Relative Contributions of Neuromuscular Factors to Muscle Strength Decline with Age

A thesis submitted in fulfilment of the requirements for the degree of Doctor of Philosophy in Electrical & Electronics Engineering

Ariba Moti Siddiqi
Bachelor of Mechatronics Engineering

School of Electrical and Computer Engineering
College of Science Engineering and Health
RMIT University

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Declaration

I certify that except where due acknowledgement has been made, the work is that of the author alone; the work has not been submitted previously, in whole or in part, to qualify for any other academic award; the content of the thesis is the result of work which has been carried out since the official commencement date of the approved research program; any editorial work, paid or unpaid, carried out by a third party is acknowledged; and, ethics procedures and guidelines have been followed.

Ariba Moti Siddiqi

18th August 2016
DEDICATION

For Mum & Dad.
Thank you for making me capable of achieving such a monumental feat.
This is for you.

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Other Publications by the Candidate

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ABSTRACT

Aging is associated with numerous changes in the human body. One of the most prominent alterations is in the decline of neuromuscular function leading to loss of muscle strength. Muscular weakness in the lower limb muscles is a risk factor for falls in the elderly, with the Tibialis Anterior (TA) playing a pivotal role. This loss in strength has been identified as being due to several age-associated neuromuscular alterations. These alterations can be unique for each muscle, depending on their functional role and composition. Nonetheless, the individual contributions of the specific altered neuromuscular properties to muscle strength decline remain unclear. A need to delineate these influences has been identified in order to provide a more targeted strength preservation strategy for the elderly.

This thesis has investigated the relative influence of neuromuscular properties on age-associated muscle strength decline in the Tibialis Anterior using a new improved computational surface electromyogram (sEMG) and muscle force model. It has further used this model to estimate the neuromuscular properties and expected strength loss in the older cohorts from the age-associated sEMG changes. It has also investigated the inhomogeneous aging of the Triceps Surae (TS) in comparison to the Tibialis Anterior using sEMG.

A new improved computational model for generation of sEMG and force was implemented specifically for the pennate Tibialis Anterior. It featured a statistical distribution of parameters, different motor unit types, and a motor unit twitch model for the force. This model was validated using the experimentally recorded sEMG. A series of experiments were performed with healthy young cohorts (age range: 20-30 years) and older cohorts (age range: 60-85 years). They performed isometric dorsi- and plantarflexion of the ankle at six fractions of their maximal voluntary contraction (MVC), and their exerted force and sEMG from the TA and TS muscles was recorded. The power spectrum (PSD) and bispectrum of the sEMG was computed for each participant. From the power spectrum, the maximal power and median frequency were computed, and from the bispectrum, the gaussianity test statistic was computed. Statistical analysis was performed to detect significant age-related differences in the sEMG features for the Tibialis Anterior, and to determine inhomogeneous aging of the TA and TS muscles.

After validation, the model was simulated with widely reported values of neuromuscular properties and their age-associated alterations and the simulated force recorded. It performed repetitive simulations to emulate the biological variability. A linear regression analysis was
performed between the neuromuscular properties simulated and the force they generated, and the slope coefficients were standardised.

Eighteen different simulations were also performed with varying age-associated parameters reported in literature that modelled the increasing exacerbation of the neuromuscular system. The difference in the maximal power of the PSD and the Gaussianity from the values simulated using the young cohorts physiological parameters was calculated for each of the eighteen simulated aging conditions. Pearson’s correlation coefficient was computed between the eighteen simulated aging differences and the experimental age-associated difference to select the aging condition that best described the neuromuscular properties of the older cohorts of this study. Once established, the simulation model was updated with these parameters and the alteration in simulated force determined.

This study has found significant age-associated changes in the maximal power of the sEMG’s PSD, and Gaussianity where older cohorts had higher maximal power and increased non-Gaussianity of their sEMG. These changes were attributable to the age-associated physiological motor unit remodelling reported in literature.

This study has also found the TA to have significantly higher age-associated increase in the maximal power of the PSD in comparison to TS. Within the Triceps Surae complex, the Soleus and Lateral Gastrocnemius were not significantly affected in comparison to Medial Gastrocnemius. These differential changes were considered to be due to different fibre composition, and rates of age-associated neuromuscular changes. However, no age-associated decline in muscle strength was observed for these muscles.

The new improved computational model of the sEMG and force was successfully validated, and was able to reproduce the variability in the signal features observed experimentally. The model was developed to include neural and muscular factors, as well as an ankle joint moment model for comparison with the experimental values. The simulation studies performed with this model found that once the effects of neuromuscular properties on muscle force were standardised, neural drive as assessed by firing rate emerged as the most influential property, followed by muscular factors. The sEMG model was also able to estimate the aging condition that best described the older cohorts of this study. The older cohorts’ TA were characterised to have undergone moderate motor unit remodelling which corresponded to a 40% loss of motor units with half the number of fast fibres. Simulation also demonstrated that loss in fast fibres contributed to the greatest decline in strength in
comparison to loss of motor units, however, the combined effect was compensatory that acted to preserve muscular force.

This study highlights that neural drive is the most influential property regulating muscle strength. It also establishes that moderate motor unit remodelling in the TA may not be accompanied with strength loss. This was also found in the TS muscles, which was differently altered to the TA. This information can be used to provide more targeted strength preservation strategies for the prevention of falls in the elderly. These findings were achieved through a novel sEMG and force model developed which was vital to this study.
Chapter 1

1 Introduction

1.1 Introduction

Australia is facing an ageing population, which is expected to grow at 3.5% per year to 4.0 million in year 2022 (Australian Bureau of Statistics 2009). This ageing population will have several significant economic and social impacts (Australian Government 2015). One social impact will be an increased demand for health care services due to increased longevity (Productivity Commission 2008). A higher incidence of falls amongst the elderly is one factor contributing to increased Australian health care system costs (Moller 2003; Shumway-Cook, Ciol et al. 2009).

A risk factor for falls in the older people is an age-related strength decline in the lower limb muscles (Wu, Callisaya et al. 2016), with the Tibialis Anterior playing a pivotal role (Daubney and Culham 1999; Moreland, Richardson et al. 2004; Robinson, Gordon et al. 2004). Several neuromuscular alterations that occur with age have been identified, contributing to strength decline (Clark and Manini 2008; Kaya, Nakazawa et al. 2013). However, their individual contributions to muscle strength regulation remain unclear (Clark and Manini 2008; Clark and Manini 2010; Clark, Law et al. 2015).

A need to delineate the relative contributions of neural and muscular factors to age-associated strength decline has been identified in order to provide a more targeted strength preservation strategy for the elderly (Clark and Manini 2008).

A comprehensive review has been performed to glean the relative contributions of neuromuscular factors to strength regulation (Clark and Fielding 2012). Several experimental studies have also been reported to address this issue (Mau-Moeller, Behrens et al. 2013; Reid, Pasha et al. 2014; Zampieri, Pietrangelo et al. 2015). These studies have been insightful, but they have employed invasive procedures which are not desirable for the frailer, elderly people.
Findings from experimental studies are also constrained to the muscle and the age group studied. This is because muscles can age at different rates depending on their functional role and composition (Simoneau, Martin et al. 2005; Clark and Taylor 2011; Gennaro, Davide et al. 2015). Hence, there is a need for a non-invasive method of addressing this issue for an elderly population that is capable of measuring inhomogeneous aging of different muscles.

1.2 Problem Statement

A suitable non-invasive technique for addressing the gap in knowledge identified is the surface electromyogram (sEMG), which is an easy to record electrical signal that is emanated by the active muscle. This signal contains useful information regarding the neuromuscular system, but is affected by several factors (Farina, Cescon et al. 2002; Farina, Merletti et al. 2004) which limits its clinical value (Hogrel 2005).

Computational models of the sEMG have been developed to better understand the relationship between sEMG signal characteristics, neuromuscular properties and confounding factors (Nandedkar and Stalberg 1983; Fuglevand, Winter et al. 1993; Dimitrov and Dimitrova 1998; Disselhorst-Klug, Silny et al. 1998; Merletti, Lo Conte et al. 1999; Stegeman, Blok et al. 2000; Mesin 2006; Cao, Boudaoud et al. 2015). A computational model of the sEMG will be advantageous to answer the research question for three key reasons:

- Quantifying the influence of each altered neuromuscular property in vivo is difficult especially when these changes exist concurrently in the aging cohort.

- A simulation model offers a practical method of isolating the effect of each neuromuscular property on muscle strength.

- A simulation model will be able to investigate age-associated sEMG changes arising from alterations in the senescent muscle.

For a computational model to address this research question, it needs to include neuromuscular parameters that are affected with aging. However, existing models (Dimitrova, Dimitrov et al. 1999; Merletti, Roy et al. 1999; Farina and Merletti 2001) have been optimised for other purposes limiting them for studying age-related changes to the
neuromuscular system. A suitable sEMG model was developed by Wheeler, Kumar et al. (2011) for investigating aging effects in the biceps brachial which could be adapted.

This thesis reports on the relative influence of neuromuscular factors on muscle strength decline in the Tibialis Anterior using a computational sEMG and muscle force model. The thesis details the development and improvement of an existing computational model of the sEMG (Wheeler, Kumar et al. 2011) for the Tibialis Anterior, for the purpose of addressing the research question identified. A series of experiments have been performed to identify age-associated sEMG changes in the Tibialis Anterior and validate the model which was used to relate the sEMG changes to neuromuscular alterations. An additional experiment was performed to identify age-associated sEMG changes in the Triceps Surae for testing its disparity to the Tibialis Anterior’s age-associated sEMG changes.

### 1.3 Research Questions

This thesis aims to answer the following research questions with a combination of experimental and simulation methods, identified through literature review:

Q1: What are the relative influences of the neural and muscular factors on muscle strength decline with aging in the Tibialis Anterior? (Simulation)

Q1a: Are there age-related surface electromyogram changes corresponding to neuromuscular alterations? (Experimental)

Q1b: Can the age-related surface electromyogram changes be quantified into neuromuscular changes in the older participants? (Simulation)

Q2: Are there inhomogeneous age-associated changes in surface electromyogram of Tibialis Anterior and Triceps Surae due to different neuromuscular composition? (Experimental)
1.4 Outline of the Thesis

This thesis is organised into nine chapters, the first chapter presenting an introduction to the research study. The neuromuscular basis of surface electromyogram and muscular force is described in Chapter 2 which also details the anatomy of the Tibialis Anterior, and Triceps Surae muscles studied. Chapter 3 provides a background to the research problems identified, and presents an overview of literature studies on surface electromyogram and muscle force modelling.

Chapter 4 reports on the hypothesized age-associated changes in the sEMG of the Tibialis Anterior and discusses the neuromuscular alterations that support or oppose the observations made. Experimental data collected for the study in Chapter 4 are used to validate the surface electromyogram and muscle force model developed for the Tibialis Anterior and is detailed in Chapter 5.

Chapter 6 used the force model developed and reports on the relative effects of neuromuscular properties on the muscle force, answering research question 1 for a broader population.

The models detailed and validated in Chapter 5 are also used to answer research question 1b in Chapter 7. This chapter describes the simulation method used to estimate the neuromuscular properties of the older participants in this study from their age-associates sEMG changes found in Chapter 4.

Chapter 8 reports on the inhomogeneous aging of the Tibialis Anterior and Triceps Surae muscles’ sEMG. It discusses the different age-altered alterations that occur in the ankle muscles, which could explain the heterogeneous age-related sEMG changes.

Chapter 9 concludes this thesis, and details the main contributions of this research arising from answering the research questions detailed in Chapter 1, Section 1.3.
Chapter 2

2 Neuromuscular System in the Generation of Surface Electromyogram

2.1 Introduction

This Chapter provides an overview of the neuromuscular system which gives rise to the surface electromyogram. It details the electrical potential generation that is detected by the surface recording electrodes, and describes the physiological process in the generation of muscle force. Anatomy of the ankle muscles, which is the focus of this thesis, is also described.

2.2 Neuromuscular System

This thesis has selected surface electromyogram (sEMG) as the biological signal to non-invasively investigate neuromuscular changes that occur with age. It has used a variety of signal processing methods to extract the neuromuscular changes, and has developed a simulation model of the sEMG and force produced by the Tibialis Anterior. Therefore, to understand the basis of the sEMG this section describes the neuromuscular elements involved in its generation.

2.2.1 Anatomy of the Nervous System

The nervous system is involved in the control of the voluntary and involuntary actions of the human body, and is divided into two main parts: central nervous system (CNS), and the peripheral nervous system (PNS). The CNS is comprised of the brain and the spinal cord, and the PNS is mainly composed of the nerves, and is responsible for transmission of signals to and from the CNS, and the rest of the body (Gray, Warwick et al. 1973).
The nerves that comprise the PNS are of two types: sensory (afferent nerves) that provide communication from the body about physical sensation to the CNS; and motor (efferent nerves) that form the communication link from the CNS to the body which is used to control muscles and glands. A schematic of the transmission between CNS and the rest of the body using the PNS is shown in Figure 2.1

**Figure 2.1** The components of the central nervous system (CNS), and the peripheral nervous system (PNS). The PNS uses sensory nerves to transmit information back to the CNS from the human body, and motor nerves to transmit signals from the CNS to the human body.

### 2.2.1.1 Nervous systems communication method: action potentials

The nerves transmit signals in the form of electrochemical signals called action potentials, where the electrical potential of the neuron cell membrane rapidly rises and falls, and consequently traverses the length of the neuron. Action potentials are generated through voltage gated ion channels within the cells membrane which open and close depending on the potential of the cell membrane (Purves D, Augustine GJ et al. 2001) (Figure 2.2).

In the absence of a transmission, a neuron is at rest and its resting cell membrane potential is typically at -70 mV (Bullock, Orkand et al. 1977; Junge 1981). This resting potential is...
achieved through a sodium-potassium pump that actively moves sodium ions outside the cell membrane, while moving potassium ions inside. At rest, there is a high extra-cellular concentration of sodium and chloride ions and intra-cellular concentration of potassium ions, giving a net negative potential.

![Figure 2.2](image-url) A schematic of the generation of the neural electrochemical signal, the action potential.

An action potential is instigated when an electrical stimulus arrives at the resting neuron’s dendrites, attempting to raise the cell membrane potential. Rising of the cell membrane potential opens the voltage-gated sodium ion channels, allowing sodium ions to enter the cell. If the stimulus is strong enough to raise the membrane potential to its threshold, the inward sodium ion current increases more rapidly. The neuron’s cell membrane potential rapidly rises until all the sodium channels are open. This phase is known as depolarisation of the cell membrane, as its potential is completely reversed from its resting value (Junge 1981).

At the peak of the action potential, the sodium channels start closing while the potassium ions start opening allowing an outward rush of the potassium current. This decreases the potential of the cell membrane, and this phase is known as repolarisation of the cell membrane. The potassium ions are slow to close as the cell membrane decreases which leads to the potential to drop below the resting potential. This phase is known as the cell membrane being hyperpolarised (Bullock, Orkand et al. 1977).
The sodium-potassium pumps bring the neuron cell membrane back to its resting potential at the end of the action potential.

The transmission of signals in neurons follow an ‘all or nothing’ principle, i.e. an action potential is instigated only if the electrical stimulus is at or above the cells’ threshold.

### 2.2.2 Anatomy of the Muscular System

The muscular system is comprised of three kinds of muscles: skeletal, smooth and cardiac. Skeletal muscles perform voluntary contractions, while smooth and cardiac muscles are directly controlled by the nervous system, and are involuntary.

The skeletal muscle is a form of striated muscle tissue, and is comprised of numerous bundles of long, cylindrical muscle cells called muscle fibres (Gray, Warwick et al. 1973) (Figure 2.3). Each bundle of muscle fibres is known as a fascicle. A muscle fibre is constructed from multiple nuclei, and myofibrils which are surrounded by the sarcoplasm (a gel-like substance much like the cytoplasm of other cells), and is enclosed in an electrically excitable cell membrane called the sarcolemma, that plays an important role in muscle contraction.

Myofibrils are the basic unit of the muscle fibre, and are mainly composed of three long, cylindrical proteins: actin, myosin and titin, which are responsible for muscle force generation. These proteins are organised into thick (actin) and thin (myosin and titin) filaments, collectively called the myofilaments. The myofilament structures repeat along the length of the myofibril, and each such unit is known as a sarcomere. Sarcomeres are the basic contractile unit of a muscle, and it is the contraction of millions of these units that give rise to a skeletal muscle contraction.
2.2.2.1 Skeletal Muscle Fibre types

There are three types of muscle fibres: Type I or slow type fibres; Type IIa or fast oxidative fibres, Type IIb or fast glycolytic fibres (Merletti and Parker 2004).

Type IIb fibres are capable of generating large amounts of force with rapid contraction. Their large fibre diameter densely packing numerous myofibrils enables them to generate more force. However, these fibres use anaerobic glycolysis for the production of adenosine triphosphate (ATP) which is utilised during a contraction. This makes them highly susceptible to fatigue. The resultant action potential generated by these muscles is shorter in duration due to the fast conduction velocity of these fibres (Eccles, Eccles et al. 1958; Kupa, Roy et al. 1995). Muscles requiring fast movements are composed of these fibres, such as the eye muscle orbicularis oculi.

Type I fibres are smaller in size, and produce smaller amounts of force in comparison to Type IIb with longer contraction time. However, these fibres are resistant to fatigue due to their aerobic cellular respiration mechanism of ATP production. They are generally well supplied by capillaries which assist in their resistance to fatigue. Anti-gravity muscles such as the Soleus generally are composed of Type I fibres.

Figure 2.3 A top-down view of the skeletal muscle fibre (Gray, Warwick et al. 1973).
Type IIa fibres fall between the Type I and Type IIb range, and this is reflected in their properties. Their mechanism for ATP production is both aerobic and anaerobic.

### 2.2.2.2 Muscle Architecture

The muscle fibres of a skeletal muscle can be arranged in a particular orientation which is based on the mechanical function it performs. The main two types of muscle architectures are parallel and pennate (Gray, Warwick et al. 1973). The architecture of a muscle is distinguishable by the orientation of the muscle fibres relative to the line of the force.

Parallel muscles have their fibres aligned in the direction of the line of the force (Figure 2.4). Parallel muscle architecture can be further subdivided to strap, fusiform, and fan shaped.

Pennate muscles have their fibres aligned at an angle to the force generating axis. This angle is known as the pennation angle of the muscle. These muscles generally have shorter fibre lengths resulting in fewer sarcomeres in series. However, their ability to pack sarcomeres more densely in parallel gives them high force generating capacity (Narici 1999). Pennate muscles can be uni-, bi- or multi-pennate (Figure 2.4).

![Figure 2.4](image.png)

**Figure 2.4** Muscle architecture types. Parallel muscles have their fibres aligned in the same direction as the line of force, while pennate muscles have oriented at an angle relative to the line of force.
2.2.3 The Neuromuscular Junction

The neuromuscular junction is the chemical synapse between the motor neuron’s axon terminals and the motor endplates (portion of the sarcolemma closest to the motor neurons axon terminal) of the muscle fibres. It facilitates the voluntary contraction of the muscle instigated by the nervous system.

When the action potential arrives at the motor neuron’s axon terminal, it instigates the release of a neurotransmitter chemical called acetylcholine into the synapse, which is the neuromuscular junction. Acetylcholine binds with its receptors located at the motor endplate, causing sodium ion channels to open which initiates an action potential on the muscle fibres cell membrane to be generated, as described in Section 2.2.1.

The group of muscle fibres that is innervated by one motor neuron is collectively called a motor unit. Therefore, once an action potential arrives at a neuromuscular junction, it will initiate a muscle action potential in each of the fibres comprising the motor unit (Figure 2.5).

**Figure 2.5** A motor unit comprised of a motor neuron and the group of muscle fibres it innervates. An intra-cellular action potential travels away from the neuromuscular junction to both ends of the muscle fibres once the motor neuron is excited.
2.2.4 Mechanism of muscle contraction

The mechanical contraction of the individual sarcomeres occurs through the process called excitation-contraction coupling. The depolarisation of the motor endplate as a consequence of the action potential also causes the sarcoplasmic reticulum (a specialised endoplasmic reticulum) to release calcium ions into the sarcoplasm, which is the cytoplasm of the muscle fibre.

The sarcomere is contracted through a cross-bridge cycling process. The calcium ions released due to the action potential binds to a protein called troponin present in the thin filaments of the myofibril. This process exposes the myosin-binding sites on the actin protein. The myosin attaches to these sites, hydrolyses the adenosine triphosphate (ATP), and swivels the myosin heads which are firmly attached to the actin protein. This causes the thin and thick filaments to slide past each other, shortening the sarcomere and causing a contraction (Figure 2.6). This process repeats as long as sufficient calcium ions and ATP are present. Once depleted, another arrival of the action potential will instigate a muscle contraction.

![Figure 2.6](image_url) The shortening of a sarcomere (basic unit of a muscle fibre) due to the interaction of actin and myosin filaments.
2.2.4.1 Muscle Contraction types

There are three types of muscular contractions – isotonic, isometric, isokinetic - depending on whether the fibre length, contraction speed or tension is changing. In an isometric contraction, the muscle generates force without a change in its length. This is typically achieved by fixing the limb and performing the work. Isotonic contractions involve constant tension while the muscle lengthens. Isokinetic contractions maintain a constant speed, while the force generated varies with the resistance applied.

In this thesis, isometric contractions have been used. This contraction type has been predominantly used in the surface electromyogram (sEMG) studies to investigate neuromuscular functions. The advantages it offers over the other contraction types are:

- Reduced movement artefact while recording the sEMG.
- Control of experiments is superior, with less likelihood of injury to participants.
- Availability of wide reported studies investigating muscles with this contraction type.

2.2.5 Force modulation of a muscle

The nervous system exerts control over the skeletal muscles through the action potential as described earlier. The nervous system can vary the force produced by the muscles through two modulation schemes: recruitment and firing rate (Milner-Brown, Stein et al. 1973; Kukulka and Clamann 1981; Moritani and Muro 1987).

Firing rate is the rate at which action potentials arrive at the neuromuscular junction of a motor unit. One action potential initiates one motor unit contraction through the excitation-contraction coupling. In absence of further action potentials, the motor unit relaxes. Therefore, at sufficiently high rates of action potential arrival more motor unit twitches (contractions) occur and the motor unit reaches tetanic contraction.

Recruitment threshold of a motor unit is related to its motor neuron’s properties, and is the force level at which the motor neuron is activated. Larger motor neurons are known to have higher thresholds, and are therefore recruited at higher force levels (Henneman, Somjen et al. 1965; Henneman 1979). The recruitment of additional motor units with increasing force demand would appropriately increase the force generated by the muscle.
Different muscles use these two strategies with different preferences, dependent on the function it performs. Muscles that require finer control generally rely on firing rate modulation as the method to control the force generation, such as the muscles in the hand (Woods and Bigland-Ritchie 1983). Muscles that do not require precise control of the force are reliant on recruitment order, such as the Tibialis Anterior that recruit motor units up to 90% of its maximal voluntary contraction (Klass, Baudry et al. 2008).

The relationship between recruitment and de-recruitment of motor units has been studied by De Luca and Hostage (2010). In young subjects the gap between recruitment and de-recruitment thresholds became larger for motor units recruited at higher thresholds (De Luca and Hostage 2010). Motor units would de-recruit at higher recruitment thresholds in comparison to when they are recruited, implying that fewer motor units produce the same level of force at de-recruitment than at recruitment. De Luca and Hostage (2010) attributed this effect to motor unit potentiation.

A study found the de-recruitment threshold of a motor unit decreases with age such that a motor unit will continue to fire below its recruitment threshold (Kamen and De Luca 1989). In contradiction, a more recent study did not find altered de-recruitment behaviour of motor units with age (Jesunathadas, Marmon et al. 2010). Fatigue, motor unit remodelling, coactivation, and methodological differences could account for the differences in de-recruitment and recruitment behaviour of motor units with age (Kamen and De Luca 1989).

### 2.2.6 Anatomy of the Ankle Muscles

In this thesis, the Tibialis Anterior, and the Triceps Surae muscles are studied (Figure 2.7). These ankle muscles play an important role in locomotion and balance, and their weakness is associated with risk of falls (Perry, Carville et al. 2007).

#### 2.2.6.1 Tibialis Anterior

The Tibialis Anterior is a major dorsiflexor and inverter of the ankle. It is innervated by the deep peroneal nerve which branches from the common peroneal nerve. The Common Peroneal nerve originates from the fourth and fifth lumbar nerves, and the first sacral nerve (Gray, Warwick et al. 1973).
2.2.6.2 Triceps Surae Muscles

The Triceps Surae is a major plantarflexor of the ankle, and is comprised of three muscles: the Soleus, Medial Gastrocnemius and Lateral Gastrocnemius. The gastrocnemii play an additional role of flexing the knee. Amongst the Triceps Surae, the Soleus plays a predominant role in plantarflexion. The Triceps Surae is innervated by the Tibial nerve which is a branch from the Sciatic nerve. The Sciatic nerve arises from the 4th lumbar segment to the 3rd sacral segment (Gray, Warwick et al. 1973).

![Diagram of the Triceps Surae muscles](image)

**Figure 2.7** The Tibialis Anterior performs dorsiflexion of the ankle, and the Triceps Surae, comprised of the Gastcnemii and Soleus, performs plantarflexion of the ankle.

2.2.7 Anatomy of the Ankle Joint

The ankle joint is the region where the leg and foot connect. It is comprised of three joints: the talocrural joint which is the main ankle joint, the subtalar joint, and the inferior tibiofibular joint (Figure 2.7) (Gray, Warwick et al. 1973). The Tibialis Anterior inserts into base of the first cuneiform, and the first metatarsal. The Triceps Surae inserts into the calcaneum via the Achilles tendon. The movements performed about this joint are dorsiflexion and plantarflexion of the foot.
Direct muscular forces are not practically measurable. Experimental studies use the externally recorded joint torque produced during a maximal voluntary contraction as representative of muscle strength. However, antagonistic muscles that oppose the action of the prime mover can significantly contribute to the resultant joint torque measured (Simoneau, Billot et al. 2009). Therefore, their contribution to the external joint torque needs to be considered.

Studies have factored in the antagonist muscles’ contribution to external torques (Simoneau, Billot et al. 2009) and estimated muscle force produced by representing the muscles and the joints they exert force about as simple lever systems (Maganaris, Baltzopoulos et al. 2001; Maganaris 2004).

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**Figure 2.8** The three ankle joints. Talocrucal or ankle joint proper is formed between Tibia and Talus; subtalar joint is formed between the talus and calcaneus, and inferior tibiofibular joint is formed between the tibia and fibula. The Triceps Surae inserts into the Calcaneus through the Achilles tendon, and Tibialis Anterior’s inserts into the first cuneiform and first metatarsal.
2.3 **Surface Electromyogram**

The surface electromyogram measures the electromagnetic fields generated by the underlying activated muscle fibre. When an action potential occurs within the muscle fibre, an extra-cellular potential is generated in its vicinity due to the transmembrane ionic currents. Depending on the distance between the active muscle fibre and the recording electrode, as well as the surrounding biological tissue, the shape of the extra-cellular potential can undergo significant changes (Farina, Cescon et al. 2002; Mesin, Merletti et al. 2011).

The potential generated by the active fibre can be measured by a needle, or a surface electrode. Measurements by the needle electrode involves insertion into the muscle fibre (needle EMG), or the extracellular matrix of the muscle (intra-muscular EMG). The surface recording electrode measures the extra cellular potentials from all of the active muscle fibres simultaneously (Merletti and Parker 2004). Consequently the signal features fractal properties (Arjunan and Kumar 2007), and interpretation of the sEMG requires in-depth knowledge of its relationship with the neuromuscular properties (Farina, Merletti et al. 2004). SEMG models have been developed for such a purpose.

2.4 **Summary**

This Chapter provided an overview of the neuromuscular system that gives rise to the surface electromyogram. A description of the action potential was given which is the main component of the sEMG. The physiological processes that lead to a muscular contraction are also described.

The following Chapter will address the motivations for this research, and provides a review of the current state-of-the-art of surface electromyogram and muscle force modelling fields.
Chapter 3

3 Literature Review

3.1 Introduction

This Chapter begins by establishing the motivation for understanding the relative influence of neuromuscular properties on muscle strength decline with age. It proceeds to direct the focus of the research question to a specific muscle, and further discovers the need to assess inhomogeneous aging of muscles. The motivation to use a computation model of the surface electromyogram and force model is discussed, and an overall review of current state-of-the-art in these fields is provided.

3.2 Dynapenia – Muscle Strength Decline with Age

‘Sarcopenia’ is a geriatric condition originally termed by Rosenberg (1989) to describe the loss of skeletal muscle mass seen in the aged. Rosenberg (1989) suggested that functional independence such as mobility was linked to loss of muscle mass and strongly encouraged research studies on the mechanism and effects of sarcopenia. This prompted a significant amount of research with this aim (Ferrucci, Guralnik et al. 1997; Baumgartner 1998; Schwartz 1998; Morley, Baumgartner et al. 2001; Janssen, Heymsfield et al. 2002; Lauretani, Russo et al. 2003; Delmonico, Harris et al. 2007). Sarcopenia was established to be linked with physical disability, risk of falls, mortality and other measures of quality of life (Abellan van Kan 2009; Narici and Maffulli 2010).

Successive studies eventually found these debilitating conditions to be more strongly correlated with muscle strength than muscle mass (Evans 1997; Ferrucci, Guralnik et al. 1997; Lauretani, Russo et al. 2003; Visser, Goodpaster et al. 2005; Newman, Kupelian et al. 2006; Abellan van Kan 2009). However, this finding was considered to be due to muscles strengths’ correlation with muscle mass (Frontera, Hughes et al. 1991; Evans 1997).
Hence, sarcopenia as a terminology evolved to encompass loss of muscle strength and a causal relationship between muscle mass and strength was assumed (Morley, Baumgartner et al.; Lauretani, Russo et al. 2003; Timothy 2003; Delmonico, Harris et al. 2007; Clark and Manini 2008; Cruz-Jentoft, Baeyens et al. 2010). This assumption was ultimately found to be unsupported (Hughes, Frontera et al. 2001; Clark and Manini 2008).

Muscle strength declines at a greater rate than muscle mass (Goodpaster, Park et al. 2006). From 50 years of age, muscle mass declines at about 1-2% per year (Hughes, Frontera et al. 2001), whereas muscle strength decreases at 1.5% per year, and accelerates to 3% per year after 60 years of age (Vandervoort 2001; Abellan van Kan 2009). Conversely, the gain of muscle mass was not found to provide immunity against an age related loss of muscle strength (Goodpaster, Park et al. 2006; Delmonico, Harris et al. 2009). Initial strength gains due to resistance training were also not accompanied by a change in the muscle morphology (McDonagh, Hayward et al. 1983; Young, McDonagh et al. 1985). This indicates that there is more to strength regulation than just an alteration of muscle mass.

A new terminology has been proposed to describe loss of muscle strength—‘Dynapenia’ (Clark and Manini 2008). The motivation for a new term was similar to Rosenberg (1989); to focus research on elucidating the mechanism of strength loss rather than loss of muscle mass by drawing a distinction between the two phenomena.

A definition of ‘Muscle strength’ is the maximum voluntary force a muscle can produce and is dependent on several neuromuscular properties. These neuromuscular properties form the pathway of muscle force production. It is initiated by the motor cortex as an electrical stimulus which propagates along the spinal cord to the relevant motoneuron pool. The motoneuron instigates an action potential to travel to the neuromuscular junction, eventually exciting the muscle fibres which produce a contraction through the excitation-contraction coupling process (Figure 3.1).

In this thesis, ‘muscle strength’ has been defined to be the maximal contraction force at 100% maximal voluntary contraction (MVC).
Figure 3.1 Neuromuscular elements involved in the production of muscle force. These include the motor cortex instigating an electrical excitation. The excitation travels along the spinal cord to the relevant motoneuron responsible for controlling a muscle. The motoneuron connects to a group of muscle fibres through the neuromuscular junction. An action potential is elicited at the muscle fibre membrane (sarcolemma) causing a muscular twitch to occur through the excitation-contraction coupling.
Several comprehensive reviews have reported on the neuromuscular factors that are involved in regulating muscular strength and how these are affected in the aging process (Clark and Manini 2008; Clark and Taylor 2011; Clark and Fielding 2012; Manini and Clark 2012). The reviews established that each site of force regulation can be affected by aging (Clark and Manini 2008; Clark and Taylor 2011) (Figure 3.2). Some of these include:

- Excitatory drive to the motor neurons from the motor cortex (Rossini, Desiato et al. 1992; Oliviero, Profice et al. 2006)
- Alpha-motoneuron excitability (Obata, Kawashima et al. 2010)
- Antagonistic muscle activity (Maganaris, Baltzopoulos et al. 1998; Simoneau, Billot et al. 2009)
- Motor unit recruitment and firing rate (Connelly, Rice et al. 1999; McNeil, Doherty et al. 2005; Klass, Baudry et al. 2008)
- Neuromuscular transmission (Wood and Slater 2001; Gordon, Hegedus et al. 2004),
- Muscle mass (Frontera, Hughes et al. 2000),
- Excitation-contraction coupling process (Ryan and Ohlendieck 2004; Fauler, Jurkat-Rott et al. 2012; Lamboley, Wyckelsma et al. 2016) and
- Muscle structure (Simoneau, Longo et al. 2012; Barber, Barrett et al. 2013)

Each of these age-associated neuromuscular changes have been thoroughly investigated; however, their individual contributions to muscle strength regulation remain unclear (Clark and Manini 2008; Clark and Manini 2010; Clark, Law et al. 2015). A need to extract the relative contributions of neural and muscular factors to age-associated strength decline has been identified in order to provide a more targeted strength preservation strategy for the elderly (Clark and Manini 2008). This knowledge is essential as a simple age-related change in a neuromuscular property does not constitute a cause and effect relationship. For a better understanding of the effects of neuromuscular properties on strength regulation, their integrative effects on muscle strength need to be examined (Clark and Manini 2008).
Several experimental studies have been performed to understand the individual contributions of neuromuscular properties to muscle strength, but these have been limited to the quadriceps muscle. One such study investigated the influence of age-related changes in neural drive, spinal excitability, contractile properties and muscle mass of the quadriceps to its strength decline (Mau-Moeller, Behrens et al. 2013). Another study undertook a longitudinal investigation to assess age-associated changes in muscle size, fibre type proportions, neuromuscular activation, and contractile properties of sedentary and active participants (Reid, Pasha et al. 2014). Relative contribution of disuse, and aging to muscle strength decline in the quadriceps have also been investigated (Zampieri, Pietrangelo et al. 2015).

These experimental studies have been insightful; however, the use of invasive procedures such as biopsies and electrical stimulation within these studies is not suited for the frailer, elderly people. The findings of these studies are also constrained to the muscle and the age group studied. This is because neuromuscular properties do not undergo a uniform rate of aging amongst muscles of different function and composition (Simoneau, Martin et al. 2005; Clark and Taylor 2011; Gennaro, Davide et al. 2015). Hence, there is a need for a non-

**Figure 3.2** Alterations of the neuromuscular properties that lead to muscle strength decline.
invasive method of addressing this research question for an elderly population that is capable of measuring inhomogeneous aging of different muscles.

Nonetheless, experimental diagnostic tools are limited in their ability to quantify the influence of each altered neuromuscular property \textit{in vivo}. Measuring the individual effects on the muscle strength would require a reference point, and prior knowledge of interplay amongst the neuromuscular properties moderating each other’s effect. Longitudinal studies may assist with the former requirement; however, these changes can be idiosyncratic. Hence, an objective quantification of the relative impacts of neuromuscular properties on muscle strength decline is difficult with experimental studies. This is particularly challenging for the aging cohort that can have numerous simultaneous alterations in their musculature.

The limitations of experimental studies can be overcome by the use of computational models which offer a practical solution. A primary purpose of mathematical models is evaluating the effects of its input parameters on the response variable. This makes them well-suited for this purpose to heuristically isolate the effect of each neuromuscular property on muscle strength (Webber, Porter et al. 2009).

In this thesis, the candidate has proposed to use the surface electromyogram as the non-invasive tool, and a computational model of this signal to extract the individual contributions of age-altered neuromuscular properties to strength decline. This is discussed in Section 3.4 of this Chapter.

3.3 Heterogeneous Age-Associated Changes in the Muscles

In Section 3.2 it was identified that the majority of experimental studies that addressed the relative influence of neuromuscular properties on strength decline was limited to the quadriceps muscle. A reason for the quadriceps to have been the focus of aging studies (Hurley, Rees et al. 1998; Roos, Rice et al. 1999; Goodpaster, Park et al. 2006; Welsh, Dinenno et al. 2007; Ihira, Shimada et al. 2012; Baroni, Geremia et al. 2013) is because age-related changes are more prominent in the lower proximal limbs than the upper (Macaluso and De Vito 2004; Mitchell, Williams et al. 2012; Nogueira, Libardi et al. 2013). However, it has also been established that age-associated changes in the neuromuscular system are more prominent in the distal rather than proximal muscles (Campbell, McComas et al. 1973;
Literature Review

Taylor 1993; Galea 1996; Kallio 2013). A study supporting this performed a comparison between the age-associated changes in the Tibialis Anterior and Vastus Medialis (a quadriceps muscle) and found comparatively more severe motor unit losses in the Tibialis Anterior (McKinnon, Montero-Odasso et al. 2015). This highlights the need for more studies investigating lower limb, distal muscles.

The ankle muscles are important for locomotion and balance, with weak dorsi-flexors associated with risk of falls (Fukagawa, Wolfson et al. 1995; Kemoun, Thoumie et al. 2002; Moreland, Richardson et al. 2004; Perry, Carville et al. 2007). Within the ankle muscles, there is a discrepancy reported in the strength decline with values ranging from 63% to 14% (Vandervoort and McComas 1986; Winegard, Hicks et al. 1996; Connelly, Rice et al. 1999; Lanza, Towse et al. 2003; Lanza, Russ et al. 2004; McNeil, Doherty et al. 2005) while some authors reported no significant decline (Simoneau, Martin et al. 2005; Power, Dalton et al. 2010; Hasson, Miller et al. 2011). A source of this discrepancy has been the neglect of antagonistic muscles’ (that oppose the motion of the prime mover, the agonist) contribution to the external joint torque recording (Simoneau, Billot et al. 2009).

Direct muscular forces are not practically measurable (Maganaris, Baltzopoulos et al. 2001). Experimental studies use the externally recorded joint torque produced during a maximal voluntary contraction as representative of muscle strength. This external torque measurement is the algebraic sum of the agonist and antagonist torque (Falconer and Winter 1984). For a correct assessment of the agonist strength, the antagonist torque needs to be assessed and added to the external torque measured.

The antagonist torque can be estimated by the antagonist’s muscle’s sEMG activity/ torque relationship constructed by several submaximal contractions when it acts as the agonist (Baratta, Solomonow et al. 1988). A study found a non-significant age-associated decline in the externally measured dorsiflexion torque (-15%), but a significant decline in the agonist torque (-39%) after the inclusion of the antagonist’s torque (Simoneau, Billot et al. 2009). This finding asserts the importance of measuring the antagonist torque for accurate measurements of muscle strength.

Nonetheless, another source of discrepancy is the different aging of the dorsiflexor, Tibialis Anterior, and plantarflexors, Triceps Surae (Simoneau, Martin et al. 2005). A study that examined both the dorsi- and plantar-flexors found the former’s strength to be preserved until
70 years of age, whereas the latter muscle group’s strength suffered earlier (Fukagawa, Wolfson et al. 1995). These differences in the rate of strength decline can be attributed to the different rates of neuromuscular changes observed in the ankle muscles. A 40% loss of motor units occurs in the Tibialis Anterior for cohorts aged 60-69 years, with an additional loss of 33% by the 8th decade (McNeil, Doherty et al. 2005). A 70% loss of motor units has been noted in the Soleus at very advanced age (Vandervoort and McComas 1986), but with no loss till 75 years (Dalton, McNeil et al. 2008). A comparable change in the number of motor units for the gastrocnemius has not been reported. An age-related decrease in muscle mass has also been found in both Triceps Surae (Barber, Barrett et al. 2013; Csapo, Malis et al. 2014) and Tibialis Anterior (Barber, Barrett et al. 2013; Power, Allen et al. 2014), but this effect is greater in the former (Barber, Barrett et al. 2013).

These inhomogeneous changes in the ankle muscles substantiate the need for studies examining both these muscle groups. Earlier studies have investigated age-related changes in the Tibialis Anterior (Connelly, Rice et al. 1999; McNeil, Doherty et al. 2005; Power, Allen et al. 2014; McKinnon, Montero-Odasso et al. 2015) and Triceps Surae musculature (Morse, Thom et al. 2005; Dalton, McNeil et al. 2008; Dalton, Harwood et al. 2009; Barber, Barrett et al. 2013; Csapo, Malis et al. 2014), but studies concurrently examining both ankle plantar-and dorsiflexors are limited. An examination of both the opposing ankle muscles will provide insight to their heterogeneous aging that will be useful for appropriate strength preservation strategies in the elderly (Gennaro, Davide et al. 2015).

In this thesis, the Tibialis Anterior has been selected as the focus of the research question 1, ‘What are the relative influences of the neural and muscular factors on muscle strength decline with aging in the Tibialis Anterior?’ The Triceps Surae muscles have been studied in conjunction with the Tibialis Anterior to investigate their inhomogeneous aging.
3.4 Surface Electromyogram Modelling for Aging

3.4.1 Surface Electromyogram Features

The surface electromyogram (sEMG) is an electrical signal recorded by surface electrodes and is the temporal and spatial superposition of the motor unit action potentials (MUAP). The sEMG provides a gross estimate of the activation state of the muscle under investigation, and therefore has applications in kinesiology, gait analysis, and prostheses control (Parker and Scott 1986; Clarys and Cabri 1993; De Luca 1997; Kleissen, Buurke et al. 1998; Hägg, Luttmann et al. 2000; Sutherland 2001). The characteristics of the sEMG signal can also be used to estimate neuromuscular properties (Disselhorst-Klug, Silny et al. 1998; Farina and Merletti 2004; Zhao and Li 2012), and several sEMG features have been studied to identify age or diseases associated neuromuscular changes (Rissanen, Kankaanpää et al. 2008; Kaplanis, Pattichis et al. 2009; Meigal, Rissanen et al. 2009; Istenič, Kaplanis et al. 2010; Arjunan, Wheeler et al. 2013; Siddiqi, Poosapadi et al. 2015).

The majority of these studies provide conflicting results on sEMG feature changes with age. Two studies did not find significant age-associated changes in the sEMG’s linear and non-linear properties; however, they did not identify their choice of features based on the underlying physiology (Kaplanis, Pattichis et al. 2009; Meigal, Rissanen et al. 2009). Other studies have found significant age-related changes in the sEMG’s complexity (Arjunan, Wheeler et al. 2013; Gennaro, Davide et al. 2016), and the amplitude (Kalra, Kumar et al. 2011), but conflicting results for the median frequency (Kalra, Kumar et al. 2011; Wheeler, Kumar et al. 2011).

Various neuromuscular alterations can affect the sEMG signal properties differently (Disselhorst-Klug, Silny et al. 1998; Meigal, Rissanen et al. 2009), and a single signal feature cannot classify all of the age-associated neuromuscular changes. The lack of consensus on age-associated changes in sEMG features emphasizes the need for a purposeful, well-informed selection of features based on the physiological neuromuscular changes.

A lack of standards about the sEMG recording electrode size, inter-electrode distance, and electrode placement could contribute to the discrepancy in age-associated sEMG changes. These factors can significantly affect the sEMG signal and its properties (Merletti, Lo Conte et al. 1999; Mademli, Arampatzis et al. 2004; Rainoldi, Melchiorri et al. 2004). SENIAM had originally established standards for sEMG recording (SENIAM 2009); however, it has since
been challenged to no longer be the best practice (Rainoldi, Melchiorri et al. 2004; Botter 2015; Lopez and Davies 2016).

Nonetheless, sEMG features can only provide an indication of neuromuscular changes but cannot quantify them. Their association with neuromuscular properties is also confounded by several extrinsic and intrinsic factors (Farina, Cescon et al. 2002; Farina, Merletti et al. 2004; Keenan, Farina et al. 2005; Farina, Merletti et al. 2014). To address this, many researchers have strived to develop sEMG models in order to better understand the neuromuscular system (Gydikov and Kosarov 1974; Nandedkar and Stalberg 1983; Roy, De Luca et al. 1986; Fuglevand, Winter et al. 1993; Dimitrov and Dimitrova 1998; Disselhorst-Klug, Silny et al. 1998; Merletti, Lo Conte et al. 1999; Stegeman, Blok et al. 2000; Mesin 2006; Cao, Boudaoud et al. 2015).

3.4.2 Surface Electromyogram Models

SEMG models can be classified as phenomenological or structural (Stegeman, Merletti et al. 2005). Phenomenological sEMG models represent the sEMG as a band-limited, Gaussian process. These models are often seen in kinesiology applications, where only the state of the muscle is required (McGill 2004). Structural sEMG models mathematically formulate the underlying physiological elements involved in the sEMG’s generation. In this thesis, a structural sEMG model is developed for answering the research questions.

SEMG models are constructed by modelling (i) the biological current source, i.e. the generation, propagation and extinction of the intra-cellular action potential; (ii) the volume conductor which is the biological medium through which the current source propagates; (iii) the recording system used to observe the sEMG.

Lorente de No (1947) pioneered research into the mathematical formulation of the intra- and extracellular potential, which was further advanced by Clark and Plonsey (1968); Plonsey (1974), and Rosenfalck (1969). Since then several authors have increasingly improved the modelling of the action potential (Dimitrova 1974; Gydikov and Kosarov 1974; Dimitrov and Dimitrova 1977; Plonsey 1977; Andreassen and Rosenfalck 1981; Griep, Gielen et al. 1982; Nandedkar 1983; Roth, Gielen et al. 1988; Gootzen 1990; Dimitrova, Dimitrov et al. 1999). Extinction and generation phases of the action potential (Merletti, Lo Conte et al. 1999; Farina and Merletti 2001), the effect of different volume conductors (Farina and Merletti 2001; Blok, Stegeman et al. 2002; Schulte, Farina et al. 2004) and the effect of
detection systems has been considered (Dimitrov and Dimitrova 1998; Farina, Cescon et al. 2002). Recent volume conductor models have simulated pennate muscles (Mesin and Farina 2004; Mesin, Merletti et al. 2011; Mesin 2013), multiple layers (Blok, Stegeman et al. 2002; Mesin 2013; Carriou, Boudaoud et al. 2016), and shortening of muscles (Schulte, Farina et al. 2004).

These models have advanced the understanding of the neuromuscular system; however, they have been optimised for purposes such as investigating muscle fatigue (Merletti, Roy et al. 1999; Callahan, Umberger et al. 2016), estimating conduction velocity (Merletti, Lo Conte et al. 1999), testing signal processing techniques (Mesin, Kandoor et al. 2008) or investigating effects of different muscular architectures (Mesin and Farina 2004).

For a sEMG model to suitably investigate the age-associated neuromuscular alterations that lead to the observed sEMG changes, it needs to meet certain specifications. The model should have parameters relating to the neuromuscular properties that are altered with age. It needs to model the variability of its outputs to be representative of the population of interest. It has multiple measurable outputs that can be validated against experimental values for unbiased validity and accuracy (Eddy, Hollingworth et al. 2012). It is not computationally time intensive, as a realistic number of motor units (200-400 in the Tibialis Anterior (Feinstein, Lindegård et al. 1955; McNeil, Doherty et al. 2005)) and muscle fibres (96,800 – 162,500 (Johnson, Polgar et al. 1973)) will need to be simulated multiple times.

Consequently, the existing models are unsuitable for studying age-associated changes in the sEMG for the following reasons:

- **Statistical distribution:** Single mean values have been applied to the model parameters, with the exception of Farina, Fattorini et al. (2002) and Mesin, Merletti et al. (2011) who described a Gaussian distribution for the conduction velocity.

- **Fibre type:** They do not distinguish between slow and fast motor unit types which are shown to be affected with age (Rowan, Rygiel et al. 2012).

- **Motor unit size:** These models do not consider different sizes and numbers of motor units with the exception of Mesin, Merletti et al. (2011).
With the exception of Fuglevand, Winter et al. (1993), another shortcoming of the earlier models is that they have implemented only a single output: the sEMG (Merletti, Lo Conte et al. 1999; Mesin, Merletti et al. 2011; Cao, Boudaoud et al. 2015). Validation of a model requires multiple data sources for it to suitably represent the population or outcomes it is intending to simulate (Eddy, Hollingworth et al. 2012). The inclusion of a second independent output for comparison with experimental measurements is strongly recommended for improved validity and accuracy of the computational sEMG model (Keenan and Valero-Cuevas 2007).

Recent models that generate force and sEMG have been investigated (Hashemi, Morin et al. 2013; Cao, Boudaoud et al. 2015; Liu, Liu et al. 2015); however, two of these models (Hashemi, Morin et al. 2013; Liu, Liu et al. 2015) have described the force as a function of sEMG and not as an independent parameter. The third study (Cao, Boudaoud et al. 2015) assigned the motor units mean forces which were summed to generate the output. This modelling approach does not reflect the neuromuscular physiology where there is the integration of twitch force generated by individual muscle fibres.

Wheeler, Kumar et al. (2011) developed a sEMG model that incorporated the two types of motor units and used a statistical distribution for the model values to resemble biological variability. This model has been used to approximate the change in number of motor units and the ratio of fast and slow motor units with aging (Arjunan, Kumar et al. 2015). In addition to the sEMG output, Wheeler, Kumar et al. (2011) also included a muscle force output that was based on the motor unit twitch model by Fuglevand, Winter et al. (1993).

The model by Wheeler, Kumar et al. (2011) is well suited to address the research question 1 as it meets the requirements discussed. However, it does not model the pennation of a muscle, or translates the force models output to an external joint torque for an accurate comparison with the experimentally recorded force. It needs to be further modified to represent the pennate Tibialis Anterior, and an ankle joint model included for validating the simulated force with the experimentally recorded force.

The candidate proposes to use this computational model to quantify the age-associated changes in the sEMG to the neuromuscular changes which is not possible solely from the experimental recorded sEMG.
In the next section, the motivation for adopting Fuglevand, Winter et al. (1993) model over other existing muscle force models is discussed.

### 3.5 Muscle Force Modelling for Aging

The muscle force model adopted by Wheeler, Kumar et al. (2011) is based on the motor unit twitch model developed by Fuglevand, Winter et al. (1993), and is also adopted in this thesis. Historically, muscle force models have been variants of Hill-type (Hill 1938), Huxley-type (Huxley 1957) or Fuglevand, Winter et al. (1993) model.

Hill-type model is a lumped parameter model that is based on the input-output functions of the muscle to a stimulation based on experimental results (Hill 1938). In the Hill-type model, the force producing capability is modelled as a contractile element in series with a series elastic element (representing the muscle-tendon’s elasticity) and parallel with a parallel elastics element (representing the muscle’s viscoelasticity) (Figure 3.3).

![Figure 3.3](image)

**Figure 3.3** Hill-type lumped parameter model with the force generating component modelled as the contractile element (CE), which is in series with a series elastic element (SE) (representing the muscle-tendon’s elasticity) and parallel with a parallel elastics element (PE) (representing the muscle’s viscoelasticity)

Huxley-type models are based on the sliding filament theory (Huxley 1957). These models describe muscle force generation at the basic cellular level, modelling the actin-myosin interaction instigated by the excitation-contraction coupling. Although the mechanism of the force produced is modelled rather than treated as a black box like Hill type models, Huxley-based models use partial differential equations to describe the actin-myosin dynamics. This
poses a numerical problem, potentially requiring up to fourteen state variables to be solved (M G Hibberd and Trentham 1986). Huxley-type models are impractical for running multiple simulations as it is computationally intensive (Wexler, Ding et al. 1997). Hence, muscle force models based on Hill-type are more popular than the Huxley-type due to the increased complexity in the latter which is not needed in applications such as gait analysis, and muscle kinematics (Carbone, van der Krogt et al.; Thelen 2003; Hasson, Miller et al. 2011; Hasson and Caldwell 2012; Romero and Alonso 2016). It has also been shown that the two model types produce equivalent mechanical behaviour which is sufficient for applications requiring estimates of muscle forces (Lemaire, Baan et al. 2016).

Hill-type models have been used to investigate age-associated changes in the muscles (Thelen 2003; Hasson, Miller et al. 2011; Hasson and Caldwell 2012). One study investigated the influence of changing muscle mechanics with aging on the isometric and isokinetic strength of the dorsi- and plantar flexors (Thelen 2003). This work was able to simulate the losses in strength and power observed experimentally (Thelen 2003). Similarly, other studies investigated the mechanical properties of the ankle muscles using Hill’s model and optimised it for the individual subjects to give a more accurate simulation (Hasson, Miller et al. 2011; Hasson and Caldwell 2012). However, these studies only consider muscular changes and do not include the neurological factors which also contribute to strength loss with age (Clark and Manini 2008). Furthermore, Hill-based models consider the muscle as a ‘black-box’, and cannot be used to study alterations in the neuromuscular properties and their impact on force generated.

Alternative models to Hill-type and Huxley-type have been developed. A comprehensive muscle-tendon model was developed that included various muscular factors such as fibre type, fatiguability, number and size of fibres, force-length relationship, force-velocity relationship, pennation angle and contraction history (Hawkins 1990). This model is suitable for studying fatigue effects and muscular factors; however, it has also not implemented neural factors (Hawkins 1990).

Another muscle force model was developed by Heckman and Binder (1991) which described the transformation of the synaptic currents input to the motoneurons, to the mechanical output from individual motor units. Hence, their model described the individual electrical and mechanical properties of the motor units and was assigned values obtained from the experimental data for the cat medialis gastrocnemius. This model was adapted by Webber,
Porter et al. (2009) which to date is the only simulation study that investigated the relative influence of age-associated neuromuscular changes on the frequency and force output of the quadriceps muscle. The model incorporated motoneuron excitability, motor unit twitch properties, rate coding and recruitment behaviour of the motor units. However, this model was not validated against experimental data and it does not simulate sEMG (Webber, Porter et al. 2009).

Fuglevand, Winter et al. (1993) developed a motoneuron pool and motor unit force output model for isometric force conditions under steady state, similar to Heckman and Binder (1991). The important improvement over Heckman and Binder (1991) model, was the inclusion of a motor unit twitch model (Fuglevand, Winter et al. 1993). This model was used to study the muscle force generation under different recruitment and motoneuron firing frequency conditions and included a second independent output: the sEMG.

Many studies have adopted Fuglevand, Winter et al. (1993) model for studying the relationship between amplitude of motor unit action potential and force (Zhou and Rymer 2004), different recruitment and firing rate strategies (Zhou and Rymer 2004), force variability (Moritz, Barry et al. 2005; Barry, Pascoe et al. 2007) and many other applications. However, the use of these models for studying age related changes has been limited (Wheeler, Kumar et al. 2011) or have only investigated muscular factors (Barry, Pascoe et al. 2007).

This thesis has adopted and further improved the muscle force model developed by Fuglevand, Winter et al. (1993) which describes the generation of the muscular force through a motor unit twitch model. It is preferred over the Hill type models which only mimic the force generation behaviour of a muscle. It is not as detailed as the Huxley type models, but it has the advantage of not being computationally intensive. The excitation-contraction coupling and the cross-bridge cycle modelled in Huxley-type model can suitably be represented by the specific force (Renganathan, Messi et al. 1997; D'Antona, Pellegrino et al. 2003). The improved force model will be used to answer the first research question, ‘What are the relative influences of the neural and muscular factors on muscle strength decline with aging in the Tibialis Anterior?’
3.6 Summary

This chapter has established the broader research context and motivation for the research undertaken in this thesis. It has identified the need to study the relative influence of neuromuscular properties on muscle strength decline with age, and discussed recent work undertaken for this purpose. The muscle of interest for investigating this research question was narrowed to Tibialis Anterior, whose weakness is associated with risk of falls.

Literature also reported that the inhomogeneous aging of the ankle muscles (Tibialis Anterior and Triceps Surae) could lead to different rates of strength decline between the muscles. Hence, identifying their heterogeneous aging for a holistic fall prevention strategy in the elderly was established.

A need for a non-invasive tool to address this issue was determined and a combination of experimental and simulation methods have been proposed. Surface electromyogram has been selected to assess neuromuscular changes as an experimental non-invasive method. A lack of consensus in literature on age-associated sEMG changes was found which warrants a purposeful and informed selection of signal features based on the neuromuscular properties. This will be addressed in Chapter 4, while the examination of inhomogeneous aging of the ankle muscles by the sEMG will be addressed in Chapter 8.

The inability to quantify the age-associated sEMG changes to the corresponding neuromuscular changes was found to be a limitation of experimental studies with sEMG. This was one of the motivations established in this chapter to use a computational model of the sEMG to overcome this shortcoming. Another motivation for a simulation model is its ability to isolate the effects of neuromuscular properties on muscle force production, typically difficult with experimental studies. This necessitates the inclusion of a muscle force model with the sEMG.

This Chapter identified that a computational model of the sEMG and force model are vital to addressing the technological gaps discussed. Hence, recent work performed in the areas of sEMG and force modelling has been discussed. An existing computational sEMG and force model has been identified meeting the majority of the requirements for investigating age-related changes in the neuromuscular system. A modification of the existing computational model is proposed which will be described and validated in Chapter 5. This model will be
used to investigate the relative influence of neuromuscular properties on muscle strength decline with age in Chapter 6. It will also be used to quantify the neuromuscular changes from the age-associated sEMG changes using a simulation model and will be addressed in Chapter 7.
Chapter 4

4 Age-Associated changes to SEMG of Tibialis Anterior

4.1 Introduction

This chapter aims to address Research Question 1a (‘are there age-related surface electromyogram changes corresponding to neuromuscular alterations?’) by investigating age-associated neuromuscular changes in the Tibialis Anterior with sEMG properties: power spectral density (PSD) and the first of the higher-order statistics, bispectrum. These features have been selected by understanding their relation to the neuromuscular properties that undergo age-related changes. The work described in this chapter has used an experimental approach to investigate the changes in the various sEMG features between the younger and older cohort at different maximal voluntary contractions (% MVC). The findings from this chapter are consequently used in Chapter 7 which will address quantifying these changes to the corresponding neuromuscular changes in the older cohorts.

4.2 Senescent Muscle Changes and Corresponding sEMG Changes

The Motor Unit Action Potentials (MUAPs) from an active population of motor units constitutes the sEMG which studies have found to undergo changes with age (Meigal, Rissanen et al. 2009; Wheeler, Kumar et al. 2011; Arjunan, Wheeler et al. 2013). Neural and muscular changes manifest as changes in the MUAP shape (Disselhorst-Klug, Silny et al. 1998) and is the probable cause of age-associated differences in the sEMG. However, there are number of other factors that can influence the sEMG (Farina, Cescon et al. 2002; Farina, Merletti et al. 2004; Keenan, Farina et al. 2005), and identifying suitable features to assess neuromuscular alterations is essential.

The expected age-associated neuromuscular alterations include, but are not limited to:
i. **Motor Unit Remodelling:** is a loss of motor units with a preferential loss of fast type fibres (Rowan, Rygiel et al. 2012). This is due to increased oxidative stress on the large alpha motor neurons, causing their axons to undergo a ‘dying back’ process (Gordon, Hegedus et al. 2004). Consequently, the affected motor neuron’s muscle fibres are denervated (Gordon, Hegedus et al. 2004). Neighbouring slow type motor units would attempt to reinnervate these abandoned fibres by axonal sprouting (Brown, Strong et al. 1988; Deschenes 2004; McNeil, Doherty et al. 2005), leading to increased motor unit size (innervation ratio) and a conversion of the fast fibres to slow type. This will manifest as high amplitude MUAP, and sparser MUAP trains due to decreased number of motor units but with increased motor unit size (Disselhorst-Klug, Silny et al. 1998).

ii. **Decreased Firing rate:** is considered to be a consequence of slowed contractile properties of the motor unit due to motor unit remodelling (Connelly, Rice et al. 1999; McNeil, Doherty et al. 2005; Dalton, McNeil et al. 2008). However, factors such as decreased corticospinal excitability (Rossini, Desiato et al. 1992; Peinemann, Lehner et al. 2001; Oliviero, Profice et al. 2006; Manini, Hong et al. 2013; Sale, Lavender et al. 2016), increased duration of motor neuron after hyperpolarisation (Engelhardt, Morales et al. 1989; Piotrkiewicz, Kudina et al. 2007), slowed nerve conduction velocity (Campbell, McComas et al. 1973; Borg, Grimby et al. 1979; Metter, Conwit et al. 1998), and increased antagonistic co-activation (Klein, Rice et al. 2001) can constitute decreased firing rate. This will decrease the number of MUAP present in the sEMG.

iii. **Decreased Muscle fibre size and number:** Atrophy of fast fibres due to motor unit remodelling can cause decreased fibre size (Coggan, Spina et al. 1992; Deschenes 2004). Another consequence of denervation outpacing reinnervation is the eventual loss of muscle fibres (Jacob and Robbins 1990; Robbins 1992). This will manifest as decreased MUAP amplitude.

By understanding how the age-associated changes in the neuromuscular system affect the MUAP shape and therefore the sEMG, suitable signal properties were selected: the power spectral density (PSD) and Higher Order Statistics (HOS) (Table 4.1).

**Table 4.1** lists the age-associated neuromuscular changes and its effect on the MUAP, and consequential effect on the sEMG. Motor unit remodelling, decreased firing rate, and decreased muscle fibre size and number have been listed as the major neuromuscular...
alterations studied. Median frequency has been selected to detect selective atrophy of fast fibres in motor unit remodelling, and higher order test statistics have been used to detect decreased number of motor units. Peak of the power spectral density curve has been selected to assess decreased number of MUAP, and their amplitude.

**Table 4.1** Age-associated neuromuscular changes, its effect on MUAP shape with corresponding effect on sEMG and features to investigate these alterations.

<table>
<thead>
<tr>
<th>Age-related Alteration</th>
<th>Corresponding changes to MUAP</th>
<th>Expected effect on sEMG</th>
<th>Suitable feature to assess sEMG change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motor Unit Remodelling</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atrophy of Fast type Units</td>
<td>Increased Duration of MUAP due to decreased average conduction velocity (Merletti, Farina et al. 2002)</td>
<td>PSD of EMG shifts to lower frequencies (Merletti, Farina et al. 2002)</td>
<td>Decreased Median Frequency of the PSD (Merletti, Farina et al. 2002; Poosapadi Arjunan, Kumar et al. 2015)</td>
</tr>
<tr>
<td>Decreased Number of Motor Units due to denervation</td>
<td>Increased time between adjacent MUAP (Disselhorst-Klug, Silny et al. 1998)</td>
<td>EMG pattern becomes sparser, EMG amplitude distribution centred closer around zero (Disselhorst-Klug, Silny et al. 1998; Istenič, Kaplanis et al. 2010)</td>
<td>Higher Order Statistics: Measure deviation from a Gaussian distribution</td>
</tr>
<tr>
<td>Increased Existing Motor Unit Size, due to reinnervation</td>
<td>Increased MUAP amplitude (Disselhorst-Klug, Silny et al. 1998)</td>
<td>Increased EMG amplitude</td>
<td>Increased Peak Power of the PSD (Farina, Merletti et al. 2014)</td>
</tr>
<tr>
<td>Decreased Firing Rate</td>
<td>Decreased Number of MUAP (Farina, Merletti et al. 2004)</td>
<td>Decreased EMG amplitude</td>
<td>Decreased Peak Power of the PSD (Farina, Merletti et al. 2014)</td>
</tr>
<tr>
<td>Decreased Muscle Fibre Size and Number</td>
<td>Decreased MUAP amplitude</td>
<td>Decreased EMG amplitude</td>
<td>Decreased Peak Power of the PSD (Farina, Merletti et al. 2014)</td>
</tr>
</tbody>
</table>
Zhao and Li (2012) simulated the effect of number of active motor units and firing rate behaviour on the higher-order statistics (HOS) of the sEMG: Gaussianity and Linearity test statistics, using a biceps brachii model. The study found a correlation between the HOS of the sEMG and the number of active motor units (Zhao and Li 2012), a concept that has been experimentally validated for the biceps brachii, which showed increased Gaussianity of the sEMG with increased force demands (Bilodeau, Cincera et al. 1997; Nazarpour, Sharafat et al. 2007; Kaplanis, Pattichis et al. 2009). These studies demonstrated that decreased number of motor units due to motor unit remodelling can be studied with the first of HOS, the bispectrum (Zhao and Li 2012). The hypothesis of an age-associated change in HOS has been investigated for the biceps brachii (Kaplanis, Pattichis et al. 2009); however, no equivalent work has been performed for the TA.

A corresponding increase in sEMG RMS due to increased MUAP amplitude has been observed with age in the TA, which was indirectly related to motor unit remodelling (R Deschenes 2011). This was further confirmed by Fling, Knight et al. (2009) who found increased macro EMG amplitude in older cohorts indicative of increased motor unit size. Nonetheless, the amplitude of the sEMG is affected by number of extrinsic and intrinsic factors (Ng and Kent-Braun 1999; Farina, Merletti et al. 2004) and neuromuscular evaluations based solely on the sEMG amplitude can be misleading. A limitation of this study is that subcutaneous fat was not measured.

4.3 Materials and Methods

4.3.1 Participants

Eighteen younger and 18 older volunteers (details in Table 4.2) with no clinical history of neuromuscular disease or ankle injury participated in this study. The experimental protocol was approved by RMIT University Human Research Ethics Committee (Ethics project reference no: 15751 (40/13)) and in accordance with Helsinki Declaration (revised 2004).
Table 4.2. Details of the participants; number, age, height, and body mass index.

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (years)</th>
<th>Height (cm)</th>
<th>Body Mass Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Young (n = 18)</td>
<td>26.1 ± 2.9 (20 – 30)</td>
<td>166.7 ± 8.9 (151 – 182)</td>
<td>22.3 ± 2.9 kg m⁻²</td>
</tr>
<tr>
<td>Old (n = 18)</td>
<td>67.7 ± 8.1 (60 – 85)</td>
<td>163.2 ± 9.1 (152-184)</td>
<td>26.0 ± 3.9 kg m⁻²</td>
</tr>
</tbody>
</table>

4.3.2 Mechanical and sEMG recording procedures

Participants were seated in a sturdy chair with right leg strapped to a support such that the hip, knee and ankle were fixed at 90°, 140° and 90° (neutral position), respectively. A force sensor, SM-100 type (Interface, Arizona, USA) was attached to measure the isometric force applied to the fixed footplate. The left leg was planted firmly on the ground. To ensure absence of foot or toe movement during dorsiflexion, the foot and ankle was secured with straps to the footplate (Siddiqi, Arjunan et al. 2015) (Figure 4.1).

Myomonitor 4 (Delsys, Boston, USA) was used to record the EMG activity which had a gain of 1000, CMRR of 92 dB and bandwidth of 20- 450 Hz, with 12 dB/ octave roll-off. The sampling frequency was set to 1000 Hz with a resolution of 16 bits/ sample. The Delsys single-channel active differential silver bar (1 mm x 1 mm) surface electrodes with an embedded preamplifier and inter-electrode distance of 10 mm were used. The skin at the electrode locations were shaved, abraded and cleansed with an alcohol swipe. EMG and force recordings were performed concurrently during the experiment.

![Figure 4.1 Experimental setup for isometric dorsiflexion of the ankle and the sEMG electrode placement for Tibialis Anterior, and Triceps Surae.](image)
4.3.3 Electrode Placements

Electrode placement must be done parallel to the muscle fibres, and placement on the innervation zones and tendons should be avoided (Farina, Cescon et al. 2002; Barbero, Merletti et al. 2012). In parallel fibre muscles the sEMG signal’s amplitude decreases, and frequency spectrum shifts to higher frequencies on these locations (Farina and Merletti 2000; Farina, Cescon et al. 2002).

In a pennate muscle the electrode mainly detects non-travelling components of the action potential due to generation at the innervation zone and extinction at the tendons (Farina, Cescon et al. 2002; Mesin, Merletti et al. 2011; Barbero, Merletti et al. 2012). Unlike parallel fibre muscles, placement of the electrode on the innervation zones and tendons cannot be avoided for a pennate muscle. Therefore, the restriction on the placement of the electrode is relaxed for muscles with pennate architecture (Farina, Cescon et al. 2002).

The electrode placement and skin preparation was done in accordance with SENIAM recommendations (SENIAM 2009). EMG activity was recorded from the dorsiflexor, TA. The surface electrode was placed at 1/3rd on the line between the tip of the fibula and the tip of the medial malleolus (SENIAM 2009) and the ground electrode was placed at the patella (Billot, Simoneau et al. 2010) (Figure 4.1).

To evaluate any age-related change in the TA’s EMG amplitude from the antagonistic muscle’s coactivation, EMG activity was also recorded from the Triceps Surae (TS) muscles during dorsiflexion as follows (Figure 4.1):

SOL: few centimetres from where the gastrocnemii (GAS) join the Achilles tendon on the midline of the leg.

MG: On the most prominent bulge of the muscle belly (SENIAM 2009).

LG: 1/3rd of the line between the head of the fibula and the heel (SENIAM 2009).

4.3.4 Experimental Protocol

Prior to maximal voluntary contraction (MVC) measurement for isometric dorsiflexion (DF), participants were trained to elicit their true MVC with a visual force feedback on the screen. After significant rest and self-administered massage, they repeated this twice and recordings were accepted if the difference was less than 5% from each other. Minimum two minute rest
period was given between each trial. Subsequently, they were instructed to perform two isometric DF repetitions, each of 10, 20, 30, 50%, 75% and 100% MVC, each for 5 seconds with a 2 minute rest period between each trial, and with the order being randomly assigned to prevent bias.

4.4 Data Analysis

4.4.1 EMG Data Analysis

The first one second and the last one second of all the recordings were discarded because the force was not steady during these segments. The following EMG features were calculated from the remaining segments:

4.4.1.1 Higher Order Statistics (HOS): Bispectral Analysis

Reduction in the number of MUAP due to decreased number of active motor units will make the sEMG signal less Gaussian (Istenič, Kaplanis et al. 2010). The Gaussianity of a signal can be assessed by negentropy (Nazarpour, Sharafat et al. 2007), probability density function (Naik and Kumar 2011) and recently developed third order cumulant based features (Orosco, Lopez et al. 2013; Orosco, Diez et al. 2015). In this study, Hinich’s non-skewness test of time series using HOS has been used (Hinich 1982), since a relationship between number of active motor units and these features has been established (Zhao and Li 2012).

The algorithm developed by Hinich (1982) tests if the bispectrum (Equation 4.1) which is the Fourier transform of the third-order cumulant (Equation 4.2) is zero. This occurs if the third-order cumulants of a process is zero, leading to the biocherence (Equation 4.3) (normalised bispectrum) to also be zero.

\[
B(\omega_1, \omega_2) = \sum_{m=-\infty}^{\infty} \sum_{n=-\infty}^{\infty} R(m, n)e^{-j(\omega_1 m + \omega_2 n)} \tag{4.1}
\]

\[
R(m, n) = E\{X(k)X(k + m)X(k + n)\} \tag{4.2}
\]

\[
B_s(\omega_1, \omega_2) = \frac{B(\omega_1, \omega_2)}{\sqrt{P(\omega_1)P(\omega_2)P(\omega_1 + \omega_2)}} \tag{4.3}
\]
Where $P(\omega)$ is the power spectrum.

If the bispectrum, $B(\omega_1, \omega_2)$, is non-zero then the underlying process or signal is classed as a non-Gaussian process. The bicoherence, $B_n(\omega_1, \omega_2)$, will be a non-zero constant if the process is linear and non-Gaussian. The non-Gaussianity test statistic ($S_g$) is chi-squared distributed with $2P$ degrees of freedom when the bicoherence is zero (Equation 4.4). $P$ is the number of points over which the squared bicoherence is summed over in the non-redundant region (Hinich 1982). Hence if the $S_g$ value is determined to be consistent with a central chi-squared distribution, the null hypothesis of assumption of Gaussianity can be made. The null hypothesis can be rejected if the probability of false alarm value, which measures the probability in accepting a non-Gaussian process is incorrect, is less than 0.05 (Hinich 1982).

$$S_g = \sum |B_n(\omega_1, \omega_2)|^2$$

(4.4)

### 4.4.1.2 Power Spectral Analysis

Amplitude measures such as Average Rectified Value (ARV) or Root Mean Square (RMS) have typically been used to study neuromuscular changes (Merletti, Roy et al. 1999; Tracy and Enoka 2002; Wheeler, Kumar et al. 2011). However, these features suffer from amplitude cancellation (Farina, Merletti et al. 2004), and an alternative measure is needed to disregard its effect on the aging analysis. The power spectrum is not influenced by amplitude cancellation (Farina, Merletti et al. 2014) and can be used to study amplitude changes in the sEMG.

The power spectral density of the sEMG was calculated for epoch lengths of 512 points with a 25% overlap (Inbar, Paiss et al. 1986). The peak of the power spectral density curve (PSD) was determined and is defined as the maximal power in dB ($P_M$) of the PSD. $P_M$ was computed as $10\log_{10}P_{xx}$ where $P_{xx}$ is the power spectral density ($V^2$ Hz$^{-1}$) computed. The Median Frequency (MDF) which represents the frequency of half the power spectrum’s energy is related to changes in the MUAP shape and conduction velocity (Stulen and De Luca 1981). Thus, the MDF can be used to identify atrophy of fast fibres (Table 4.1) as previously shown in the biceps brachii (Wheeler, Kumar et al. 2011). A note of caution regarding the MDF is that it is influenced by several other factors, and its relationship with the conduction velocity is controversial (Farina, Merletti et al. 2004).
The TS coactivation analysis and results are described in Appendix A.

4.5 Statistical Analysis

Statistical Analysis was performed using the MATLAB and Statistics Toolbox Release 2011a (The MathWorks Inc., Massachusetts, USA). One-way ANOVA was performed on the EMG power spectral and bispectral features with age as a factor with two levels; Young and Old. This was repeated for each of the MVC levels; 10%, 20%, 30%, 50%, 75% and 100% MVC. Prior to ANOVA calculations normality of the test data was performed using Shapiro-Wilk test at $\alpha = 0.05$. If the test data was determined to be not normal, it was transformed using the Aligned Rank tool (ARTool) developed by Wobbrock, Findlater et al. (2011). This tool was developed to address the need for performing factorial analysis on nonparametric data and has been verified to be accurate.

The ARTool aligns the response variable for each main or interaction effect by stripping all effects but one of interest from the response variable. The aligned responses are assigned ranks, and averaged in the case of ties. A full factorial ANOVA is performed on the aligned and ranked responses calculated for each main and interaction effect. For more details, the reader is directed to (Wobbrock, Findlater et al. 2011; Wobbrock 2016). All the statistical results are tabulated in Table 4.3.
4.6 Results

The relationship of the Bispectral and Power spectral features; Gaussianity Test Statistic, maximal power of the PSD and median frequency, with MVC for the two age groups are shown in Figures 4.2, 4.3 and 4.4 while the significant statistical values are described in Table 4.3

4.6.1 HOS: Gaussianity Test Statistic ($S_g$)

Figure 4.2 Changes in the Gaussianity Test Statistic value (Mean + SD) of the young and old cohort’s sEMG with increasing force level measured as a percentage of maximal voluntary contraction. Significant age-associated difference indicated by ** $p < 0.05$.

Figure 4.2 illustrates the changes in the Gaussianity Test Statistic ($S_g$) of sEMG recorded from the young and older cohorts’ with increasing force level. The results show decrease in $S_g$ with increasing force level, indicating that sEMG is increasingly Gaussian at higher force levels. While the change in Gaussianity was more evident for the older cohort, the younger cohort had on overall higher Gaussianity at all force levels.

Except at 100% MVC for young cohorts, the $S_g$ values were found to be not normally distributed for either of the cohorts at all the MVCs. Hence the data was transformed using the ARTool developed by Wobbrock, Findlater et al. (2011) prior to ANOVA calculations.
The difference between the two age cohorts was significant at 20% and 50% MVC (Table 4.3).

4.6.2 Power Spectral Density (PSD)

![Figure 4.3](image)

**Figure 4.3** Maximal power in dB (P_M) of the sEMG signal’s PSD (Mean ± SD) as a function of force (% MVC) in young and old cohorts. Significant age-associated difference indicated by ** p < 0.05 and *** p < 0.01.

**Figure 4.3** shows the P_M measured in dB from the participant’s sEMG power spectral density for different force levels. While both cohorts display increasing P_M with force, the older cohorts always maintained a higher P_M than young.

The P_M data was found to be normally distributed for both the cohorts at 10%, 20% 30% and 100% MVC. The PM was not normally distributed at 50% MVC for young cohorts and at 75% MVC for older cohorts. Therefore, the young and old cohorts’ data at 50% and 75% MVC was transformed using the ARTool prior to ANOVA calculations. A main effect for age was found at all the MVC’s except at 75% and 100% MVC (Table 4.3).
Figure 4.4 shows changes in the median frequency of the young and old cohorts’ for EMG with increasing force level measured as the percentage of MVC. The older cohorts had higher median frequencies than the young, but no significant differences were found at any of the MVCs ($p > 0.05$).

Figure 4.4 Changes in the median frequency (Mean ± SD) of the young and old cohorts’ sEMG with increasing force measured as a percentage of maximal voluntary contraction.

Figure 4.5 SEMG signals for a young participant's Tibialis Anterior at six different %MVC levels.
Table 4.3. ANOVA Significant statistical results for the EMG features.

<table>
<thead>
<tr>
<th>EMG Feature</th>
<th>Effect</th>
<th>MVC (%)</th>
<th>F(1, 35) =</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gaussianity Test Statistic (Sg)</td>
<td>20</td>
<td>5.18</td>
<td>0.0292 **</td>
<td></td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>4.84</td>
<td>0.0347 **</td>
<td></td>
</tr>
<tr>
<td>Maximal Power (dB)</td>
<td>Age</td>
<td>10</td>
<td>7.07</td>
<td>0.0119 **</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>15.58</td>
<td>0.0004 ***</td>
<td></td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>13.5</td>
<td>0.0008 ***</td>
<td></td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>9.96</td>
<td>0.0033 ***</td>
<td></td>
</tr>
</tbody>
</table>

Significant difference between young and old cohorts indicated by ** p < 0.05 and *** p < 0.01.

4.7 Discussion

This chapter has described an experimental investigation of the age–related change in sEMG of TA muscle using features from the power spectrum, \( P_M \) and MDF; and from the bispectum; \( S_g \). From the results, it is confirmed that the maximal power of the PSD and Gaussianity increases with increased levels of muscle contraction, although MDF remained independent of the force level. Significant differences in the \( P_M \) and Gaussianity of the sEMG recorded from the TA muscle between the younger and older cohort were also observed which shows that age-related changes can be assessed with these features. To interpret the results of these experiments, these features need to be examined individually.

Maximal power of the PSD which is a representation of the sEMG amplitude can be an indicator of increased size or firing rate of the motor unit (Disselhorst-Klug, Silny et al. 1998; Farina, Merletti et al. 2004). In older cohorts, increased sEMG amplitude could also be because of increased antagonistic coactivation (Kent-Braun and Ng 1999; McNeil, Doherty et al. 2005). From literature it is evident that firing rate reduces with age (McNeil, Doherty et al. 2005; Klass, Baudry et al. 2008), and TS coactivation in this study was not significantly altered with age (Appendix A, Figure A.1). Another factor that can lead to increased sEMG
amplitude is a reduction in subcutaneous fat (Farina, Cescon et al. 2002) but this hypothesis is not supported by literature which have found an age-associated increase in subcutaneous fat (McNeil, Vandervoort et al. 2007; Csapo, Malis et al. 2014; Power, Allen et al. 2014). Thus the age-associated increase in maximal power of the PSD can only be attributed to the size of the motor units. Although the strength of this finding is limited due to the subcutaneous fat not being measured in this study.

The increased sEMG amplitude in older cohorts has also been observed by other studies (Kent-Braun and Ng 1999; McNeil, Doherty et al. 2005; Fling, Knight et al. 2009). Motor unit remodelling is the increased MUAP amplitude due to increased innervation ratio (Disselhorst-Klug, Silny et al. 1998; R Deschenes 2011; Rowan, Rygiel et al. 2012) and could explain the increase in sEMG amplitude (Kent-Braun and Ng 1999; McNeil, Doherty et al. 2005; Fling, Knight et al. 2009).

The longer duration of the MUAP due to remodelling would shift the frequency spectrum to the left; however, the opposite trend is observed in our results (Figure 4.4). Similar to Meigal, Rissanen et al. (2009), our old cohorts were characterised by higher MDF, although this was not significantly different to the younger cohorts MDF. The lack of an age-related change in the MDF could be due to the high percentage of slow fibres in TA (~70%). The MDF is sensitive to conduction velocity (Stulen and De Luca 1981), but is also influenced by other factors (Lowery, Vaughan et al. 2000; Farina, Merletti et al. 2004). Therefore, the loss of fast fibres in a predominantly slow type muscle may not significantly alter the MDF.

Based on the central limit theorem, a system distribution becomes closer to Gaussian as the number of independent components increases (Rice 1995). Decreases in the Gaussianity Test Statistics ($S_g$) value shows the system to be closer to Gaussian distribution, and indicates a larger number of motor units (Zhao and Li 2012). Reduction of $S_g$ of sEMG can be interpreted as reduced number of motor units.

Increasing force demands are met through two schemes: recruitment and rate coding. Both of these will increase the MUAP content of the sEMG which will increase the PSD amplitude (Kaplanis, Pattichis et al. 2009; Wheeler, Kumar et al. 2011) and Gaussianity of the EMG signal (Bilodeau, Cincera et al. 1997; Nazarpour, Sharafat et al. 2007; Kaplanis, Pattichis et al. 2009). This is readily observed in this study. This is also supported by Istenič, Kaplanis et
al. (2010) study who suggests that increased force would lead to greater number of MUAP contributing to the amplitude distribution and hence higher Gaussianity.

The sEMG is found to become increasingly Gaussian with increased force level due to an increased number of MUAP (Kaplanis, Pattichis et al. 2009; Naik and Kumar 2011). The lack of significance at MVC levels greater than 50% MVC could be due to increased number of MUAP with force levels that would mask any age-associated decreases in number of motor units. High inter-subject variability in the $S_g$ feature at 10% MVC was noted for the older cohorts that could account for the lack of significance noted.

Conversely, decrease in the number of active motor units would contribute a lesser number of MUAP to the EMG signal and lead to a narrower amplitude distribution centred about zero (Istenič, Kaplanis et al. 2010). Since, Gaussianity is correlated with number of active motor units (Zhao and Li 2012), its decrease in the older cohorts’ sEMG is indicative of decreased number of motor units in the TA.

### 4.8 Summary

This chapter has investigated the effect of age on the Gaussianity and the PSD of the sEMG for the Tibialis Anterior at different force levels. The chapter answers Research Question 1A by demonstrating that the SEMG of the older cohorts had significantly higher amplitude and more non-Gaussianity, which was especially evident at submaximal contractions. The combination of these features maybe associated with motor unit remodelling and would be useful for non-invasively tracking neuromuscular changes with age and implementing rehabilitation strategies to prevent strength degradation.

The next chapter will introduce the sEMG and Force Model for the purpose of answering the Research Question 1 (Chapter 6), and quantifying the sEMG changes observed in this chapter to changes in the neuromuscular system (Chapter 7).
5 Electromyogram and Force Model of the Tibialis Anterior: Implementation and Experimental Validation

5.1 Introduction

The aim of the work described in this chapter is to develop a new computational model for sEMG of unipennate TA and the force generated, measured at the ankle joint to address the Research Question 1 (‘What are the relative influences of the neural and muscular factors on muscle strength decline with aging in the Tibialis Anterior?’). This model aims to overcome the shortcomings in past models, and has been tested using the sEMG power spectral density (PSD) and Median Frequency (MDF).

The sEMG and force model presented also assigns a statistical distribution of values to its parameters to represent intra- and inter subject variability, and distinguishes the fast and slow motor unit types. The novelty of the force model is the integration of twitch force with realistic parameters instead of arbitrary units, and an ankle joint moment model to compute the torque.

5.2 Previous Surface Electromyogram Models Limitations

Surface electromyogram (sEMG) is an easy to record, non-invasive signal of the muscle activity. It is generated by the superposition of an electrical potential induced by active motor units in the muscle, namely the motor unit action potential (MUAP). Studies have demonstrated age-associated changes in the sEMG (Meigal, Rissanen et al. 2009; Wheeler, Kumar et al. 2011; Arjunan and Kumar 2013; Siddiqi, Poosapadi et al. 2015). However, the cause of this change is difficult to identify because the sEMG is influenced by multiple parameters; rate of activation (Farina, Merletti et al. 2004), size and type of active motor units (Ayachi, Boudaoud et al. 2014), conduction velocity (Farina, Merletti et al. 2004; Ayachi,

To understand the relationship between these changes and neuromuscular parameters, computational sEMG models have been developed (Nandedkar and Stalberg 1983; Fuglevand, Winter et al. 1993; Dimitrov and Dimitrova 1998; Desselhorst-Klug, Silny et al. 1998; Merletti, Lo Conte et al. 1999; Stegeman, Blok et al. 2000; Mesin 2006; Cao, Boudaoud et al. 2015). While these models are suitable for generic explanation of sEMG, these make a number of approximations that makes them unsuitable for investigating age or disease associated changes to the parameters. Some of the limitations in the design of the model are:

1. Statistical Distribution: These models generally have applied single values to their parameters, with exceptions such as Farina, Fattorini et al. (2002) and Mesin, Merletti et al. (2011) who implemented a distribution for conduction velocity.

2. Fibre type: These models do not distinguish between fast and slow motor unit types, which are shown to be affected with age (Rowan, Rygiel et al. 2012).

3. Motor unit size: These models do not consider different sizes and numbers of motor units with the exception of Mesin, Merletti et al. (2011) and Wheeler, Kumar et al. (2011).

One shortcoming of the earlier computational sEMG models is that these have been implemented for generic parallel fibre muscles (Nandedkar and Stalberg 1983; Fuglevand, Winter et al. 1993; Merletti, Lo Conte et al. 1999; Stegeman, Blok et al. 2000). To study muscles such as the Tibialis Anterior (TA) that are vital for posture stability and gait (Moreland, Richardson et al. 2004), it is important to model the pennation of the muscle fibres. Although recent modelling work has produced volume conductor solutions to pennate muscle architecture (Farina, Mesin et al. 2004; Mesin and Farina 2004; Mesin 2006; Mesin,
Merletti et al. 2011; Mesin 2013), they are inadequate due to the previously described limitations.

Most of the earlier models described only have one independent output; the sEMG (Merletti, Lo Conte et al. 1999; Mesin, Merletti et al. 2011). Validation of a model requires multiple data sources for it to suitably represent the population or outputs it is intending to simulate (Eddy, Hollingworth et al. 2012). The inclusion of a second independent output for comparison with experimental measurements can improve the validity and accuracy of the computational model (Keenan and Valero-Cuevas 2007). Recent models that generate force and sEMG have been investigated (Hashemi, Morin et al. 2013; Cao, Boudaoud et al. 2015; Liu, Liu et al. 2015); however, two of these models (Hashemi, Morin et al. 2013; Liu, Liu et al. 2015) have described the force as a function of sEMG and not as an independent parameter. The third study (Cao, Boudaoud et al. 2015) assigned the mean forces to the motor units which were summed to generate the output. This modelling approach does not reflect the neuromuscular physiology where there is the integration of twitch force generated by individual muscle fibres.

5.3 Surface Electromyogram Theory

A motor unit is comprised of a single motor neuron and the muscle fibres it innervates (Figure 5.1). A motor unit twitch, which is the smallest unit of muscular force, is instigated when its motor neuron is excited. An action potential propagates along the excited motor neuron’s fibre, eventually arriving at the neuromuscular junction where the motor neuron attaches to its muscle fibres.

Two intracellular action potentials (IAP) are generated at the neuromuscular junction that travel to either ends of the muscle fibre and extinguishes at the tendon (Figure 5.1). This process occurs to all the muscle fibres that constitute the motor unit, albeit at slightly different initiation times. This is due to different arrival times of the action potential owing to the variability of the neuromuscular junction locations within the motor unit.

The intracellular action potential is typically triphasic in shape and is the consequence of rapid depolarisation and repolarisation of the fibre membrane. The depolarisation and repolarisation of the membrane is accompanied by the influx of sodium ions and exit of potassium ions from the membrane which is known as the transmembrane current. The
intracellular action potential recorded by an electrode from a single fibre is known as a single fibre action potential. Collectively, these single fibre action potentials (SFAP) create the motor unit action potential (MUAP). The superposition of MUAPs from the active motor units that is recorded by a surface electrode is known as the surface electromyogram (EMG). This process is illustrated in Figure 5.2.

**Figure 5.1** A motor unit comprised of an alpha motoneuron and the group of muscle fibres it innervates. An intra-cellular action potential travels to both ends of the muscle fibres once the motoneuron is excited.

**Figure 5.2** A schematic of the sEMG generation. A train of impulses is instigated once the motoneuron is excited \((Im(t))\). This propagates to the neuromuscular junction \((NMJ)\) which generates two action potentials \((AP)\). The AP undergo shape changes due to the volume conductor that is surrounding biological tissue, before it is detected by recording electrodes. The summation of the action potentials from the motor units comprises the sEMG.
5.4 Surface Electromyogram Model Description

The computational model described in this paper has been adapted from the biceps brachii sEMG model (Wheeler, Kumar et al. 2011; Poosapadi Arjunan, Kumar et al. 2015). This model incorporates the following; statistical distribution of parameters, type 1 and 2 fibres, motor units of varying sizes and non-linear recruitment based on literature (Klass, Baudry et al. 2008). It has added many new features such as the use of single fibre action potential, and considered the pennation angle. These adaptations and additions have been described below.

5.4.1 Single Fibre Action Potential

The single fibre action potential (SFAP) can be deduced using volume conductor theory and solving for the Poisson’s Equation (5.1)

$$ \nabla \cdot ( \sigma \nabla \phi ) = -I \text{ in } \Omega $$

(5.1)

Where $\sigma$ is the conductivity tensor (S/m), $\phi$ is the extracellular potential (V) or the SFAP, $I$ is the current density source (A/m$^3$) or the transmembrane current, and $\Omega$ is the volume conductor domain.

Historically, several authors have contributed to the development of an expression to determine the extracellular potential (Wilson, Macleod et al. 1933; Lorente de No 1947; Clark and Plonsey 1968; Plonsey 1974; Andreassen and Rosenfalck 1981). The solution can largely be expressed as follows (Wilson, Macleod et al. 1933; Dimitrov and Dimitrova 1998):

$$ \phi(x_o, y_o) = -\frac{\sigma_i}{4\pi\sigma_e} \left[ dS \int_{-\infty}^{\infty} \frac{\partial \varphi_i(x)}{\partial x} \cdot \frac{\partial (1/r)}{\partial x} \cdot dx \right] $$

(5.2)

Where $\sigma_i$ and $\sigma_e$ are the intra- and extracellular conductivities, $\varphi_i(x)$ is the intracellular action potential (IAP) and $r$ is the distance from the source to the observation point.

Further simplification of Equation (5.2) has been done to present an easy volume conductor function, whereby the extracellular potential is obtained as the convolution of the bioelectric source and the impulse response of the volume conductor (Plonsey 1974; Andreassen and Rosenfalck 1981; Nandedkar and Stalberg 1983). The earlier model (Wheeler, Kumar et al. 2011) used this approach to compute the signal at the surface after considering the volume conduction and a fixed shape to describe the MUAP at the fibre.
This volume conductor function of the previous model (Wheeler, Kumar et al. 2011) lacks the ability to study the effect of generation and extinction of the action potential as along the muscle fibre. While this approximation is valid for biceps where the muscle fibres are parallel, this cannot be applied to a pennate muscle (Mesin, Merletti et al. 2011). The approach used by Dimitrov and Dimitrova (1998) to generate the SFAP has been used to overcome this shortcoming. SFAP is generated by the convolution of the first derivative of the IAP and the first derivative of the weighting function detailed in Section 5.4.2.

5.4.2 Volume Conductor for a Pennate Muscle

The weighting function in Equation (5.3) represents the impulse response of the volume conductor which is the tissue surrounding the bioelectric source. It acts as a low pass filter and attenuator of the signal as the distance increases from the source to the observation point. While the biceps brachii sEMG model (Wheeler, Kumar et al. 2011) represented the volume conductor for a fusiform muscle, this needs to be modified for the bipennate TA which is depth inclined.

The conductivity tensor in a bipennate muscle changes directions between the unipennate halves, making it inhomogeneous (Mesin 2006). Therefore, the analytical solution to the volume conductor used in the previous model (Wheeler, Kumar et al. 2011) would not be suitable. While numerical solutions to model volume conductor of bipennate muscles have been developed (Mesin and Farina 2004; Mesin 2013) these are computationally very complex. An analytical solution to the volume conductor problem is preferred for reduced computation time (Farina, Mesin et al. 2004; Mesin 2013).

It has been shown that surface electrode recordings are unaffected by sources that are further away in a pennate muscle (Mesin, Merletti et al. 2011). This suggests that the deeper half of the TA would not contribute significantly to the sEMG. Therefore, as a first approximation the TA can be modelled as unipennate. This enables an analytical volume conductor solution to be implemented so long as the electrode detection system is rotated with respect to the muscle fibres (Mesin 2006). This approximation has been shown to be valid for studying sEMG’s amplitude and median frequency (Siddiqi, Kumar et al. 2014).
For a muscle fibre that is inclined at $\Theta$ degrees to the recording electrode (Figure 5.3), the volume conductor function is given as (5.3) (Appendix B, Section 11.2.1)

$$ft = \frac{\partial}{\partial z} \left( \frac{\sigma_i}{4\pi \sigma_e} \sqrt{(z_o - (z_{NMJ} \pm z' \cos \Theta))^2 + K_{an} (x_o - x_{NMJ})^2 + (y_o - (y_{NMJ} \pm z' \sin \Theta))^2} \right)$$

(5.3)

Where $ft$ is the impulse response of the volume conductor in space domain, $\sigma_i$ and $\sigma_e$ are the intra- and extracellular conductivities; $K_{an}$ is the anisotropic factor which is the ratio of conductivities parallel and perpendicular to the muscle fibre ($\sigma_i / \sigma_e$). The neuromuscular junction is located at $(X_{NMJ}, Y_{NMJ}, Z_{NMJ})$ with respect to the recording electrode coordinates $(X_o, Y_o, Z_o)$ origin. The Origin of the muscle fibre coordinates $(X', Y', Z')$ is located at the motor unit’s neuromuscular junction. The muscle fibre coordinates indicate the position of the action potential travelling the length of the fibre $(x', y', z')$. (Figure 5.3).

5.4.3 Source description

The bioelectric source used in the formulation of Equation (5.2) is the first derivative of the IAP ($\phi_i$). An analytical expression of the IAP will be used in this study which was first
described by Rosenfalck (1969) and has been translated to spatial domain (Merletti, Lo Conte et al. 1999)

\[ V_m(z) = A(\lambda z^3)e^{-\lambda z} - B \]  

(5.4)

Where \( V_m \) is the IAP, \( A \) is the action potential amplitude, \( B \) is the resting membrane potential, \( z \) is the distance along the muscle fibre and \( \lambda \) is a scaling factor to alter the action potential’s waveform. A scaling factor of 2 has shown good comparison to experimental IAP (Nandedkar and Stalberg 1983; Duchene and Hogrel 2000). The values of \( A \) and \( B \) have been reported to be 96 mV and -90 mV, respectively. This function can be transformed to time-domain with the assumption of constant conduction velocity (Equation 5.5) (Wheeler, Kumar et al. 2011)

\[ V_m(t) = A(\lambda(\nu t)^3)e^{-\lambda(\nu t)} - B \]  

(5.5)

### 5.4.4 Surface Electromyogram

The IAP shape and conduction velocity can be assumed to be constant along a muscle fibre length (Dimitrova, Dimitrov et al. 1999), which enables the fibre to be modelled as linear and space-invariant. Consequently, the single fibre action potential is simply the convolution of the volume conductor function (5.3) and the first derivative of the IAP (\( V_m \)) in time domain as used by Dimitrova, Dimitrov et al. (1999). Hence, the sEMG can be represented as in equation (5.6):

\[ s\text{EMG} = \sum_{i=1}^{n} \sum_{j=1}^{m} \int \frac{\partial V_{i,j}(t)}{\partial t} * \delta \left( t - \frac{k}{fr} - \tau_i \right) \]  

(5.6)

Where \( n \) is the total number of motor units, \( m \) is the number of muscle fibres in the \( i^{th} \) motor unit, \( \delta(t) \) function is the train of impulses arriving from the motor neuron to the neuromuscular junction at firing rate of \( fr \) with an initial temporal offset of \( \tau_i \) for the \( i^{th} \) motor unit, with \( k \) number of pulses. The initial temporal offset is relative to the instance when the motor unit is first recruited. This offset is randomly assigned to each motor unit and is used to ensure asynchronous firing of the motor units.
5.5 Model Implementation

The computational model for sEMG and force of TA was populated with neuromuscular parameters reported in literature and summarized in Table 5.1. Column 1 lists the model parameters simulated; Column 2 lists the range of values reported in literature for the various neuromuscular properties simulated highlighting the innate variability of this muscle. Column 3 lists the nominal values used for the Young Model simulation. Column 4 lists the additional values simulated to represent the inter-subject variability. Hence, different ranges of number of motor units, muscle fibres, fast-slow fibre ratio, muscle fibre length, and pennation angle described in Table 5.1, Column 4 have also been simulated to compare the variability offered by the model against the experimental variability.

The motor unit firing rate and recruitment pattern was modelled and have been described in Section 5.5.1 and 5.5.2.

5.5.1 Motor unit firing rate strategy

De Luca and Hostage (2010) estimated the firing rate of the Tibialis Anterior using a decomposition technique that has been proven to be 92.5% accurate on average. Equation (5.7) represents the ‘onion skin’ phenomenon which describes that; (i) earlier recruited motor units achieve higher firing rates compared with motor units recruited later, and (ii) the discharge rate increases with maximum voluntary contraction (MVC). The equation is a function of the MVC ($\Phi$) and the motor unit’s recruitment threshold ($\kappa$). The range of the firing rate is from 8 to 30 Hz.

$$\lambda(\phi, \kappa) = D \cdot \phi + (C \cdot A \cdot e^{B \cdot \kappa}) \cdot \kappa + E$$  \hspace{1cm} (5.7)

Where $\lambda$ is the firing rate; $\Phi$ is defined as the MVC level; $\kappa$ is the motor unit’s recruitment threshold; and the constants were derived from the best fit line equation, such that $A = 65$, $B = 0.3$, $C = -15$, $D = .54$, and $E = 20.2$ (De Luca and Hostage 2010).

To model the variability of the firing rate, its variance was modelled such that the coefficient of variance decreases exponentially with increasing MVC based on Jesunathadas, Klass et al. (2012) study.
SEMGG and Force Model of the TA

\[ CV = A + \left( \frac{\kappa_i}{25} \right) + \left( \frac{\phi}{4} \right) e^{(-\Delta \phi)} \]  

(5.8)

Where \(\kappa_i\) is the recruitment threshold of the \(i^{th}\) motor unit, \(\Phi\) is the MVC level and \(CV\) is the coefficient of variation in the firing rate of the motor unit. The firing rate spectrum and its variability at different MVC level are illustrated in Figure 5.4.

![Figure 5.4 Firing rate and its variability at 6 different force levels for the 360 motor units. Distinction is made when the fast type motor units are recruited.](image)

5.5.2 Recruitment Pattern

We have incorporated the results from Klass, Baudry et al. (2008), who determined that the young subjects demonstrate continuous recruitment of motor units from 1% - 90.2% MVC. This recruitment range was a skewed distribution, described as having a median of 26.3% MVC, Skewness: 0.641 and Kurtosis -0.491.

An additional consideration was given for determining the recruitment range of the two motor unit types. In the absence of any direct experimental study of the difference between slow and fast fibres recruitment in the TA, this study has applied Henneman’s ‘size principle’ (Henneman, Somjen et al. 1965) to the motor unit’s recruitment thresholds, whereby the smaller slow type motor units are recruited first.
**Table 5.1** Range of values reported in literature, model values used for simulation of Tibialis Anterior sEMG and force and for simulating inter-subject variability. Parameters listed with a single mean value are fixed, and parameters listed with $\mu \pm \sigma$ are generated as a Gaussian distribution. Other distributions used to represent a parameter are explicitly stated.

<table>
<thead>
<tr>
<th>Model Parameter</th>
<th>Values reported in literature</th>
<th>Value used for ‘Young’ Tibialis Anterior Simulation</th>
<th>Values simulated to depict inter-subject variability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1 muscle fibre cross sectional area ($\mu$m²)</td>
<td>3950 ± 950 (<a href="#">Jakobsson, Borg et al. 1988</a>), 4830 – 5290 (<a href="#">Edstrom and Nystrom 1969</a>)</td>
<td>3950 (<a href="#">Henriksson-Larsén, Lexell et al. 1983</a>)</td>
<td></td>
</tr>
<tr>
<td>Type 2 muscle fibre cross-sectional area ($\mu$m²)</td>
<td>8070 ± 1850 (<a href="#">Jakobsson, Borg et al. 1988</a>), 8060 - 8800 (<a href="#">Edstrom and Nystrom 1969</a>)</td>
<td>8070 (<a href="#">Henriksson-Larsén, Lexell et al. 1983</a>)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fast fibres conduction velocity m/s</td>
<td>Slow fibres conduction velocity m/s</td>
<td>Total number of muscle fibres</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>-------------------------------------</td>
<td>-------------------------------------</td>
<td>------------------------------</td>
</tr>
<tr>
<td></td>
<td>2.6 – 5.3 (Farina, Fattorini et al. 2002)</td>
<td>4.9 ± 0.3 (Farina, Fattorini et al. 2002)</td>
<td>3.9 ± 0.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>131 000 (Jakobsson, Borg et al. 1988)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>96 800, 162 500</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>292 500 (Feinstein, Lindegård et al. 1955)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>96 800, 162 500</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>96 800, 162 500</td>
</tr>
<tr>
<td>Innervation ratio (# of muscle fibres per motor unit)</td>
<td>329 – 657 (Feinstein, Lindegård et al. 1955; Gath and Stålberg 1981)</td>
<td>Poisson distribution with λ = 364</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muscle length (cm)</td>
<td>28.4 – 32.2 (Wickiewicz, Roy et al. 1983), 30.0 ± 0.8 (Fukunaga, Roy et al. 1996)</td>
<td>29.8 (Edstrom and Nystrom 1969)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muscle fibre length (cm)</td>
<td>6.9 – 9.3 (Wickiewicz, Roy et al. 1983), 4.5 ± 0.4 (Maganaris 2001), 7.0 ± 1.3 (Simoneau, Longo et al. 2012)</td>
<td>7.7 (Wickiewicz, Roy et al. 1983)</td>
<td>4.0, 4.5, 6.9 (Wickiewicz, Roy et al. 1983; Maganaris 2001; Maganaris, Baltzopoulos et al. 2001; Simoneau, Longo et al. 2012)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parameter</td>
<td>Value</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>------------------------------------------------</td>
<td>----------------------------------------------------------------------</td>
<td>-----------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Duration of AP along fibre (mm)</td>
<td>11 (Lowery, Vaughan et al. 2000), 16 (Dumitru, King et al. 1999)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intra-cellular Conductivity (Smm$^{-1}$)</td>
<td>1.01 (Nandedkar and Stalberg 1983; Lowery, Vaughan et al. 2000); 0.45–0.75 (Albers, Rutten et al. 1988)</td>
<td>1.01 (Nandedkar and Stalberg 1983; Lowery, Vaughan et al. 2000)</td>
<td></td>
</tr>
<tr>
<td>Extra-cellular conductivity (Smm$^{-1}$)</td>
<td>0.089 (Disselhorst-Klug, Silny et al. 1998); 1.8–2.5 (Albers, Rutten et al. 1988)</td>
<td>0.089 (Disselhorst-Klug, Silny et al. 1998)</td>
<td></td>
</tr>
<tr>
<td>Anisotropic ratio Kan</td>
<td>5.2 (Nandedkar and Stalberg 1983; Lowery, Vaughan et al. 2000); 1.8–15.3 (Griep, Gielen et al. 1982); 1.39 (Disselhorst-Klug, Silny et al. 1998)</td>
<td>5.2 (Nandedkar and Stalberg 1983; Lowery, Vaughan et al. 2000)</td>
<td></td>
</tr>
<tr>
<td>Subcutaneous tissue (mm)</td>
<td>Single, 3mm isotropic layer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Slow type specific force (Ncm$^{-2}$)</td>
<td>8.5 ± 1.6 (Lowery, Vaughan et al. 2000); 13.1 ± 2.0 (Morse, Thom et al. 2005)</td>
<td>15.5 ± 5.0 (Krivickas, Dorer et al. 2011)</td>
<td></td>
</tr>
<tr>
<td>Fast type specific force (N cm$^{-2}$)</td>
<td>4.9 ± 0.06 (Fukunaga, Roy et al. 1996); 3.4 ± 0.3 (Maganaris 2001)</td>
<td>4.9 ± 0.4 (Maganaris 2001)</td>
<td></td>
</tr>
<tr>
<td>Tibialis Anterior tendon moment arm (cm)</td>
<td>4.9 ± 0.06 (Fukunaga, Roy et al. 1996); 3.4 ± 0.3 (Maganaris 2001)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
5.6 Force Model Equations and Implementation

Force models can be described as either Hill-type (that mimics the behaviour of a muscle (Morris, Osborne et al. 2004)), or Huxley type (that includes the excitation-contraction coupling and actin myosin interaction to produce force (Huxley 1957)). Hill-type models consider the muscle as a ‘black-box’, and therefore are not appropriate for studying alterations in neuromuscular properties. While Huxley-type models best represent the structure and behaviour of a muscle, these models are often complicated.

Fuglevand, Winter et al. (1993) developed a motor unit force model for isometric force conditions under steady state conditions, which has been adopted for this study. While this model does not account for the excitation-contraction effects, it is still a structure based model that allows investigators to study alterations in neuromuscular properties and its effect on force.

5.6.1 Motor unit twitch force

Muscular force is achieved through the tetanic summation of individual motor unit twitches. The motor unit twitches are found to follow a critically damped second order system and has been represented by Equation (5.9) developed by Fuglevand, Winter et al. (1993) based on Milner-Brown, Stein et al. (1973) experimental study:

\[ g_i(t) = \frac{P_i T_i}{T_i} e^{1 - \frac{t}{T_i}} \]  

Where \( P_i \) is the twitch amplitude of the \( i^{th} \) motor unit, and \( T_i \) is the contraction time or the rise time to peak twitch force.

In the model presented by Fuglevand, Winter et al. (1993), the peak twitch amplitude was assigned arbitrary units that followed a skewed distribution. While this is suitable to demonstrate the concept, this is not accurate because different muscle fibres generate varying levels of force. In this study, the peak twitch amplitude has been computed using the fundamentals of neurophysiology (Sacks and Roy 1982; Narici, Landoni et al. 1992) and a function of three factors; cross-sectional area of the muscle fibre, muscle fibre type (modelled by specific force), and number of muscle fibres constituting the motor unit (Equation 5.10).

\[ P_i = \text{specific tension} \cdot \text{CSA} \cdot \# \text{ of fibres} \]  

(5.10)
This model incorporates the twitch force integration, for which the contraction time of a motor unit has been modified to follow a normal distribution ($\mu = 45 \text{ ms}, \sigma = 13.6 \text{ ms}$) based on Cutsem, Feiereisen et al. (1997) experimental findings of the TA. In the absence of any experimental data differentiating the fast and slow fibres, this study has approximated the contraction time of slow motor units to correspond to $\mu + \sigma$, while the fast to $\mu - \sigma$.

### 5.6.2 Tetanic summation of motor unit twitches

The individual motor unit twitches eventually start to fuse once its firing rate increases beyond the relaxation time of the motor unit. The twitches summate non-linearly and follow a sigmoid relationship, the shape of which is dependent on the motor unit twitch characteristics (Fuglevand, Winter et al. 1993). This non-linearity between twitch force and the firing rate can be described by the gain factor $g_{i,j}$ (Equation 5.11) developed by (Fuglevand, Winter et al. 1993) based on experimental studies (Bigland and Lippold 1954; Rack and Westbury 1969; Burke, Rudomin et al. 1976).

\[
g_{i,j} = \frac{S\left(\frac{T_i}{ISI_j}\right)}{\frac{T_i}{ISI_j}} \text{ for } \frac{T_i}{ISI_j} > 0.4
\]

\[
g_{i,j} = 1.0 \text{ for } \frac{T_i}{ISI_j} < 0.4
\]

Where $T_i$ is the contraction time of the $i^{\text{th}}$ motor unit, and $ISI_j$ is the jth interspike interval, $S$ is the sigmoid function.

The total muscle force is simply the summation of the consecutive motor unit twitches of all the active motor units.

\[
F_M = \sum_{i=1}^{n} F_i(t) = \sum_{i=1}^{n} \sum_{j=1}^{k} f_{i,j}(t - t_{i,j}) = \sum_{i=1}^{n} \sum_{j=1}^{k} g_{i,j} \cdot \frac{p_i(t-t_{i,j})}{T_i} e^{-\left(\frac{t-t_{i,j}}{T_i}\right)} \text{ for } t - t_{i,j} \geq 0
\]

Where $F_M$ is the total muscle force, $F_i$ is the total twitch for the $i^{\text{th}}$ motor unit and $j^{\text{th}}$ impulse.
5.6.3 Resultant Torque measured by the force sensor

Figure 5.5 Experimental setup to measure dorsiflexion and plantarflexion forces and the electrode recording locations for the TA and TS muscles. \( x_1 \) is the distance from the first interphalangeal joint of the foot to the footplate hinge point; and \( x_2 \) is the distance from the first interphalangeal joint of the foot to the tibiotalar joint.

For comparison with the experimental torque recordings, the simulated muscle force needs to be converted to the joint moment as measured in the experimental setup (Figure 5.5). This is performed by converting the muscular force to the tendon force and then determining the appropriate moment equation to calculate the joint moment (Figure 5.6).

Figure 5.6 Muscular forces and its relation to the tendon force.

The force generated by the model is converted to the tendon force as follows (Figure 5.6):
$F_t = F_m \cdot \cos \alpha \quad (5.13)$

Where $\alpha$ is the pennation angle of the tibialis anterior, $F_t$ is the tendon force and $F_m$ is the muscle force.

The joint moment is determined by taking moments centred on the tibiotalar joint, where, $d$ is the tendon moment arm of the TA (Maganaris 2001) and is described by Equation 5.14. The resultant torque which is measured by the force sensor is obtained by taking moments centred about the equipment hinge point and is described by Equation 5.15.

Joint Moment = $F_t \cdot d \quad (5.14)$

Resultant Torque = $\frac{\text{Joint Moment} \cdot x_1}{x_2} \quad (5.15)$

Where the resultant torque is computed as the force recorded by the force sensor multiplied by the moment arm of 18cm as measured from the hinge point of the footplate to the location of the force sensor; $x_1$ is the distance from the first interphalangeal joint of the foot to the footplate hinge point; and $x_2$ is the distance from the first interphalangeal joint of the foot to the tibiotalar joint.
**Figure 5.7** A schematic view of the sEMG and Force model input and outputs. The inputs are the motor unit properties and the excitation level. Each motor unit is assigned a specific activation pattern corresponding to its firing rate and recruitment threshold. This activation pattern is used to generate the stimulus that leads to the generation of sEMG and Joint Torque.
An overview of the sEMG and Force Models’ implementation is shown in Figure 5.7. This figure shows the input parameters to the model which are the motor unit properties and the excitation level representing the force demand (%MVC). The motor units have a specific activation pattern described in Section 5.5.1 and 5.5.2 which is used to generate the stimulus, representative of a train of neural impulses descending from the Central Nervous System (CNS). The stimulus instigates a train of action potentials which further causes the motor unit twitch leading to a muscular contraction through the excitation-contraction process (Fauler, Jurkat-Rott et al. 2012). The summation of the MUAP observed by the recording electrodes after volume conduction effects is the sEMG.

5.7 Materials and Methods

5.7.1 Participants

Eighteen young volunteers (9 males and 9 females; 26.1 ± 2.9 years; 166.7 ± 8.9 cm; BMI: 22.3 ± 2.9 kg m⁻²) were recruited to participate in the experiments. The experimental protocol was approved by RMIT University Human Research Ethics Committee (Ethics project reference no: 15751 (40/13)) and was performed in accordance with Helsinki Declaration (revised 2004). Any volunteers with a history of neuromuscular disease or lower limb injury were excluded from the study.

5.7.2 Surface Electromyogram recordings

Surface Electromyogram (sEMG) was recorded from the Tibialis Anterior (TA) and Triceps Surae (TS) muscles using Delsys bipolar single-channel active differential surface electrodes. The signals were recorded on Delsys myomonitor 4 (DELSYS, Boston, USA) system, having gain of 1000, CMRR greater than 92dB and bandwidth of 20-450 Hz, with 12dB/ octave roll-off. The silver (99.9%) contacts on the electrodes (10mm x 1mm) were at a fixed inter-electrode distance of 10mm, with the preamplifier embedded on the electrode. The sampling frequency was set at 1000Hz with a resolution of 16 bits/sample.

The skin at the electrode locations were shaved, lightly abraded and cleansed with an alcohol swipe. EMG activity was recorded from the dorsiflexor TA, and the plantar flexor; TS, comprising of m. medial gastrocnemius (MG), m. lateral gastrocnemius (LG), and m. soleus (SOL). The TS EMG was recorded to evaluate the coactivation level and its antagonistic
force contribution during dorsiflexion. The ground electrode was placed at the patella (Billot, Simoneau et al. 2010), while except for SOL; the electrodes were placed on the recommended locations (SENIAM 2009) as described below:

TA: 1/3rd on the line between the tip of the fibula and the tip of the medial malleolus.

SOL: few centimetres from where the gastrocnemii join the Achilles tendon on the midline of the leg.

MG: On the most prominent bulge of the muscle belly.

LG: 1/3rd of the line between the head of the fibula and the heel.

5.7.3 Force Recordings

The participants were seated in a chair with hip flexed at 90°, knee at 140° and ankle at 90°. To prevent any foot or toe movement or heel lift during dorsi- and plantarflexion, the foot and ankle was strapped to the footplate (Siddiqi, Arjunan et al. 2015). Strapping of the foot and toes ensured participants were not incorrectly everting and inverting their ankle while performing dorsi-and plantarflexion movements. An S type force transducer, SM-100 type (Interface, Arizona, USA) was attached to the footplate and measured the force produced by the ankle. The resultant torque is computed as the force recorded by the force sensor multiplied by the moment arm of 18cm as measured from the hinge point of the footplate to the location of the force sensor.

Prior to sEMG recordings, the participants underwent training to elicit their true maximal voluntary contraction (MVC) during both isometric plantar- and dorsiflexion (DF). They were provided visual force feedback and given verbal encouragement. They repeated the MVC trials until their consecutive force recordings differed less than 5%. The volunteers subsequently performed two isometric dorsiflexion at 10%, 20%, 30%, 50%, 75%, and 100% MVC in a random order, for 5s, with a 2 minute rest between each trial.

Antagonistic muscles can significantly contribute to the external joint torque measured and this needs to be considered (Simoneau, Billot et al. 2009). To quantify the antagonist force produced by the TS, an EMG-force relationship was constructed for the TS during plantarflexion (PF) (Baratta, Solomonow et al. 1988). Participants were instructed to perform
several submaximal contractions at 10, 20, 30, and 50% MVC for 5 seconds and a 2 minute rest period between each trial.

### 5.8 Simulation Protocol

The model was simulated with a sampling frequency of 10,000 Hz using the values in Table 5.1, Column 3, at 10%, 20%, 30%, 50%, 75% and 100% MVC for 6s. This was repeated eighteen times and each simulation regenerated parameters that were modelled as a distribution (Table 5.1). A sampling frequency of 10,000 Hz was used to correctly construct the action potential source shape, which if under sampled at 1000 Hz introduces aliasing effects and is not able to give the correct resolution needed.

In addition to this, five parameters that were originally fixed were also varied according to the values listed in Table 5.1, Column 4. These were the number of motor units, muscle fibres, fast-slow fibre ratio, fiber length and pennation angle. The purpose of this was to simulate the variability observed in the experimental sEMG, thereby being symbolic representation of the 18 young volunteers that were tested. A total of 1994 simulations were performed.

For a comparison with the experimental sEMG, the simulated sEMG was digitally filtered with a 2nd order Butterworth filter with a band pass frequency of 20 Hz and 450 Hz. Furthermore, the sEMG signal was down sampled at 1000 Hz to mimic the sampling frequency of the experimentally recorded sEMG.
5.9 Data Analysis

5.9.1 Surface Electromyogram Data Analysis

The first and last one second of the TA’s sEMG recorded with single differential electrodes (Section 5.7.2) and force data was discarded because of the presence of transients in these sections. Power spectral density (PSD) and median frequency (MDF) was calculated for both the experimental and simulated sEMG. The sEMG’s PSD was calculated using epoch lengths of 512 points and a 25% overlap (Inbar, Paiss et al. 1986). The peak of the power spectral density curve (PSD) was determined and is defined as the maximal power in dB ($P_M$) of the PSD. $P_M$ was computed as $10\log_{10}P_{xx}$ where $P_{xx}$ is the power spectral density ($V^2 \text{ Hz}^{-1}$) computed. The Median Frequency (MDF) which represents the frequency of half the power spectrum’s energy was also calculated.

For computing the TS antagonistic torque, the TS sEMG RMS was computed at the submaximal contractions recorded described in Section 5.7.3.

5.9.2 Torque Data Analysis

The mean torque was computed for the force recording for each experiment and simulation. The antagonistic torque generated by TS was estimated using methods previously reported (Baratta, Solomonow et al. 1988) which generates a EMG/torque relationship for the TS using submaximal contractions. The antagonistic TS torque estimated was added to the resultant dorsiflexion torque at each %MVC measured to obtain the agonist TA torque (Billot, Simoneau et al. 2010). A summary of these steps are detailed below which has been described previously (Simoneau, Billot et al. 2009):

1. The total TS sEMG RMS was calculated as a summation of the MG, LG and SOL sEMG RMS (Simoneau, Billot et al. 2009):

$$TS_{RMS} = MG_{RMS} + LG_{RMS} + SOL_{RMS}$$

(5.16)

2. The coactivation level of the TS as an antagonist was calculated as the ratio of its sEMG RMS during dorsiflexion (DF) and plantarflexion (PF) MVC (Falconer and Winter 1984).

$$TS\% = \frac{TS_{RMS-DF}}{TS_{RMS-PFMVC}}$$

(5.17)
3. A polynomial equation of the sEMG/force relationship of the TS was constructed from the submaximal contractions performed by the participant. A second degree polynomial equation was used if the second-degree polynomial coefficient was found to be higher than the linear coefficient (Baratta, Solomonow et al. 1988; Billot, Simoneau et al. 2010).

4. The coactivation level of the TS was used to estimate the antagonist force produced from the constructed sEMG/force relationship.

5. The agonist force of the Tibialis Anterior was calculated as the summation of the resultant DF and antagonist TS force.

5.9.3 Regression Analysis

Statistical Analysis was performed using the MATLAB and Statistics Toolbox Release 2011a (The MathWorks Inc., Massachusetts, USA). A linear regression was performed at $\alpha = 0.05$ for the sEMG features & torque with MVC for the experimental and simulated values. F-test statistic and coefficient of determination ($R^2$) were computed to determine goodness of fit of the linear regression model to the simulated and experimental sEMG features and normalised torque.
5.10 Results

Figure 5.8 shows a scatter plot of the simulated and experimentally observed maximal PSD of sEMG, and the least square line of best fit for the simulated and experimental values. The scatter plot of the simulated sEMG generated using model parameters listed in Table 5.1, Column 3 and 4. The plots show that maximal power of the PSD increases with increasing force levels for both the simulated (slope = 0.1136) and experimental sEMG (slope = 0.2042). The average slope is greater for the experimental sEMG of young cohorts.

Regression analysis results in Table 5.2 show that experimental maximal power of sEMG PSD correlation with MVC, ($R^2 = 0.3462$) was similar to the simulation correlation with MVC ($R^2 = 0.3438$). The range of simulated values is within the experimentally observed values.
Figure 5.9 Scatter plots with line of best fit of the simulated and young cohort’s median frequency of their EMG with increasing force level measured as the percentage of MVC.

Figure 5.9 shows a scatter plot of the simulated and experimentally observed MDF, and the least square line of best fit for the simulated and experimental values. The scatter plot of the simulated sEMG generated using model parameters listed in Table 5.1, Column 3 and 4. The plots show the MDF of the experimental sEMG increases slightly with increasing force levels (slope =0.2478), but the simulated sEMG’s MDF remains constant with MVC (slope = 0.0992). Table 5.2 shows neither experimental nor simulated MDF has strong correlation with levels of MVC ($R^2$= 0.0452 and 0.1153). The range of simulated values is within the experimentally observed values.

Figure 5.10 shows the plot of the normalised simulated torque against the normalised experimental torque. A strong correlation was found between the simulated normalised torque and experimentally recorded torque ($R^2$ = 0.9240). This is confirmed by the F statistical test performed to determine if the linear regression was significant.
Figure 5.10 A scatter plot of the simulated vs. young cohort’s agonist normalised torque that represents 18 repetitions (or subjects) x 6 MVC levels =108 simulated and experimental data points.

Table 5.2 Regression coefficients and goodness of fit statistics (F-test and $R^2$) for sEMG features and Torque for simulated and experimental conditions.

<table>
<thead>
<tr>
<th></th>
<th>Maximal Power of PSD (dB)</th>
<th>Median Frequency (Hz)</th>
<th>Normalised Torque</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Simulation</td>
<td>Experiment</td>
<td>Simulation</td>
</tr>
<tr>
<td>Intercept</td>
<td>-117.9</td>
<td>-119.75</td>
<td>120.19</td>
</tr>
<tr>
<td>Slope</td>
<td>0.1136</td>
<td>0.2042</td>
<td>0.0992</td>
</tr>
<tr>
<td>$R^2$</td>
<td>0.3438</td>
<td>0.3462</td>
<td>0.1153</td>
</tr>
<tr>
<td>$F$</td>
<td>1042.56</td>
<td>56.14</td>
<td>259.42</td>
</tr>
<tr>
<td>p-value</td>
<td>$p&lt;0.0001$</td>
<td>$p&lt;0.0001$</td>
<td>$p&lt;0.0001$</td>
</tr>
</tbody>
</table>
5.11 Discussion

This chapter has described a computational model that simulates sEMG and the agonist torque generated by the TA during dorsiflexion. This has been validated using two independent parameters; sEMG and force. The model has considered the details of the neuromuscular parameters such as the non-linearity of motor recruitment, differences between type 1 and 2 fibres, and integration of twitch force of individual muscle fibre.

The model was tested by comparing the simulated and experimentally recorded sEMG’s and torque. The experiments were conducted on 18 participants, and to match, simulation was repeated 18 times, with values randomly obtained from within the statistical distribution of each parameter (Table 5.1). In addition to the 18 simulations, parameters that were initially fixed such as number of motor units and muscle fibres, fast-slow fibre ratio, fiber length and pennation angle were also varied to compare the variability of the sEMG model against the experimental sEMGs.

PSD maximal power and MDF were used as the features to compare sEMG while the normalised torque was used for the force model. The simulated and experimental results showed an increase in PSD maximal power with %MVC and this observation is supported from literature (Gander and Hudgins 1985; Kaplanis, Pattichis et al. 2009). The experimental and simulated results also showed that MDF does not correlate with levels of muscle contraction (%MVC), which is supported by observations of Inbar, Paiss et al. (1986), but contradictory to the results of Gander and Hudgins (1985) and Kaplanis, Pattichis et al. (2009).

5.11.1 Inter-Subject Variability of sEMG power spectrum.

The experimental inter-subject variability is observed to be higher than the simulation, particularly for MDF. Table 5.1 Column 3 and 4 shows the wide ranging values that have been reported for parameters simulated. For example, the number of motor units reported for the TA is highly variable, from 125 to 652 (Feinstein, Lindegård et al. 1955; Cutsem, Feiereisen et al. 1997; McNeil, Doherty et al. 2005). Likewise, the muscle fibres in the TA can vary from 96,000 to 292,500 (Feinstein, Lindegård et al. 1955; Henriksson-Larsén, Lexell et al. 1983; Enoka 1995). To test the hypothesis that increased variation in the parameters simulated would increase the variance observed in the sEMG power spectrum, additional values for the parameters were tested using Table 5.1 Column 4. The number of
motor units, muscle fibres, fast-slow fibre ratio, fiber length and pennation angle that were originally fixed to values from **Table 5.1**, Column 3 were varied according to values listed in **Table 5.1**, Column 4.

The increased variability of the input parameters corresponded to an increase in the simulated PSD maximal power and MDF in comparison to the original simulation with model values from **Table 5.1**, Column 3 (Appendix B, Figure B.2, and B.3). The results show the sEMG model is capable of simulating the inter-subject variability observed in the young cohorts’ sEMG.

An additional factor that may contribute to the high inter-subject variability observed experimentally is the intra- ($\sigma_i$) and extra-cellular conductivity ($\sigma_e$) and the muscles’ anisotropy ratio ($K_{an}$). A large variability exists in the intra- (Andreassen and Rosenfalck 1981; Griep, Gielen et al. 1982; Albers, Rutten et al. 1988; van Veen, Wolters et al. 1993; Lowery, Vaughan et al. 2000; Röhrle, Davidson et al. 2012) and extracellular conductivities (van Veen, Wolters et al. 1993; Disselhorst-Klug, Silny et al. 1998; Röhrle, Davidson et al. 2012) reported as well as the anisotropy ratio of the muscle fibre.

The intra- and extra-cellular conductivity ratio that appears in Equation (5.2) influences the SFAP’s amplitude (Nandedkar and Stalberg 1983; Albers, Rutten et al. 1988), while the anisotropy can affect both its amplitude and wave shape (Nandedkar and Stalberg 1983). Increasing anisotropy will decrease the amplitude of the action potential as well as ‘stretch’ it’s wave shape (Appendix B, Figure B.4). Hence, a variation of these parameters in the participants tested could also contribute to the high inter-subject variability observed. This is further illustrated in (Appendix B, Figure B.5).

In this study, the most commonly implemented values for intra- and extracellular conductivity, and anisotropic ratio were used. An intra-cellular conductivity of 1.01 Smm$^{-1}$ was used similar to authors (Nandedkar and Stalberg 1983; Lowery, Vaughan et al. 2000), while the conductivities for the skin, fat and muscle was averaged to give a value of 0.089 Smm$^{-1}$ for the extra-cellular conductivity following Disselhorst-Klug, Silny et al. (1998) study. For the anisotropy, the conductivities parallel and perpendicular to the muscle fibres of 0.33 Smm$^{-1}$ and 0.0633 Smm$^{-1}$ were used similar to other authors (Nandedkar and Stalberg 1983; Lowery, Vaughan et al. 2000).
5.11.2 Force Model Validation

The force model for the TA presented in this paper has been adapted from Fuglevand, Winter et al. (1993). A significant improvement was made to their model by assigning realistic twitch force values to the motor units, instead of arbitrary units. The peak twitch force is a function of the number of muscle fibres, fibre cross-sectional area and specific force; this is the adaptation of accepted muscle physiology (Sacks and Roy 1982; Narici, Landoni et al. 1992). This changes the relationship between the peak twitch force and the contraction time from a power (Fuglevand, Winter et al. 1993) to a linear function, which best represents the TA’s motor unit behaviour (Jesunathadas, Klass et al. 2012). The separation of motor units in the sEMG is also reflected in the properties simulated in the force model, namely the peak twitch force and contraction time. This enables the sEMG force model to be coupled; therefore, any changes to the sEMG model would also affect the force output. Lastly, the force model incorporates an ankle joint model which converts the simulated muscle force to the torque measured by the sensor in the experiment. This facilitates the comparison of experimentally recorded torque and simulation, since direct muscular forces cannot be measured (Maganaris 2001).

5.11.3 Limitations

The model presented in this study featured a number of assumptions:

(i) The TA’s volume conductor is represented as unipennate instead of bipennate.

(ii) The volume conductor is a 2D simplified planar representation of the muscle and ignores curvature or shortening of muscle fibres.

(iii) The calculation of the simulated resultant torque assumes the ankle as 2D and ignores any variation in the moment arms $x_1$ and $x_2$ appearing in equation (5.15).

These assumptions lead to the limitations of the present sEMG and Force Model. More complicated and realistic representations of volume conductor have been presented by other studies (Farina, Mesin et al. 2004; Mesin and Farina 2004; Mesin 2006). However, in this study we opted for a simpler volume conductor, which has also been used by implemented in other models (Dimitrov and Dimitrova 1998; Merletti, Lo Conte et al. 1999; Wheeler, Kumar et al. 2011).
Shortening of muscle fibres can impact the MDF (Schulte, Farina et al. 2004; Rodriguez-falces and Place 2014), and could explain the higher inter-subject variability observed experimentally in comparison to simulation. It has been shown that pennate muscles can still undergo a decrease in fiber length and increased pennation angle under isometric contraction (Fukunaga, Ichinose et al. 1997; Maganaris and Baltzopoulos 1999; Simoneau, Longo et al. 2012). Future studies can significantly improve the correlation between simulated and experimental sEMG.

The ankle model that has been used to compute the resultant torque from the generated muscle force is represented as 2D with fixed moment arms. The force is assumed as a point load, rather being a distributed over the footplate. These assumptions could explain the variability observed in experimental torque with respect to the simulated torque.

The TA is one of four dorsiflexor muscles that act to dorsiflex the ankle (Gray 1973; Marsh, Sale et al. 1981). In this study, only the TA has been modelled which could explain the lower torque values simulated in comparison to experimental torque leading to a slope of 0.9762 which is less than 1 (Table 5.2).

5.12 Summary

A computational surface electromyogram model for the Tibialis Anterior is presented that describes in detail the neuromuscular activity and models biological variability. The model also incorporates a twitch force model that emulates the generation of force and resultant torque. This model would be useful to study changes to the Tibialis Anterior neuromuscular system and answering Research Question 1 (‘What are the relative influences of the neural and muscular factors on muscle strength decline with aging in the Tibialis Anterior?’). The realistic force model provides an independent output that is necessary for validation of the model. It also provides the versatility to investigate the effect of neural and muscular factors on strength decline which has been studied in Chapter 6 and 7.
Chapter 6

6 The Relative Effects of Neuromuscular Properties on Torque–A Simulation Study

6.1 Introduction

The aim of the work described in this chapter is to use the force model of the Tibialis Anterior developed in Chapter 5 to answer Research Question 1 - ‘What are the relative influences of the neural and muscular factors on muscle strength decline with aging in the Tibialis Anterior?’ - in a broader capacity. Hence, several neuromuscular properties with values reported in literature for young and the elderly are simulated to evaluate individual contributions of neuromuscular properties to muscle force regulation. The findings of this chapter establish the most influential neuromuscular property involved in regulating the Tibialis Anterior’s muscle strength.

6.2 Muscle Force Models and their Capacity to Study Senescent Musculature

A risk factor for falls in older people is an age-related strength decline in the lower limb muscles (Wu, Callisaya et al. 2016), in particular the Tibialis Anterior (TA) (Daubney and Culham 1999; Moreland, Richardson et al. 2004; Robinson, Gordon et al. 2004). To mitigate this decline, it is essential to identify the underpinning factors that cause this loss of strength. There are several neuromuscular properties that are responsible for its age-associated strength reduction (Clark and Manini 2008). The key well-studied changes are:

(i) Muscle architectural changes in fibre length and pennation due to loss of sarcomeres in series and parallel (Morse, Thom et al. 2005; Mitchell, Williams et al. 2012).

(ii) Motor unit remodelling which is the reduction of fast-slow fibre ratio, and increased motor unit size (R Deschenes 2011; Kaya, Nakazawa et al. 2013).
(iii) Muscle fibre loss due to impaired reinnervation (Lexell, Taylor et al. 1988; Rowan, Rygiel et al. 2012; Kwan 2013)
(iv) Decreased motor unit firing rate and altered recruitment pattern of motor units (Klass, Baudry et al. 2008; Manini and Clark 2011).
(v) Reduced specific force and prolonged contraction time of motor units (Vandervoort and McComas 1986; Clark and Manini 2008)

Age association of these factors with force of muscle contraction has been extensively studied (Vandervoort and McComas 1986; Connelly, Rice et al. 1999; Klass, Baudry et al. 2008; Hasson and Caldwell 2012; Reid, Pasha et al. 2014; McKinnon, Montero-Odasso et al. 2015; Zampieri, Pietrangelo et al. 2015). However, their relative contributions to strength decline are not fully explained (Clark and Manini 2008; Webber, Porter et al. 2009; Clark, Law et al. 2015). Experimental studies are unsuitable for isolating these factors because it is impractical to control and alter these parameters. Computational models provide a practical way of determining the influence of each neuromuscular property on muscle force generation (Webber, Porter et al. 2009).

There are a number of studies reported in literature that have developed computational models for muscles (Hawkins 1990; Fuglevand, Winter et al. 1993; Wexler, Ding et al. 1997; Thelen 2003; Moritz, Barry et al. 2005; Barry, Pascoe et al. 2007; Hasson, Miller et al. 2011; Contessa and Luca 2013; Romero and Alonso 2016). However, there is only one study that has reported the investigation of the individual contributions to muscle force, and this was performed on the quadriceps muscle (Webber, Porter et al. 2009). Yet this does not accurately represent the muscle force generation as it has several shortcomings, such as parameters do not represent their innate biological variability (Webber, Porter et al. 2009), joint moment has not been modelled (Webber, Porter et al. 2009; Contessa and Luca 2013) and the simulation has not been verified against experimental values (Webber, Porter et al. 2009).

The Force model that was presented in Chapter 5 will be used to answer Research Q1 in this chapter. It models the ankle joint mechanics to investigate the effect of neuromuscular properties on the simulated dorsiflexion torque. This model incorporates the neural and muscular factors; generation of twitch force; differentiates between fast and slow muscle
fibre types; and assigns a statistical distribution of values to its parameters. The model is used to simulate a combination of young and senescent neuromuscular parameters to determine their relative contributions to torque generated. A key outcome of this study will be to better target strength preservation strategies in the elderly.

6.3 Materials and Methods

The Force model developed in Chapter 5 for the Tibialis Anterior will be used to investigate the effect of the parameters listed in Table 6.1. The modified force model is an accurate representation of force generated by the TA muscle as it incorporates a motor unit recruitment threshold (Klass, Baudry et al. 2008) and firing rate scheme (De Luca and Hostage 2010) that has been specifically developed for the TA based on experimental studies. The Table 6.1 lists the values of the parameters used to represent the range of differences corresponding to differences in age and gender.

6.3.1 Simulation Protocol

The simulation of the force model with the parameters listed in Table 6.1 was performed in two stages. The first stage was to generate the direct effects of the parameters on the simulated torque; the second stage was to investigate interaction effects amongst the parameters.

i. **Direct Effects:** The model was simulated for six seconds for each set of parameter values and this was repeated ten times to generate a distribution of values resembling inter-subject variability. This was repeated for six fractions of maximal voluntary contraction (MVC); 10%, 20%, 30%, 50%, 75% and 100% MVC. The relative effect of the neuromuscular parameters on torque was measured using standardised slope coefficients obtained from a linear regression model detailed in Section 6.4. This is a measure of the slope corresponding to one standard deviation change in response to one standard deviation change in the predictor.

ii. **Interaction Effects:** Moderation of one parameter’s effect on the simulated torque due to another parameter was investigated by holding one parameter constant, while varying the other. The rest of the simulation protocol remained the same as detailed above. The interaction effects between the following parameters was investigated:
Relative Influence of Neuromuscular Properties on Torque

- Number of motor units, and fast-slow fibre ratio
- Number of motor units and total number of muscle fibres
- Number of motor units and recruitment distribution
- Fast-slow fibre ratio and fast fibre size
- Fibre length and pennation angle

Table 6.1 A combination of young and age modified parameters used for the simulation of the dorsiflexion torque to investigate their relative effects.

<table>
<thead>
<tr>
<th>Parameters Simulated</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of motor units ‡</td>
<td>50, 100, 150, 200, 250, 300, 360 (Cutsem, Feiereisen et al. 1997; Trojaborg, Kaufmann et al. 2002; McNeil, Doherty et al. 2005; Fling, Knight et al. 2009)</td>
</tr>
<tr>
<td>Fast-Slow Fibre Ratio</td>
<td>0.1, 0.2, 0.3, 0.5 (Edstrom and Nystrom 1969; Johnson, Polgar et al. 1973; Henriksson-Larsén, Lexell et al. 1983)</td>
</tr>
<tr>
<td>Pennation Angle</td>
<td>0°, 5°, 10°, 20°, 30° (Wickiewicz, Roy et al. 1983; Maganaris 2001; Simoneau, Longo et al. 2012)</td>
</tr>
<tr>
<td>Fibre length (mm)</td>
<td>40, 45, 69, 77 (Wickiewicz, Roy et al. 1983; Maganaris 2001; Maganaris, Baltzopoulos et al. 2001; Simoneau, Longo et al. 2012)</td>
</tr>
<tr>
<td>Total number of muscle fibres †</td>
<td>131500 (Young) (Jakobsson, Borg et al. 1988) 85150 (35% decrease with age (Deschenes 2004))</td>
</tr>
<tr>
<td>Fast Fibre Size</td>
<td>8070 ± 1850 μm² (Young) 5700 ± 1970 μm² (29% decrease with age) (Jakobsson, Borg et al. 1988)</td>
</tr>
<tr>
<td>Firing Rate †</td>
<td>18% decrease with age (McNeil, Doherty et al. 2005) <strong>Young firing rate range:</strong> 8-30 Hz.</td>
</tr>
<tr>
<td>Recruitment Distribution †</td>
<td><strong>Young:</strong> to 90.2% MVC (median: 26.3%; skewness: 0.641; kurtosis: -0.491) (Klass, Baudry et al. 2008)  <strong>Old:</strong> 0.4 to 64% MVC (median: 15.6%; skewness: 1.093; kurtosis: 0.781) (Klass, Baudry et al. 2008)</td>
</tr>
<tr>
<td>Specific Force †</td>
<td>30% decrease with age (Morse, Thom et al. 2005)</td>
</tr>
<tr>
<td>Contraction Time †</td>
<td>23% increase with age (McNeil, Doherty et al. 2005; Klass, Baudry et al. 2008)</td>
</tr>
</tbody>
</table>

† Age-altered parameter that is assigned a value of 1 to represent the elderly, and a value of 0 to represent the young, in the linear regression model.
‡Number of motor units was used to represent changes in the innervation ratio, and is modified to reflect the simulated innervation ratio to investigate its effect on the simulated torque.
6.4 Data Analysis

The first and last second of the simulated force was discarded, as the signal is transient in these segments. The mean value of the simulated torque was computed for the remaining data.

The relationship between firing rate, recruitment of motor units and force of muscle contraction is (Milner-Brown, Stein et al. 1973; Kukulka and Clamann 1981; Moritani and Muro 1987). In this study, we isolated the effect of changes in firing rate and motor unit recruitment due to MVC by normalising the group mean for different levels of MVC. This removes the effect of increased firing rate and increased number of motor units recruited with MVC on the simulated torque, so that any variations are exclusively due to the parameters simulated.

6.4.1 Regression Analysis

Prior to performing the regression analysis, the innervation ratio was computed as the ratio of the number of muscle fibres and number of motor units simulated, and this value was used in the regression model. Number of motor units are more commonly reported in ageing studies of the TA (Trojaborg, Kaufmann et al. 2002; McNeil, Doherty et al. 2005; Fling, Knight et al. 2009; McKinnon, Montero-Odasso et al. 2015) compared to the innervation ratio which is not well-studied (Feinstein, Lindegård et al. 1955; Gath and Stålberg 1981). Increased innervation ratio as assessed by EMG is often observed in the elderly (Kent-Braun and Ng 1999; McNeil, Doherty et al. 2005) and is a consequence of decreased motor unit numbers, but with minimal loss in muscle fibres. Therefore, for an accurate investigation of its effect on the simulated force generated, the parameter number of motor units is suitably modified to reflect the innervation ratio.

An initial linear regression analysis at $\alpha = 0.05$ was performed between all the simulated parameters, and their interactions (Table 6.1) and the simulated torque. In this model, parameters from Table 6.1 that are identified to have a specific age-related alteration were assigned a value of 1, while those corresponding to young were set to 0 as a reference point. The parameters were ranked based on the $p$ values, and those corresponding to higher $p$ values ($p>0.05$) had lower significance and were removed. Subsequently, the regression model was iteratively updated to reduce Root Mean Square Error (RMSE) until minima was
Relative Influence of Neuromuscular Properties on Torque

obtained. The parameters and corresponding RMSE was recorded. The relative effect of the neuromuscular parameters on torque was measured using standardised slope coefficients.

6.5 Results

Table 6.1 lists all the neuromuscular parameters that were used to analyse the model. Figure 6.1 shows the standardised slope coefficient for the neuromuscular parameters that have significant effect (p<0.05) on simulated torque. Five parameters had direct significant effect - firing rate, number of muscle fibres, specific force, pennation angle, and innervation ratio. While two had significant interaction effect - fast-slow fibre ratio with innervation ratio and

**Figure 6.1** The relative influences of the neuromuscular properties on the resultant force measured by standardised slope coefficients. All standardised slope coefficients were significant p < 0.05.

Table 6.1 lists all the neuromuscular parameters that were used to analyse the model. Figure 6.1 shows the standardised slope coefficient for the neuromuscular parameters that have significant effect (p<0.05) on simulated torque. Five parameters had direct significant effect - firing rate, number of muscle fibres, specific force, pennation angle, and innervation ratio. While two had significant interaction effect - fast-slow fibre ratio with innervation ratio and...
fast fibre diameter. The recruitment distribution, contraction time, and fibre length were found to be below the significant $\alpha = 0.05$ threshold.

Estimation of the torque from the regression model with values corresponding to the elderly showed reduction in the torque produced at the ankle. Table 6.2 shows the reduction in torque produced by parameter values corresponding to the elderly reported in literature. It is observed that single biggest cause of reduction in torque was due to age-expected reduction in firing rate which caused 19.6% drop in torque. The total reduction in torque due to the combined effect of all the parameters was 35.2%.

Table 6.2 Percentage loss in simulated torque estimated from the regression model due to individual neuromuscular property altered with age based on literature.

<table>
<thead>
<tr>
<th>Age-Related Change in Parameter</th>
<th>Change in simulated torque</th>
</tr>
</thead>
<tbody>
<tr>
<td>18% decrease in firing rate (McNeil, Doherty et al. 2005)</td>
<td>-19.6%</td>
</tr>
<tr>
<td>35% decrease in muscle fibres (Deschenes 2004)</td>
<td>-6.7%</td>
</tr>
<tr>
<td>30% decrease in specific force (Morse, Thom et al. 2005)</td>
<td>-7.2%</td>
</tr>
<tr>
<td>62% increase in innervation ratio estimated by the ratio of muscle fibres and 40% remaining motor units (McNeil, Doherty et al. 2005)</td>
<td>-2.7%</td>
</tr>
<tr>
<td>Interaction of innervation ratio and 50% loss of fast fibres (Jakobsson, Borg et al. 1988)</td>
<td>1.5%</td>
</tr>
<tr>
<td>Interaction of fast-slow fibre ratio and 29% decrease in fast-fibre diameter (Jakobsson, Borg et al. 1988)</td>
<td>-0.5%</td>
</tr>
<tr>
<td><strong>Total Loss</strong></td>
<td><strong>-35.2%</strong></td>
</tr>
</tbody>
</table>
6.6 Discussion

The results show that simulation of the force model accurately predicts the age-associated reduction in the torque. The simulated decline of 35% is similar to experimental observation for elderly aged 80+ years (McNeil, Doherty et al. 2005; McNeil, Vandervoort et al. 2007).

This study shows that changes to firing rate of the Tibialis Anterior were the most influential in regulating the ankle torque. This was followed by number of muscle fibres, specific force, pennation angle, innervation ratio, fast-slow fibre ratio and fast fibre size. The relative influence of the neural and muscular factors to strength regulation observed in the simulation study concurs with experimentally obtained strength training and de-training literature (Häkkinen K and PV. 1983; Narici, Roi et al. 1989; Gondin, Guette et al. 2006). These relationships are discussed in the following sections.

6.6.1 Firing Rate

The simulation study shows that decreased firing rate is a major contributor to reduced torque. This concurs with the exercise studies that have shown that initial strength gains are primarily due to increased neural drive with later gains due to muscular properties (Häkkinen K and PV. 1983; Narici, Roi et al. 1989; Gondin, Guette et al. 2006). Strength loss during detraining followed the reverse process, i.e. decreased neural drive, followed by deterioration of muscular properties (Häkkinen K and PV. 1983; Gondin, Guette et al. 2006).

There are a number of causes for reduced firing rate. The three main causes are:

(i) Decreased cortical excitability (Rossini, Desiato et al. 1992; Peinemann, Lehner et al. 2001; Oliviero, Profice et al. 2006; Manini, Hong et al. 2013; Sale, Lavender et al. 2016)
(iii) Altered coactivation (Klein, Rice et al. 2001).

6.6.2 Motor Unit Remodelling and Loss of Muscle Mass

Age-associated motor unit remodelling is an increase in innervation ratio and decreased fast-slow fibre ratio due to the selective atrophy of fast fibres (R Deschênes 2011). The simulation shows that both increased innervation ratio and reduction in fibre diameter can contribute to loss of strength (Krivickas, Dorer et al. 2011).
Experimental studies show that motor unit remodelling in the TA may not significantly reduce strength until a critical threshold of motor units has been reached (McNeil, Doherty et al. 2005; McKinnon, Montero-Odasso et al. 2015). At this threshold, loss of muscle fibres due to impaired reinnervation is likely to be the cause of decreased strength (Kent-Braun and Ng 1999; McNeil, Doherty et al. 2005). This is demonstrated by the simulation results (Figure 6.1) that show the effect of loss of muscle fibres is much more prominent in comparison to motor unit remodelling.

6.6.3 Pennation Angle and Fibre Length

The simulation shows pennation and torque to be negatively correlated, but no significant correlation was found with the fibre length. The lack of a relation between torque generated and fibre length could be because sarcomeres in series are responsible for shortening speed, while sarcomeres in parallel are responsible for maximal voluntary force (Narici and Maganaris 2006).

There is no age-associated decrease reported in the pennation angle of the TA (Jesunathadas, Rudroff et al. 2010); however, the pennation angle reported in literature for the TA is quite varied (Wickiewicz, Roy et al. 1983; Maganaris 2001; Simoneau, Longo et al. 2012). Hence, variations and/or reductions in pennation angle can increase variability of the torque measured.

6.6.4 Specific Force

Specific force is the force generated per cross-sectional area of the muscle. Simulation has determined that decrease in this is a prominent factor to decline in muscle strength. Decreased number of actin-myosin cross bridges (D'Antona, Pellegrino et al. 2003), excitation-contraction uncoupling (Renganathan, Messi et al. 1997) and changes in the muscle architecture (Morse, Thom et al. 2005) are responsible for altered specific force. The TA is reported to maintain its specific force up till the 8th decade (Kent-Braun and Ng 1999; McKinnon, Montero-Odasso et al. 2015), but decline in specific force with advanced aging can account for the majority of strength loss in absence of other neuromuscular alterations (McNeil, Vandervoort et al. 2007).
6.6.5 Other Non-significant parameters

Altered recruitment pattern, fibre length and slowed contraction time were not found to significantly affect the torque in comparison to other factors. However, recruitment pattern and contraction time, though not investigated in this study, could affect the steadiness of the torque (Patten and Kamen 2000; Jesunathadas, Klass et al. 2012).

6.6.6 Limitations of this Study

There are some neuromuscular factors that have not been explored by this study as they have not been explicitly modelled in the sEMG and force model use.: These factors include changes in the neuromuscular junction (Manini, Hong et al. 2013), excitation-contraction uncoupling (Renganathan, Messi et al. 1997), alterations in the tendon (Narici and Maganaris 2006) and infiltration of fat (Delmonico, Harris et al. 2009). However, these could be considered from the reduction in specific force (D'Antona, Pellegrino et al. 2003; Narici and Maganaris 2006).

6.6.7 Novelty and Applications of this Study

This simulation study has investigated the most widely reported alterations in the TA musculature to investigate their relative effects on the torque generated. A comprehensive simulation of the reported neuromuscular properties in the TA has been performed, and consideration given to interaction effects amongst the properties. This is valuable for future experimental studies to consider when assessing the relative effects of altered neuromuscular properties on TA’s muscle strength for a more targeted strength preservation strategy in the elderly.
6.7 Summary

This Chapter addresses Research Question 1: ‘What are the relative influences of the neural and muscular factors on muscle strength decline with aging in the Tibialis Anterior?’ A detailed force model of the TA developed in Chapter 5 was used to evaluate the relative contributions of neuromuscular properties on torque generated. The effects of neuromuscular properties on torque were standardised for comparison of their influence. Neural drive as assessed by firing rate was the most prominent effect on torque, followed by muscular factors: number of muscle fibres, specific force, pennation angle, and motor unit remodelling. This study presents valuable information for future experimental investigations and strength rehabilitation strategies for the senescent TA muscle.

The following chapter will quantify the age-associated sEMG changes found in Chapter 4 to neuromuscular changes with the use of the sEMG and force model developed in Chapter 5. It will further quantify the effect of age-altered neuromuscular properties (determined to occur in the older cohorts of this study) on the force exerted.
Chapter 7

7 Surface Electromyogram Simulation of Aging Tibialis Anterior and Changes in Muscle Force

7.1 Introduction

Dynapenia is the age-associated loss of muscle strength that occurs due to numerous age-related neuromuscular changes and can impact quality of life (Clark and Manini 2008; Manini and Clark 2011). Neuromuscular assessments are typically performed by invasive and painful procedures such as biopsies and needle EMG, which is not suitable for frailer, elderly people. Hence, there is a need to assess these changes non-invasively and identify their contribution to strength loss for timely and targeted strength preservation strategies in the elderly (Clark and Manini 2008; Clark, Law et al. 2015).

Age-related changes in the neuromuscular system are known to manifest as alterations in the surface electromyogram, an easy to record non-invasive electrical signal (sEMG) (Huppertz, Desselhorst-Klug et al. 1997; Meigal, Rissanen et al. 2009; Arjunan and Kumar 2013; Siddiqi, Poosapadi et al. 2015). Several sEMG features have been heuristically studied to identify age-associated neuromuscular changes (Kaplanis, Pattichis et al. 2009; Meigal, Rissanen et al. 2009; Arjunan, Wheeler et al. 2013; Siddiqi, Poosapadi et al. 2015). These studies give an indication of a neuromuscular alteration, but cannot quantify them from the sEMG changes. Extracting the altered neuromuscular property from the modified sEMG signal feature requires an in-depth understanding of their relationship, which can be achieved through computational models of the sEMG (Merletti, Roy et al. 1999; Farina and Merletti 2001; Merletti, Farina et al. 2002; Wheeler, Kumar et al. 2011; Zhao and Li 2012).

This Chapter addresses Research Q1b (‘Can the age-related surface electromyogram changes be quantified into neuromuscular changes in the older participants?’) by using the sEMG and Force model developed and validated in Chapter 5. This model will be used to delineate age-related neuromuscular changes in the Tibialis Anterior (TA) from the recorded sEMG, and their impact on isometric force simulated. The sEMG model was used to simulate several
SEMG simulation of Aging TA

aging conditions with increasing severity of neuromuscular alterations. The power spectrum and higher order statistics computed from the sEMG was used to distinguish between the simulated conditions that best described the aging cohort studied.

7.2 Methods and Materials

7.2.1 Participants

Thirty-six volunteers with equal number of young and older cohorts (details in Table 7.1) with no clinical history of neuromuscular disease or ankle injury participated in this study. The experimental protocol was approved by RMIT University Human Research Ethics Committee (Ethics project reference no: 15751 (40/13)) and in accordance with Helsinki Declaration (revised 2004).

Table 7.1 Details of the participants; number, age, height, and body mass index.

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (years)</th>
<th>Height (cm)</th>
<th>Body Mass Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Young (n = 18)</td>
<td>26.1 ± 2.9 (20 – 30)</td>
<td>166.7 ± 8.9</td>
<td>22.3 ± 2.9 kg m⁻²</td>
</tr>
<tr>
<td>Old (n = 18)</td>
<td>67.7 ± 8.1 (60 – 85)</td>
<td>163.2 ± 9.1</td>
<td>26.0 ± 3.9 kg m⁻²</td>
</tr>
</tbody>
</table>

7.2.2 SEMG Recordings

Myomonitor 4 (Delsys, Boston, USA) was used to record the sEMG activity which had a gain of 1000, CMRR of 92 dB and bandwidth of 20-450 Hz, with 12 dB/ octave roll-off. The sampling frequency was set to 1000 Hz with a resolution of 16 bits/ sample. The Delsys single-channel active differential silver bar (1 mm x 1 mm) surface electrodes with an embedded preamplifier and inter-electrode distance of 10 mm were used. The skin at the electrode locations were shaved, abraded and cleansed with an alcohol swipe. SEMG and force recordings were performed concurrently during the experiment.

The electrode placement and skin preparation was done in accordance with SENIAM recommendations (SENIAM 2009). SEMG activity was recorded from the dorsiflexor, TA. The surface electrode was placed at 1/3rd on the line between the tip of the fibula and the tip
of the medial malleolus (SENIAM 2009) and the ground electrode was placed at the patella (Billot, Simoneau et al. 2010) (Figure 7.1).

The Tricep Surae’s sEMG was also recorded to measure the coactivation level and therefore, its antagonistic force during dorsiflexion. This was performed to obtain the experimental agonist force of the TA for comparison with the simulated force. The electrodes were placed on the recommended locations (SENIAM 2009) as described below:

Soleus (SOL): few centimetres from where the gastrocnemii join the Achilles tendon on the midline of the leg.

Medial Gastrocnemius (MG): On the most prominent bulge of the muscle belly.

Lateral Gastrocnemius (LG): 1/3rd of the line between the head of the fibula and the heel.

![Figure 7.1 Experimental setup for isometric dorsiflexion and plantarflexion of the ankle and the sEMG electrode placement for Tibialis Anterior and Triceps Surae.](image)

7.2.3 Experimental Protocol

Participants sat in a sturdy chair with their right leg strapped to a support such that the hip, knee and ankle were at 90°, 140° and 90° (neutral position), respectively. The left foot was positioned firmly on the floor. A force sensor, SM-100 type (Interface, Arizona, USA) was attached to measure the isometric force applied to the fixed footplate. The right foot and ankle was secured with straps to the footplate (Siddiqi, Arjunan et al. 2015) to ensure lack of
foot or toe movement during dorsiflexion, and heel lift during plantarflexion (Siddiqi, Arjunan et al. 2015) (Figure 7.1).

The participants were trained to produce their true maximal voluntary contraction (MVC) during both isometric plantar- and dorsiflexion (DF). They were given visual feedback of their exerted torque and verbal encouragement to elicit their MVC. They repeated the MVC trials until their consecutive force recordings differed less than 5%. The trained participants performed two isometric dorsiflexion at 10%, 20%, 30%, 50%, 75%, and 100% MVC, for 5s, with a 2 minute rest between each trial.

The antagonist force produced by the TS was quantified using an EMG-force relationship constructed for the TS during plantarflexion (PF) (Baratta, Solomonow et al. 1988). Participants were instructed to perform several submaximal contractions at 10%, 20%, 30%, and 50% MVC for 5 seconds and a 2 minute rest period between each trial.

7.2.4 Simulation Protocol

7.2.4.1 SEMG simulation

The surface EMG and force model developed for the Tibialis Anterior was used in this chapter, and its details are presented in Chapter 5. The model was used to simulate three different losses of motor units ten times at six different aging conditions based on literature (Table 7.2) using the sEMG model. The aging conditions emulate increasing changes in the neuromuscular system due to aging. This was done at 10%, 20%, 30%, 50%, 75%, and 100% MVC, similar to the experimental recordings.

In summary, 3 motor unit losses x 6 different aging conditions x 6 MVC levels x 10 repetitions of simulations were performed, and 6 MVC levels x 10 repetitions of simulation was performed with the Young Model values listed in Table 7.2. A total of 1,140 simulations were conducted.

7.2.4.2 Force Simulation

After determining the aging condition that best suited the older cohorts of this study, the Young Model’s parameters were replaced one at a time by each age-altered parameter and the force model simulated at 100% MVC. The change in force from the Young Model’s force value due to each altered parameter was calculated. Lastly, the Young Models’ parameters
were replaced by all of the age-altered parameters and the force model simulated. The total change in simulated force due to aging was calculated.

**Table 7.2 Young and Aging parameters for simulation.**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Increasing severity of aging</th>
<th>Aging Model Value</th>
<th>Young Model Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>40 – 60% loss of Motor Units without loss of muscle fibres (McNeil, Doherty et al. 2005; Power, Dalton et al. 2010)</td>
<td>144, 180, 216</td>
<td>360</td>
</tr>
<tr>
<td>B</td>
<td>Decreased number of motors and fast-slow fibre ratio.</td>
<td>0.16 (Jakobsson, Borg et al. 1988)</td>
<td>0.3 (Johnson, Polgar et al. 1973; Henriksson-Larsén, Lexell et al. 1983)</td>
</tr>
<tr>
<td>C</td>
<td>Decreased number of motors, fast-slow fibre ratio and fast fibre diameter.</td>
<td>29 % decrease (Jakobsson, Borg et al. 1988)</td>
<td>8070 μm² (Jakobsson, Borg et al. 1988)</td>
</tr>
<tr>
<td>D</td>
<td>Decreased number of motors, fast-slow fibre ratio, altered recruitment pattern.</td>
<td>Old: 0.4 to 64% MVC (median: 15.6% MVC; skewness: 1.093; kurtosis: 0.781) (Klass, Baudry et al. 2008)</td>
<td>Range: 1% - 90.2% MVC (median 26.3% MVC, skewness: 0.641 ; Kurtosis -0.491)(Klass, Baudry et al. 2008)</td>
</tr>
<tr>
<td>E</td>
<td>Decreased number of motors, fast-slow fibre ratio, fast fibre diameter and altered recruitment pattern.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>Decreased number of motors, fast-slow fibre ratio, fast fibre diameter and altered recruitment pattern and total number of muscle fibres.</td>
<td>35% decrease (Deschenes 2004)</td>
<td>131 000 fibres (Henriksson-Larsén, Lexell et al. 1983)</td>
</tr>
</tbody>
</table>
Table 7.2 lists the 6 aging conditions A-F that simulate increasing severity of aging. Column 3 lists the corresponding aging value used in the simulation model. Column 4 lists the base model values for the young which is used to compare the age-associated change due to the six different aging conditions at 3 different losses of motor units.

7.3 Data Analysis

7.3.1 Surface Electromyogram Data Analysis

The first and last one second of both the experimental and simulated sEMG was discarded as the force was usually transient in these sections.

A single feature would not be sufficient to classify all the neuromuscular alterations that occur with aging as various neuromuscular alterations can affect the sEMG signal properties differently (Disselhorst-Klug, Silny et al. 1998; Meigel, Rissanen et al. 2009). Signal processing techniques that assess separate attributes of the sEMG need to be used to wholly discern these neuromuscular changes (Morrison and Newell 2012).

The following features were calculated to measure expected age-related changes (Disselhorst-Klug, Silny et al. 1998; Farina, Merletti et al. 2004; Istenič, Kaplanis et al. 2010; Zhao and Li 2012) (Table 7.3) for both the experimental and simulated sEMG:

1. **Power spectral density**: The power spectrum of the sEMG depends on the muscle fibre membrane properties, and the timing of the MUAP (Farina, Merletti et al. 2004). Therefore, the sEMG’s power spectral density (PSD) was calculated using epoch lengths of 512 points and a 25% overlap (Inbar, Paiss et al. 1986). The peak of the power spectral density curve (PSD) was determined and is defined as the maximal power in dB ($P_M$) of the PSD. $P_M$ was computed as $10\log_{10}P_{xx}$ where $P_{xx}$ is the power spectral density ($V^2 \text{Hz}^{-1}$) computed. This was used to measure changes in the sEMG’s amplitude due to motor unit remodelling, decreased muscle fibre size or loss of muscle fibres (Table 7.3).

2. **Bispectral analysis**: Fourier transform of the third order cumulant (a higher order statistic, representing the skewness) is known as the bispectrum. Based on Hinich’s non-skewness test (Hinich 1982), the Gaussianity test statistic ($S_g$) and the Linearity Test Statistics ($S_l$) are computed. Briefly, the sEMG’s bicoherence will be constant and zero if the sEMG is a linear and Gaussian process, respectively. It follows that the $S_g$ which is the mean bicoherence power will be chi-squared distributed for a Gaussian process (Kaplanis, Pattichis...
et al. 2009). Likewise, the difference between the theoretical, and the estimated inter-quartile range, derived from the estimated mean bicoherence power is the $S_l$ which will be less than twice the theoretical inter-quartile range for a constant bicoherence (Kaplanis, Pattichis et al. 2009). $S_g$ and $S_l$ were computed because they have been found to be correlated with number of active motor units (Zhao and Li 2012).

**Table 7.3** Age-related changes in the physiology, sEMG and its features.

<table>
<thead>
<tr>
<th>Age-related Alteration</th>
<th>Corresponding changes to MUAP</th>
<th>Expected effect on sEMG</th>
<th>Expected change in sEMG feature</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Motor Unit Remodelling</strong></td>
<td>Increased time between adjacent MUAP (Disselhorst-Klug, Silny et al. 1998)</td>
<td>EMG pattern becomes sparser, EMG amplitude distribution centred closer around zero (Disselhorst-Klug, Silny et al. 1998; Istenič, Kaplanis et al. 2010)</td>
<td>Higher Order Statistics: Measure deviation from a Gaussian distribution Increased Gaussianity and Linearity Test Statistic (Zhao and Li 2012).</td>
</tr>
<tr>
<td>Decreased Number of Motor Units due to denervation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased Existing Motor Unit Size, due to reinnervation</td>
<td>Increased MUAP amplitude (Disselhorst-Klug, Silny et al. 1998)</td>
<td>Increased EMG amplitude</td>
<td>Increased Peak Power of the PSD (Farina, Merletti et al. 2004).</td>
</tr>
<tr>
<td><em>Atrophied fast fibres, decreased Muscle Fibre Size and Number</em></td>
<td>Decreased MUAP amplitude (Disselhorst-Klug, Silny et al. 1998)</td>
<td>Decreased EMG amplitude</td>
<td>Decreased Peak Power of the PSD (Farina, Merletti et al. 2004).</td>
</tr>
</tbody>
</table>

**Table 7.3** lists the age-related changes in the neuromuscular system, its effect on the MUAP property, and corresponding effect on the sEMG. Higher order statistics have been selected to investigate decreased number of motor units, and peak of the power spectral density curve has been selected to measure changes in the sEMG amplitude due to increased innervation ratio or decreased number of muscle fibres.
7.3.2 Computation of Age-related difference in the simulated and experimental sEMG features

The sEMG features (maximal power of the PSD, $S_g$, and $S_l$) calculated from one simulated aging condition’s sEMG was subtracted from the sEMG features computed from the Young Model at the 6 MVCs (Equation 7.1, 7.2, 7.3). This was repeated for each of the 6 aging conditions simulated (Table 7.2).

$$\Delta S_g (MVC) = S_g (% Motor Unit Loss, Aging Condition, MVC) - S_g (Young Model, MVC)$$  \hspace{1cm} (7.1)

$$\Delta S_l (MVC) = S_l (% Motor Unit Loss, Aging Condition, MVC) - S_l (Young Model, MVC)$$  \hspace{1cm} (7.2)

$$\Delta P_M (MVC) = P_M (% Motor Unit Loss, Aging Condition, MVC) - P_M (Young Model, MVC)$$  \hspace{1cm} (7.3)

The age-related difference between the experimental sEMG features: maximal power of the PSD, $S_g$, and $S_l$, was also computed at the 6 measured MVCs.

7.3.3 Experimental Force Data Analysis

To estimate the agonist dorsiflexion force, the antagonistic force of the TS needs to be computed. The antagonist force produced by the TS was estimated using the EMG/force relationship constructed for the TS (Baratta, Solomonow et al. 1988). The antagonist force was added to the resultant dorsiflexion force to obtain the agonist dorsiflexion force (Billot, Simoneau et al. 2010)

7.4 Statistical Analysis

7.4.1 Protocol to determine the aging condition

The best aging condition that describes the older cohorts of this study was determined in two steps:

(i) The Pearson Correlation was computed between two calculated differences with increasing MVC. The first difference is the experimental age-related change in the higher order statistics: $\Delta S_g$(experiment), $\Delta S_l$(experiment). The second difference is in the higher order statistics calculated for the simulated aging conditions, A and D, at 3 different losses of motor units from the Young Models $S_g$ and $S_l$ values described in section 7.2.4.1 and
illustrated in Figure C.1 and C.2 (Appendix C). A total of 6 Pearson’s correlation coefficients were computed for each higher order statistic (detailed in Table 7.4).

Only aging conditions with significant positive correlations were selected. The percentage loss in motor units and the presence/absence of altered recruitment pattern (Condition D/A) in the older cohorts was determined by selecting the strongest correlation for \( S_g \) and \( S_l \). If there was a disparity between the selected condition from the \( S_g \) and \( S_l \) statistics, preference was given to the condition selected by \( S_g \) as its relation to number of motor units is well established in literature (Kapelanis, Pattichis et al. 2009; Zhao and Li 2012; Siddiqi, Poosapadi et al. 2015).

Table 7.4 The Pearsons Correlation Coefficient computed between the experimental age-related change in higher order statistics, and difference calculated for the simulated aging conditions A and D at different losses of motor units.

<table>
<thead>
<tr>
<th>Experimental Age-related Difference in higher order statistics</th>
<th>Simulated Aging Conditions Difference from the Young Models’ estimated in the higher order statistics</th>
<th>Pearsons Correlation Coefficients</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \Delta S_g(\text{experiment}) )</td>
<td>( \Delta S_g(40%\text{Motor Unit Loss,Condition A}) )</td>
<td>( \rho_{1,1} )</td>
</tr>
<tr>
<td></td>
<td>( \Delta S_g(50%\text{Motor Unit Loss,Condition A}) )</td>
<td>( \rho_{1,2} )</td>
</tr>
<tr>
<td></td>
<td>( \Delta S_g(60%\text{Motor Unit Loss,Condition A}) )</td>
<td>( \rho_{1,3} )</td>
</tr>
<tr>
<td></td>
<td>( \Delta S_g(40%\text{Motor Unit Loss,Condition D}) )</td>
<td>( \rho_{1,4} )</td>
</tr>
<tr>
<td></td>
<td>( \Delta S_g(50%\text{Motor Unit Loss,Condition D}) )</td>
<td>( \rho_{1,5} )</td>
</tr>
<tr>
<td></td>
<td>( \Delta S_g(60%\text{Motor Unit Loss,Condition D}) )</td>
<td>( \rho_{1,6} )</td>
</tr>
<tr>
<td>( \Delta S_l(\text{experiment}) )</td>
<td>( \Delta S_l(40%\text{Motor Unit Loss,Condition A}) )</td>
<td>( \rho_{2,1} )</td>
</tr>
<tr>
<td></td>
<td>( \Delta S_l(50%\text{Motor Unit Loss,Condition A}) )</td>
<td>( \rho_{2,2} )</td>
</tr>
<tr>
<td></td>
<td>( \Delta S_l(60%\text{Motor Unit Loss,Condition A}) )</td>
<td>( \rho_{2,3} )</td>
</tr>
<tr>
<td></td>
<td>( \Delta S_l(40%\text{Motor Unit Loss,Condition D}) )</td>
<td>( \rho_{2,4} )</td>
</tr>
<tr>
<td></td>
<td>( \Delta S_l(50%\text{Motor Unit Loss,Condition D}) )</td>
<td>( \rho_{2,5} )</td>
</tr>
<tr>
<td></td>
<td>( \Delta S_l(60%\text{Motor Unit Loss,Condition D}) )</td>
<td>( \rho_{2,6} )</td>
</tr>
</tbody>
</table>
(ii) After narrowing the specific loss in motor units, a Pearson correlation was calculated between (a) the experimental age-related change in maximal power of the PSD ($\Delta P_M$(experiment)), and (b) the difference in maximal power calculated for all of the aging conditions (A-F) at that number of motor units (Table 7.5). This is shown in Figure C.3 (Appendix C). A total of 6 Pearson’s correlation coefficient was computed. The aging condition that had the strongest significant positive correlation was selected.

Table 7.5 The Pearson's Correlation Coefficient computed between the experimental age-related change in maximal power of the PSD, and difference calculated for the simulated aging conditions A to F at estimated percentage loss of motor units.

<table>
<thead>
<tr>
<th>Experimental Age-related Difference in maximal power of the PSD</th>
<th>Simulated Aging Conditions Difference from the Young Models’ estimated in the maximal power of the PSD at the specified motor unit loss.</th>
<th>Pearson's Correlation Coefficients</th>
</tr>
</thead>
<tbody>
<tr>
<td>($\Delta P_M$(experiment))</td>
<td>$\Delta P_M$(Condition A)</td>
<td>$\rho_{3,1}$</td>
</tr>
<tr>
<td></td>
<td>$\Delta P_M$(Condition B)</td>
<td>$\rho_{3,2}$</td>
</tr>
<tr>
<td></td>
<td>$\Delta P_M$(Condition C)</td>
<td>$\rho_{3,3}$</td>
</tr>
<tr>
<td></td>
<td>$\Delta P_M$(Condition D)</td>
<td>$\rho_{3,4}$</td>
</tr>
<tr>
<td></td>
<td>$\Delta P_M$(Condition E)</td>
<td>$\rho_{3,5}$</td>
</tr>
<tr>
<td></td>
<td>$\Delta P_M$(Condition F)</td>
<td>$\rho_{3,6}$</td>
</tr>
</tbody>
</table>
7.5 Results

The results are represented as bar graphs of the Pearson’s correlation coefficient computed between the simulated and experimental age-associated differences for the various aging conditions. These are detailed in Table 7.4 and Table 7.5

Figure 7.2 shows the correlation coefficients computed between the experimental and simulated age-related difference in the higher order statistics: (a) $S_g$ and (b) $S_l$ for aging conditions A and D, at 3 different motor unit losses. The higher order statistics were used to distinguish between the losses of motor units and to determine if the recruitment pattern was altered. The results show a significant correlation for the aging condition A with 216 remaining motor units, corresponding to a 40% loss of motor units.

Figure 7.3 shows the significant correlation coefficient computed between the experimental and simulated age-related difference in the maximal power of the PSD. This feature was used to distinguish any further muscular changes that may have occurred with age. The results show only condition B corresponding to decreased fast-slow fibres, with 216 remaining motor units had a significant correlation.
Figure 7.2 The pearsons correlation coefficients computed between experimental and simulated sEMG differences in a) Gaussianity Test Statistic $S_g$ and (b) Linearity Test Statistic $S_l$. The experimental difference was the age-associated change in the experimental sEMG’s higher order statistics with MVC. The simulated change was between the Young Models and the simulated sEMGs higher order statistics for two aging conditions, A- motor unit loss, and D- altered recruitment pattern, at three motor unit losses. (**) significant correlation coefficient $p < 0.05$. 
Figure 7.3 The Pearson's correlation coefficients computed between experimental and simulated sEMG differences in maximal power of the PSD. The experimental difference was the age-associated change in the experimental sEMG’s maximal power with MVC. The simulated change was between the Young Models and the simulated sEMG’s maximal power for six aging conditions, A-F, at a 40% loss in motor units. (**) significant correlation coefficient p < 0.05.

Figure 7.4 shows the change in experimental agonist dorsiflexion force with age, and the change in simulated force due to the different age-altered properties and their combined effect. The loss in simulated force was greatest due to loss of fast-fibres, but the combined effect of loss of motor units and decreased fast-fibres is less. This is because in the absence of loss in total number of muscle fibres, the decreased number of motor units reflected increased innervation ratio. The increased size of the motor units could have moderated the effect of loss of fast fibres. The experimental age-related change in force was not significant (p = 0.1362).
The percentage change in experimental and simulated force due to the combined and individual age-altered change in motor units and fast fibres.

### 7.6 Discussion

The results show that the higher-order statistics were able to distinguish between differing losses of motor units simulated, while the power spectrum further discriminated changes in the musculature. A 40% loss of motor units with halved the number of fast fibres best represented the age-related change in the experimental sEMG features. This change corresponded to an 8% decrease in simulated force. The ability of the sEMG features to distinguish between aging conditions and the effect of altered neuromuscular properties on strength decline is discussed.

#### 7.6.1 SEMG features and Aging

The aging conditions varied in severity to simulate the exacerbation of the neuromuscular system that occurs with age. The higher-order statistics and the power spectrum were used to distinguish amongst the aging conditions and numbers of motor units.

The higher-order statistics, Gaussianity ($S_g$) and Linearity Test Statistics ($S_l$), have been shown to be non-linearly correlated with the number of active motor units (Zhao and Li 2012). The power spectral features are influenced by several other neuromuscular properties in addition to number of motor units and recruitment pattern (Farina, Merletti et al. 2004).
The different sensitivity of the power spectral and higher-order statistics to neuromuscular factors was exploited to discriminate between the various aging conditions simulated.

The simulation concurs with experimental studies that have found a loss of 40% motor units to occur between 60-69 years of age (McNeil, Doherty et al. 2005; Power, Dalton et al. 2010), while the decrease in fast fibres tends to occur at the end of the 6th decade of life (Jakobsson, Borg et al. 1988; Power, Allen et al. 2014). A later study by Power, Allen et al. (2014) found only a 25% loss of motor units for cohorts aged 60 – 73 years, but they tested a much smaller sample of only 6 men.

The study also shows that it is important to assess different aspects of the sEMG signal properties to categorise the state of neuromuscular system better. The higher order test statistics were able to specify the loss of motor units, but the maximal power of the PSD further identified the atrophy of fast fibres.

### 7.6.2 Effect of Neuromuscular properties on strength decline

The simulation shows that decline in fast fibres causes the greatest change in force, but this is compensated by increased motor unit size. Ultimately, the total loss of simulated strength was only 8% with 40% loss of motor units and fast-slow fibre ratio of 0.16 from 0.3. The simulation is in line with studies that showed strength was not reduced despite a loss of 40% motor units (McNeil, Doherty et al. 2005; Power, Dalton et al. 2010), until the 8th decade (McNeil, Doherty et al. 2005; McNeil, Vandervoort et al. 2007), whereby an additional 33% motor units were lost (McNeil, Doherty et al. 2005). Maintenance of strength in the 6th decade of age could be due to the compensatory nature of motor unit remodelling that acts to preserve excitable mass (Desypris and Parry 1990).

Contrary to the simulation, the experimental results show a non-significant decline of 22%. The discrepancy between the simulation and experimental strength decline could be due to the larger age bracket and heterogeneous group tested. A similar loss of strength with 56% loss of motor units was found at an earlier age of 76 years by McKinnon, Montero-Odasso et al. (2015), who tested a heterogeneous group.
7.6.3 Limitations

Determining the altered neuromuscular properties in the older participants from the age-associated changes in the sEMG represents an inverse modelling problem. Inverse problems require a reduction in model parameters to obtain convergence to a solution if one exists (Groetsch and Groetsch 1993; Farina, Merletti et al. 2004). However, inverse problems can also result in multiple solutions which are not necessarily stable (Groetsch and Groetsch 1993).

In this study, the solution to the inverse problem posed was limited to three losses of motor units at six levels of age-associated degradation in the neuromuscular function. The combination of these aging conditions could have yielded similar age-associated changes, and therefore, multiple solutions (Appendix C, Section 11.3.1). This limitation was overcome by finding the strongest, significant correlation between experimental and simulated age-associated changes in the sEMG that enabled narrowing the potential solution. Nonetheless, a better understanding of the relationship between model parameters and sEMG signal features is needed, and the combinations of model parameters leading to similar sEMG signals investigated.

7.7 Summary

This Chapter addresses the Research Question 1b (‘Can we quantify the experimental age-related changes in the older cohorts using simulation?’) The Gaussianity and Linearity test statistics were able to specify the loss of motor units, while the maximal power of the power spectrum was able to distinguish between muscular changes. It found that the age-related differences in the sEMG features of the Tibialis Anterior were best explained by moderate motor unit remodelling. These changes corresponded to an 8% decrease in simulated force, despite a non-significant decline of 22% found in the experiment.

The following chapter address Research Question 2 that is investigating inhomogeneous aging of TA and TS muscles using sEMG.
Chapter 8

8 Inhomogeneous Age-Related Surface Electromyogram Changes between the Tibialis Anterior and Triceps Surae

8.1 Introduction

This chapter aims to investigate the difference in age-associated changes to Tibialis Anterior (TA) and Triceps Surae’s (TS) sEMG to determine inhomogeneous aging of TA and TS muscles. The power spectrum of the sEMG, coactivation of the TA and TS muscles and force of maximal voluntary contraction will be compared. The findings of this Chapter will answer Research Question 2 (‘Are there inhomogeneous age-associated changes in surface electromyogram of Tibialis Anterior and Triceps Surae due to different neuromuscular composition?’), and demonstrate that while examining the muscle strength of elderly, disproportionate changes in sEMG should be considered, failing which the disparity in the strength of ankle muscles may not be observed.

8.2 Inhomogeneous Aging of the Ankle Muscles

Tibialis Anterior (TA) and the Triceps Surae (TS) are opposing muscles at the ankle and important for locomotion and postural stability (Moreland, Richardson et al. 2004; Hale, Fergus et al. 2014). Their weakness can be detrimental for daily activities and this has been correlated with increased risk of falls (Moreland, Richardson et al. 2004; Hale, Fergus et al. 2014). Although not a unanimous finding (Vandervoort and McComas 1986; Simoneau, Billot et al. 2009), studies have shown that the performance of the TA and TS are differently altered with aging, with the TS showing a greater degradation (Simoneau, Martin et al. 2005; Simoneau, Martin et al. 2007; Hasson, Miller et al. 2011; Hasson and Caldwell 2012). Moreover, the deterioration of TS is also not uniform amongst its constituent muscles (Barber, Barrett et al. 2013).
An imbalance amongst the TA and TS muscles with aging would affect surface electromyogram (sEMG) measures that are used to investigate their neuromuscular function (McNeil, Doherty et al. 2005; Simoneau, Martin et al. 2007; Rodriguez-Falces, Izquierdo et al. 2014) or to represent muscle strength (Shao, Bassett et al. 2009; Amarantini and Bru 2015; Ravera, Crespo et al. 2016; Zhang, Guo et al. 2016). Disproportionate changes in the sEMG in the absence of strength deficits would thus violate the use of sEMG for estimating muscle activation. Earlier studies have investigated age-related changes in the TA (Connelly, Rice et al. 1999; McNeil, Doherty et al. 2005; Power, Allen et al. 2014; McKinnon, Montero-Odasso et al. 2015) and TS musculature (Morse, Thom et al. 2005; Dalton, McNeil et al. 2008; Dalton, Harwood et al. 2009; Barber, Barrett et al. 2013; Csapo, Malis et al. 2014), but there is no study that has simultaneously compared the sEMG changes of TA and TS. Therefore, it is not possible to confirm whether such examinations are appropriate.

8.3 Materials and Method

8.3.1 Participants

Thirty-six volunteers participated in this study; 18 young volunteers (age range: 20 – 30 years; height: 166.7 ± 8.9 cm; bmi: 22.3 ± 2.9 kg m⁻²) and 18 older volunteers (age range: 60 – 85 years; height: 163.2 ± 9.1; bmi: 26.0 ± 3.9 kg m⁻²) with no history of neuromuscular disease or ankle injury. The experimental protocol was approved by RMIT University Human Research Ethics Committee (Ethics project reference no: 15751 (40/13)) and in accordance with Helsinki Declaration (revised 2004).

8.3.2 Force and sEMG recording procedures

Participants sat on a custom built chair with their right leg strapped to a support fixing the hip, knee and ankle at 90°, 140° and 90° (neutral position) respectively while their left leg rested on the ground, (Figure 8.1). A SM100-type strain gauge force sensor (Interface S type) was used to measure the isometric force applied to the fixed footplate. The left leg was planted firmly on the ground. Absence of heel lift, and foot or toe movement during plantarflexion and dorsiflexion was ensured by securing the foot and ankle with straps to the footplate (Siddiqi, Arjunan et al. 2015).
The sEMG was recorded from the dorsiflexor Tibialis Anterior (TA), and plantar flexor: Triceps Surae (TS), comprising of m. soleus (SOL) and gastrocnemius (GAS), which is made up of m. medial gastrocnemius (MG), m. lateral gastrocnemius (LG) (Figure 8.1). The ground electrode was placed at the patella (Billot, Simoneau et al. 2010), while the electrodes with the exception of SOL were placed on the recommended locations (SENIAM 2009) as described below:

TA: 1/3rd on the line between the tip of the fibula and the tip of the medial malleolus.

SOL: few centimetres from where the gastrocnemii (GAS) join the Achilles tendon on the midline of the leg.

MG: On the most prominent bulge of the muscle belly.

LG: 1/3rd of the line between the head of the fibula and the heel.

The skin was prepared to ensure good contact prior to placement of electrodes. It was shaved, mildly abraded and cleansed with an alcohol swipe. The sEMG was collected using the Myomonitor 4 (Delsys, Boston) which had a gain of 1000, CMRR of 92 dB and bandwidth of

Figure 8.1 Experimental setup for performing isometric dorsi- and plantarflexion and the electrode locations for the TA and TS muscles.
Inhomogeneous Age-related sEMG changes between TA and TS

2-450 Hz, with 12 dB/octave roll-off. The sampling frequency was set to 1000 Hz with a resolution of 16 bits/sample. Delsys single-channel active differential silver bar (1 mm x 1 mm) surface electrodes with an embedded preamplifier and inter-electrode distance of 10 mm were used.

8.3.3 Experimental Protocol

Participants were encouraged to elicit their true isometric dorsiflexion and plantarflexion maximal voluntary contraction (MVC) using visual force feedback on the screen and verbal encouragement. They were also made to exert at their MVC for short time and repeat this until the consecutive recordings differed less than 5% from each other. Two minute rest was given between each attempt.

After obtaining the MVC of the participant, they were made to perform isometric dorsiflexion at 30% MVC for 5 seconds and were given visual feedback for identifying their 30% level. Submaximal contraction at 30% MVC were used because muscular changes maybe more evident at lower contractions (Siddiqi, Poosapadi et al. 2015) which could otherwise be masked at MVC due to increased interference of motor unit action potentials causing amplitude cancellation (Keenan, Farina et al. 2005). After two minute rest, they repeated this to obtain the second sample. After allowing rest to ensure that there was no fatigue, the above experiment was repeated for isometric plantarflexion.

Participants were also instructed to perform additional submaximal dorsi- and plantarflexion contractions at 10, 20, and 50% MVC for 5 seconds and a 2 minute rest period between each trial. These submaximal contractions were used to construct an EMG-force relationship for estimating the agonist TA and TS force (Baratta, Solomonow et al. 1988).

The data was observed and it was noticed that during the start and end of the exercise, the force of contraction was not steady but had transience. To ensure that the signal recordings were comparable and represented isometric contraction, the first and last one second of the sEMG and force recordings was discarded.
8.4 Data Analysis

8.4.1 SEMG analysis

Maximal power spectral density ($P_M$) is a measure of the gross signal strength and $P_M$ is a robust indicator of strength of muscle contraction (Kaplanis, Pattichis et al. 2009). Power Spectral Density (PSD) of the sEMG recordings for the 4 muscles was calculated for epoch lengths of 512 points with a 25% overlap (Inbar, Paiss et al. 1986). The peak power, $P_M$ was the maximum point of the PSD curve. $P_M$ was computed as $10\log_{10}P_{xx}$ where $P_{xx}$ is the power spectral density ($V^2 Hz^{-1}$) computed.

Coactivation of TA and TS was assessed at 30% MVC. Root Mean Square (RMS) of the TA and the collective TS muscles was computed, and the coactivation was measured as the ratio between the muscles’ antagonistic and agonist sEMG amplitude (Falconer and Winter 1985; Baratta, Solomonow et al. 1988).

8.4.2 Force Analysis

Direct muscular forces are not measurable; therefore, external force recordings are used to represent muscle strength. The antagonistic muscles’ contribution to the force recording may not be negligible and therefore needs to be considered when computing the true agonist force (Simoneau, Billot et al. 2009).

The antagonist TS force was estimated using Baratta, Solomonow et al. (1988) protocol which generates an EMG/force relationship for TS using submaximal contractions. The antagonistic TS force was added to the measured resultant TA force at 100% MVC to obtain the agonist TA force. Similarly, the antagonist TA force was estimated and summed with the TS’ resultant force measured at 100% PF MVC to obtain the TS’ agonist force.

8.5 Statistical Analysis

Statistical Analysis was performed using the R Stats Package (R Foundation for Statistical Computing, Vienna, Austria) (Team 2015). Prior to the analysis Shapiro-Wilk test (Razali and Wah 2011), was applied to the $P_M$ from the 4 muscles and it was determined that these were not normally distributed ($\alpha = 0.05$). Subsequently, the $P_M$ data was transformed using
the Aligned Rank Tool (ARTool) developed by Wobbrock et al (2011) (Wobbrock, Findlater et al. 2011) which addresses the need for performing factorial analysis on nonparametric data.

The ARTool aligns the response variable for each main or interaction effect by stripping all effects but one of interest from the response variable. The aligned responses are assigned ranks, and averaged in the case of ties. A full factorial ANOVA is performed on the aligned and ranked responses calculated for each effect. For more details, the reader is directed to (Wobbrock, Findlater et al. 2011; Wobbrock 2016).

### 8.5.1 Different age-related changes in the Maximal Power of the PSD between muscles

A 2-way ANOVA was performed on the transformed $P_M$ data with the factors being; age (Young and Old) and muscle type (TA, SOL, MG and LG) ($\alpha = 0.05$). A significant interaction between age and muscle type was further investigated by post hoc pairwise comparisons according to Wobbrock’s (2016) protocol for ARTool transformed data (Wobbrock 2016).

### 8.5.2 Differences in the Maximal Power of the PSD between muscles

The post-hoc contrasts tests for testing interactions described in Section 8.5.1 is unsuitable for testing the differences between muscle types levels ‘within the age’ factor (Wobbrock 2016). Please see (Wobbrock 2016) for more detailed explanation.

To determine the statistical significance of the difference between $P_M$ values of the four muscles for individual age group, a One-Way ANOVA ($\alpha = 0.05$) was performed separately for the young and old age groups where muscle type was the single factor. This was followed by a post hoc pairwise comparison ($\alpha = 0.05$) according to Wobbrock (2016) protocol to establish which of four muscles had significant differences.

### 8.5.3 Age-related differences in coactivation

The antagonistic coactivation values of TA and TS muscles were not normally distributed as investigated by the Shapiro-Wilk test ($\alpha = 0.05$) (Razali and Wah 2011). The nonparametric Wilcoxon rank sum test at $\alpha = 0.05$ was performed between the young and older cohorts for TA and TS antagonistic coactivation at 30% MVC.
8.5.4 Age-related differences in muscle strength

Shapiro- Wilk test (Razali and Wah 2011) found the TA and TS agonist force data to be normally distributed for both the young and older cohorts (p< 0.05). One-tail student t-test was performed to determine a significant age-related change in TA and TS muscle strength.

8.6 Results

8.6.1 Maximal Power of the PSD

Figure 8.2 shows the interaction plot of \( P_M \) between age (younger and older cohort) and muscle type at the 30% MVC. The values are represented by the median and the inter-quartile range since their distributions were not normal. The plot shows that \( P_M \) for TA and GAS (MG and LG) was greater among the older participants. However, no change was observed in SOL.

Table 8.1 shows the ANOVA results for the interaction of age and muscle type (\( p < 0.05 \)). Post-hoc analysis shown in Table 8.2 reveal that the TA’s age-related increase in \( P_M \) is significantly different to SOL and LG, but not to MG (\( \chi^2 (1,143) = 2.27, p= 0.3969 \)).

One-way ANOVA for the two age groups found a significant main effect of muscle type on \( P_M \) (Table 8.1). Post-hoc analysis are shown in Table 8.3 and these show that the \( P_M \) values of MG and LG were significantly different to TA and SOL for the young cohorts while for the older cohorts’ \( P_M \) for TA was significantly different to all 3 muscles of the TS.

Table 8.1 ANOVA results for the interaction of age and muscle type, and main effect of muscle type within young and old cohorts at significance level \( \alpha = 0.05 \) at 30% MVC.

<table>
<thead>
<tr>
<th>Effect</th>
<th>F statistic</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age*Muscle</td>
<td>F (3, 143) = 5.18</td>
<td>0.0023</td>
</tr>
<tr>
<td>Muscle (Within Young)</td>
<td>F(3, 71) =14.88</td>
<td>( p&lt;0.0001 )</td>
</tr>
<tr>
<td>Muscle (Within Old)</td>
<td>F(3, 71) = 44.70</td>
<td>( p&lt;0.0001 )</td>
</tr>
</tbody>
</table>
Inhomogeneous Age-related sEMG changes between TA and TS

**Table 8.2** Post-hoc pairwise comparisons for the significant interaction effect of age and muscle type at 30% MVC.

<table>
<thead>
<tr>
<th>Contrast Pairs</th>
<th>$\chi^2 (1,143) =$</th>
<th>$p$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TA-SOL</td>
<td>14.13</td>
<td>0.0010</td>
</tr>
<tr>
<td>TA-LG</td>
<td>7.04</td>
<td>0.0400</td>
</tr>
</tbody>
</table>

**Figure 8.2** Interaction plot between muscle type and age group for the maximal power of the PSD of the sEMG at 30% MVC. Median PM values are used with the whiskers representing the inter-quartile range.
Table 8.3 Post-hoc pairwise comparisons for the significant main effect of muscle type within young and old cohorts at 30% MVC.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Contrast Pairs</th>
<th>( t(71) = )</th>
<th>( p )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Young</td>
<td>LG-SOL</td>
<td>-4.12</td>
<td>0.0006</td>
</tr>
<tr>
<td></td>
<td>LG-TA</td>
<td>-4.94</td>
<td>( p&lt;0.0001 )</td>
</tr>
<tr>
<td></td>
<td>MG-SOL</td>
<td>-4.43</td>
<td>0.0002</td>
</tr>
<tr>
<td></td>
<td>MG-TA</td>
<td>-5.25</td>
<td>( p&lt;0.0001 )</td>
</tr>
<tr>
<td>Old</td>
<td>LG-SOL</td>
<td>-5.91</td>
<td>( p&lt;0.0001 )</td>
</tr>
<tr>
<td></td>
<td>LG-TA</td>
<td>-10.47</td>
<td>( p&lt;0.0001 )</td>
</tr>
<tr>
<td></td>
<td>MG-SOL</td>
<td>-4.45</td>
<td>0.0002</td>
</tr>
<tr>
<td></td>
<td>MG-TA</td>
<td>-9.00</td>
<td>( p&lt;0.0001 )</td>
</tr>
<tr>
<td></td>
<td>SOL-TA</td>
<td>-4.56</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

8.6.2 Coactivation of TA and TS muscles

Figure 8.3 is a bar plot of the coactivation of TA and TS to compare the young and older cohorts. The TS coactivation is higher than the TA’s coactivation for both the age groups but no significant age-related difference was found for TA (\( p = 0.6016 \)) or TS (\( p = 0.6464 \)).

Figure 8.3 Coactivation of TA and TS at 30% MVC in the young and old cohorts. No significant age-related difference was found for either of the muscle groups (\( p > 0.05 \))
8.6.3 Age-associated Strength Decline in TA and TS muscles.

Figure 8.4 is a bar plot to compare the force of maximal voluntary contraction produced by the young and old cohorts for both, TA and TS muscles. The statistical student t-test found $p = 0.1362$ for TA and $p=0.7352$ for TS, and this indicates that there was no statistically significant age-related change found for the MVC produced by the two opposing ankle muscles.

![Figure 8.4](image_url)  
*Figure 8.4* Maximal force produced by TA and TS at MVC by the young and older cohorts. No significant age-related difference was found for either of the muscle groups ($p > 0.05$)
Inhomogeneous Age-related sEMG changes between TA and TS

8.7 Discussion

This chapter has shown that $P_m$ of TA and TS sEMG was altered differently, with age-associated increase in maximal power of the PSD higher for TA than the TS muscles. Previous studies have shown an age-related increase in the TA (Kent-Braun and Ng 1999; McNeil, Doherty et al. 2005; Fling, Knight et al. 2009) and MG sEMG’s amplitude but not for SOL (Dalton, Harwood et al. 2009) which supports our results. However, there is no reported study of the age-related change in the LG’s sEMG.

To summarise, there was differential change in sEMG with no evidence of change in the strength of contraction and in coactivation. Section 8.7.1 discusses briefly the supporting literature for the absence of significant change in muscle strength observed, while Section 8.7.2 discusses the possible causes for the differential change in sEMG.

8.7.1 Muscle strength

The TA’s strength is found to be well preserved until a significant number of motor units are lost (McNeil, Doherty et al. 2005). Likewise, the preservation of SOL which is a major plantar flexor (Morse, Thom et al. 2005) can act to preserve plantar flexor strength. The discrepancy between the strength and sEMG age-related changes highlights that they are affected at different rates with age.

8.7.2 Differential age-related changes in the TA and TS sEMG

Age-related increase in the sEMG’s amplitude can be attributed to a number of factors: (i) increased antagonistic coactivation (Kent-Braun and Ng 1999; McNeil, Doherty et al. 2005), (ii) motor unit remodelling (Kent-Braun and Ng 1999; McNeil, Doherty et al. 2005), and (iii) change in muscle architecture (Morse, Thom et al. 2005; McNeil, Vandervoort et al. 2007; Jesunathadas, Rudroff et al. 2010; Csapo, Malis et al. 2014; Power, Allen et al. 2014). We have considered the effect of each of these below.

i. Coactivation: Our study has shown that there is no significant age-related alteration in the TA or TS’ coactivation (Figure 8.3), while other studies have found small reduction for TS (Simoneau, Billot et al. 2009). Hence coactivation is not the cause of the increased sEMG amplitude among older cohort.

ii. Motor Unit Remodelling: Studies have demonstrated that there is loss of fast fibres and increase in innervation ratio (Rowan, Rygiel et al. 2012). While increased innervation
Inhomogeneous Age-related sEMG changes between TA and TS

ratio will increase the sEMG amplitude (Disselhorst-Klug, Silny et al. 1998), the loss of fast fibres would decrease it and the net impact will depend on the proportion of fast and slow fibres (Gennaro, Davide et al. 2015).

It has been reported that 40% loss of motor units occurs in the TA for cohorts aged 60-69 years, with an additional loss of 33% by the 8th decade (McNeil, Doherty et al. 2005). In comparison, 70% loss of motor units was found in the SOL at very advanced age (80-100 years) (Vandervoort and McComas 1986), but with no loss till 75 years (Dalton, McNeil et al. 2008). A comparable change in the number of motor units for the GAS has not been reported.

The TA experiences a loss of fast fibres from 14% to 24% with age (Jakobsson, Borg et al. 1988). In LG the number of fast fibres remains unchanged with age while their size decreases (Coggan, Spina et al. 1992). Age-related changes in the fast-slow fibre ratio of SOL and MG are not reported in literature for a suitable comparison, but a decrease in muscle mass has been found in TS (Barber, Barrett et al. 2013; Csapo, Malis et al. 2014) which was larger than the reduction in TA (Barber, Barrett et al. 2013). Reduction in TS found in study (Barber, Barrett et al. 2013) was mainly due to GAS and the preservation of SOL attributed to the greater proportion of slow fibres (89%) (Johnson, Polgar et al. 1973; Gollnick, Sjödin et al. 1974) in comparison to the GAS (50%) (Johnson, Polgar et al. 1973), as well as their different functional role (anti-gravity vs. phasic) (Morse, Thom et al. 2005; Dalton, Harwood et al. 2009). This relationship is complex and better understanding of the effect of motor unit remodelling will require modelling of the different ankle muscles.

iii. Change in Muscle Architecture: Loss of muscle mass can manifest as decreased number of sarcomeres in parallel and series, and therefore decreased pennation angle and fibre length, respectively (Morse, Thom et al. 2005; Mitchell, Williams et al. 2012). The muscles investigated are all pennate and have short fibre lengths (Fukunaga, Roy et al. 1992), with the TS muscles having higher pennation angle and shorter fibres than TA (Fukunaga, Roy et al. 1992).

The pennation angles of TS are known to decrease with age (Morse, Thom et al. 2005), while the angle for TA does not change (Jesunathadas, Rudroff et al. 2010). Modelling has shown that increased pennation angle would increase the non-propagating components of sEMG (Mesin, Merletti et al. 2011), and thus broaden the power spectrum and decrease the $P_M$ (Farina, Cescon et al. 2002). Conversely, reduced pennation angle with age would increase
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the $P_M$. Another modelling study has shown that decreased fibre length can decrease the $P_M$ (Dimitrova, Dimitrov et al. 1990). Decreased fibre length has only been reported for MG, while SOL and LG’s fibre length remain unchanged with age (Morse, Thom et al. 2005).

To summarise, motor unit remodelling and decreased pennation angle can increase the $P_M$, while decreased fast-slow fibre ratio, and fibre length can decrease it. The combination of these changes could be such that TA and SOL’s $P_M$ similarity and difference to the GAS observed in the young cohorts is lost with aging at 30% MVC, when age-altered TA becomes different to SOL.

8.7.3 Consequences of differently aged TA and TS muscles

This study has shown that there is an inhomogeneous change in sEMG of TA and TS, indicating that measurements of the relative changes in strength of these two muscles based on sEMG may lead to incorrect assessment. A consequence of differently altered neuromuscular properties in TA and TS will be evident in the gait and postural stability.

Weakness in the TA can lead to a medial/lateral postural sway during gait (Gefen 2001) and increased likelihood of a fall due to inability to correctly invert the ankle at heel contact or clear toes during swing phase (Gefen 2001). Weakness in TS can lead to anterior/posterior postural sway and overall decreased postural stability and is evident at mid- and late stance among the elderly (Bok, Lee et al. 2013).

A limitation of this study is that motor unit numbers, muscle architecture changes, and subcutaneous fat were not measured. This has limited the strength of the conclusions.
8.8 Summary

This chapter investigated inhomogeneous aging of the TA and TS muscles’ sEMG to answer Research Question 2 (‘are there inhomogeneous age-associated changes in surface electromyogram of Tibialis Anterior and Triceps Surae due to different neuromuscular composition?’). It has found significant age-associated change of $P_M$ in the sEMG of TA and TS while their coactivation and force of maximal voluntary contraction did not change significantly. The results have also shown that the change of $P_M$ for TA was higher than TS while SOL and LG were not significantly affected in comparison to MG.

The findings of this Chapter demonstrate that age-related changes in ankle musculature are not homogeneous. Thus the relationship between muscle strength and sEMG would change at a different rate with ageing for different muscles. This indicates that while examining the muscle strength of elderly, disproportionate changes in sEMG should be considered, failing which the disparity in the strength of ankle muscles may not be observed. Such disparity can be a cause of medial/lateral postural sway due to aging of the phasic muscles, TA and GAS.

A summary of the findings and main contributions of this thesis are detailed in the following chapter.
Chapter 9

9 Conclusion

9.1 Introduction

This thesis has investigated the relative influence of neuromuscular properties on muscle strength decline with age in the Tibialis Anterior. This knowledge would be useful to better target strength preservation strategies in the elderly for the prevention of falls. The biosignal, surface electromyogram (sEMG) has been successfully used to assess age-related alterations in the Tibialis Anterior’s musculature detailed in Chapter 4.

As a first step to answer the research questions, the sEMG and force model was simulated and validated for the young people using the values of the parameters from literature (Chapter 5). The novelty of this model simulation was the use of statistical distribution of the parameters and repetitive simulations to obtain more representative simulation. Another novelty was that the model simultaneously simulated the force and sEMG and provided a two point validation which is known to improve the accuracy of the model (Keenan and Valero-Cuevas 2007). This is highly significant because earlier models have simulated with only one measurement which makes the validation process biased. Validation of a model requires multiple data sources for it to suitably represent the population or outputs it is intending to simulate (Eddy, Hollingworth et al. 2012).

The model validated for the young cohorts was used to estimate age-altered neuromuscular properties in older participants from their sEMG features, discussed in Chapter 7. This involved modifying the sEMG and force model to represent several age-associated changes in the neuromuscular parameters and using the experimental sEMG changes to statistically determine the best aging condition of the older cohorts of this study. After determining the altered neuromuscular properties, the force model was updated with the aging parameters and their effect on force decline was determined. The muscle force model was also used to simulate several neuromuscular properties with a wide range of values reported in literature,
and there alteration with age. This provided a more broader answer to the first research question, detailed in Chapter 6.

Lastly, inhomogeneous aging of the Tibialis Anterior and Triceps Surae muscles was experimentally investigated using sEMG to answer the second research question, and its findings are presented in Chapter 8.

9.2 Main Contributions

This thesis has addressed the following research questions, detailed in Chapter 1, Section 1.3:

Q1: What are the relative influences of the neural and muscular factors on muscle strength decline with aging in the Tibialis Anterior? (Investigated in Chapter 6 & 7)

Q1a: Are the age-related surface electromyogram changes corresponding to neuromuscular alterations? (Investigated in Chapter 4)

Q1b: Can the age-related surface electromyogram changes be quantified into neuromuscular changes in the older participants? (Investigated in Chapter 7)

Q2: Are there inhomogeneous age-associated changes in surface electromyogram of Tibialis Anterior and Triceps Surae due to different neuromuscular composition? (Investigated in Chapter 8)

A combination of simulation and experimental methods was used to answer these research questions. The new and improved computational surface electromyogram and force model developed for the Tibialis Anterior detailed in Chapter 5 was vital to answering Research Q1 and Q1b.

The following presents the main contributions of this thesis:

- This thesis has established the effect of age on the Gaussianity and the maximal power spectral density amplitude of the sEMG for the Tibialis Anterior at different force levels. SEMG of the older cohorts had higher amplitude and more non-Gaussianity, which was especially evident at submaximal contractions. The combination of these features were considered to be associated with motor unit remodelling. This study adds new knowledge to
the existing literature that have investigated these features for aging in the biceps brachii, but not for the Tibialis Anterior (Kaplanis, Pattichis et al. 2009; Meigal, Rissanen et al. 2009).

- This thesis has implemented a new and improved computational model for the pennate muscle, Tibialis Anterior, with two independent outputs: sEMG and force, which has been vital for investigating the research questions posed by the candidate. The model incorporates a statistical distribution of values to its parameters to represent intra- and inter-subject variability, and distinguishes between the two motor unit types. The novelty of the force model is the integration of twitch force with realistic parameters instead of arbitrary units, and an ankle joint model to compute the torque. This work provides an alternative approach to modelling a pennate muscle in comparison to more complicated approaches in literature (Mesin and Farina 2004; Mesin, Merletti et al. 2011). An alternative description of the motor unit force model has also been provided to produce a realistic force output instead of arbitrary units (Fuglevand, Winter et al. 1993). The model also incorporates neural and muscular factors which has been lacking in literature (Thelen 2003; Barry, Pascoe et al. 2007; Hasson and Caldwell 2012).

- It has been demonstrated through a simulation study performed with the sEMG and force model developed for the Tibialis Anterior in this thesis that once the effects of neuromuscular properties on muscle strength were standardised, neural drive as assessed by firing rate emerged as the most influential property, followed by muscular factors: number of muscle fibres, specific force, pennation angle, and motor unit remodelling. This has been the first study that has studied the relative influence of neuromuscular properties using a force model experimentally validated.

- It has been demonstrated with the aid of the sEMG and force model presented in this thesis that the age-associated changes to the older cohorts’ Tibialis Anterior sEMG of this study was best explained by moderate motor unit remodelling. This corresponded to a 40% loss of motor units with halved the number of fast fibres. Simulation also demonstrated that loss in fast fibres contributed to the greatest decline in strength in comparison to loss of motor units, however, the combined effect was compensatory that preserved strength.

- This thesis has established significant heterogeneous age-associated changes in the maximal power spectral density amplitude of the sEMG of the Tibialis Anterior and Triceps Surae muscles. The change in the spectral maximum for Tibialis Anterior was higher than
Conclusion

Triceps Surae. Within the Triceps Surae complex, the Soleus and Lateral Gastrocnemius were not significantly affected in comparison to Medial Gastrocnemius. Coactivation of the ankle muscles and force of maximal voluntary contraction were not found to be significantly altered with age. This work provides a different perspective to heterogeneous age-related changes in the Triceps Surae and Tibialis Anterior using sEMG and adds value to the growing body of literature in this area (Simoneau, Billot et al. 2009; Barber, Barrett et al. 2013; Csapo, Malis et al. 2014; McKinnon, Montero-Odasso et al. 2015).

9.3 Impact and Applications

Australia is facing an ageing society (Australian Bureau of Statistics 2009), and that has several significant economic and social costs (Australian Government 2015). An identified social cost to the Australian health care system is the increased hospitalisation of the elderly due to injuries sustained during falls (Moller 2003; Shumway-Cook, Ciol et al. 2009). This also comes at a personal cost to the person suffering and their family, as falls are the leading cause of accidental death amongst older people (Morris, Osborne et al. 2004).

One of the factors contributing to risk of falls is declining muscle strength of the ankle muscles (Moreland, Richardson et al. 2004). Several neuromuscular properties are known to contribute to strength loss, but their relative effects were unknown (Clark and Manini 2008). The need for isolating the relative influence of neural and muscular properties on age-associated muscle strength decline was identified in order best tailor strength preservation strategies in the elderly (Clark and Manini 2008).

This thesis has presented a novel sEMG and force model which has been able to establish the ‘linchpin’ of age-associated muscle strength decline in the Tibialis Anterior. It has successfully quantified the neuromuscular changes from the sEMG changes of the older cohorts and analysed the individual and cumulative effect of the age-altered neuromuscular properties on the muscle force. It has also predicted the individual contributions of age-altered neuromuscular factors to muscle strength decline in the Tibialis Anterior with advanced aging.

By using a non-invasive tool, the sEMG and a computational sEMG and force model, this thesis has identified neural drive to be the most influential factor contributing to strength
decline in the Tibialis Anterior, followed by muscular factors. It has also identified that neuromuscular factors influencing muscle strength can be different for different muscles.

9.4 Limitations and Future Perspectives

The research conducted in this thesis was not without limitations which presents an opportunity for future studies to improve upon.

This thesis has established age-associated changes in the sEMG of the Tibialis Anterior, and that it can be different from the age-associated changes in its neighbouring muscle, the Triceps Surae. However, the strengths of the conclusions made were limited by the lack of information on the participants’ subcutaneous fat, muscle architecture, and number of motor units. By analysing the inter-subject variability in the sEMG due to anatomical differences, the experimental variance observed could be better explained.

The assumptions used in the development of the sEMG and force model presented also contributed to the limitations of this research and has been discussed in Chapter 5. The main limitations were in the volume conductor chosen to represent the Tibialis Anterior, and the representation of the ankle torque exerted as a point load. The subject-specific physiological properties could also be used to improve the sEMG and force model developed. Future studies could investigate the improvement in the model’s accuracy with more sophisticated volume conductor models and ankle joint biomechanics.

Lastly, the age-altered neuromuscular parameters of the older participants in this study were estimated by an inverse approach with the use of the sEMG model developed. Inverse problems suffer from existence, uniqueness and stability of the solution (Groetsch and Groetsch 1993; Farina, Merletti et al. 2004). For the sEMG and its model to be applicable clinically, the combinations of model parameters leading to similar solutions needs to be understood. This would increase the confidence in the utilisation of sEMG for diagnostic purposes.
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11 Appendices

11.1 Appendix A

The experimental protocol described in Chapter 4 has been used. Participants were instructed to perform two isometric plantarflexion (PF) repetitions at 100% MVC to measure the antagonistic TS muscles’ coactivation level. Root Mean Square (RMS) of SOL, MG and LG was calculated at the 100% MVC trials during the DF and PF; RMS\textsubscript{MG}, RMS\textsubscript{LG} and RMS\textsubscript{SOL}. The RMS of TS was computed as follows:

\[
\text{RMS}_{TS} = \text{RMS}_{MG} + \text{RMS}_{LG} + \text{RMS}_{SOL}.
\]

The coactivation level of the TS was calculated by dividing its antagonist EMG RMS by its agonist EMG RMS (Falconer and Winter 1985; Baratta, Solomonow et al. 1988) as described as follows.

\[
\text{TS Coactivation} = \frac{\text{RMS}_{TS \ DORSIFLEXION}}{\text{RMS}_{TS \ PLANTARFLEXION}}
\]

After determining the normality of the TS coactivation data with the Shapiro-Wilk test at \( \alpha = 0.05 \), a two-tail student t-test was performed between the young and older cohort’s TS antagonistic coactivation levels at \( \alpha = 0.05 \).
Figure A.1 Antagonistic coactivation level (Mean ± SD) of the TS during dorsiflexion measured at 100% MVC for young and older cohorts. No significant age-related difference was found.

Figure A.1 shows the TS muscles’ coactivation level at 100% MVC for young and old cohorts, during dorsiflexion when it behaves as the antagonist. The TS coactivation level in the young cohorts is higher than the older cohorts, although no significant difference was found ($p = 0.0954$).
Figure A.2 Bar graph of the dorsiflexion agonist force (Mean ± SD) of the young and older cohorts at the six different maximal voluntary contraction levels (%MVC).

Figure A.2 shows the bar graph of the exerted dorsiflexion force by young and older cohorts at 10%, 20%, 30%, 50%, 75%, and 100% MVC. The young cohorts produced greater dorsiflexion force than older cohorts at all of the MVCs measured. One-way student $t$-test did not find a significant age-associated change in the exerted dorsiflexion force ($p > 0.05$).
11.2 Appendix B

11.2.1 Volume Conductor Function Derivation for a unipennate muscle

As a first approximation, a unipennate muscle can be modelled as a space-invariant parallel fibre system that is rotated with respect to the recording electrode (Mesin 2006). This approximation allows the extracellular action potential to be determined as the convolution of the intra-cellular potential and the impulse response of the volume conductor (Plonsey 1974; Nandedkar 1983). The rotation of the muscle fibres with respect to the electrode system will require the transformation of the parallel fibre coordinates to the new rotated coordinate system. This transformation will affect the formulation of the impulse response of the volume conductor (Dimitrova, Dimitrov et al. 1999).

For a space-invariant model, the impulse response of a parallel fibre volume conductor can be described as follows (Plonsey 1974; Wheeler, Kumar et al. 2011):

\[
\tilde{f}(t) = \frac{\sigma_i}{4\pi \sigma_e} \frac{1}{\sqrt{(z - z')^2 + Kan[(x - x')^2 + (y - y')^2]}}
\]

(B.1)

Where \(\tilde{f}(t)\) is the impulse response of the volume conductor in space domain, \(\sigma_i\) and \(\sigma_e\) are the intra- and extracellular conductivities; \(K_{an}\) is the anisotropic factor which is the ratio of conductivities parallel and perpendicular to the muscle fibre \((\sigma_i / \sigma_e)\). \((X', Y', Z')\) is the coordinate axes of the parallel muscle fibres with its Origin at the neuromuscular junction,
and \(x', y', z'\) are coordinate points of the bioelectric source travelling along the muscle fibre in the coordinate axes \((X', Y', Z')\) (Figure B.1).

The coordinates \((x', y', z')\) of the action potential field need to be transformed to a rotated coordinate system \((X_o, Y_o, Z_o)\) that is depth inclined at \(\theta\) degrees in the \(Z'-Y'\) plane. This requires resolving the components of the action potential to the new coordinate system’s axes \((X_o, Y_o, Z_o)\):

\[
\begin{align*}
    z' &\Rightarrow z' \cos \theta \\
y' &\Rightarrow z' \sin \theta \\
x' &\Rightarrow x'
\end{align*}
\] (B.2)

The transformed coordinates from Eq (B.2) are substituted into Eq (B.1) and the linear translation of the coordinate axis from the neuromuscular junction to the recording electrode \((X_o, Y_o, Z_o)\) is included. The modified impulse response of the volume conductor is described as:

\[
f_t = \frac{\partial}{\partial z} \left( \frac{\sigma_l}{4\pi\sigma_i} \frac{1}{\sqrt{(z_o - (z_{NMJ} \pm z' \cos \theta))^2 + K_{NMJ} [(x_o - x_{NMJ})^2 + (y_o - (y_{NMJ} \pm z' \sin \theta))^2]}} \right)
\] (B.3)
Figure B.2. Scatterplot of the simulated and young cohort’s maximal power of their sEMG PSD with increasing force level measured as the percentage of MVC. The sEMG was simulated from the parameters in Table 5.1, Column 3, that had fixed number of motor units, muscle fibres, fast-slow fibre ratio, fiber length and pennation angle.
Figure B.3. Scatterplot of the simulated young cohort’s MDF of their EMG with increasing force level measured as the percentage of MVC. The sEMG was simulated from the parameters in Table 5.1, Column 3, that had fixed number of motor units, muscle fibres, fast-slow fibre ratio, fiber length and pennation angle.
Figure B.4. (a) Effect of different intra- & extra-cellular conductivity ratios on the SFAP waveform with in an isotropic medium. Higher ratios lead to increased amplitude. (b) Effect of different anisotropic ratios on the SFAP waveform. As the anisotropy increases, the waveform stretches and its amplitude decreases.
Figure B.5. The effect of different intra- & extra-cellular conductivity ratios ($\sigma_i/\sigma_e$) and anisotropic ratio ($K_{an}$) on the (a) Maximal Power of the PSD and (b) Median Frequency. Higher ($\sigma_i/\sigma_e$) ratios lead to increased amplitude but it has minimal effect on MDF. As the anisotropy increases, both sEMG amplitude and MDF decreases.
11.3 Appendix C

Figure C.1. A plot of the age-related difference in Sg obtained experimentally with increasing MVC, and the difference in Sg computed between the Young Simulation Model and simulated aging conditions A (motor unit loss) and D (motor unit loss with altered recruitment pattern) at 40%, 50%, 60% loss of motor units, with increasing MVC.
Figure C.2. A plot of the age-related difference in SI obtained experimentally with increasing MVC, and the difference in SI computed between the Young Simulation Model and simulated aging conditions A (motor unit loss) and D (motor unit loss with altered recruitment pattern) at 40%, 50%, 60% loss of motor units, with increasing MVC.
Figure C.3. A plot of the age-related difference in maximal power obtained experimentally with increasing MVC, and the difference in maximal power computed between the Young Simulation Model and simulated aging conditions A–F at 40% loss of motor units. Details of condition A–F is given in Table 7.2 in Chapter 7.
11.3.1 Inverse Modelling Multiple Solutions

The similarity of sEMG signal features at different aging conditions as described in Chapter 7 has been explored in this Appendix.

The following sEMG signal features were computed at 10%, 20%, 30%, and 50% MVC from the sEMG signals generated with the sEMG model in Chapter 7 at three different motor unit losses and six different aging conditions:

- Gaussianity Test Statistic (Sg)
- Linearity Test Statistic (Sl)
- Peak power of the power spectral density (PMAX)
- Median Frequency (MDF)

A feature vector \( Z \) was computed for each simulated signal:

\[
Z = [\text{PMAX}, \text{MDF}, \text{Sg}, \text{Sl}]
\]

The approach by Rissanen, Kankaanpää et al. (2008) for feature extraction and cluster analysis has been implemented. Briefly, the dimensionality of the feature vector was reduced by applying the principal component analysis (Rissanen, Kankaanpää et al. 2008). K-means Cluster Analysis was performed on the principle components to determine the differences in the simulated aging conditions’ signal features (Rissanen, Kankaanpää et al. 2008).

To understand which sEMG signal features are represented in each of the computed principle component, pearsons correlation between the feature vector \( Z \), and the principle components were computed. Significant correlations were selected to indicate the relationship between the signal feature and the principle component.

Figure C.4 shows the clusters that were generated at 10%, 20%, 30% and 50% MVC. The clusters show membership of simulated aging conditions that varied in the % loss of motor units, and at 6 different severity of aging. At 10% MVC, the young healthy condition is mostly contained in cluster 1, but there is overlap with other simulated aging conditions. A similar observation is also made for 20% - 50% MVC.
Figure C.4. Clusters generated using K-means cluster method shows the simulation conditions that yielded similar sEMG signal features at 10%, 20%, 30%, and 50% MVC. The clusters show membership of the simulated aging condition which is comprised of the loss in number motor units, and the 6 different aging conditions detailed in Table 7.2.
11.4 Appendix D

NOTICE OF HUMAN RESEARCH ETHICS COMMITTEE APPROVAL
Notice of Approval

Date: 12 December 2013
Project number: 40/13
Project title: Effects of height on muscle activity
Risk classification: More than low risk
Investigator: Prof Dinesh Kumar
Approved: From: 12 December 2013 To: 31 December 2016

Terms of approval:

1. Responsibilities of investigator
   It is the responsibility of the above investigator to ensure that all other investigators and staff on a project are aware of the terms of approval and to ensure that the project is conducted as approved by HREC. Approval is only valid whilst investigator holds a position at RMIT University.

2. Amendments
   Approval must be sought from HREC to amend any aspect of a project including approved documents. To apply for an amendment use the request for amendment form, which is available on the HREC website and submitted to the HREC secretary. Amendments must not be implemented without first gaining approval from HREC.

3. Adverse events
   You should notify HREC immediately of any serious or unexpected adverse effects on participants or unforeseen events affecting the ethical acceptability of the project.

4. Plain Language Statement (PLS)
   The PLS and any other material used to recruit and inform participants of the project must include the RMIT university logo. The PLS must contain a complaints clause including the above project number.

5. Annual reports
   Continued approval of this project is dependent on the submission of an annual report.

6. Final report
   A final report must be provided at the conclusion of the project. HREC must be notified if the project is discontinued before the expected date of completion.

7. Monitoring
   Projects may be subject to an audit or any other form of monitoring by HREC at any time.

8. Retention and storage of data
   The investigator is responsible for the storage and retention of original data pertaining to a project for a minimum period of five years.

9. Special conditions of approval
   Nil.

In any future correspondence please quote the project number and project title above.

A/Prof Barbara Polus
Chairperson
RMIT HREC

cc: Dr Peter Burke (Ethics Officer/HREC secretary), Sruthi Sahebjada (student researcher).
Notice of Approval of Amendment

Date: 15 April 2015
Project number: 15751 (40/13)
Project title: Effect of height on muscular activity
Risk classification: More than low risk
Investigator: Prof Dinesh Kumar
Expiry: 31 December 2016

The request to amend the above project was approved by the Human Research Ethics Committee on 15 April 2015.

The following amendments are therefore approved:
   a. An increase for the age range of participants to 18 - 85 years for the second phase of the experiment protocol only.

Please retain this notice for future reference.

Regards

A/Prof Barbara Polus
Chairperson
RMIT HREC

cc: Dr Peter Burke (HREC secretary), Ms Ariba Siddiqi (research student)