A K-W test was performed to understand the directional difference. It revealed significant differences in the muscle pattern among the directions in the control group: control aged (except for DMID and DANT; $p < 0.02$), control adult (except for BICP and DANT; $p < 0.002$). For the stroke participant 1 no significant differences were observed across different directions (except for BRAC and BICP; $P < 0.01$) whereas participant 2 showed significance in directional difference (except for DMID and DANT; $p > 0.01$).

6.4 DISCUSSION

In this chapter, I assessed the motor performance of three groups of subjects: control adult, control aged, and stroke participants by kinematic and EMG-based metrics to understand and identify the differences across directions, subjects and their relation with the type and level of impairment.

For the assessment, the kinematic and physiological parameters were selected for assessing a subject's ability to perform a planar reaching task within his or her workspace: 1) Smoothness of the reaching task: the ability of the participants to complete the task with a minimum number of sub movements is assessed using SAL. 2) Time to peak velocity normalized: the time taken by subjects to reach the peak of their speed profile with respect to the total time to complete the task. This measure gives the temporal efficiency and planning strategy of the subject. 3) The activation pattern of different upper limb muscles across the shoulder and elbow analyzed by monitoring the IAV value of their EMG activity. This provides an insight into the neuromuscular co-ordination by understanding the major and minor contributors of the task and the

Figure 6.5: IAV-EMG value for all muscles across the three directions in control adult, control aged and two stroke participants. The data is shown for the following muscles: Brachioradialis (BRAC), Biceps Brachii (BICP), Triceps lateral head (TRIC), Deltoid Medial (DMID), Deltoid Anterior (DANT), Deltoid Posterior (DPOS), and Trapezius Superior (TRAP)

variability in recruiting among different groups. We briefly discuss the results here and their implications.

The kinematic end effector parameters demonstrate a clear difference in the control and stroke subject performance. Smoothness (as in SAL) is characterized as having no or few sub-movements spaced closely in time [19, 97]. Control participants (both adult and aged groups) exhibited fewer sub movements as indicated by SAL values closer to zero than the stroke-affected participants (Figure 6.2). Similarly, when comparing corresponding directions between control and stroke participants, a significant difference was observed. These results indicate that using smoothness - and SAL, in particular - can be used as a motor assessment measure, since it gives information about co-ordination at task space. The time to peak velocity measure showed a difference in the control adult and aged group. The aged group took a longer movement time to perform the reaching task when compared to the young adult group as expected. The stroke subjects exhibited even lower values and a significant difference between the control and stroke subjects was observed. The normalized time to peak velocity is a

sensitive and reliable measure and, in combination with the smoothness, can be used to get a preliminary understanding of a person's impairment and functionality.

The kinematic task parameters showed limited correlation with the clinical status of the subject. For example, one would expect the patient 1 with FMA: 45/66 would perform better than the patient 2 with FMA: 20/66 and may be similar the control subjects in smoothness and temporal efficiency. But, we observe both the stroke subjects show equally poor performance. Moreover, the patient 1 has high variability in the measure i.e., he is unable to repeat the movements in similar fashion. The reason behind such discrepancies can be understood by looking deeper, for instance, at the movement origin level i.e., their muscle activation. The IAV measure of the muscles provided additional and most important information about the subject's strategies and compensatory movements. In general, the prime movers for the planar reaching task in control subjects for forward motion are the shoulder joint deltoid muscles (DMID, DANT) with the maximum IAV being observed in DANT, along with supportive muscles (TRIC, TRAP). The activation pattern within the control groups (adult vs aged) is similar, except that control aged group seems to have increased activity in supporting muscle (TRIC, TRAP).

The patient 1, with a moderate FM score of 45, a co-contraction of the agonist-antagonist pair of the deltoid muscles (DANT, DPOS) is observed. This might be due to ataxia (verified from the clinical tests). Patient 2, a severely impaired subject with a low FM score of 20 seems to use the primary mover (DANT) in greater amounts in proportion to other upper limb muscles, indicating that the subject requires more strength and uses abnormal activation patterns when compared to the control. The results are in accordance with recent studies that showed impairment level dependent muscular activity pattern alterations among different stroke group subjects (mild, moderate and chronic) when compared to control subjects [215, 219]. This difference in the muscle activation and co-ordination among stroke participants might account for the type and severity of the stroke. This can be used as feedback by therapists to identify the subject's deficit and train those muscles that showed abnormal activation patterns.

6.4.1 LIMITATIONS

The limitation of using EMG signals is that they are highly variable signals depending on many anatomical, physiological and technical factors reviewed in [214] and requires expertise in electrode placement and measuring a noise free qualitative signal [220]. A limitation of this study includes the limited number of stroke participants. For effi-

cient and faster recovery, there is a need to understand the reason behind motor control deficit from a neuromuscular perspective i.e., modular organization of motor control. To account for the limitations in collecting and analysing EMG alone, the later chapters introduce and analyse muscle synergy (the co-ordination of muscles to act in groups) patterns to understand the impaired motor control by adding multiple task constraints.

6.5 CONCLUSION

From this case study, it can be derived that unlike the kinematic measures that provide information about the level of in-coordination alone, EMG-based measures provide explanations for such movements.

- The healthy **adult and aged** behave similarly in kinematic task parameters in a planar reaching task with difference in performance across directions. In the muscle recruitment, healthy aged show increased activity in supporting muscles in comparison to adult population.
- Analysis of muscle activity in **stroke** subject highlights the **altered muscle patterns** from healthy control. This helps in investigating the underlying strategies of each user.
- This study promotes the employment of **EMG-based** metrics or muscle synergies as **indicators of impairment** to track the recovery process along with typically used kinematic based task space parameters.

In this chapter, the potential of employing EMG signals to describe stroke subjects unique behaviour is demonstrated. From this, we aim to investigate the muscular organization and how the muscle activity is transformed to task space forces at the end-effector to perform a desired task in the following chapter.

"I could either watch it happen or be a part of it".

Elon Musk

Innovator and Entrepreneur

7

Augmented synergies to identify task relevance of muscle synergies from an isometric task in healthy control subjects

In this chapter, the muscle synergies during an isometric task involving shoulder muscles from the healthy control subjects are presented. A novel method to extract synergies, called '**Augmented Synergies**', is introduced to estimate the task-space contributions of muscle synergies. **Isometric task** is chosen as the assessment task, as it is one of the effective methods to look into the muscle coordination from the **endpoint force information**. It is simple to infer the results and is devoid of any other factors in dynamic motion that may contribute to the undesirable task forces. This chapter is a **preliminary** step to better understand motor control and to assess the feasibility of the use of muscle synergy based control schemes in rehabilitation robotics. ¹

¹A part of this work is a revised version of paper published in ICORR 2017. Budhota, A., Tommasino, P., Hussain, A., and Campolo, D. (2017, July). **Identification of shoulder muscle synergies in healthy subjects during an isometric task**. In Rehabilitation Robotics (ICORR), 2017 International Conference on (pp. 134-139). IEEE.

7.1 INTRODUCTION

A muscle synergy is defined as the **coordinated recruitment of a group of muscles** with specific activation weights to act as a functional unit [30]. Muscle synergy hypothesis is one of the widely used solutions proposed to solve the '**redundancy**' problem in motor control. Bernstein in 1967 proposed that CNS activates muscles in groups solving the problem of motor and muscle redundancy and reduce the computational complexities in motor planning and execution of a voluntary movement [29]. **Synergies** are regarded as the building blocks of motor control that hold a characteristic relationship across **set of similarly activating muscles** to produce **wide variety of tasks**. According to this hypothesis, *a muscle synergy constitutes activation of multiple muscles and one muscle can be part of multiple synergies*. Muscle synergies, that are a grouping of functionally similar muscle have been observed in humans across many tasks such as reaching [127], grasping [221], walking and running [131], postural response [222], and isometric force generation [144]. It has also been observed that the synergies are shared across different tasks [223, 224] and their activation is modulated by a sensory feedback [225]. Moreover, these muscular synergies are **shared** across different subjects [226] and also **subject-specific** synergies are observed accounting for varying bio-mechanical properties [134]. The post-stroke alterations in different motor tasks have been studied in human upper arm [33, 36, 215, 227] and in lower extremities in [153] and revealed an altered number, structure, and activation of muscle synergies depending on the level of impairment. However, a consensus has not been reached about the neural origin of muscle synergies [146].

Kutch and colleagues in their research [141, 142] **challenged the muscle synergy hypothesis** by showing that, for the index finger, muscles can be recruited either *individually or synergistically* leading to the hypothesis of a flexible activation scheme rather than a synergistic one. This is extended to a major view called '**prime mover strategy**', in which a single muscle is activated in dominance if the target force direction is aligned with the action direction of a muscle and results suggested flexible recruitment of synergies depending on the task rather than a hardwired neural representation. Between these diverse competing hypotheses and other theories, no consensus has yet been reached. Hence, it is essential to understand how muscle synergies manifest onto task forces at end-effector. Some studies in literature have attempted to associate the task force to the synergy activation in [31, 147, 179]. All such studies attempt to

establish relation to the forces and muscle synergy either by correlation or regression analysis after processing them as separate entities. Nevertheless, this is not suffice to how to explain the task relevance of these muscle synergies, i.e., to directly correspond the task force to the estimated synergies. Moreover, in calculation of synergies, most of the studies **normalized** the input muscle activity to have **unit variance**, to prevent any bias towards highly-variance muscle. According to Signal Dependent Noise (**SDN**) principle by [148] and minimum-variance hypothesis of motor control [228] a motor output is composed of desired endpoint force and fluctuations. It is hypothesized that if motor output is corrupted by neuronal noise, it manifests as fluctuations at motor level and is scaled with respect to the magnitude of the desired force/motor activity. Hence these fluctuations (variance) could **reflect the lower level neural activity** and might constitute the underlying muscle properties such as mechanical muscle action direction or the evidence for the neuronal existence of muscle synergies. Hence "**variance**" in a signal might consist of vital information and normalizing the signals to have unit variance might devoid us from analyzing critical information.

In this experiment, we include the **task-space forces along with the EMG in the muscle synergy extraction**. To do this we propose a novel approach to calculate synergies termed as '**Augmented Synergies**'. Also, the variance in the force and EMG signals is added as a weight matrix to the modified version. We hypothesize that by this approach, we could identify the synergies that contribute to the task, and any additional synergies that required to support the posture, or those that arise due to *compensatory actions*. Five control healthy subjects performed an isometric, two-dimensional force-matching task in **twelve planar directions** with two force levels across shoulder joint. The target forces for the experiment are set at two force levels scaled to **15% and 30%** of Maximum Voluntary Force (MVF). The results from **healthy control subjects** are analyzed to establish normative data in isometric tasks involving shoulder muscles and preliminary analysis on the 'Augmented Synergies' to estimate the task contributions of muscle synergies.

7.2 METHODS

7.2.1 PARTICIPANTS

Five right-handed healthy subjects [Age: 23 ± 2.6 ; Gender: 3M, 2F] are recruited for the study to perform an isometric force-matching task with the dominant hand. All the par-

ticipants had corrected to normal vision and had no known neuromuscular disorders. The methodology and written consent form for the experiments were approved by the Domain Specific Institutional Review Board (IRB) of the Nanyang Technological University.

7.2.2 APPARATUS

The experimental setup is a custom-made apparatus as shown in Figure 7.1 with a load cell attached to a 3D printed wrist support. This is supported onto a height adjustable aluminum bar. The isometric end-point forces and torques in Para-Sagittal plane were acquired at a sampling rate of 1000Hz by a six-degree-of- freedom (DOF) load cell (ATI MINI-80). The isometric condition allows to map directly Flexion-Extension (FE) and Abduction-Adduction (AA) shoulder torques into the vertical and lateral forces at the load cell. These forces denoted F_{FE} and F_{AA} respectively, were mapped and represented onto lateral (x) and vertical (z) axes of the screen. These mapped forces were used to control the cursor to move to the required target direction during isometric task in the virtual game developed in UNITY.

ELECTROMYOGRAPHY

The EMG activity of the following upper nine limb muscles: Brachioradialis (BRAD), Biceps Brachii (BICP), Triceps long head (TRIC), Triceps lateral head (TRIL), Deltoid Anterior (DELA), Deltoid Medial (DELM), Deltoid Posterior (DELP), Trapezius Superior (TRAU), and Pectoralis Major (PECM) was analyzed. Muscle selection was based on the task requirement [227]. The EMG data was synchronized with the data from the isometric task via QUANSER controller that contains information about the forces and game conditions through a common trigger to both systems.

7.2.3 STUDY PROTOCOL

Isometric task is one of the methods to look into the muscle coordination from the end-point force information. A typical isometric task setup is to constrain the body segment and let the endpoint exerts force against a sensor. More interpretable experimental findings can be obtained from isometric tasks [141]. Also, muscle activation patterns can be evaluated through muscle activities and force production during the isometric tasks owing to their linear relationship [158]. It has been shown that peak force

Figure 7.1: (Top) Subject performing the isometric task with wrist strapped onto the load cell. (Bottom) Visual target forces (blue circles) and real-time force (yellow bar) and task definition with directions notation. The forces denoted respectively, were mapped and represented onto lateral (x) and vertical (z) axes of the screen

produced by strongest subjects and weakest subjects have very large difference. There were no significant differences in the force variability at their 100% of Maximum Voluntary Contractions between the two groups [229]. Therefore, compared with the absolute force levels, force levels that relative to the MVC perform act as a better indicator for the force variability across different subjects, especially in the range below 60% MVC. Since it is tedious and redundant to measure MVC of each muscle involved in the task individually, we measured the end-effector and EMG activity during the Maximum Voluntary Force (MVF) exertion task in four task directions (in the Shoulder Abduction, Adduction, Flexion and Extension respectively).

The subjects performed in total 24 isometric force matching tasks in the Para-Sagittal plane across 12 directions at two force levels across the shoulder joint as shown in the 7.1. The custom-made setup apparatus was placed on fixed table and a visual feedback

with task instructions was provided on a flat screen monitor [23 inches] placed in front of the subject. The apparatus was adjusted relative to the subject's height so that the shoulder joint was aligned horizontally with the wrist in neutral position. Here, the neutral position is defined as the position where the wrist is in straight alignment with the forearm: no flexion, extension, radial or ulnar deviation. The load cell was calibrated prior to the task to remove any bias in the force signals due to the limb weight, and forces against gravity.

Prior to the isometric task, subjects performed MVF (Maximum Voluntary Force) trials in four respective directions (in the Shoulder Abduction, Adduction, Flexion and Extension). During these MVF trials, the subject was instructed to apply their maximum force in each of the four directions (two axes: A-A and F-E) for 5 seconds. The minimum of the two peak values in each of the axis was considered as the overall MVC force of the subject in that axis. This measure was used to scale the target forces for the experiment to two levels at 15% and 30% of MVF in the respective axis. The target forces were evenly distributed in twelve directions and at two force levels at an increment of 30 degrees as shown in Figure 7.1

Followed by calibration and MVC estimation to scale the target forces individually, the subject performed isometric force matching task. The targets were displayed on the game screen as blue circles and their locations were set according to the desired force (15 % or 30% MVF) and direction (one of the 12 direction) in a randomized order to eliminate any incidence of learning. The inner layer and outer layer targets (in blue) correspond to 15 % or 30% MVF respectively. At the start of each trial, the subject placed the cursor at the home position with the wrist-shoulder joint in neutral position and was asked to slowly produce force to reach the a random target force and maintain it for at least five seconds. The subject viewed the desired force as a target (blue circle) and the real time endpoint force as a moving cursor (yellow bar) on a screen. The targets were shown on screen as blue circles and their locations were set according to the desired force level and direction in a randomized order. Subjects could practice for a few rounds to familiarize themselves with the task. A rest period of 10 sec after each trial was provided to avoid muscle fatigue. The torque across the pronation-supination direction is monitored during the task and when the torque is greater than 0.5Nm the game is paused and a visual feedback instruction to avoid the rotation of the arm is shown. The electromyography activity from nine upper limb (shoulder and elbow) muscles was also

collected for future analysis. The detailed task protocol is presented in Figure 7.2. Data acquisition and experiment control were designed and performed in MATLAB scripts and Simulink models interfacing with QUANSER (a real-time controller). The game interface was designed in Unity3D. All data analysis was performed with scripts written in MATLAB (Mathworks, Natick, MA).

Figure 7.2: The task protocol of the isometric task implemented in this study. Prior to the isometric task, subjects performed MVF (Maximum Voluntary Force) trials in four respective directions (the Shoulder Flexion, Extension, Abduction, and Adduction) for 10 sec each. Followed by this, the subjects performed in total 24 isometric force matching tasks in the Para-Sagittal plane across 12 directions at two force levels (15% and 30% MVF) across the shoulder joint. The subjects exerted desired force direction and had to maintain it for at least five seconds before the next trial.

7.3 DATA ANALYSIS

7.3.1 PRE-PROCESSING OF FORCES FROM THE ISOMETRIC TRIAL

The raw force data obtained from the load cell was low pass filtered with cut-off frequency 20 Hz (similar to the muscular activity). The force data during the hold period from each trial are cropped to 3sec for further analysis by removing the first and last sec to avoid any variations due to external disturbances as they might contain the transient phase of force development.

7.3.2 PRE-PROCESSING OF MUSCLE ACTIVITY (EMG)

The EMG data during the hold period (5 sec) from each trial are cropped to 3sec for further analysis by removing the first and last sec to avoid any variations due to external disturbances. This is to ensure that we analyze only relatively constant forces eliminate any traces of transient phase of force development. The acquired raw EMG signal, cropped to 3 sec hold period was pre-processed offline to a demeaned (removing any offset), rectified and low pass filtered signal (Butterworth: 4th order, cut off Fc: 20Hz) to obtain an EMG envelope for further processing. The Integrated Average Value (IAV) of EMG activity was calculated to analyze and compare the muscle activity across different directions by estimating muscle tuning curves from a cosine fit to the IAV data as described in [230].

7.3.3 SYNERGY EXTRACTION WITH THE TRADITIONAL NNMF METHOD: WITH MUSCLE ACTIVITY ONLY

Prior to synergy extraction, EMG envelope recorded from each muscle followed by pre-processing was down-sampled to 100Hz assuming relatively constant activation in EMG signal across the trial. Following the literature, this EMG envelope is normalized to have unit variance to remove any bias towards highly varying muscles. The muscle synergies were extracted from the EMG matrix that is comprised of muscle activity across various conditions by employing non-negative matrix factorization (NNMF) algorithm described in 3.3.2.

$$EMG_{(M \times T)} = W_{(M \times N)} \times C_{(N \times T)} + RES \quad (7.1)$$

- EMG: pre-processed EMG signals of size [Number of muscles (M) × Time Samples (T)]; T= [Directions × Force Levels × Time Bins]. Here, EMG matrix was of size [9 × (12 × 2 × (3sec × 100))].
- W: Synergy weight matrix [Number of muscles (M) × Number of Synergies (N)];
- C: Co-activation of synergy matrix across the trials [Number of Synergies (N) × Time Samples (T)];
We extracted the synergies for all for N= 1 to 9 (number of muscles monitored).
- Residual error

7.3.4 SYNERGY EXTRACTION WITH THE PROPOSED WEIGHTED NNMF ALGORITHM
METHOD: EMG AND TASK FORCES TO DERIVE "AUGMENTED SYNERGIES"

. In this proposed method, since the forces at the tasks-space are the outcomes of muscular activity, we evaluate them as inputs to the dimension reduction algorithm and combine them into single matrix by appending forces with EMG. Both the EMG and forces signals are pre-processed as described in the above section, 7.3.2. The forces are decomposed into their respective directions. As the inputs to the NNMF algorithm are required to be all positive, the forces in the negative x (Flexion), and z (Adduction) directions are rectified. This is formulated as given below:

$$A_{((M+4) \times T)} = \begin{bmatrix} EMG(t) \\ Task - space Forces(t) \end{bmatrix} = \begin{bmatrix} \mathbf{m}_1(t) \\ \mathbf{m}_2(t) \\ \vdots \\ \mathbf{m}_M(t) \\ \mathbf{F}_{x^+}(t) \\ \mathbf{F}_{x^-}(t) \\ \mathbf{F}_{z^+}(t) \\ \mathbf{F}_{z^-}(t) \end{bmatrix} = W_{(M+4) \times N} \times C_{N \times T} + RES \quad (7.2)$$

The task space forces are represented as below to have all positive values (as required by NNMF algorithm):

$$\begin{aligned} \mathbf{u}^+(t) &:= \frac{1}{2}(1 + \text{sign}(u(t))) \times u(t) \\ \mathbf{u}^-(t) &:= \frac{1}{2}(1 - \text{sign}(u(t))) \times u(t) \end{aligned} \quad (7.3)$$

- **A**: pre-processed Augmented matrix with EMG and forces [Number of muscles and force (M+4) × Time Samples (T)];
T= [Directions × Force Levels]. Here, matrix 'A' was of size [13 × (12 × 2)]
- **W**: Augmented synergy weight matrix [13 × Number of Synergies (N)];
- **C**: Co-activation of synergy matrix across the trials [Number of Synergies (N) × Time Samples (T)];

- *RES*: Residual Error;

We extracted the synergies for all for $N= 1$ to 13 (number of input signals in the augmented matrix). And for this method, we employ a modified weighted NMF algorithm described in section section:Formulation of Augmented Synergies. The variance of EMG and the force signals during across the targets is given as the weight to the K matrix.

7.3.5 STATISTICAL ANALYSIS

ESTIMATING THE OPTIMAL NUMBER OF SYNERGIES: FOR TRADITIONAL AND AUGMENTED SYNERGIES

The optimal number of synergies sufficient to effectively represent the variability in the given input data set was determined based on a Variance Accounted For (VAF) criterion. This is a measure of how the reconstructed dataset from the synergies best match the original dataset. Following similar methodology from literature [231], the minimum number of muscle synergies required to achieve a mean global VAF $> 90\%$ and a mean VAF for each input signal (signal VAF) that exceeded 80% was considered as the optimal number of synergy (N_{syn}) of the subject. This is to ensure that the estimated number of synergies could reconstruct each input signal individually as well as the overall input matrix appropriately. For the case with traditional NMF, the input matrix consists of muscle activity alone (hence signal VAF is referred as muscle VAF). In the proposed weighted algorithm, the input is a composite of muscle activity and task space forces.

GLOBAL, SHARED, AND SUBJECT-SPECIFIC SYNERGIES

To identify shared and subject specific muscle synergies functional sorting was performed by calculating cosine similarity across muscle synergies of all subjects to group similar synergies. Cosine similarity (r) of two synergy vectors is their dot product scaled by the product of their magnitudes. This measure of similarity is independent to the magnitude and lies between 0 and 1. Global synergy is an average set calculated from the synergies that are shared across subjects. Estimating global synergies is a 3-step process.

- In the initial stage, called functional sorting detailed in [178], i.e an arbitrary subject was selected as a reference subject and cosine similarity across all synergies is calculated. Synergies with the highest correlation or similarity values ($r>0.6$,

$p < 0.05$) are grouped together in hierarchical order and this process is iterated across subjects. It ensures that similar muscles synergies were grouped together for further comparison.

- The second step is estimation of global synergy set, computed by averaging the respective set of synergies sorted from the initial stage. The similarity between global and each subject synergies was quantified using cosine similarity to identify shared (that exhibit high similarity) and subject specific synergies [232]. Synergy that has the minimum cosine similarity ($r < 0.4$, $p > 0.05$) with any of the global synergy set was considered as subject specific synergy, that may arise due to different biomechanical properties across different subjects and removed from the averaging step. This process is iterated till all the subject specific synergies are identified.
- At the end, we obtain a global synergy set that is an averaged set of shared muscle synergies across the subjects. Along with this, we also identify the shared and subject specific synergies.

7.4 RESULTS

The representative subject's force and muscle activity from the Maximum Voluntary Force calibration phase is presented in Figure 7.3. Within each axis, the average forces in FE and AA directions for all the subjects from the MVC task are given by $26.06 \pm 7.7\text{N}$ and $20.49 \pm 4.1\text{N}$. The subjects exerted higher forces in FE direction in comparison to the AA Axis. The force level was scaled to % of MVF of each subject unlike the absolute force levels set in literature [142, 233] as we observed difference in strength across different subjects and directions. The force trajectories of a representative subject for the 24 targets during the 5 sec hold periods are presented in the Figure 7.4.

7.4.1 DIRECTIONAL TUNING OF MUSCLES

The average EMG activity (IAV) of all the upper limb muscles monitored during the task with respect to each direction (in increments of 30 degrees) across all subjects is presented in Figure 7.5. The directional tuning of each muscle is estimated by a cosine fitting to the IAV data and plotting a muscle tuning curve shown in the figure as a red

Figure 7.3: A) Band pass filtered forces in the FE and AA axis, during the Maximum Voluntary Force (MVF) task. The person exhibited MVF in the order of Abduction, Adduction, Flexion, and Extension respectively. B) Raw muscle activity of Pectoralis Muscle (PECM) , a representative subject in the calibration phase during the Maximum Voluntary Force (MVF) task

line. The EMG activity pattern of synergistic muscles is observed to be similar and in accordance to the anatomical task requirement. The TRIC and TRIL muscles, dominant in an extension task show high activity in shoulder extension direction [330-30degrees]. Similarly, DELA, DELM and PECM show higher activity in the Abd-Flex plane whereas the higher activity in DELP is observed in the adduction plane signifying the muscle tuning with respect to the direction of task. The TRAP muscle that is activated during shrug motion of the shoulder is highly active in the abduction direction, whereas the PECM responsible for stability and horizontal flexion shows major activity flexion direction.

Figure 7.4: Force trajectories of representative subject performing the isometric task across 24 targets for the hold period (5sec) is shown. The force measurements were band-pass filtered at 8 and 30 Hz using a zero- phase-lag fourth-order Butterworth filter. The displayed forces are magnified by 3 times for visual purpose.

BRAD and BICP seems to be activated uniformly all over the plane with a slightly higher activity in the horizontal flexion plane along with PECM and DELA. The uniform activity in BRAD and BICP muscles across the 12 directions might be due to averaging across subjects and also the experimental setup position, where the muscles are activated from the initial stages to hold the arm against gravity. The results suggest that the IAV of EMG signals is reliable measure to interpret the directional tuning of respective muscles and can be used to investigate the motor control strategy across subjects.

7.4.2 MUSCLE SYNERGIES FROM TRADITIONAL APPROACH

The surface EMG collected from the upper limb muscle during an isometric force matching task is decomposed into muscle synergies (W) and their activation patterns (C) across 12 directions. Number of Synergies vs VAF for N=1 to number of muscles (here 8) for all the participants is presented in Figure 7.6 A. On average, 3.6 ± 0.54 number of synergies were necessary to achieve a mean global VAF > 90% and a mean VAF for each muscle (muscle VAF) > 80%. So we adopt four synergies as an optimal number to compare across subjects based on the VAF criteria.

Figure 7.5: The EMG IAV activity (Blue) and cosine fitted tuning curve (Red) of the muscles: Brachioradialis (BRAC), Biceps Brachii (BICP), Triceps lateral head (TRIC), Deltoid Medial (DMID), Deltoid Anterior (DANT), Deltoid Posterior (DPOS) and Trapezius Superior (TRAP). Directional tuning of the respective muscles can be inferred from the muscle tuning curves. For visualization purposes, the IAV of each muscle is normalized to its maximum activation value

The Global synergies (Weights: W) and their activation coefficients (C) extracted after functional sorting are presented in Figure 7.6B. The activation coefficients are averaged across the 3 sec hold period for each direction. The mean (thick line) and SD (shaded region) values of activation coefficients across the force levels (15% MVF and 30% MVF are presented) are presented. The muscles with weight greater than 0.5 are considered to be the major contributor to the respective synergy. These four muscle synergies with the corresponding activation coefficients are recruited to maintain the specified force across prescribed direction.

- The first synergy W_1 , is mainly composed of Anterior Deltoid (DELA) and Pectoralis Major (PECM), along with the Biceps Brachii (BICP). These muscles are major contributors to the flexion and abduction movements. Similarly, from the activation curve (C_1) it is observed that these muscle are activated primarily in the Flex-Abd plane.

Table 7.1: Number of optimal synergies, synergy similarity to the global synergy set, overall VAF, average Muscle VAF of all the subjects from the traditional muscle synergy extraction : NNMF algorithm.

ID	No.of syn	Average cosine similarity	VAF (%)	Muscle VAF (%)
Sub1	3	0.97 ± 0.01	94.31	85.5 ± 13.1
Sub2	3	0.57 ± 0.40	96.28	90.06 ± 8.96
Sub3	4	0.96 ± 0.02	94.55	83.80 ± 11.02
Sub4	4	0.80 ± 0.12	95.01	87.88 ± 12.06
Sub5	4	0.62 ± 0.35	94.43	84.94 ± 14.05
Avg	3.6 ± 0.54	0.79 ± 0.20	94.91 ± 0.8	86.43 ± 11.83

Figure 7.6: **A.** Number of optimal synergies estimation. The VAF (Variance Accounted For) is taken as goodness of fit measure and is plotted across the number of synergies. The number of muscle synergies was determined as the minimum number that achieved a mean global VAF $>90\%$ (dashed line) and a mean VAF for each muscle (muscle VAF) $>80\%$. Each subject is represented by different color. On an average 4 Synergies are required to sufficiently explain the EMG variability.

B. Global muscle synergies (left) and their activation coefficients (right) extracted from the EMG data matrix using non-negative matrix factorization (NNMF) followed by functional sorting. Each muscle-weighting vector of muscle synergies was normalized to the maximum value in the synergy vector. The mean (thick line) and SD (shaded region) values of activation coefficients across the force levels (15% MVF and 30% MVF are presented) are presented

- The second synergy W_2 , contains major weighting from the bi-articular muscles Triceps long head (TRIC), Triceps lateral head (TRIL), contributing to the

shoulder extension and adduction task with higher activation in Ext-Abd and its oriented directions.

- The third synergy W_3 , is mainly made up of the anterior and medial Deltoid (DELA and DELM) responsible for shoulder abduction and is highly activated in the Flex-Abd plane.
- The fourth synergy is dominated by the activity of the DELA and Trapezius TRAU in comparison with other muscles. Uniform activation of W_4 across all directions is observed to maintain stability in the initial task position. Higher activation was observed in 90° corresponding to the pure shoulder abduction task and high trapezius activity.

SIMILARITY OF MUSCLE SYNERGIES ACROSS SUBJECTS

The synergies of each subject along with their similarity to the global synergy (in the order of decreasing correlation) is presented in Figure 7.7. The first synergy W_1 , was highly similar across all subjects (on an average $r > 0.84$) and is composed of DELA, DELM and PECM. W_4 synergy is observed to be highly similar across SUB₁, SUB₃ mostly. In the other subjects W_4 is also composed of TRAP muscles, instead of PECM as both are stabilizing muscles. Subject specific synergies observed in SUB₂ and SUB₅ are highlighted in dashed rectangles. W_2 synergy in SUB₂, is composed of all the muscles distributed in random weights and the load might be shared across different muscles. This is similar to the case of SUB₅ in W_3 synergy. Existence of this specific synergy might account for low cosine similarity of other synergies in SUB 2 and 5 respectively.

7.4.3 AUGMENTED SYNERGIES AND THEIR CO-ACTIVATION PATTERN: INTEGRATION OF VARIANCES AND FORCES TO EXTRACT TASK RELEVANT SYNERGIES

The augmented synergies are derived from the task space forces and respective muscle activity (EMG) together as described in the methods section. As the forces(N) and EMG(mV) are different measurement (hence-units) we use the modified NNMF detailed in section 3.3.2. The forces are decomposed into their positive and negative parts and with respect to the task directions. The pre-processed EMG activity and force tuning curves during the isometric task in 12 directions across two force level is presented in Figure 7.8. The directional tuning of the respective forces can be inferred directly from the polar plots. Due to the addition of end effector forces relative to the

Figure 7.7: Muscle synergies estimated for all the subjects from traditional NNMF algorithm. The cosine similarity of each subject's synergy with the respective global synergy is presented by its r value. The subject specific synergies whose $r < 0.5$ and $p > 0.05$, are highlighted in dashed rectangles

degrees of freedom of the task the dimensionality of the input matrix is increased from 9 (*No.of.Muscles*) to 13 (*No.of Muscles + Forces in 4 task directions*). Number of Synergies vs VAF for $N=1$ to 13 for all the participants is extracted. Following the criteria from section 7.3.5, On average 6.28 ± 0.72 number of synergies were necessary to achieve a mean global VAF $> 90\%$ and a mean VAF for each input signal $> 80\%$. So we adopt six synergies as an optimal number to compare across subjects based on the VAF criteria.

From the augmented synergy method, the synergies and their co-activation patterns extracted with the modified NNMF algorithm is presented in Figure 7.9

- The first synergy W_1 , is mainly composed of Pectoralis Major (PECM), along with the Biceps Brachii (BICP) specifically. These muscles are major contributors to the flexion and abduction movements. Also from the force distribution, it can be observed that this synergy contributes F_{x-} and F_{z-} significantly, i.e., Flexion and Adduction.
- The second synergy W_2 , is primarily made up of the shoulder muscles - anterior and medial Deltoid (DELA and DELM) and Trapezius (TRAU). This synergy contributes to the forces in abduction motion i.e in F_{z+} direction as seen in the Figure.

Figure 7.8: The pre-processed muscle activity and force tuning curves during the isometric task in 12 directions across two force levels for a representative subject is presented. The inner level of force i.e **15% MVF (green line)** and the upper level of force i.e **30% MVF is (red line)**. The directional tuning of the respective forces can be inferred from the polar plots.

- The synergy W_3 , contains major weighting from the bi-articular Triceps long head (TRIC) and all the Deltoid muscles. Due to the uniform activation of agonist and antagonist pair (i.e., anterior and posterior Deltoid), this did not show any significant contribution in any task force, and only a small weighting in F_{z+} is observed.
- The fourth synergy is dominated by the activity of the Triceps (TRIL, TRIC) muscles in comparison with other muscles. In the task space forces, this synergy contributed to F_{x-} i.e extension significantly.
- The fifth synergy W_5 , mainly consists Brachioradialis muscle and a minor contribution from TRIL and TRAU with minor task force effect in F_{z-} direction.

Figure 7.9: Global Augmented synergies (left) and their activation coefficients (right) extracted from the data matrix using the novel (weighted) modified non-negative matrix factorization (NNMF) is presented. Each muscle-weighting vector of muscle synergies was normalized to the maximum value in the synergy vector. The shaded bar represents the mean (thick line) and SD (shaded region) values of activation coefficients across the two force levels (15% MVF and 30% MVF)

- The last synergy W6, higher activation of the posterior Deltoid (DELP) and Trapezius (TRAU) muscles is observed in comparison with other muscles. In the task space forces, this synergy contributed had no significant contribution except for a minor activation in in F_{x+} direction.

RECONSTRUCTION OF THE TASK FORCES AND MUSCLE ACTIVITY FROM THE AUGMENTED SYNERGIES

Reconstruction of EMG and forces from the Augmented Synergies and their activation co-efficient curve is performed by $A^*=W.C$. Each synergy contribution is summed to obtain the reconstruction Signal similar to the original signal i.e **part-by-part reconstruction**. Their similarity quantified by VAF % is also presented. From the six synergies, most of the EMG and force is reconstructed.

7.5 DISCUSSION

This chapter presents results on muscle organization during an isometric force matching task using traditional approach and preliminary results with a modified NNMF algorithm. The results showed that the muscle activity is recruited and tuned with respect to the task direction in congruence with the biomechanical properties. The force level was scaled to 15% and 30 % MVF of each subject unlike the absolute force levels set in the literature, to account for variation in strength across different subjects. Further, the target forces are scaled with respect to axis direction. It is found that subjects exert different range of forces in F-E and A-A axis.

The results obtained with the **traditional NNMF** implied that **four synergies** are sufficient to explain the spatio-temporal variability in EMG observed from nine upper limb muscles across 12 directions in the para-sagittal plane. The **shared and subject specific synergies** are also presented. Subject specific synergies observed in two subjects might be due to variable biomechanical properties or a difference in strategy. The high similarity values of synergies across different subjects highlight an impetus to understand the task relevance of muscle synergies by analyzing the changes in the synergy structure and their co-activation patterns w.r.t to the task space forces.

In the new method, we include the **task-spaces force along with the EMG** and their corresponding variance in the synergy analysis to derive '**Augmented Synergies**'. The results indicated its potential use to estimate the synergies that contribute to the task.

Figure 7.10: Reconstruction of EMG and forces from the Augmented Synergies for a representative subject in Lower force level: 15% MVF. Each synergy contribution is summed to obtain the Reconstruction Signal similar to the original signal. Their similarity quantified by VAF % is to also presented.

Moreover, from the results it can be seen that to produce force in a specific direction, one synergy called **primary synergy** is employed. Example: In **W₁** augmented synergy from Figure 7.9 contributes to mostly movement in **Flexion direction**, whereas **W₄** synergy is responsible for movement in Extension direction. Similarly **W₂** results in Abduction forces. Unlike the other directions, the force production in **Adduction direction** is not limited to one primary synergy, but is a **combination of multiple synergies**. So to move in a specific direction, one might have to recruit a single or combination of muscle synergies that would result in appropriate muscle activity to produce the required forces. Also, the advantage of this method is that one could identify the synergies that do not contribute to the task, i.e. here example **W₃**. Synergies that might be activated due to some co-contractions or to support against gravity etc, or task independent muscular activations. Also, with augmented synergies, more synergies (6 on an average) were required to fulfill the 90 % VAF criteria compared to the traditional method (4 on average). This could also be because of the difference in the force and EMG variability across targets.

Hence from this method, I try to identify which synergies contribute to the desired task and how they are inter-related. This is essential when we want to extend the use of muscle synergy analysis in clinical rehabilitation settings. As discussed earlier, stroke patients tend to have **altered synergies (W)** or **impaired co-activation patterns (C)** in comparison with the healthy population and the difference can be taken as measure of error and motivation for the recovery of synergy activation by minimizing the error. Since recovery can be functional changes in the neuro-motor control or learning new compensatory movements. If we do not establish the task-relevance of muscle synergy, and simply aim to modify/correct the altered synergies in the post-stroke it might result in faulty learning of movements and might train/ develop in incorrect muscular organization. Hence, this proposed method could provide a direction for better understanding of motor control and designing optimal rehabilitation paradigms.

7.5.1 LIMITATIONS

In the present study, limited number of subjects and the possibility of fatigue (can be translated in EMG) due the task i.e., holding the limb against gravity to maintain the shoulder horizontal to the ground with the wrist strapped onto a load-cell for prolonged time is seen as the potential might have effected the results. We average the IAV EMG value across the two levels of forces to analyze the directional tuning of muscles under the assumption that force is in linear relation with the EMG. We assume linear relation

between task and muscle movements, but in reality the musculoskeletal is a non-linear system and reconstructed EMG may not result in the observed task [234] as there might be a chance of generating achievable joint torques profiles.

7.6 CONCLUSION

In this study, the muscle synergy analysis involving shoulder muscles during an isometric tasks is presented. Five subjects performed an 2D-isometric force-matching task in twelve planar directions with two force levels across shoulder joint. Muscle synergies and their respective activation curves were computed from nine upper limb muscles via a non-negative matrix factorization (NNMF) algorithm. We introduced the concept of '**Augmented Synergies**' derived from modified NNMF with the nine upper limb muscles and task-space forces in four directions to explain the task relevance of muscle synergies.

- In the isometric task, the target forces were scaled to % of Maximum Voluntary Force (15 % and 30 % MVF) of each subject unlike the absolute force levels. Within each axis, the average forces in Flexion-Extension and Abduction-Adduction directions for all the subjects from the MVC task are given by 26.06 ± 7.7 N and 20.49 ± 4.1 N. This highlights the difference in strength across different subjects and also directions.
- The results obtained from the traditional NNMF approach suggested that four synergies are sufficient to explain the spatio-temporal variability in EMG observed from nine upper limb muscles across 12 directions in the para-sagittal plane. The *shared and subject specific* synergies are also presented.
- With the novel approach proposed in this chapter, we included the task space forces with EMG to derive 'Augmented Synergies', that could explain the task relevance of muscle synergies. Based on this results, we could identify the *primary* synergy and *secondary* synergies recruited for a movement in a specific direction. Six synergies were required to meet 90 % VAF criteria to explain the variability in EMG and the task-space forces.
- Further studies need to be carried out to assess their reliability and robustness across different task and also to understand their relation to degrees of freedom of the task.

As mentioned earlier the results presented in this study are preliminary step towards understanding the relation between the EMG, muscle synergies, and isometric forces/torques. This concept can be extrapolated to understand how the merging/fragmentation of existing synergies, or development of new synergies in severe stroke subjects are related to compensatory actions that result in abnormal joint movements and altered EMG activations.

"The answer to the ancient question, 'why is there something rather than nothing?' would then be that 'nothing' is unstable."

Frank Wilczek

2004 Nobel Prize in Physics for the discovery of
asymptotic freedom in the theory of the strong
interaction

8

Conclusions and Future Works

This chapter presents the conclusions of the two major works discussed in this thesis with the directions for future works. Section 8.1 summarizes each chapter, highlighting the results and their implications for enhanced robotic rehabilitation. Based on the results, the contributions from this thesis are discussed in section 8.2. The scope for further research in the development and clinical applications is presented in section 8.3

8.1 CONCLUSIONS

The ever increasing burden of stroke and its consequences is presented in the introduction chapter 1. Hemiparesis is one of the major impairments due to stroke, causing disability in activities of daily living and quality of life. To overcome the needs of increasing aging population coupled with limited availability of therapists and financial resources rehabilitation robots were introduced to train and assess motor function abilities. However, their utilization is limited and more research needs to be done in the development of control algorithms and validation of the motor learning benefits. Rehabilitation robots are employed to reduce therapist workload in repetitive task movements and provide task oriented training. Most of the research in literature

has focused in developing different devices and varied robotic control strategies. In order to design better control algorithms, it is **essential** to investigate their influence on motor learning effects and their implications in the **improving the functional abilities** of stroke subjects. A clear understanding of motor control is also essential to design better robotic control paradigms. Hence there is the scope to design and validate **better training and assessment paradigms** for enhance rehabilitation post stroke.

Chapter 2 presents the literature review on the present state of art adaptive robotic control strategies developed. The potential of robotic devices for sensorimotor assessment along with its limitations is discussed. Consequently, the muscle synergies derived from physiological signals (Electromyography) have been introduced to discern the intricate control of movements by Central Nervous System (CNS). Dimension reduction algorithms such as Non-Negative Matrix Factorization (NNMF) is explained and its adaption in different muscle synergy studies is reviewed. However, the existing methods are unable to deduce the direct relation/ consequence of muscle synergy to the resultant motor task. Deriving this relation might have the potential to optimize robotic controller design for augmented rehabilitation.

Chapter 3 provides the details of the different analysis and materials used in this thesis. The **mathematical formulation of task metrics/indices** used to assess motor performance is described. A step by step procedure to extract and analyze muscle synergies using a Non negative matrix factorization (NNMF), a widely used dimension reduction algorithm popularized by Lee and Seung [181, 182] is presented. Mathematical details of the a **novel approach with modified version of NNMF** and weighted distance metrics proposed in this thesis. This is followed by the experiments and analysis performed in this thesis to validate and assess learning benefits of novel robotic control strategies for a better understating of motor control and improved rehabilitation. The summary of main results from this thesis, chapter-wise is presented in Figure 8.1

In chapter 4, the **learning and retaining of motor functionality** in stroke is assessed by comparing the motor improvement results of subjects that underwent robotic therapy with subjects who did conventional therapy alone. The robotic therapy was provided by a **novel control scheme** based on '*challenge point framework*', that adapts haptic interaction forces according to the movement smoothness performance of the user. The haptic forces ranged from assistance i.e., **performance enhancement**, if the subject

Chapter	Title	Synopsis
4	Assessment and modelling of motor learning effects from novel control algorithm design in post-stroke subjects: a randomized control study	A validation study on the efficacy of a control strategy with underlying principles from 'challenge point framework' in rehabilitation post-stroke (26 subjects) is presented. The results showed robotic group had better improvements in functional abilities compared to the control group in training and follow-up assessments.
5	Relationship between upper-extremity robotic tasks measures and associated metrics- A novel study to improve robotic assessments	To bridge the gap in clinical outcome measures and quantitative robotic scales, the potential of H-man as an assessment tool is investigated. The reliability and sensibility of quantitative task metrics depend on nature of the task and impairment level.
6	Role of EMG as a complementary tool for assessment of motor impairment and performance marker	Analysis of muscle activity (EMG) in stroke subject highlights the altered muscle patterns from healthy control. This aids in investigating the underlying strategies of each user - to provide explanations for stereotyped movements, identify compensatory actions, and provide a refined assessment of the user.
7	Augmented synergies to identify task relevance of muscle synergies from an isometric task in healthy control subjects	The task space forces along with the typically used EMG activity are combined to derive 'Augmented Synergies' using novel approaches. Preliminary results on the task-relevance of associated muscle synergies derived from an isometric shoulder task with healthy control subjects are presented.

Figure 8.1: The summary of main results presented in this thesis

cannot perform well to disturbance i.e, **performance degradation** if subjects improved smoothness above a threshold level) in the movements to give optimal challenge to the user for better gains. The data collected from 26 stroke subjects divided into robotic (13 subjects) and conventional therapy groups is presented.

The longitudinal changes in both the clinical outcome measures and the quantitative metrics (derived from two robotic tasks) from assessment of the subject's performance at four-time points over 3 months: base-line (week 0), mid-training (week 3), post-training (week 6) and follow-up (week 12) is discussed. The results indicated that Robotic therapy group had significant improvements in functional abilities compared to the conventional therapy group post training. Also, the therapy benefits were retained in the follow-up assessments implying the continued learning in the robotic therapy group. This is an evidence that better functional gains are achieved with this novel approach of combining assistance and disturbance corresponding to one's skill and impairment level to provide optimal training.

Along with the training, robotic devices has the potential to provide **objective and accurate sensorimotor assessment**. This is investigated in chapter 4, 5. Specifically in chapter 5 in a pilot study with 12 stroke and 9 control subjects, the ability of 'H-man' to detect differences in planar self-paced reaching task performance within stroke and age-matched healthy control subjects is illustrated. This is followed by a study with large cohort of stroke subject's motor performance in two unique robotic tasks : line tracing and circle tracing in chapter 4. **Regression models** were developed to estimate the *clinical outcomes from kinematic metrics* to characterize the sensorimotor impairment status of the participant. From this it is derived that, 'H-man' robot used in the experiments has the potential to provide *continuous, objective, and quantitative motor assessment* to keep track of the recovery progress. Adoption of technology aided measures for assessment in clinical settings requires further research. The main challenge is in identifying and evaluating the robotic metrics that are valid, clinically relevant, reliable, robust, and sensitive to changes from the robotic tasks independent of robotic setup. Variations in study protocols, task definitions, and availability of different metrics to evaluate same task measure limit their reliability and generalization of a task measure to compare robotic measures across different studies unlike the standard clinical studies. A better understanding of the relation between performance measure, derived task metric and the task itself is imperative. So in the chapter 5, I analyzed the effects of (intra and inter) task variations on robotic measures and associated metrics.

The results show that the reliability and sensitivity of a metric highly depends on the definition of assessed task. Hence, it is recommended to develop a normative series of robotic tasks and task metrics with increasing level of difficulty to have a more detailed picture of patients' performance. Furthermore, the feasibility of employing **Electromyography(EMG)** signal based measure as a complementary assessment metric to end-effector kinematic task metrics is evaluated in the chapter 6. Monitoring and analyzing the alterations in EMG patterns during a specified task in healthy-control and post-stroke subjects will provide deeper understanding of the cause and result of impaired movements irrespective of the task or robotic setup used. This will also aid in identifying and quantifying the compensatory strategies used by the stroke subjects to perform the motor tasks.

Following this, muscular synergies are employed as a medium to comprehend the motor control principles. In chapter 7, I introduced a novel method to explore the task relevance of muscle synergies. The muscle synergies are believed to be the building blocks of CNS to simplify motor control. In the **traditional** method, synergies are identified from the *muscle activity* alone. To seek their task association, some studies relate the task forces and synergy activation after processing them separately, but fail to explain which synergy is responsible /or needed for movement in specified degree of freedom of the task. In the current approach developed in this thesis, I employ *both forces and EMG* signals from the task with their corresponding variance to derive "**Augmented Synergies**". Results from a 2D force-matching task isometric task in twelve planar directions with two force levels across shoulder joint with five subjects are presented. A novel approach with modified version of NNMF algorithm with weight (kernel) matrix and distance metrics (Mahalanobis distance) is developed to extract augmented synergies. The results indicated its potential to decrease the computational complexity and extract the synergies that contribute to the task and to identify '*primary synergy*' and '*secondary synergy*' for movement in respective directions. Through this method, one could also determine the synergies that do not contribute to the task but are still activated. This is very essential as each subject might have unique strategies/ synergies owing to their bio-mechanical configuration that do not result in the desired task forces. Also, extending this approach to studies in stroke subjects will enable us to associate the alteration in synergy (structure and activation's) post-stroke to their stereotyped compensatory movements and devise subject-specific therapy.

8.2 CONTRIBUTIONS

To summarize, my contributions to this field from this thesis are as follows:

1. **Validating the efficacy of a novel robotic control strategy to improve motor function post-stroke**

In a randomized control trial (longitudinal study) with sub-acute to chronic stroke subjects, **robotic** therapy group had significant improvements in **functional abilities** and retained the learning effects post-training with a short training period of 6 weeks. A novel robotic control strategy based on '**Challenge Point Framework**', that adapts haptic interaction forces from *assistance to disturbance* mode according to the user's movement smoothness is validated to provide optimal training benefits.

2. **Development of regression models to estimate the clinical outcome measures from quantitative robotic tasks**

Clinical scales were derived from regression models with robotic scales indicating the potential of 'H-man' robot to provide continuous, objective, and quantitative feedback to promote their use in sensorimotor assessment. **Mixed model** with quantitative metrics from **two robotic tasks** had **better estimation of clinical scales** compared to individual task signify that inclusion of *more diverse tasks* will provide a better understanding of sensorimotor state.

3. **Evaluation of task dependency of robotic metrics and potential of EMG as a complementary measure for an improved sensorimotor assessment**

The task dependency of robotic task metrics could hinder their adaption in clinical setting to assess motor impairments. The data analyzed from two clinical studies provides recommendations to reduce the gap in translating technology aided measures for clinical use. Including Electromyography(EMG) signal based measures in addition to task based measures enables us to identify learning from *functional recovery* vs recovery through *compensatory actions*.

4. **A novel approach to derive 'Augmented Synergies' for the estimation of task relevant muscle synergies from both EMG and task space forces**

Traditionally, synergies are extracted from muscular activity using NNMF algorithm and has limited information regarding the the task space forces. With the

novel approach presented in this thesis, by modifying the NNMF, I attempt to explain the task relevance of muscle synergies by '*Augmented Synergies*'. This analysis includes muscular activity along with the resultant task forces and enable us to identify synergies that *contribute to the task* from the synergies required to support the posture, or those that arise due to *compensatory* actions. Such association of synergies to task-forces would aid in designing subject specific training paradigms for better gains.

8.3 FUTURE WORKS

This thesis aims to validate and assess the efficacy of robotic therapy to improve motor functions in stroke subjects. There is still scope for improvements in both **theoretical** (*development and validation*) and **application** (*in rehabilitation of motor impaired subjects*) areas.

From development perspective, further research in developing better robot control algorithms and diversified assessment tasks could improve the experience of rehabilitation robotics as a training and assessment tool. The robotic therapy presented in this thesis adapts the haptic forces to the user based on participants **smoothness** performance alone. In future, it would be beneficial if patients with different impairments could focus on the respective impairment, like e.g. *strength, movement speed, smoothness*. Consequently, a fusion of **smart algorithms** to incorporate performance enhancement as well as performance degradation with '*flexibility in the selection of a performance metric*' is the urgently needed for patient adapted rehabilitation with robotics to gain individual therapy. This kind of approach would benefit a larger patient group.

To enhance the learning process, it is recommended to include more reliable physiological signal based measures as feedback. We introduced **Augmented Synergies** as a medium to understand the motor control and their task relevance in 2-D **isometric conditions**. However, this has to be validated in more control subjects with varied tasks (*planar reaching, tracing, and other dynamic tasks*). Further investigation of this methodology with stroke participants would aid us in assessing the alteration of synergy structure and calibrate the compensatory effects to devise better training protocols. Adopting such **synergy based measures as performance metrics** in the above

mentioned hybrid control algorithms will amplify the means to achieve an adaptable subject-specific rehabilitation.

On the clinical direction, the experiments presented in this thesis were conducted with sub-acute to chronic stage stroke participants. A higher degree of improvement is expected for **acute stage stroke population** as the recovery potential is shown to be higher in first 3 months post-stroke from neuroimaging and electrophysiology studies [4, 51, 197]. Hence, the effectiveness of motor learning using present control algorithms needs to be validated with acute stroke subjects to achieve larger reductions in impairment and maximum therapy benefits. The regression models developed to estimate the clinical scales specific to impairment level could be refined from this large pool of data for more reliable and accurate sensorimotor assessment.

Moreover, to use robot aided assessment in clinical practise there is a need for employing standard set of robotic tasks and metrics based on the nature and the level of impairment independent of the robotic/sensory device employed. More algorithms/metrics that can classify healthy and stroke subjects performance with optimal reliability and sensitivity may be explored based on the recommendations from this thesis. As large pool of data is collected from standard robotic tasks, a database of normative motor function specific to the H-Man assessment can be formed. This would provide *clinicians* with the opportunity to compare a patient's performance against the reference values based on that data. This would allow **customization of rehabilitative therapy** to make appropriate treatment decisions for greater learning benefits.

As discussed earlier, **stroke** patients exhibit **altered muscle synergies (w) or impaired co-activation patterns(c)** in comparison with the healthy population [36]. With the proposed novel approach (of combining forces and EMG for synergy analysis), one can identify the abnormal synergies that do not aid in performing the task, synergies that are result of the compensatory actions or the synergies that limit the subject from completing the desired task. Such consequences can be accounted as measure of error, and reducing them can improve motor functionality. This can be achieved by implementing a controller that provides a **feedback** (visual/haptic; assistive/resistive forces) proportional to the error and train accordingly to achieve smooth movements and to improve the dysfunctional synergy to match the healthy

population. The qualitative differences across different stroke subjects will enable to explain the variability in the task performance. This provides a theoretical base and an impetus for the development of well-controlled, subject-specific, optimal training protocols with effective neuro-rehabilitative therapy.

List of Publications

JOURNAL PUBLICATIONS

- Hussain, Asif, Aamani Budhota, Charmayne Mary Lee Hughes, Wayne D. Dailey, Deshmukh A. Vishwanath, Christopher WK Kuah, Lester HL Yam et al. "Self-paced reaching after stroke: A quantitative assessment of longitudinal and directional sensitivity using the H-man planar robot for upper limb neurorehabilitation." *Frontiers in neuroscience* 10 (2016): 477.
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- S. Kager, Asif Hussain, Aamani Budhota, Vishwanath A Deshmukh, Christopher WK Kuah, Lester HL Yam, Liming Xiang, Karen SG Chua, Domenico Campolo et al., "Performance-based interaction controller incorporating natural movement variability for motor learning: A clinical validation," *Trans. Neural Syst. Rehabil. Eng.*, p. Submitted, 2018.

CONFERENCE PROCEEDINGS

- Aamani Budhota, Paolo Tommasino, Asif Hussain, and Domenico Campolo. Identification of shoulder muscle synergies in healthy subjects during an isometric task. In *Rehabilitation Robotics (ICORR), 2017 International Conference on*, pages 134–139. IEEE, 2017

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