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Mohamad Yazan Sadoun

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DEVELOPMENT OF HARDWARE AND SOFTWARE FOR SENSORY AND MOTOR NEUROPATHY DETECTION

A THESIS APPROVED FOR THE

SCHOOL OF ELECTRICAL AND COMPUTER ENGINEERING

BY

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Dedication

As I conclude this chapter of my journey, I do so with deep gratitude, acknowledging that “Every blessing I have is from God. To Him belongs all praise and thanks.” And as I embark on my next chapter, I begin with “BismiAllah Alrahman Alrahim”.

There are some people who had a deep and lasting impact on my experience at OU, and I wish to dedicate my heartfelt gratitude to them:

To Dr. Hazem Refai: Some debts are life-debts because you can't repay them, no matter what you do. That is how much I owe Dr. Refai.

He brought out the best in me and went beyond the classrooms to pass on lessons that will stay with me for a long time.

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To My Father, My Mother, Moutamn, and Hoomam, you have always done everything to support and encourage me. To whom stands by me in every step of my journey. To my biggest blessing in life.

Mohamad Yazan Sadoun

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Table of Contents

List of Figures

Abstract

This thesis presents the development of a comprehensive hardware and software system aimed at improving the detection of sensory and motor neuropathy, particularly in cancer patients undergoing treatments like chemotherapy. The project integrates three key components: the improvement of the Quantification of Hallux Strength Assessment (QuHalEx) device, the introduction of advanced data analysis techniques, and the development of a novel, integrable vibration system for sensory neuropathy testing.

Building on previous work, we developed the patented QuHalEx 2.0 device, featuring significant improvements in accuracy and usability for hallux strength evaluations. This new version includes a new pressure sensing module, faster data processing via new electronic boards, wireless communication, and a more durable mechanical design. Mobile applications for iOS and Android enable real-time data collection, analysis, and user feedback. These advancements increase the device's sensitivity and make it more accessible even for independent use by non-specialists, reducing the need for clinical oversight. Initial testing shows that QuHalEx 2.0 can detect subtle variations in motor function and force application patterns, aiding rehabilitation and providing a standardized approach to foot biomechanics evaluation.

In parallel, we explored an innovative method for analyzing motor function data using unsupervised machine learning and linear algebraic decomposition techniques. By applying hierarchical clustering and Singular Value Decomposition (SVD), we were able to cluster subjects into distinct groups solely based on their muscle activation patterns using the extracted features. This approach was particularly effective in identifying differences between control subjects and cancer patients going through chemotherapy treatments. The insights gained from

this analysis offer a deeper understanding of the physiological changes that occur in these patients, with implications for improving therapeutic interventions and rehabilitation programs.

To further support the detection of sensory neuropathy, we developed a vibration-based device integrated with the QuHalEx system. This device uses a Linear Resonant Actuator (LRA) to deliver precise vibrations to the patient's toe, targeting a key area that potentially might be affected by sensory neuropathy. Its customizable settings for intensity and timing, along with its portability, make it an ideal tool for early detection, helping to prevent further nerve damage in cancer patients.

Together, these innovations provide an integrated solution for assessing sensory and motor neuropathy, enhancing diagnostic accuracy and patient care. Beyond chemotherapy-related neuropathy, the system's adaptability extends to athlete performance monitoring, rehabilitation tracking, and fall prediction in the elderly. This work represents a significant step toward more accessible and personalized healthcare solutions.

1 Introduction

Sensory and motor neuropathies are significant complications affecting various patient populations, particularly individuals undergoing chemotherapy, which can impair muscle strength, coordination, and sensation. These conditions greatly impact quality of life, leading to functional limitations and an increased risk of falls, especially in elderly and cancer patients. Early detection and monitoring are crucial for timely intervention, rehabilitation, and improving patient care.

Traditional methods for assessing neuropathy typically involve manual muscle testing and subjective sensory evaluations. However, these approaches often fail to capture the complexity of muscle activation patterns and nerve responses. To address these limitations, advanced quantitative tools are necessary to provide detailed insights into motor and sensory impairments. This thesis focuses on developing and integrating hardware and software systems to enhance the detection and analysis of both motor and sensory neuropathies.

The first part of this project builds on previous work with the Quantification of Hallux Strength Assessment (QuHalEx) device, which evaluates Hallux strength—a critical factor in maintaining balance and stability. The updated QuHalEx 2.0 system offers significant advancements, including a new pressure unit and enhanced electronics to improve data precision and processing speed. Wireless communication capabilities and mobile applications that allow real-time data collection and feedback, making the system more accessible and user-friendly for both patients and clinicians. The improved sensitivity of QuHalEx 2.0 to various movement patterns enables more standardized and independent assessments, reducing the need for trained specialists in routine evaluations.

The second part of the thesis introduces a novel analysis method to detect changes in force patterns between healthy individuals and cancer patients undergoing chemotherapy.

Chemotherapy-induced peripheral neuropathy (CIPN) often leads to complex changes in muscle behavior that are difficult to quantify using traditional methods. By applying unsupervised machine learning techniques and linear algebraic decomposition, such as hierarchical clustering and Singular Value Decomposition (SVD), this analysis identified distinct behavioral groups. This approach provided deeper insights into how chemotherapy affects motor function, revealing key differences between cancer patients and control subjects, as well as supporting more tailored therapeutic interventions.

The third part of this thesis involves integrating a sensory neuropathy detection device with QuHalEx 2.0. Sensory neuropathy, often marked by numbness, tingling, or pain in the extremities, is a common side effect of chemotherapy. To provide a more portable and integrated solution, a vibration-based device was developed to be incorporated into the QuHalEx system. This device utilizes a Linear Resonant Actuator to deliver precise vibrations to the toe, enabling the detection of sensory deficits that traditional methods might miss. By allowing simultaneous testing of motor and sensory functions within a single, customizable platform, this system offers a more comprehensive and efficient means of evaluating neuropathy in clinical settings.

These developments offer a unified approach to the detection and analysis of sensory and motor neuropathies, combining advanced hardware with sophisticated data analysis techniques. The integration of motor and sensory assessments into a single device simplifies the testing process, enhances portability, and improves accessibility across various healthcare environments. As such, this thesis presents a significant contribution to neuropathy detection,

rehabilitation, and even athletic training, with the potential to enhance clinical care and broaden the understanding of neuropathic conditions in both research and clinical practice.

Thesis Contributions Summary

This thesis presents several key contributions to the field of sensory and motor neuropathy detection and analysis:

1- **Development of QuHalEx 2.0**: Hardware advancements, including improved sensors, electronics, wireless communication, and real-time feedback, significantly enhance precision and usability in clinical environments.

2- **Introduction of Novel Force Pattern Analysis**: The application of unsupervised machine learning techniques and linear algebraic decomposition, including hierarchical clustering and SVD, provides new insights into the impact of chemotherapy on motor function, allowing for more tailored therapeutic interventions for individuals affected by CIPN.

3- **Integration of Sensory Neuropathy Detection**: The incorporation of a vibration-based device for sensory testing, in combination with motor assessment, introduces a more holistic approach to neuropathy evaluation. This system is designed to detect subtle sensory deficits, providing a comprehensive platform for both motor and sensory function evaluation.

Thesis Structure

This thesis is organized into five chapters. Chapter 1 introduces sensory and motor neuropathy, highlighting the limitations of current detection methods and outlining the thesis objectives and contributions. Chapter 2 reviews related work, covering the literature and technologies for neuropathy detection, including hardware and clinical applications. Chapter 3 details the development of the QuHalEx 2.0 system, including its hardware improvements, user interface, and sensory testing. Chapter 4 discusses the analysis techniques and machine learning algorithms used for force pattern analysis, hierarchical clustering, and SVD, along with the evaluation of results in distinguishing between healthy individuals and cancer patients. Finally, Chapter 5 summarizes the findings, discusses and outlines future research directions to advance neuropathy detection systems and explore broader applications.

2 Background and Related work

Recent research has highlighted the significance of hallux strength across different demographics, from athletic performance to fall prevention in older adults. The measurement of hallux strength has gained attention as a potential indicator of overall lower limb function, a marker for various neurological conditions. [3, 4, 5]

Importance of Hallux Strength:

1. Balance and Postural Control:
    - Studies have shown that hallux strength is associated with better balance performance (Chou et al., 2009; Tanaka et al., 1996). [3, 11]
    - The big toe plays a key role in the "toe-off" phase of gait, contributing to forward propulsion and stability during walking.
2. Fall Prevention:
    - In older adults, reduced hallux strength has been linked to an increased risk of falls (Mickle et al., 2009). [7]
    - Menz et al. (2006) found that hallux plantar flexion strength independently predicts mobility performance and falls in older individuals. [6]
3. Athletic Performance:
    - Yamauchi and Koyama (2020) demonstrated the importance of toe flexor strength in vertical jump performance, highlighting its relevance in sports. [13]

- Morita et al. (2015) also identified toe flexor strength as a factor in children's performance in dynamic sports, indicating its role in supporting athletic abilities that require explosive movements. [8]

4. Indicator of Overall Foot Health:
    - Quek et al. (2015) emphasized that hallux flexor strength, particularly of the flexor hallucis brevis, is crucial for arch integrity, supporting foot stability and balance while reducing fall risk. [11]
    - Chou et al. (2009) also highlighted the importance of the hallux in balance, with their study suggesting that greater toe strength positively impacts foot stability, even when under load. [3]

Devices and Methods for Measuring Hallux Strength:

Several approaches have been developed to quantify hallux strength, each with its own advantages and limitations:

1. Manual Muscle Testing (MMT):
    - The traditional clinical approach, using the Medical Research Council (MRC) scale.
    - Limitations: Subjective, lacks sensitivity to detect subtle changes, and has a ceiling effect.
2. Hand-Held Dynamometry (HHD):
    - Provides a more quantitative measure than MMT.

- Limitations: Requires tester strength to match patient force; less reliable for weaker muscles.

3. Paper Grip Test:
    - A simple method where patients grip a piece of paper with their toes.
    - Limitations: Primarily assesses flexion strength, may lack precision, and lacks automation.
4. Pressure Mat Systems:
    - Measures plantar pressure during toe flexion.
    - Advantages: Can assess multiple toes simultaneously; provides visual pressure maps.
    - Limitations: Limited accuracy; might not isolate individual toe strength effectively; and expensive.
5. Isokinetic Dynamometry:
    - Gold standard for strength testing in research settings.
    - Limitations: Expensive; not portable; typically not available for hallux testing.

6. QuHalEx Device (Hile et al., 2023):[4]
    - A novel, portable device specifically designed to measure hallux extension strength.
    - Advantages: a) Quantifies both extension and flexion strength; b) Does not require tester strength to match patient force; c) Provides continuous force-time data; d) May detect subtle asymmetries and weaknesses missed by MMT.
    - Limitations: New technology requires further validation in diverse populations.
7. Other custom prototype devices
    - Several custom prototypes have been introduced to assess hallux and toe strength for clinical applications, each with specific limitations and customizations, including those by Andrade et al. (2022), Chatzistergos et al. (2020), Chou et al. (2009), Morita et al. (2015), Ogawa et al. (2024), Quek et al. (2015), Tsuyuguchi et al. (2019), and Yamauchi and Koyama (2019), [1, 2, 3, 8, 9, 10, 12, 14].

3 Hardware Design

3.1 QuHalEx 2.0 Device

The QuHalEx 2.0 device builds upon the device presented in (Hile et al. 2023)[4], offering significant improvements in both hardware and functionality. While the original device set a new standard for the quantitative assessment of hallux strength, moving away from subjective manual testing, continuous testing, and user feedback revealed several areas for enhancement. These improvements aim to provide a more advanced, user-friendly, and highly accurate tool for both clinical and non-clinical applications.

One major upgrade in QuHalEx 2.0 is the integration of a sensitive pressure sensing platform. The original device measured only the force applied by the hallux, which, while useful, did not fully capture the dynamics of foot movement during testing. The new system provides high-resolution data on foot positioning and force application patterns throughout the test, allowing for a more detailed analysis of hallux extension and flexion movements. This upgrade reveals subtle changes in strength or coordination that may indicate compensatory patterns or neuromuscular impairments.

Figure 3.1. The QuHalEx 2.0.

The increased precision of these sensors ensures that the data collected is not only more accurate, but also more comprehensive. QuHalEx 2.0 can now detect variations in foot pressure and movement that were previously undetectable, making it useful for monitoring gradual changes during rehabilitation or disease progression. The additional pressure data also helps identify external factors, such as compensatory movements or uneven force distribution, that could affect the accuracy of test results. This level of details supports more personalized diagnosis and treatment strategies.

Another significant improvement is in the electronics of QuHalEx 2.0. Updated electronic boards enable faster data processing, ensuring real-time capture and display of sensor data. This boost in processing power reduces latency, providing immediate feedback for both clinicians and patients. QuHalEx 2.0 also features wireless communication, transmitting data directly to companion mobile apps available on iOS and Android. These apps provide an intuitive interface for monitoring progress, analyzing data, and receiving real-time feedback, without requiring additional hardware, which enhances the device's usability in both clinical and home environments. Future updates to the mobile application will introduce the possibility of remote monitoring, allowing clinicians to track patient progress during rehabilitation, even when patients perform tests independently at home. This feature is particularly valuable for those in remote areas or with limited mobility, where in-person visits may not be feasible.

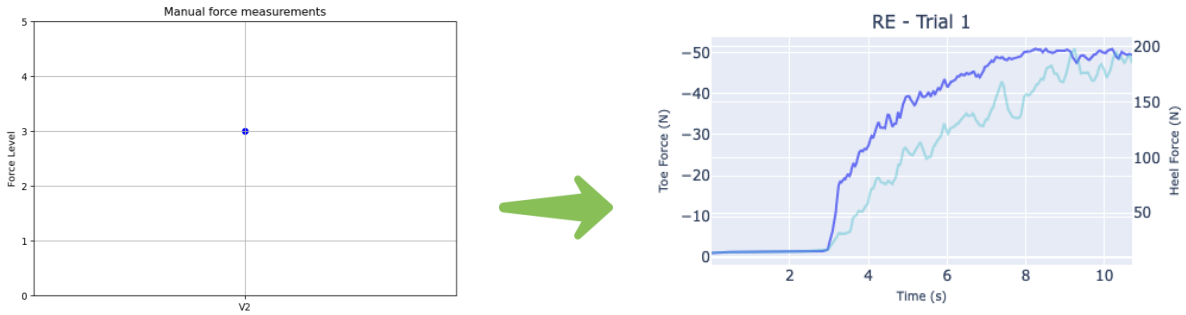

Figure 3.2. Manual force measurement vs QuHalEx 2.0 force measurements.

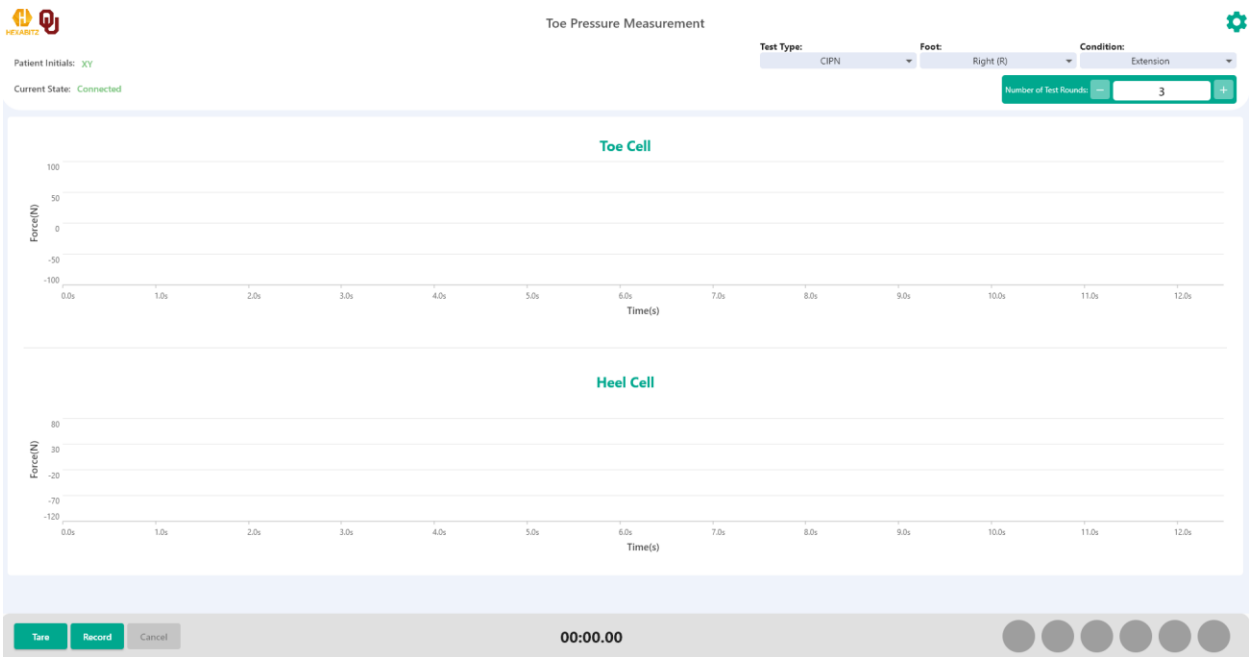

Figure 3.3. The apps' user interface.

In terms of physical design, QuHalEx 2.0 features a more robust mechanical structure. While the original design was functional, improvements were needed in stability and durability. The new design incorporates stronger materials and a sturdier build, making the device suitable for daily use in various environments, including clinics and home-based rehabilitation. Additionally, the redesign enhances device stability during testing, minimizing unwanted movements that could affect results. Improvement ensures consistent and reliable measurements across different users and settings.

This new design opens opportunities for applications ranging from outpatient clinics to research labs and athletic training facilities. The combination of advanced hardware, high-precision sensors, real-time feedback, and user independence makes QuHalEx 2.0 a versatile and impactful tool in foot biomechanics. Whether used to diagnose hallux strength deficits, study foot mechanics in a research setting, or assist patients during rehabilitation, QuHalEx 2.0 offers a comprehensive, accurate, and user-friendly solution. Its versatility also extends to athletic

performance enhancement, where precise hallux strength measurement plays a critical role in injury prevention and performance optimization.

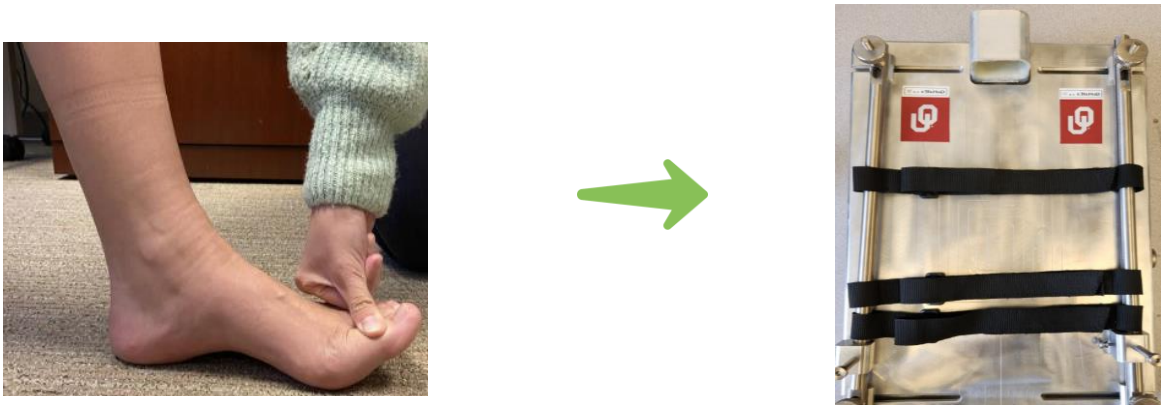

Figure 3.4. Manual testing [4] vs QuHalEx 2.0.

The validation and bench testing results, as shown in figure 3.5, demonstrate the accuracy and linearity of the sensor readings for both the hallux and heel sensors. The applied weight was plotted against the sensor readings, and the graph shows an almost perfect linear relationship for both the toe and heel measurements, indicating an accurate and consistent response to applied force. These results validate the sensor's precision in measuring applied forces, which is critical for ensuring accurate assessments in real-world applications like clinical testing or rehabilitation scenarios.

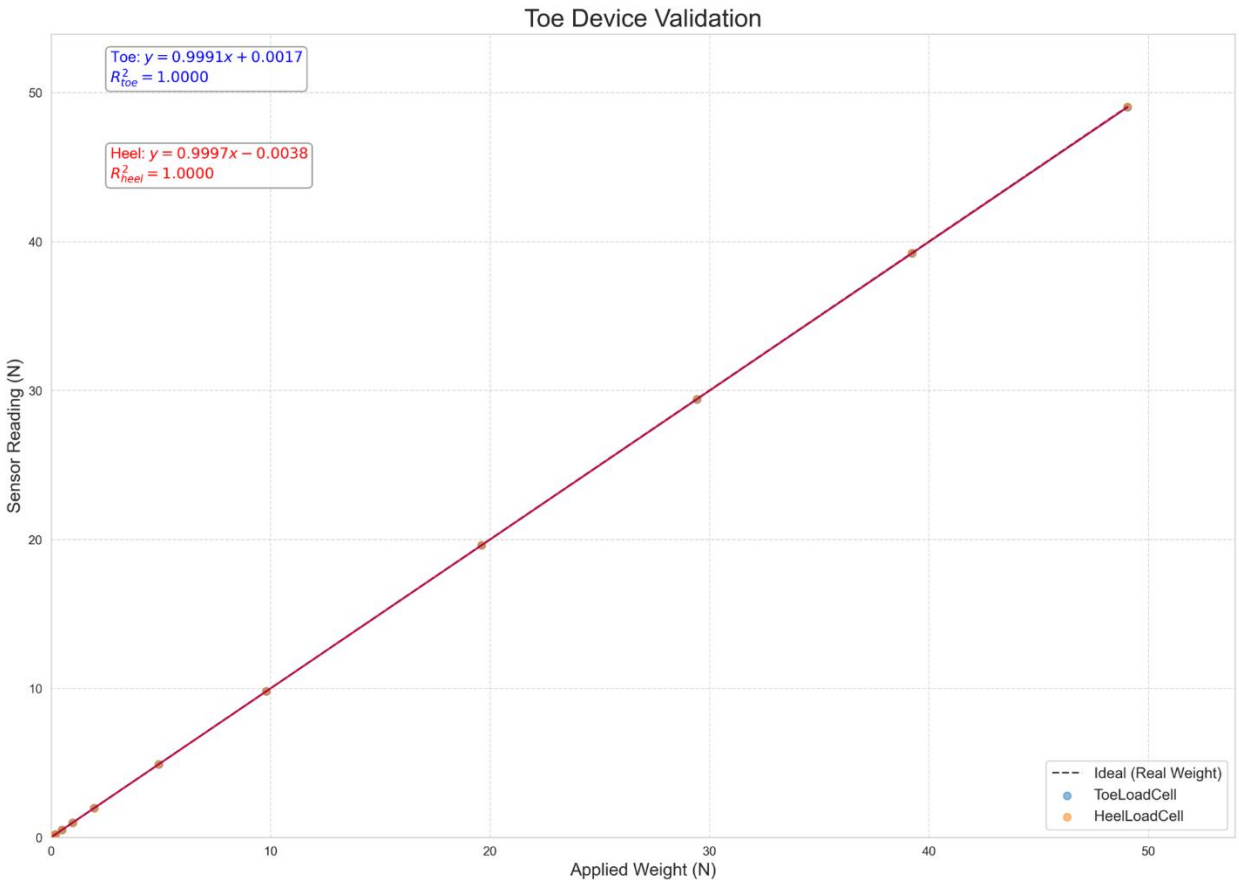

Figure 3.5. QuHalEx 2.0 bench testing and validation.

To highlight the significance of incorporating the heel sensing unit, we present examples from preliminary analysis that explore the relationship between signals collected from both the hallux strength sensor and the heel sensing plate during testing. The heatmaps below clearly demonstrate the high correlation between these two data streams, showcasing how different patients exhibit varying motor functions depending on the type of test performed.

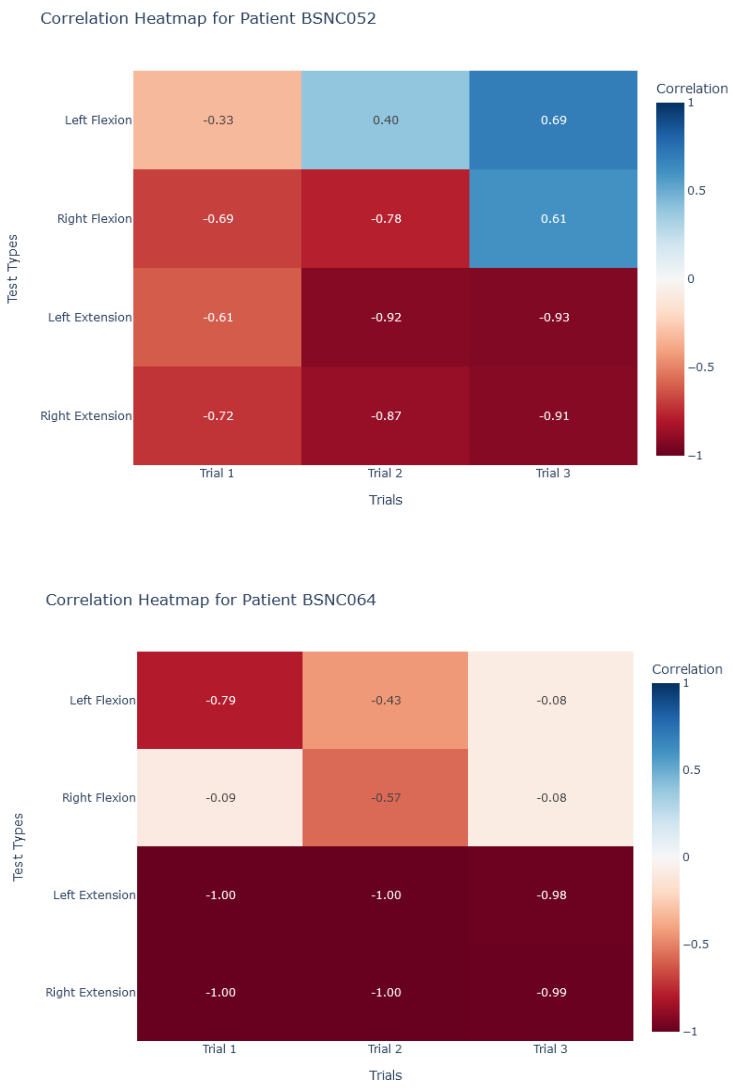

Figure 3.6. Correlation heatmaps for different types of tests for 2 different patients.

Additionally, the plots in figure 3.7 provide real test examples, further illustrating the close relationship between hallux strength and heel pressure. These examples emphasize how the integration of this additional sensing layer allows for a more nuanced understanding of foot biomechanics, capturing both movement patterns and compensatory behaviors.

Figure 3.7. Real example plots.

Figure 3.8. Correlation distributions for over 200 tests.

3.2 Vibration System for Sensory Neuropathy Detection

In addition to improving the QuHalEx 2.0 device for motor function testing, we have developed a sensory neuropathy detection device to address the growing need for comprehensive assessments of both motor and sensory impairments. Sensory neuropathy is a common complication in patients undergoing chemotherapy, which can lead to nerve damage and significantly impair quality of life. Traditional approaches to detecting sensory neuropathy often require specialized, standalone devices. To overcome this, we developed a versatile vibration-based system that can be seamlessly integrated with the existing QuHalEx 2.0 platform, offering a more efficient, portable, and customizable solution for evaluating sensory function.

This newly developed vibration system is designed to detect sensory deficits by using precise vibrations applied directly to the patient's toe—a common area for sensory neuropathy testing. The system employs a Linear Resonant Actuator (LRA) mounted on a custom-designed toe cap to deliver controlled vibrations to the targeted area. The LRA can produce vibrations with variable intensity, frequency, and duration, allowing for a tailored testing experience. This flexibility in vibration settings enhances the system's ability to detect subtle changes in sensory perception, which might be missed by more traditional methods.

At the core of the vibration system is the Haptic Driver - DA7280, a specialized controller that enables precise adjustments to the LRA's vibration output. The haptic driver allows us to fine-tune the vibration parameters to match the sensitivity levels required for each patient. This level of control is critical in testing patients and be able to quantify various degrees of neuropathy, as the system can be adapted to detect even the most minimal sensory deficits in patients with early-stage neuropathy, as well as more pronounced deficits in those with advanced nerve damage.

Figure 3.9. Haptic Driver - DA7280.

The integration of the vibration system into the QuHalEx 2.0 platform provides a unified approach to neuropathy assessment by enabling simultaneous testing of both motor and sensory functions. Combining these two assessments into a single, cohesive platform significantly streamlines the testing process, eliminating the need for separate devices or multiple assessments. This integration not only simplifies the workflow for clinicians but also reduces the burden on patients as well.

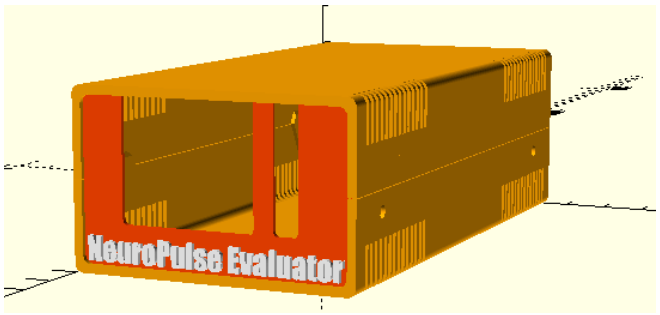

Figure 3.10. Vibration device enclosure.

The entire vibration system is housed in a compact, portable enclosure that ensures ease of use across different clinical settings.

Another feature of the vibration system is its customizable vibration modes, which allow for different types of sensory testing. The system currently supports three vibration modes: Continuous Increase, Delayed Start, and Randomized Start. Each mode offers unique testing parameters to ensure a comprehensive assessment of the patient's sensory response:

- Mode I: Continuous Increase initiates vibrations immediately, increasing the intensity steadily over a 10-second period. This mode is useful for evaluating the patient’s response to a gradually intensifying stimulus, which can help detect thresholds of sensory perception.
- Mode II: Delayed Start introduces a short delay before the vibrations begin, followed by a similar 10-second period of increasing intensity. This mode allows clinicians to assess the patient's response after a brief pause, testing the effect of latency in sensory detection and preventing false sensations.
- Mode III: Randomized Start incorporates an element of unpredictability by initiating the vibration after a random delay (between 4 and 7 seconds). This mode is also useful for eliminating any anticipation bias from the patient, as it tests their ability to detect the vibrations without prior expectation.

These varying modes provide flexibility for clinicians to tailor the sensory test to the specific needs of their patients. For example, randomized start times are particularly valuable in preventing the patient from anticipating the vibration, ensuring a more accurate measure of sensory response.

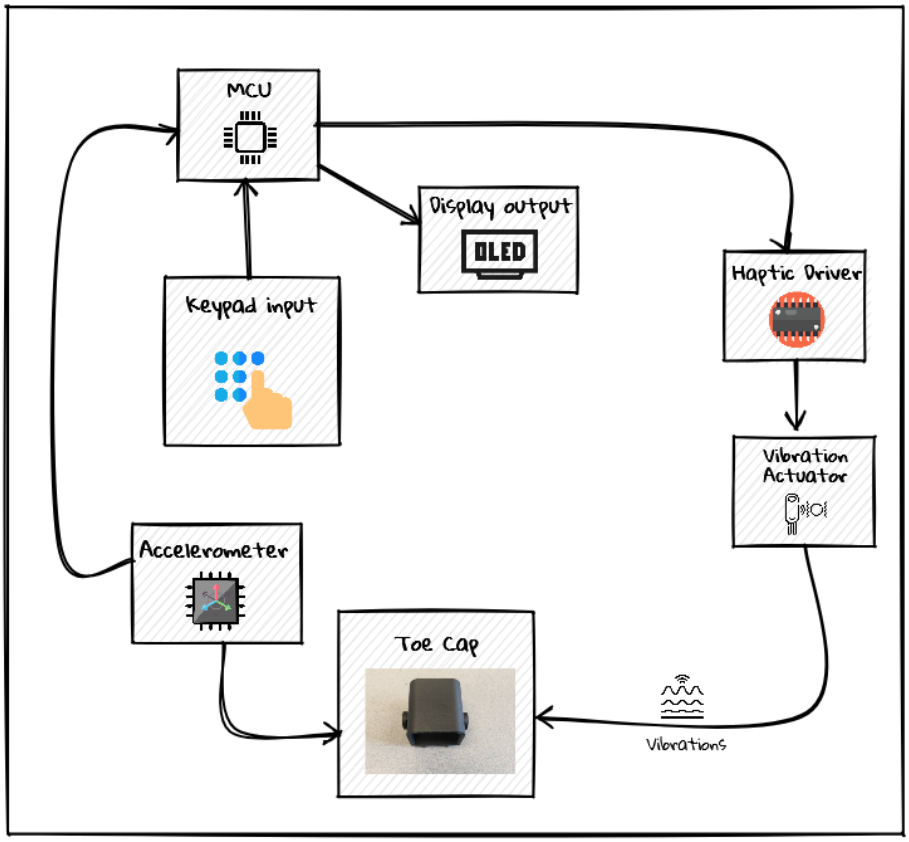

Figure 3.11. Vibration system diagram.

The system's user interface is designed for simplicity and ease-of-use. A membrane switch allows the user to select the desired vibration mode, while an OLED display shows the current mode and vibration level in real time. This straightforward interface ensures that the device can be operated efficiently by clinicians and even non-specialists, with minimal training required. Furthermore, the OLED display provides clear, real-time feedback, helping the operator monitor the test parameters and ensure that the appropriate settings are used for each patient.

In addition to its role as a standalone sensory testing tool, the vibration system offers significant potential for future developments in sensory rehabilitation. The system's control over vibration parameters could be utilized in therapeutic contexts, where targeted sensory stimulation is used to retrain nerve function or alleviate symptoms of neuropathy. By delivering controlled

vibrations to areas affected by nerve damage, the system could also help stimulate nerve regeneration or improve the patient's ability to detect sensory stimuli.

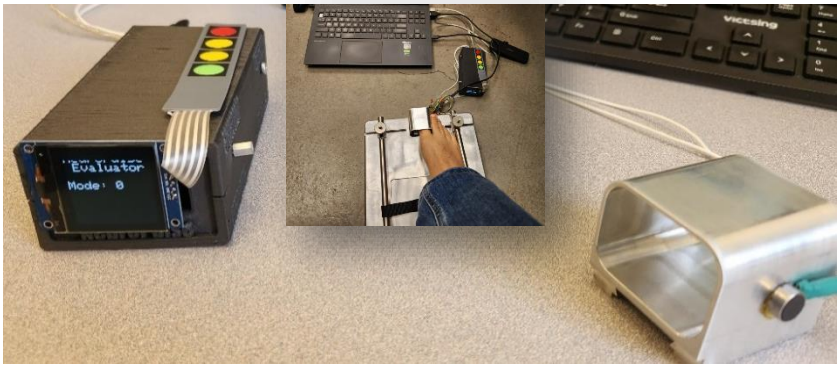

Figure 3.12. Vibration setup.

To ensure the accuracy and reliability of the vibration system, testing was conducted using the LSM9DS1 9-axis motion sensor, which includes an accelerometer to measure the vibration patterns produced by the LRA. The accelerometer provided important data on the intensity, frequency, and consistency of the vibrations, demonstrating that the system produces consistent and reliable output.

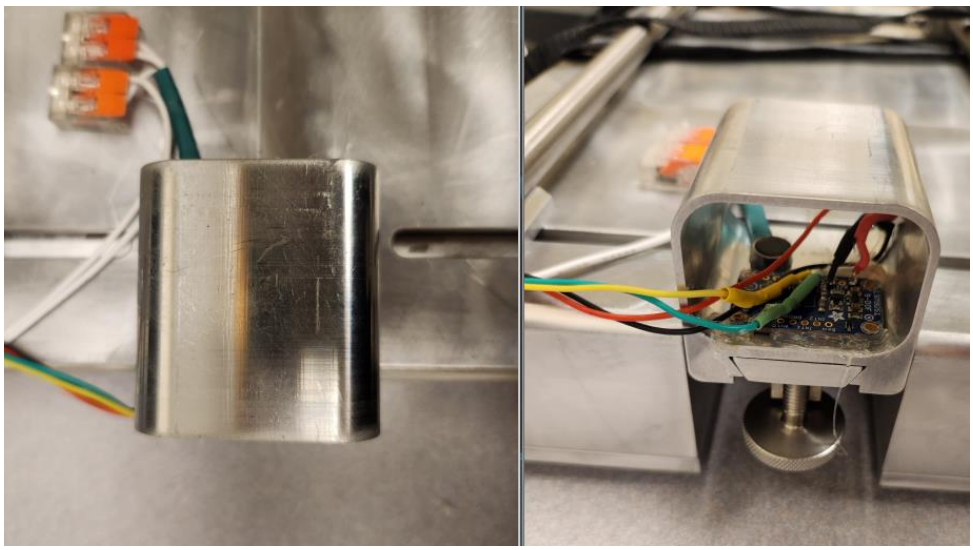

Figure 3.13. The toe cap with the LRA and the motion sensor.

Tests were conducted to study the vibration behaviors under different conditions. The control plots shown in figure 3.14 present measurements taken with no vibration applied, establishing baseline readings for environmental noise. In the absence of intentional vibration, the accelerometer detected minimal background noise, with no dominant frequencies.

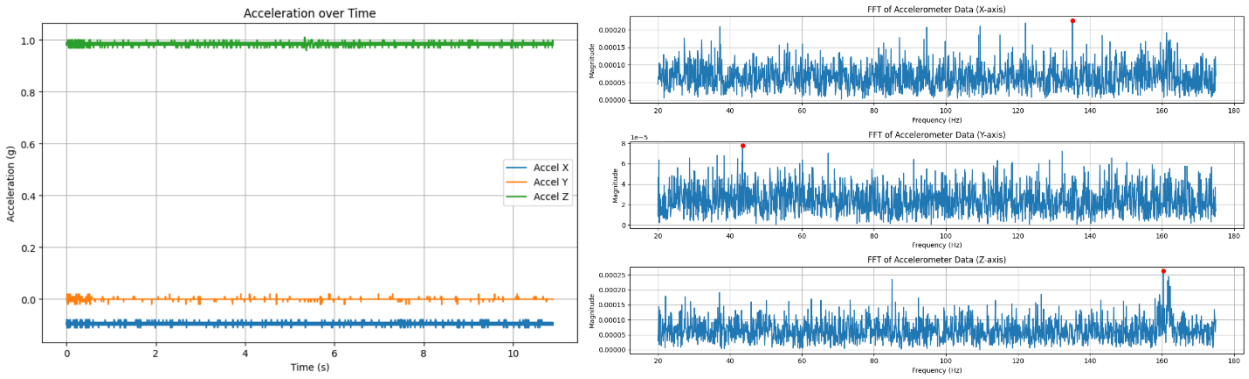

Figure 3.14. Control Time and frequency measurements (Without Vibration).

In the second setup, vibrations were applied to observe the system's response in real-time. Plot 3.15 shows the gradually increasing vibration pattern applied in Mode I, confirming the device's ability to generate the desired vibration pattern. A main dominant frequency is visible, indicating the specific frequency at which the LRA vibrates.

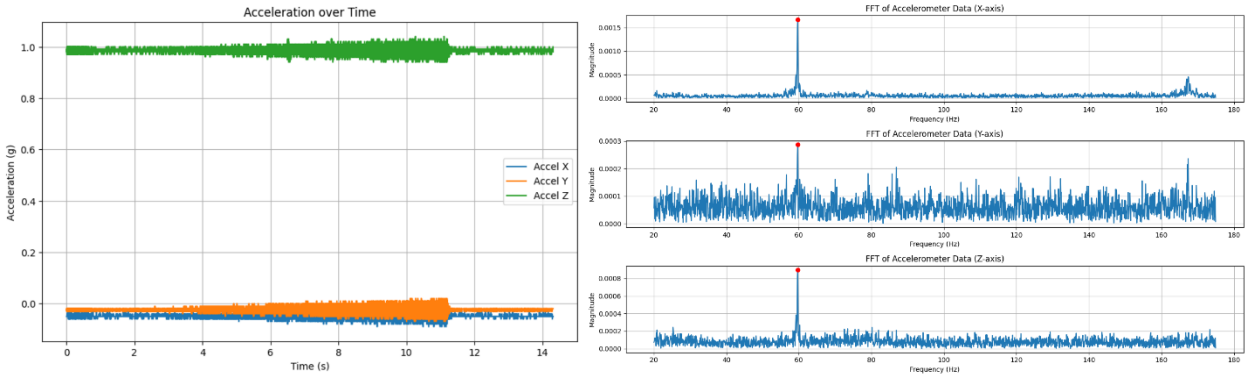

Figure 3.15. Time and frequency measurements (With Vibration).

For the third setup, the LSM9DS1 sensor was positioned just outside the cap, at the location closest to where the user's foot would be, to simulate real-world tests, figure 3.16. This setup was performed to capture whether vibrations would propagate from the toe cap to the foot. Results showed no propagation of vibrations between the LRA and the LSM9DS1 sensor in either time or frequency domains, ensuring that vibrations remain localized to the target area without unintended interference elsewhere in the system.

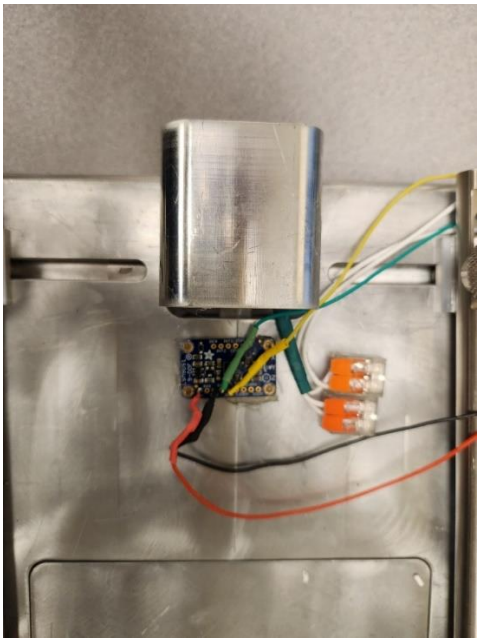

Figure 3.16. The motion sensor is positioned at the foot location.

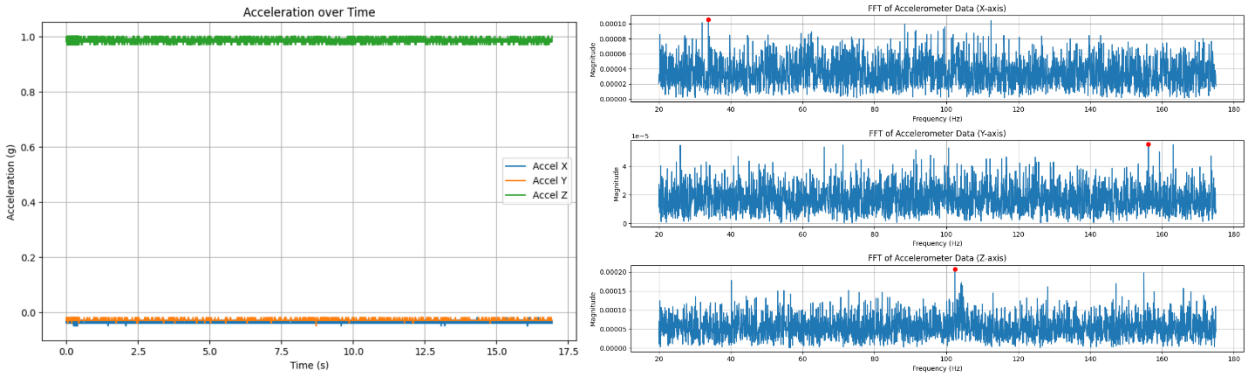

Figure 3.17. Time and frequency measurements (With Vibration, with the sensor on the platform).

In summary, the integration of the vibration system into the QuHalEx 2.0 platform represents a significant advancement in the assessment of sensory neuropathy. By combining motor and sensory testing into a single, portable device, we offer a comprehensive, efficient solution for evaluating neuropathy in clinical environments. The ability to customize vibration parameters, along with the device's portability and user-friendly interface, enhances its applicability across a wide range of healthcare settings.

4 Analysis and Model Development

The complexity of muscle activation and coordination, particularly in conditions like chemotherapy-induced peripheral neuropathy (CIPN), poses a significant challenge for clinicians and researchers. Traditional manual methods of assessing muscle strength, such as manual muscle testing (MMT), are limited in their ability to capture the full extent of the neuromuscular impairments that often arise from CIPN. Manual testing tends to focus on a subjective measure of the peak strength values, overlooking the intricate dynamics of muscle behavior over time, such as the force generation and decay patterns, fluctuations, and the distribution of muscle activation across different phases of movement.

To address these limitations, the QuHalEx device was designed to provide more detailed and objective insights into toe strength, capturing high-resolution data on force generation throughout the different testing ranges. While QuHalEx has proven to be an effective tool for gathering such data, the complexity of the resulting datasets necessitates advanced analytical techniques to extract meaningful information. Simply analyzing peak strength values would overlook the nuanced changes in muscle behavior that could signal the early onset of neuropathy or other impairments.

Thus, this chapter focuses on the development of computational models and data analysis techniques to detect and quantify differences in force patterns between healthy individuals and patients undergoing chemotherapy. By applying these methods, we aimed to capture the nuanced, multidimensional nature of muscle behavior that is otherwise difficult to interpret through traditional analysis. The combination of unsupervised machine learning techniques and linear algebraic decomposition, such as hierarchical clustering and Singular Value Decomposition (SVD), forms the backbone of this analysis, enabling the identification of distinct behavioral patterns among different subject groups.

4.1 Feature Extraction for Force Pattern Analysis

The force data collected by the QuHalEx device goes beyond simple measures of maximum strength or average force. To fully understand the underlying muscle function, we extracted features from the force-time data that encapsulate various aspects of muscle behavior. These features captured information from different domains. By examining these multiple domains, we could provide a more comprehensive picture of how muscle strength developed, fluctuated, and decayed over the duration of the test.

Feature extraction is a critical step in our methodology, as it allows us to transform raw force data into meaningful metrics that characterize muscle functions. We extracted more than 25 features from the force data, encompassing time domain, frequency domain, and force distribution characteristics. These features are designed to provide a comprehensive understanding of the dynamic aspects of muscle strength.

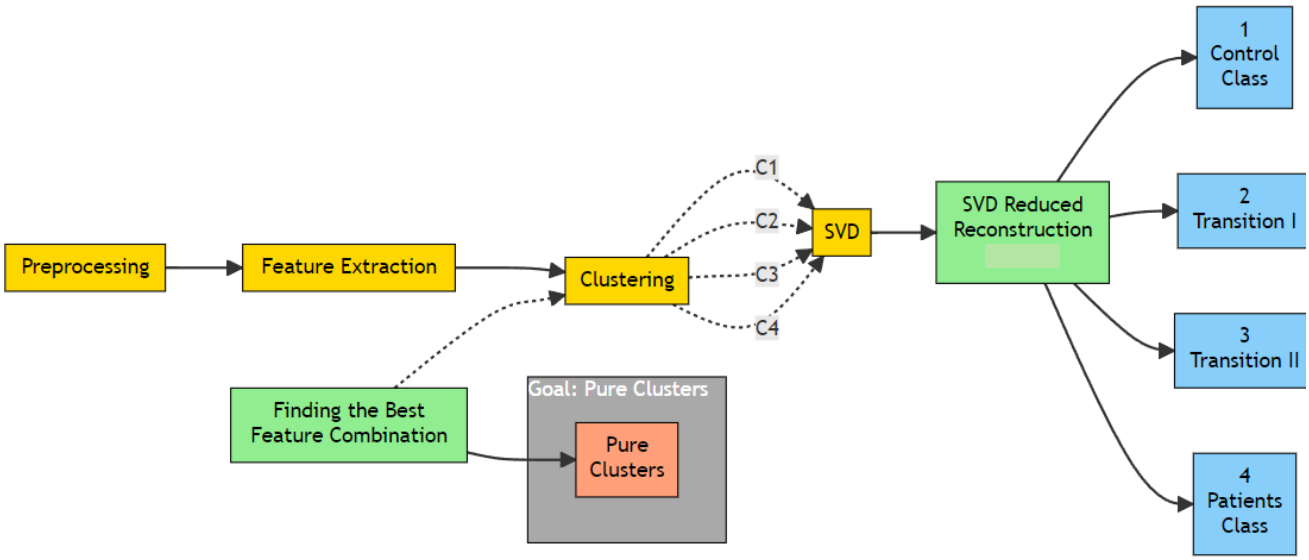

Figure 4.1. Workflow diagram.

Example of features:

Mean Force: This feature calculates the average force applied during the test, providing a basic measure of the overall force exerted by the toe.

Time to Max: This feature measures the time taken to reach the maximum force, aiding in understanding the speed and efficiency of the maximum muscle activation.

Time to 90% Force: Time taken to reach 90% of the maximum force. This metric is a more robust time to max estimate since it's less prone to noise.

Time Below: Total time spent below a certain force threshold. This feature highlights periods of low force application, which can indicate muscle weakness or poor endurance.

Time Mid: Total time spent within a mid-range force threshold. This metric is essential for understanding the consistency and control of force application.

Time Above: Total time spent above a certain force threshold. This feature indicates periods of high force application, which are critical for tasks requiring substantial muscle strength.

Max Force: The maximum force achieved during the test, providing a measure of the peak strength exerted by the muscle.

90% Force: Force value at 90% of the maximum force. This feature provides a less noisy max force measurement.

Force Below: Sum of force values below a certain threshold. This metric helps identify the total sum of minimal force application, indicating weaker muscle strength or less effort during the test.

Force Mid: Force value within a mid-range threshold. This metric provides a balanced view of force application during the test, reflecting average muscle performance.

Force Above: Force value above a certain threshold. This feature helps identify instances of maximal force application, indicating stronger muscle strength or peak effort during test.

Standard Deviation: Variability of force during the test. High variability can indicate inconsistent muscle performance.

Number of Crossings of Mean: Number of times the force crossed the mean value. This feature measures the stability and consistency of force application.

Number of Crossings 90% force: Number of times the force crossed 90% of the maximum value. This feature indicates the frequency of variation around near-maximal force.

Crossings per Second: Number of times the force crossed the mean threshold in each second.

Crossings per Second 90%: Number of times the force crossed the 90% force threshold in each second.

Total Power 0-1Hz: Total power of the force signal within the 0-1Hz frequency range. This range captures the most fundamental aspects of force application.

Total Power 1-2Hz: Total power of the force signal within the 1-2Hz frequency range. This range is associated with slower muscle activation patterns.

Total Power 2-5Hz: Total power of the force signal within the 2-5Hz frequency range. This frequency band is associated with muscle variability and fatigue.

Total Power Bigger 5Hz: Total power of the force signal above 5Hz. This feature captures higher frequency components, which may relate to rapid muscle movements.

Entropy Value: Measure of randomness in the force signal. High entropy indicates a more chaotic muscle activation pattern.

Difference Between 90 Value Mean: Difference between the 90% force value and the mean force. This metric helps assess the consistency of high-force application.

Kurtosis: A measure of the peakness of the force distribution. High kurtosis indicates sharper, more consistent force application.

Skewness: A measure of the asymmetry of the force distribution. Positive skewness suggests more frequent forceful peaks, while negative skewness indicates more frequent low-force periods.

Coefficient of Variation: Ratio of standard deviation to mean force. CV provides a normalized measure of variability.

Slope for the rise: The rate of increase in force. This metric helps in understanding the acceleration of force application.

Slope by section: The rate of change in force over different sections of the test. This metric provides a detailed view of how force rate varies throughout the test duration.

AUC (Area Under the Curve): The total area under the force-time curve. This metric represents the overall force exerted over the test period.

AUC difference from baseline: The difference between the actual AUC and an ideal baseline AUC. This comparison helps in identifying deviations from expected force patterns across multiple visits.

These features provide a rich dataset for comprehensively analyzing muscle function. The choice of features ensures that the properties of muscle activation are captured, allowing for a detailed characterization of muscle performance.

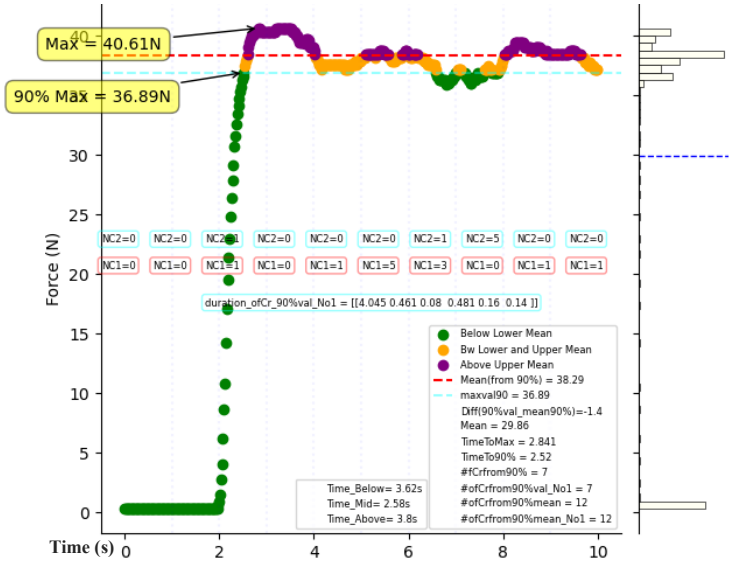

Figure 4.2. Statistical and force distribution analysis.

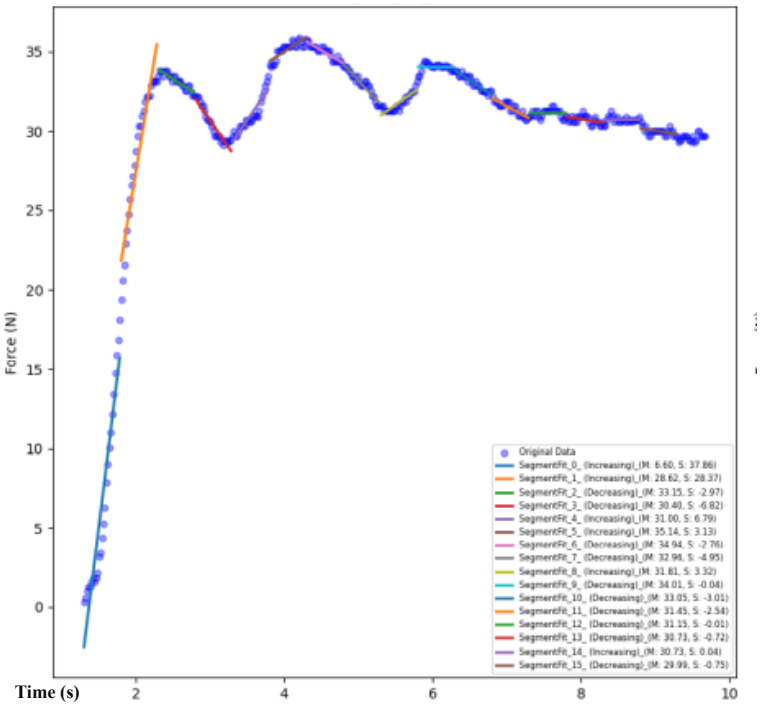

Figure 4.3. Temporal rate of change (Section by section fitting).

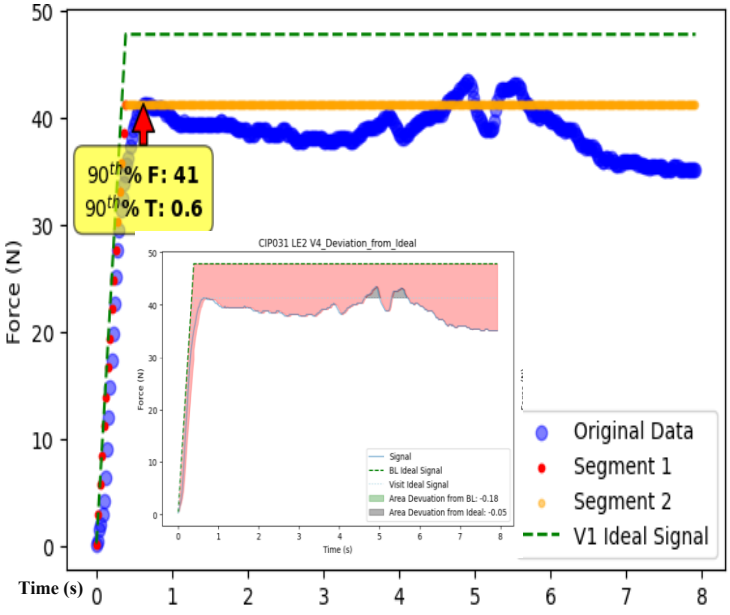

Figure 4.4. Ideal vs, baseline, and AUC difference.

By extracting over 25 features across multiple domains, we were able to generate a detailed characterization of each subject's muscle function. These features serve as the input for the subsequent clustering and decomposition methods used to identify behavioral patterns and group subjects based on their neuromuscular performance.

4.2 Clustering Analysis: Hierarchical Clustering

To uncover distinct patterns in muscle behavior, we applied hierarchical clustering, an unsupervised machine learning technique that groups subjects based on the similarity of their features without predefined labels. This approach is particularly well-suited for organizing the data into a hierarchy of nested clusters, revealing both fine and coarse groupings. By employing hierarchical clustering, we can identify distinct groups of subject tests based on muscle function characteristics, with the added benefit of an intuitive dendrogram representation that enhances our understanding of the relationships between data points.

Feature Selection for Clustering: Not all extracted features are equally responsible for accurate clustering. We defined an iterative approach to iterated over various combinations of features to identify those that maximize cluster purity. The selection process was evaluated using entropy and purity measures. Entropy measures the randomness within clusters, while purity measures the extent to which clusters contain a single class (e.g., control or CIPN patients).

In this process, we tried to find the optimal combination of features for clustering our data. The goal was to minimize entropy or maximize purity in the resulting clusters, based on two types of subjects (Control, CIPN). Following is a detailed explanation of the steps:

1. We start by generating all possible combinations of features from our feature set F.
2. For each feature combination C: a) We standardize the features to ensure they're on the same scale, preventing any feature from dominating due to its magnitude; b) We apply PCA; c) We perform hierarchical clustering forming clusters; d) For each of the clusters:

    We calculate entropy, and purity. Entropy will measure the mix of classes within the cluster. Lower entropy indicates better separation of classes.

    e. We compute the average entropy and purity across all clusters.

3. We keep track of the feature combinations that yield the lowest average entropy and highest average purity.
4. After processing all combinations, we return these optimal feature sets. We reevaluated with different numbers of clusters.

This process allows us to identify which features are most informative for separating the control and CIPN classes in our dataset.

Finding Best Combination Algorithm

Given:

$F = \{\text{mean}, \text{time\_max}, \text{time\_90}, ..., \text{skewness}\}$ (26 features)

$$\text{Total combinations} = \sum_{k=1}^{26} \binom{26}{k} = 2^{26} - 1 = 67,108,863$$

For each feature combination $C \subseteq F$:

1. Standardize features:

$$X_C = \frac{X_C - \mu_C}{\sigma_C}, \quad \mu_C = \frac{1}{n}\sum_{i=1}^{n} X_{C,i}, \quad \sigma_C = \sqrt{\frac{1}{n-1}\sum_{i=1}^{n}(X_{C,i} - \mu_C)^2}$$

2. Apply PCA:

$X'_C = \text{PCA}(X_C, n\_components = \min(|C|, 10))$

3. Perform hierarchical clustering:

$\text{linked} = \text{linkage}(X'_C, \text{method='ward'})$

$\text{clusters} = \text{fcluster}(\text{linked}, t = 4)$

4. For each cluster $i \in \{1, \ldots, 4\}$:

a. Calculate entropy:

$$H_i = -\sum_{c \in \{0,1\}} p_{i,c} \log_2(p_{i,c})$$

$$\text{where } p_{i,c} = \frac{|\{x \in \text{cluster}_i : \text{class}(x) = c\}|}{|\text{cluster}_i|}$$

b. Calculate purity:

$$P_i = \max_{c \in \{0,1\}} p_{i,c}$$

5. Compute average metrics:

$$\bar{H}_C = \frac{1}{4}\sum_{i=1}^{4} H_i, \quad \bar{P}_C = \frac{1}{4}\sum_{i=1}^{4} P_i$$

Find optimal combinations:

$$C^*_H = \arg\min_C \bar{H}_C$$

$$C^*_P = \arg\max_C \bar{P}_C$$

Figure 4.5. Finding the best combination.

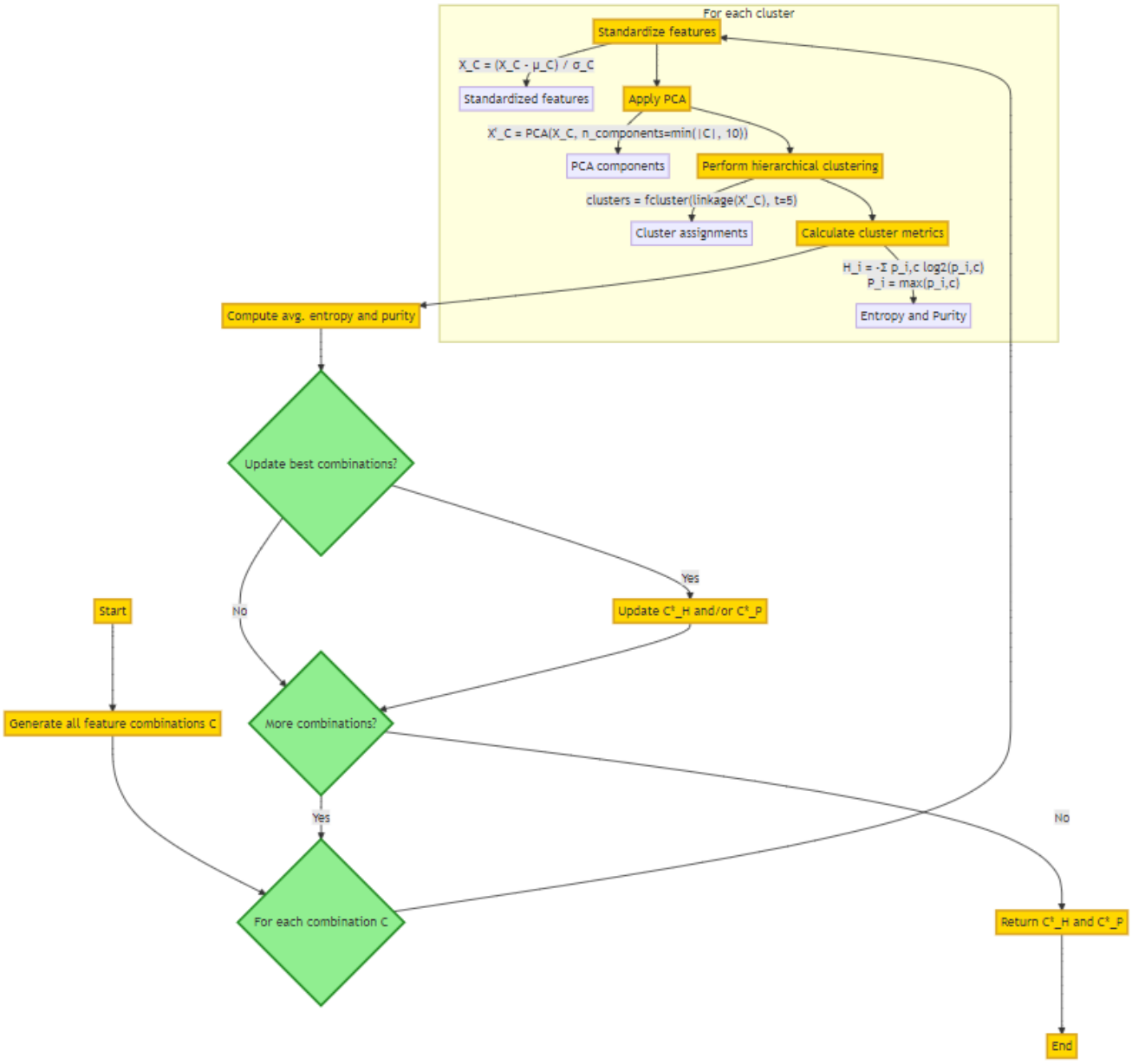

Figure 4.6. Finding the best combination flowchart.

Hierarchical Clustering: Hierarchical clustering was performed using Ward's method, which minimizes the variance within each cluster. The algorithm starts by treating each data point (test) as a separate cluster, and then iteratively merges the two clusters resulting in the smallest increase in total within-cluster variance.

Dendrogram Analysis: The resulting dendrogram provides a visual representation of the clustering process. By examining the dendrogram, we can determine the optimal number of clusters.

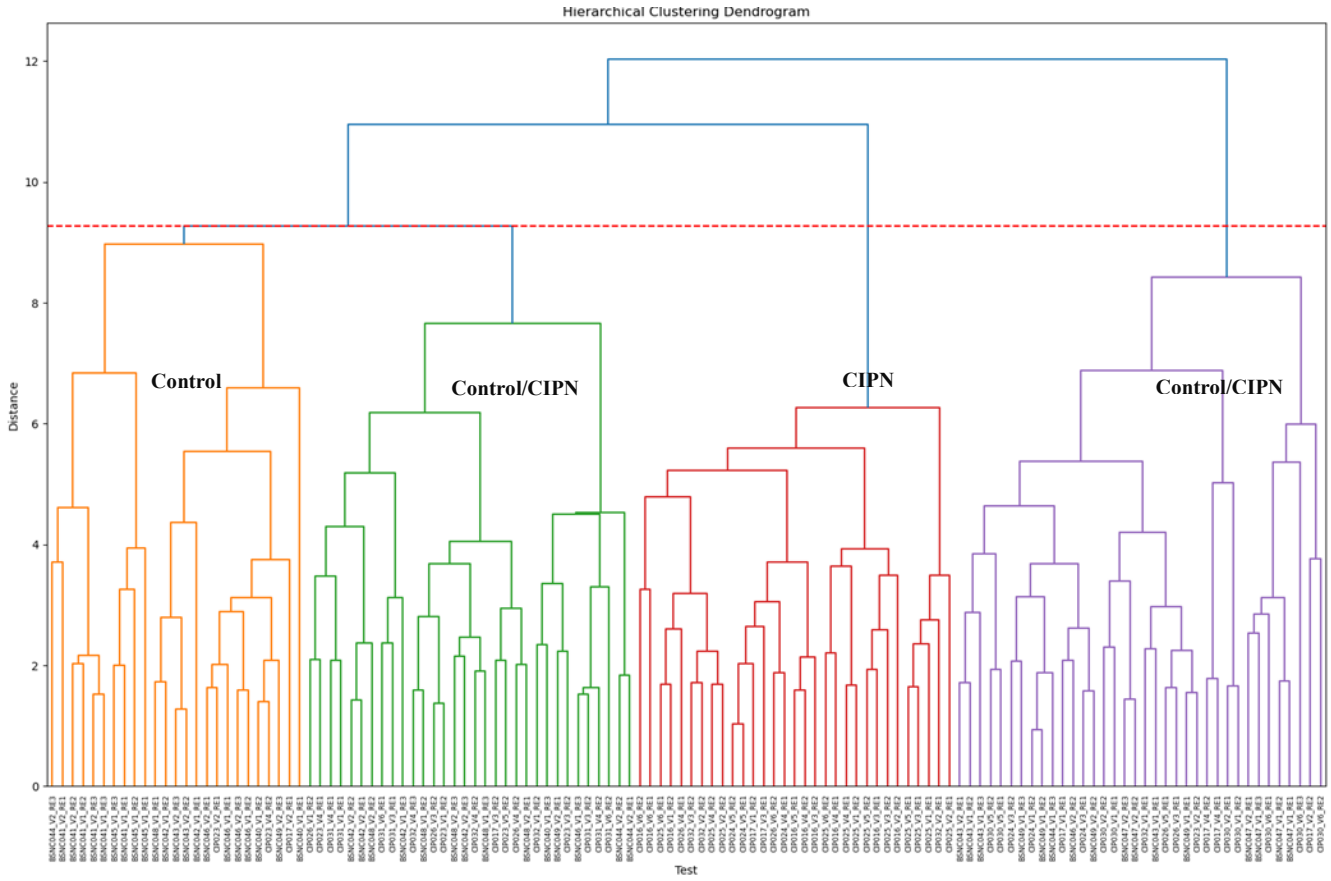

Figure 4.7. Hierarchical clustering dendrogram.

4.3 Singular Value Decomposition (SVD)

Singular Value Decomposition is a powerful technique used to simplify and interpret the complex data by breaking it down into its principal components. This step is crucial for understanding the main patterns within each cluster and for visualizing the key characteristics that differentiate the clusters. Based on the analysis of the reconstructed signals using SVD, we characterized our resultant clusters into four groups distinct groups.

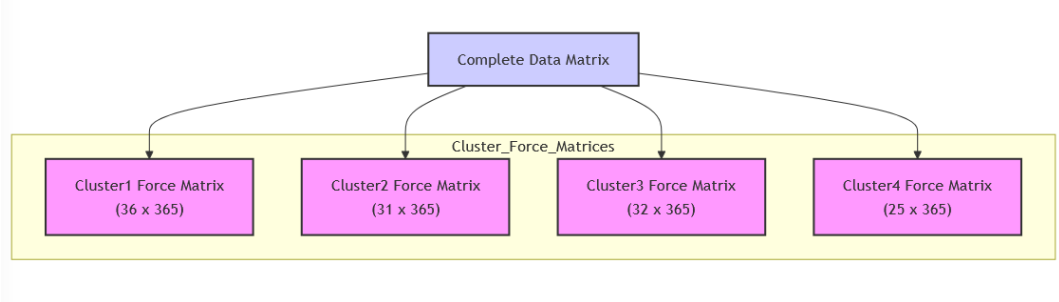

Figure 4.8. Each cluster force matrix.

Reconstuction Algorithm

For each cluster $i \in \{1, 2, 3, 4\}$:

I. Non-centered SVD:

1. Perform SVD:

$$X_i = U_i \Sigma_i V_i^T$$

2. Calculate scores:

$$\text{score}_i = U_i[:, : r]\Sigma_i[: r, : r]$$

3. Reconstruct:

$$\hat{X}_i = U_i[:, : r]\Sigma_i[: r, : r](V_i^T)[: r, :]$$

II. Centered SVD:

1. Center the matrix:

$$X_i^c = X_i - \bar{X}_i, \quad \text{where } \bar{X}_i = \frac{1}{n}\sum_{j=1}^{n} X_{i,j}$$

2. Perform SVD on centered matrix:

$$X_i^c = U_i^c \Sigma_i^c (V_i^c)^T$$

3. Calculate scores:

$$\text{score}_i^c = U_i^c[:, : r]\Sigma_i^c[: r, : r]$$

4. Reconstruct:

$$\hat{X}_i^c = U_i^c[:, : r]\Sigma_i^c[: r, : r]((V_i^c)^T)[: r, :] + \bar{X}_i$$

Where:

$X_i \in \mathbb{R}^{m \times n}$ is the original force matrix for cluster i

$\bar{X}_i \in \mathbb{R}^{1 \times n}$ is the mean of X_i along axis 0

$U_i, U_i^c \in \mathbb{R}^{m \times m}, \Sigma_i, \Sigma_i^c \in \mathbb{R}^{m \times n}, V_i, V_i^c \in \mathbb{R}^{n \times n}$

r is the number of singular values used (here, $r = 1$)

Figure 4.9. SVD and Reconstruction algorithm.

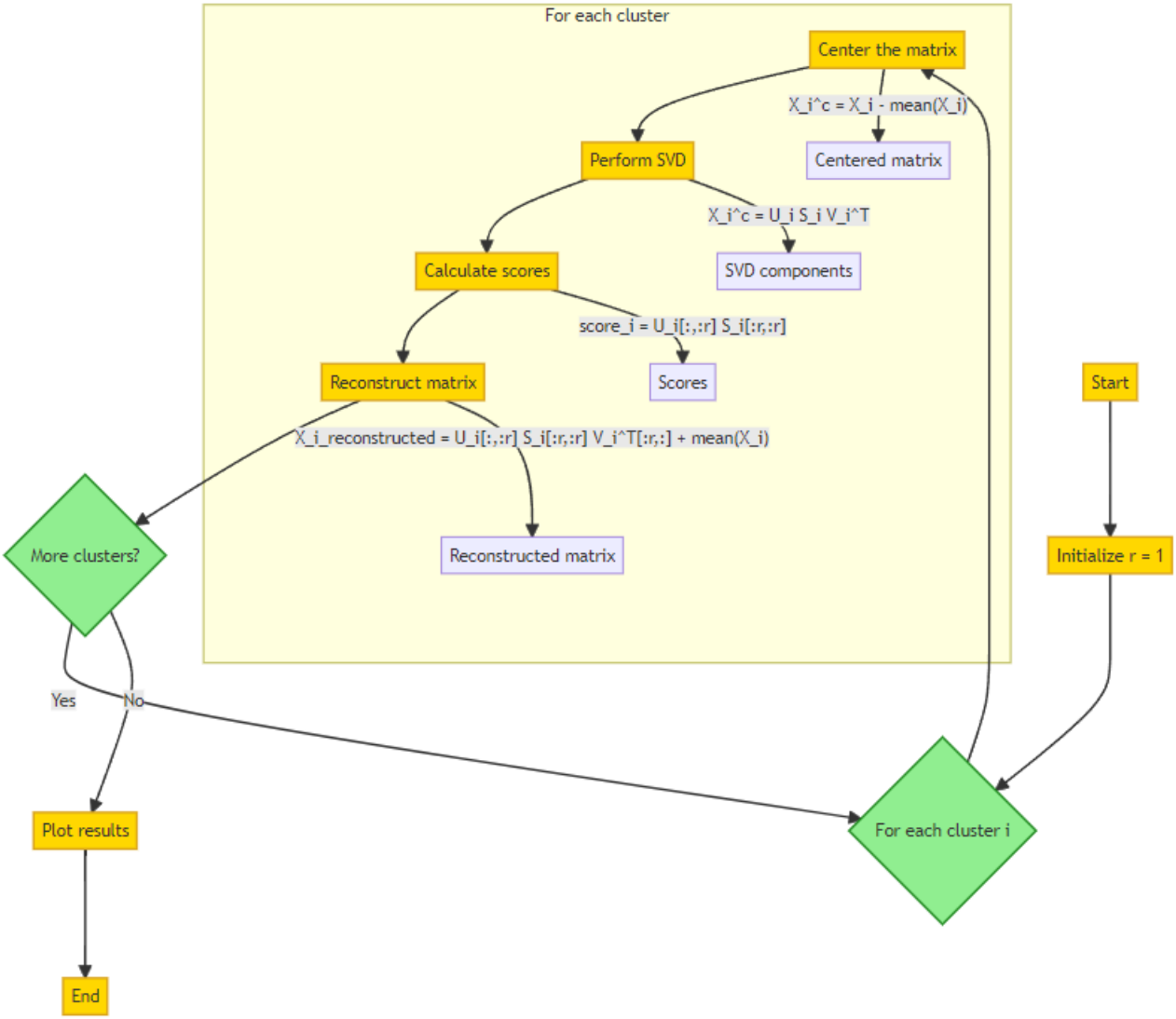

Figure 4.10. Flow diagram of the process.

4.4 Results

Using the methodology outlined earlier, we evaluated the feature combinations to identify the set that yielded the best clustering results, successfully separating it into four distinct clusters with the lowest entropy values. Two of these clusters were dominated by a single group—healthy controls or CIPN patients—while the remaining two represented transitional groups, Transition I and Transition II, where control subjects and patients displayed mixed characteristics.

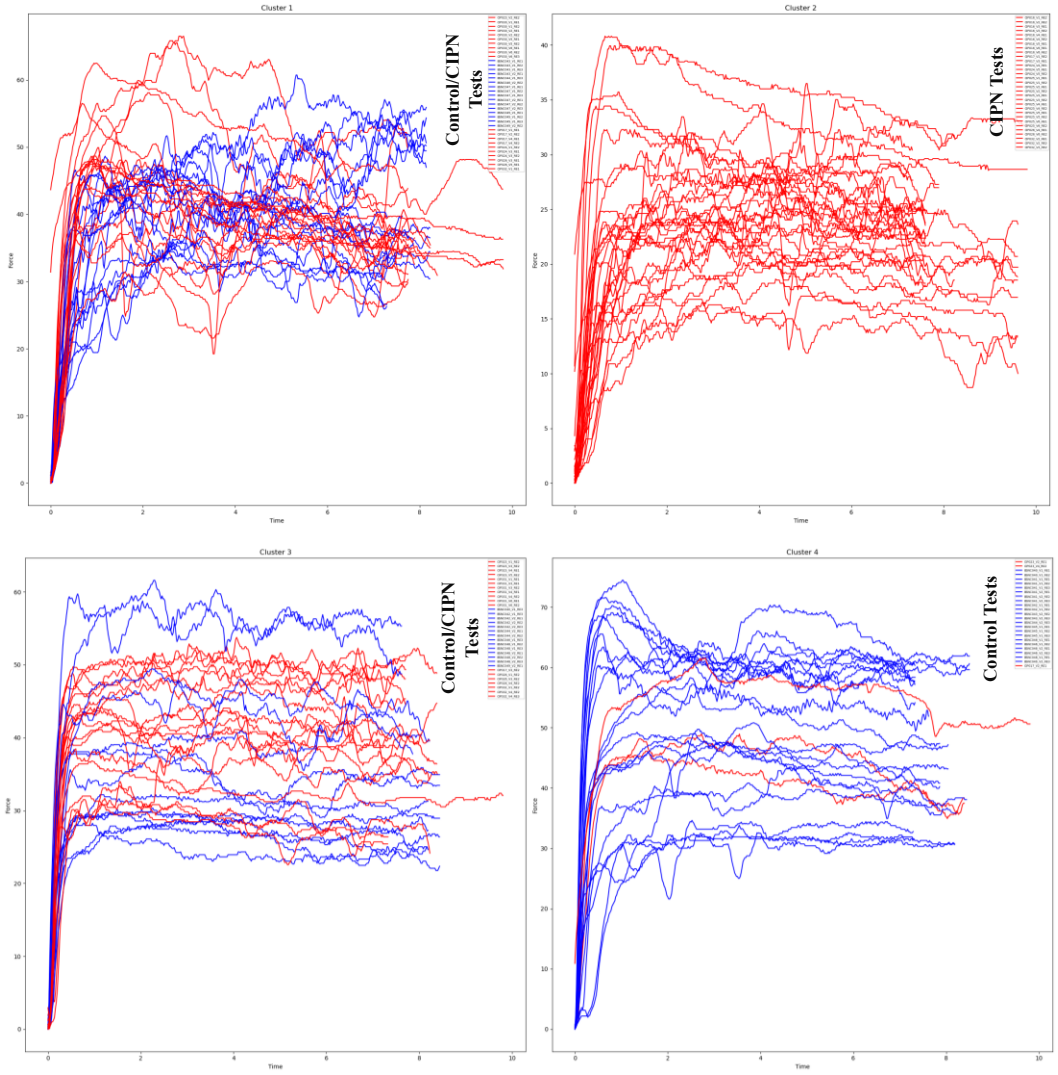

Figure 4.11. Four clusters containing two clusters with majority class and two mixed clusters

To further investigate the underlying patterns within each cluster, we applied SVD to the matrix representing each cluster. This dimensionality reduction technique allowed us to reconstruct the original signals using only a small number of principal components and capture the most critical

information exhibited in each cluster set while filtering out the rest. Through this process, we refined the tests into four distinct groups: healthy controls, CIPN patients, and the two transitional groups.

By closely analyzing the reconstructed signals, we could detect clear differences in muscle function patterns between healthy individuals, cancer patients undergoing chemotherapy, and the two transitional groups. The use of SVD helped isolate the key patterns in each group, simplifying the differentiation between normal and abnormal muscle behavior. This analysis is essential for identifying early signs of CIPN and capturing gradual changes in muscle function that conventional methods might overlook.

By breaking down the complex features set into a few key patterns, SVD allowed us to better interpret the differences between clusters and understand the muscle function characteristics specific to each group. These insights highlight how changes in muscle behavior can lead to the formation of distinct clusters.

To provide a more detailed examination of each group and highlight the key differences that define them, we broke down the specific muscle function characteristics observed in each cluster:

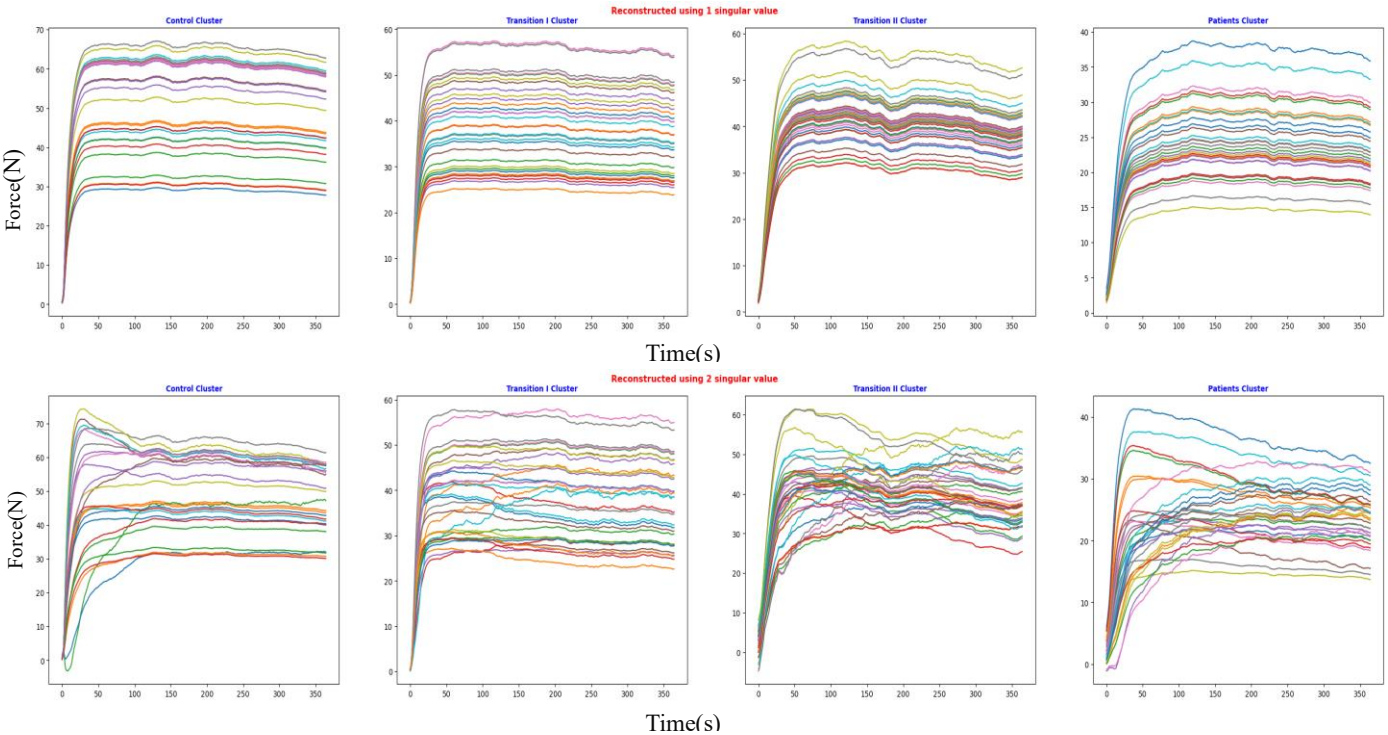

Figure 4.12. The four-group reconstructed with different number of principle components.

1. Control Group: Early Peak in Force, Steady High Value, Minimal Fluctuations

In the control group, we saw strong and stable muscle function patterns. The toe strength peaked early and stayed high with very little fluctuation. This consistency indicated healthy muscle function, typical of people without neuropathy.

2. Transition Group I: Early Peak, Steady Strength, Minimal Decay Trend

This group showed an early peak in strength pattern like the control group but exhibiting slightly more fluctuations. The strength remained steady with minimal decline, suggesting early signs of muscle function changes, possibly due to early-stage neuropathy or mild impairments.

3. Transition Group II: Delayed Peak, More Fluctuations, Stronger Decay Trend

In this group, the peak strength pattern was delayed, and there were more fluctuations and a noticeable decline over time. This indicates more advanced muscle function impairment, with slower muscle activation and increasing fatigue, which could mean progressing neuropathy.

4. Patients Group: Weaker Overall Strength, Slower Rise, and More Fluctuations, indicating the impact of chemotherapy and neuropathy.

The patients undergoing chemotherapy had weaker overall strength pattern, slower rise to peak strength levels, and more fluctuations in their toe strength. These variations show the significant impact of chemotherapy-induced neuropathy on muscle function, affecting their strength and strength steadiness over time.

Our approach to analyzing toe strength patterns provides valuable insights into how muscle function changes in cancer patients undergoing chemotherapy by capturing patterns of change beyond maximum force. Utilizing the QuHalEx device along with our analysis methods, we gain a deeper understanding of muscle function. This significant advancement in assessing neuromuscular health not only enhances the accuracy of our diagnoses but also aids in developing more targeted treatments, ultimately improving the quality of life for our patients.

5 Conclusion and Future Work

5.1 Conclusion

This thesis has introduced a novel integrated hardware-software system to advance the detection and analysis of motor and sensory neuropathy, focusing on cancer patients undergoing chemotherapy and presenting innovations across three areas: the development of the QuHalEx 2.0 device for precise motor function assessment, the implementation of advanced data analysis techniques for deeper insights into toe muscle activation patterns, and the integration of a vibration-based sensory testing device for early sensory neuropathy detection. Significant enhancements in the QuHalEx 2.0 system were introduced, including improved sensors, faster data processing, wireless communication, and mobile applications, which have made it more accessible and reliable for both clinical and independent use. This enhanced device demonstrates high sensitivity to subtle variations in hallux motor function and movement patterns, allowing for precise evaluation of hallux strength. Its robust and user-friendly design facilitates broader adoption across clinical settings, rehabilitation programs, and potentially even home care scenarios, minimizing the need for specialist supervision.

Moreover, the application of hierarchical clustering and Singular Value Decomposition (SVD) in analyzing motor function has provided novel insights into chemotherapy-induced muscle behavior impacts. By clustering and reconstructing different muscle activation patterns, this thesis has provided valuable tools for identifying distinct neuromuscular profiles between patients, healthy individuals, and transitional groups. These findings support early diagnosis of chemotherapy-induced peripheral neuropathy (CIPN), equipping clinicians with data-driven methods for timely interventions with an ultimate goal of improving patient quality of life.

The inclusion of a vibration-based sensory testing device expands the system's functionality, providing a comprehensive neuromuscular assessment within a single platform and enhancing diagnostic accuracy with a dual-modality approach. This holistic view of motor and sensory function strengthens the system’s applicability and accessibility, contributing to an improved understanding of neuromuscular health.

Overall, this thesis significantly advances neuropathy assessment, merging state-of-the-art hardware with data analytics for immediate clinical application and potential adaptation to athletic performance tracking and fall risk assessment in elderly populations. This work not only enriches current understanding of neuropathy effects on motor function but also provides a pathway for future innovations in personalized healthcare solutions.

5.2 Future Work

This thesis opens up several promising avenues for future research and development. Below are key areas where further work could be pursued:

- Cloud-Based Data Storage and Analysis

  An important enhancement to the system could involve the integration of cloud-based services for real-time data storage and analysis. This addition would allow clinicians and researchers to remotely monitor patient progress, access historical data, and track the progression of strength over time. Centralizing the data would also facilitate large-scale studies and comparisons across different patient populations, enabling more comprehensive, data-driven insights.

- Incorporation of Additional Parameters

  Adding other relevant metrics, such as hand grip strength, gait parameters, knee extension, and general health data, to the centralized cloud repository would further enhance the holistic view of patient health. This broader range of metrics would enable more personalized assessments and support longitudinal analysis, providing insights into health trends over extended periods.

- Automated Pattern Recognition and Diagnosis

  Implementing advanced machine learning algorithms, including deep learning, to analyze muscle activation, sensory data, and other patient information could automate the early diagnosis of neuropathy. These models could be trained to detect patterns and

anomalies indicating the initial stages of neuropathy, potentially offering clinicians automatic warnings or recommendations for intervention.

- Building a model for heel-toe relation

Developing a model to quantify compensation patterns between the heel and toe during tests. This model would enable real-time detection of compensatory behaviors and provide automatic alerts to clinicians when such patterns are identified. Additionally, the model could potentially be used to reverse compensatory behaviors in the data when they occur, enhancing analysis and prediction.

- Applications in Athletic Performance and Injury Prevention

The system's adaptability allows applications beyond clinical settings. For example, QuHalEx 2.0 could be used for athletic performance monitoring, where precise muscle function measurements are crucial. In this context, the system could assist athletes in optimizing training routines, tracking rehabilitation progress, and potentially preventing injuries by detecting early declines in muscle performance.

- Gamification for Patient Engagement

To increase patient engagement in rehabilitation, gamification techniques could be integrated into the mobile apps. For instance, transforming rehabilitation exercises into interactive games where patients earn points or advance through levels based on their performance could enhance the experience, making it more enjoyable and motivating consistent use. This approach is especially beneficial in long-term rehabilitation programs, where maintaining adherence can be challenging.

- Further Hardware improvement and Integration of Sensory Simulation Electronics

Adding a battery unit to the device would increase its portability and ease of use. Another area for improvement is enhancing the integration of the vibration-based sensory testing device into the core QuHalEx 2.0 electronics and apps. Embedding the vibration control unit directly into the main hardware would simplify the design and production process and enable vibration control via the mobile apps, enhancing the system's portability and usability.

- Vibration Therapy Research and Neuromuscular Stimulation

An interesting area for future exploration is the therapeutic potential of vibration therapy and neuromuscular stimulation using QuHalEx 2.0 in rehabilitation settings. Research could investigate how controlled vibration therapy might aid in muscle recovery, reduce pain, or improve nerve response.

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