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**DIRECT AND REFLEX MOTOR EFFECTS OF CONVENTIONAL  
AND CATCH-LIKE ELECTRICAL STIMULATION FOR  
DROPPED FOOT CORRECTION**

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## ABSTRACT

FACULTY OF PHYSICAL SCIENCES AND ENGINEERING  
Doctor of Philosophy

# **DIRECT AND REFLEX MOTOR EFFECTS OF CONVENTIONAL AND CATCH-LIKE ELECTRICAL STIMULATION FOR DROPPED FOOT CORRECTION**

Darren John Hart

Electrical stimulation applied to the common peroneal nerve during the swing phase of gait is an established clinical technique for the correction of dropped foot following upper motor neuron injury. The catch-like effect of skeletal muscle refers to force augmentation resulting from the inclusion of an initial high frequency burst of two or more stimuli prior to conventional low frequency electrical stimulation. There is interest in clinical utilisation of catch-like stimulation during functional applications; however the mechanism of the effect is not fully understood. The purpose of this research was to determine if the catch-like effect is a property of the muscle alone or related to spinal reflex mediated activation. In order to investigate this, direct and reflex motor effects of conventional and catch-like stimulation during dropped foot correction and other controlled conditions were assessed in unimpaired (n=12) and stroke (n=13) populations through use of electromyography. A system was developed to enable analysis of electromyography activity shortly after the application of configurable stimulation patterns. Innovative design minimised effects of stimulation artefact such that electromyography of the tibialis anterior and soleus muscles during dropped foot correction could be assessed. This system was utilised and further refined during exploratory investigations prior to structured use with study participants. Both direct and reflex motor effects of conventional stimulation were found to vary with muscle length. At typical stimulation intensities and frequencies used during dropped foot correction, direct (orthodromic) motor activation dominates voluntary or reflex mediated activation of the tibialis anterior. Enhanced contractile force when utilising catch-like stimulation with human participants, appears an effect solely inherent to muscle with no excitatory or inhibitory spinal reflex contribution. Facilitation of reflected antidromic motor activation (F-waves) with voluntary effort, observed only within the unimpaired participant group, may be an indicator of normal neuroplasticity at the spinal cord. Findings highlight the need to consider antidromic motor effects of electrical stimulation when combining its use with voluntary function during future clinical development.





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# Declaration of Authorship

I, DARREN HART

declare that the thesis entitled

## **DIRECT AND REFLEX MOTOR EFFECTS OF CONVENTIONAL AND CATCH-LIKE ELECTRICAL STIMULATION FOR DROPPED FOOT CORRECTION**

and the work presented in the thesis are both my own, and have been generated by me as the result of my own original research. I confirm that:

- this work was done wholly or mainly while in candidature for a research degree at this University;
- where any part of this thesis has previously been submitted for a degree or any other qualification at this University or any other institution, this has been clearly stated;
- where I have consulted the published work of others, this is always clearly attributed;
- where I have quoted from the work of others, the source is always given. With the exception of such quotations, this thesis is entirely my own work;
- I have acknowledged all main sources of help;
- where the thesis is based on work done by myself jointly with others, I have made clear exactly what was done by others and what I have contributed myself;
- none of this work has been published before submission,

Signed: .....

Date: .....



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# List of Symbols

ABS	Acrylonitrile Butadiene Styren
Ach	Acetylcholine
AFO	Ankle Foot Orthotic
ADP	Adenosine Diphosphate
Ag-AgCl	Silver - Silver Chloride
ATP	Adenosine Triphosphate
CNS	Central Nervous System
CSV	Comma Separated Values
DAQ	Data Acquisition
EMG	Electromyography
EPSP	Excitatory Post Synaptic Potential
FES	Functional Electrical Stimulation
IPSP	Inhibitory Post Synaptic Potential
IRAS	Integrated Research Application System
LMN	Lower Motor Neuron
MVC	Maximal Voluntary Contraction
NHS	National Health Service
NRES	National Research Ethics Committee
PCB	Printed Circuit Board
PIC	Peripheral Interface Controller
PNS	Peripheral Nervous System
RLD	Right Leg Driven system
RDS	Research Design Service
SENIAM	Surface ElectroMyoGraphy for the Non-Invasive Assessment of Muscles

SPASM	Support Programme for Assembly of database for Spasticity Measurement
SPI	Serial Peripheral Interface
UMN	Upper Motor Neuron
USB	Universal Serial Bus

# Chapter 1 Introduction

## 1.1 Overview of Research

Functional Electrical Stimulation (FES) involves the artificial electrical activation of motor neurons supplying muscle paralysed by Upper Motor Neuron (UMN) injury in order to achieve a functional task. It can provide therapeutic, functional and rehabilitative benefits to individuals with UMN dysfunction [1-3]. In 2009 the National Institute for Health and Clinical Excellence (NICE) UK completed a structured review of clinical evidence and recognised FES as an effective clinical treatment for people with dropped foot following UMN injury [4]. Assessing the clinical effectiveness of FES for dropped foot correction is not the primary objective of this research. Instead it focuses upon addressing unanswered fundamental questions about the physiological effect electrical stimulation has upon the complex nervous system.

There are notable differences between the accepted physiological action of electrical stimulation and the body's efficient natural activation of muscle [5]. Despite this, the constant frequency stimulation currently applied clinically differs very little from that first proposed by Liberson in 1961 [6] for the functional application of dropped foot correction. Although functional with clinical benefit, it is the authors' perspective that this is in part born out from historical engineering design as opposed to a scientific basis in which natural firing patterns of the voluntary motor control system are mimicked.

In 1970 Burke first reported the "catch-like effect" of electrical stimulation in which substantial force augmentation of muscle was demonstrated by the inclusion of an initial, high-frequency burst of two (doublet) or more pulses at the start of a low-frequency train of electrical stimulation [7]. The effect shows similarities to the naturally occurring initial high frequency burst of motor nerve action potentials (akin to doublet stimuli) the unimpaired central nervous system can utilise when producing large



or sudden muscular forces [8-11]. Although numerous studies report favourable characteristics when utilising the catch-like effect with unimpaired participants [12], mixed findings are reported in the few to investigate its effect with UMN injury participants [13-19]. A lack of understanding of the effect and its mechanism emphasised by such varied outcomes, may account for the catch-like effect remaining a largely experimental finding yet to be utilised within clinical FES systems.

As defined and demonstrated by Burke *et al.* [20], the catch-like effect is an innate property of the muscle. Collins *et al.* [21-25] have highlighted the significance of additional 'central components' of motor activation caused by orthodromic sensory conduction following high frequency bursts of electrical stimulation. It appears a limitation of some studies to only consider the direct motor effects of electrical stimulation. Of key interest to this research is the spinal reflex response to catch-like stimulation during dropped foot correction.

Within this study it was hypothesised that favourable observations noted when using catch-like stimulation may be partly due to spinal excitation and inhibition effects. Three research questions were formulated in order to investigate this hypothesis.

1. *How significant are reflexes to conventional and catch-like stimulation?*
2. *Is increased torque commonly observed when utilising catch-like stimulation caused, in part, by enhanced excitatory spinal reflex components which activate additional muscle fibres to those activated by direct  $\alpha$ -motor neuron excitement?*
3. *Do the use of doublet stimuli have an enhanced reciprocal inhibition effect on an active antagonist muscle; thus in part explaining the enhancement in torque commonly observed when utilising catch-like stimulation?*

Electromyography (EMG) was the primary outcome measure for this research and was used to assess the excitatory and inhibitory reflex effects on muscle activation whilst stimulating the common peroneal nerve. The onset of the tibialis anterior EMG direct motor response to a stimulation pulse used for dropped foot correction will typically be observed within 10ms. This feature is approximately a magnitude of  $10^4$  smaller than

the applied stimulation pulse and occurs in the presence of the artefact tail that follows it. Recovery of this signal from stimulation artefact represents a significant physiological measurement challenge and may account for limited research reporting the EMG response to FES.

This research was instigated from within the field of Clinical Science and Engineering which has substantially aided its success. This was because complete ownership of clinical hypothesis, study design, instrumentation development and data analysis was possible. Performance of existing design concepts were refined and advanced in order to extend measurement and research capabilities. Whilst this was important for sub-systems it was the interaction and coordination of these which permitted successful investigation of the posed research questions.

## 1.2 Thesis Outline

Aspects of this research bridge clinical engineering, applied neurophysiology and clinical rehabilitation. Chapter 1 places the thesis within the context of existing knowledge and research in these fields in order to enable the wider context of the research topic to be considered during its investigation.

Chapter 2 begins by providing a neurophysiological background relevant to control of voluntary human movement before reviewing muscle anatomy and function. It focuses on aspects relevant to the research topics which are drawn upon in greater detail when examining concepts and effects in later chapters. This chapter provides the reader with the necessary neurophysiological and muscle function knowledge to place this research in its clinical context.

Chapter 3 describes phenomena associated with Upper Motor Neuron (UMN) syndrome and the complex effect this can have on the control of movement. Whilst the presentation of these effects vary amongst individuals, the overview given is of relevance when contrasting findings from participants with unimpaired and impaired UMN function in later chapters.

Chapter 4 introduces the principal topic of this research: the clinical use of artificial electrical stimulation. The chapter begins by providing an overview of the diagnostic and therapeutic uses of electrical stimulation. A review of the neuromuscular response

to transcutaneous electrical stimulation is provided before the ‘catch-like’ effect is introduced. The broad knowledge base formed in earlier chapters enables findings from applied, in-vivo studies through to clinically based trials to be critically assessed and discussed when forming an understanding of the research field surrounding the catch-like effect. Finally the effects of conventional and catch-like stimulation on the central nervous system are discussed. This is of direct relevance to the research hypothesis outlined in the next chapter.

Chapter 5 begins by synthesising the fundamental findings and concepts outlined in Chapters 2, 3 and 4 and the limitations of previous studies. This leads to the formulation of the research hypothesis and the three research questions outlined. Study design decisions addressing the research questions are described before investigational system requirements are summarised.

A more detailed system topology and performance specification of the investigational system is presented in Chapter 6. The novel design and development of its composing sub-systems are described throughout the chapter. A substantial engineering challenge was to improve the performance of existing design concepts to allow the direct motor and reflex mediated activity following a stimulation pulse to be recorded in the tibialis anterior during stimulation for the correction of dropped foot. This chapter concludes with images of the developed investigational system.

In order to inform and refine development of both the research protocol and the investigational setup, initial exploratory data collected from the author is presented in Chapter 7. Following the first exploratory investigation further refinements to the instrumentation setup were made in order to improve the performance in light of stimulation artefact. Three further exploratory investigations assess the isotonic and isometric responses to conventional and catch-like stimulation applied as a twitch or burst. Having noted unexpected variations in M-wave amplitude with muscle length, three further experimental investigations test hypotheses accounting for this effect. Two of these hypotheses were supported and are referred to in later chapters.

Informed by the preceding chapter, Chapter 8 describes the design of a single investigation session comprising of six phases which could be completed within approximately 90 minutes. This protocol was implemented within the software controlling the instrumentation and hence details of the configuration and prompts conveyed by this system are included. The six investigation phases and associated sub-tests are summarised in Table 8-2. The naming convention of individual sub-tests

within this table is used from this point forward within the thesis. Later sections of the chapter describe research governance measures enabling the study to be successfully completed with unimpaired and impaired participants.

Whilst relatively easy to record, EMG represents a complex neurophysiological process and can be difficult to interpret quantitatively. Chapter 9 describes the development of an automated data analysis method and the analysis tools that enabled this. Automated data analysis was vital to the successful interpretation and reporting of findings within this study due to the substantial volume of collected data. The author utilised experience and skills within clinical science and engineering to enable complex software development aiding meaningful interpretation and comparison of EMG and other outcome measures.

Results of data analysis are described and presented in Chapter 10. Sub-tests are grouped and introduced before data from unimpaired and impaired participants are contrasted and discussed. Where appropriate, trends are identified and discussed with relevance to the results of other phases as well as published studies.

Conclusions of the study are presented in Chapter 11. Broader conclusions relevant to the field of neurophysiological research are first described. Conclusions relating to individual research questions are then addressed. Implications for combining FES with voluntary activation are discussed.

Chapter 12 identifies and discusses areas for future clinical investigation arising from the study conclusions.

This research set out to extend understanding of the catch-like effect such that it may be used to functional benefit in future clinical FES systems. In doing so, this research has also investigated direct and reflex motor effects of conventional electrical stimulation. By furthering underlying understanding, the clinical efficacy of conventional electrical stimulation can be informed and enhanced.

### 1.3 Publications and Presentations

Throughout this study opportunities to disseminate and gain critical feedback upon research findings have been utilised. Below is a list of presentation and publications that resulted from this research.

- (Presentation - Best Abstract Award) Hart D, Wood D, Taylor P, Chappell P. Optimally spaced stimulation for clinical use with Functional Electrical Stimulation - the effect on spinal reflexes and muscle activation in unimpaired and stroke participants. 2<sup>nd</sup> Annual Conference of the International Functional Electrical Stimulation Society (UK and Ireland Chapter). University of Dublin, Ireland. March 10<sup>th</sup> –12<sup>th</sup>, 2011.
- (Presentation) Hart D, Wood D, Taylor P, Chappell P. Optimally spaced stimulation for clinical use with Functional Electrical Stimulation - its effect on spinal reflexes & muscle activation. Guest speaker at Medical Physics department meeting, Royal United Hospital, Bath. November 2010.
- (Presentation) Hart D, Wood D, Taylor P, Chappell P. Catch-like Stimulation – its Effect on Spinal Reflexes and Muscle Activation. 1<sup>st</sup> Annual Conference of the International Functional Electrical Stimulation Society (UK and Ireland Chapter). University of Salford. April 14<sup>th</sup> -15<sup>th</sup> 2010.
- (Poster) Hart D, Wood D, Taylor P, Chappell P. Optimally spaced stimulation for clinical use with Functional Electrical Stimulation - its effect on spinal reflexes & muscle activation. IFESS 2008 Proceedings: From Movement to Mind. 13th Annual International FES Society Conference: Freiburg, Germany. 21<sup>st</sup> - 25<sup>th</sup> September 2008.
- (Presentation) Hart D, Wood D, Taylor P, Chappell P. Optimally spaced stimulation for clinical use with Functional Electrical Stimulation - its effect on spinal reflexes & muscle activation. FES User-day 2008. National Clinical FES Centre, Salisbury.
- (Poster) Hart D, Chappell P, Wood D, Taylor P. Investigation of the ‘catch effect’-its clinical use with Functional Electrical Stimulation. Medicine, Health and Life Sciences Postgraduate Conference. Boldrewood Campus, University of Southampton. June 2007.
- (Quarterly presentations). Internal ‘postgraduate forum’ meetings at the National Clinical FES Centre, Salisbury. 2006-2010.

## **Chapter 2   Neurophysiology of Human Movement**

A remarkable feature of human movement is simply how easy it can appear to the casual observer. Simply typing this sentence relies upon the complex translation, filtering and integration of information over numerous structures and levels of the author's nervous system. To consider this from an engineering perspective represents an amazing interplay of numerous complex sensors, actuators, controllers and feedback mechanisms. In order to introduce the research topic, a critical review of anatomy and physiology components relevant to motor control is presented with an emphasis upon those affected by the application of artificial electrical stimulation.

The chapter begins by providing a brief overview of the components of the nervous system involved when completing a movement. This introduces mechanisms of particular relevance to placing this research in context which are then considered in greater detail. Once neurophysiology relevant to motor control by Functional Electrical Stimulation (FES) has been discussed, the effects of an UMN injury on the described system are considered.

### **2.1   Principal Components of the Neuromuscular System**

The actions and functions of the body are principally controlled by the nervous system. It has two main divisions: the Central Nervous System (CNS) or Upper Motor Neuron (UMN) system, consisting of brain and spinal cord, and the Peripheral Nervous System (PNS) or Lower Motor Neuron (LMN) system, being all nervous tissue outside the CNS connecting to the rest of the body. Nerves that convey information away from the CNS

are termed motor or efferent nerves, and those conveying information towards the CNS, sensory or afferent nerves. Efferent nerves of the PNS form part of either the somatic or autonomic nervous systems and are operated voluntary (with conscious control) and involuntary (without conscious control) respectively.

A brief overview of the principal processes involved when completing a voluntary movement begins with a decision to commence a voluntary movement. In order to form this function, numerous excitatory and inhibitory signals are generated within complex networks of neurons at multiple processing levels within the brain. A number of areas and tracts function in combination to formulate and regulate control of UMNs, ensuring that movements are performed with spatial and temporal precision. Generated efferent signals travel down UMN axons of the spinal cord to different levels at which they are communicated to the cell bodies of LMNs. These induced action potentials then travel along somatic alpha ( $\alpha$ ) motor neurons where when close to the muscle, branch and connect to individual muscle fibres. At the neuromuscular junction to each muscle fibre the signal is communicated across an electro-chemical interface before it causes the generation of electrical activity in the fibre. This activity can trigger a chemical process causing the muscle fibres innervated by a common  $\alpha$ -motor neuron to contract which may then result in movement. In order to provide a coordinated movement the process does not stop here however. Afferent information about muscle length, rate of stretch and tension is reported back to the spinal cord through afferent neurons. At the spinal cord this afferent feedback may cause the relaxation or excitation of other neurons forming spinal reflexes in addition to being passed up to higher centres in the brain. So as to continue a smooth coordinated movement the brain may modulate spinal reflexes whilst continuing to provide efferent control.

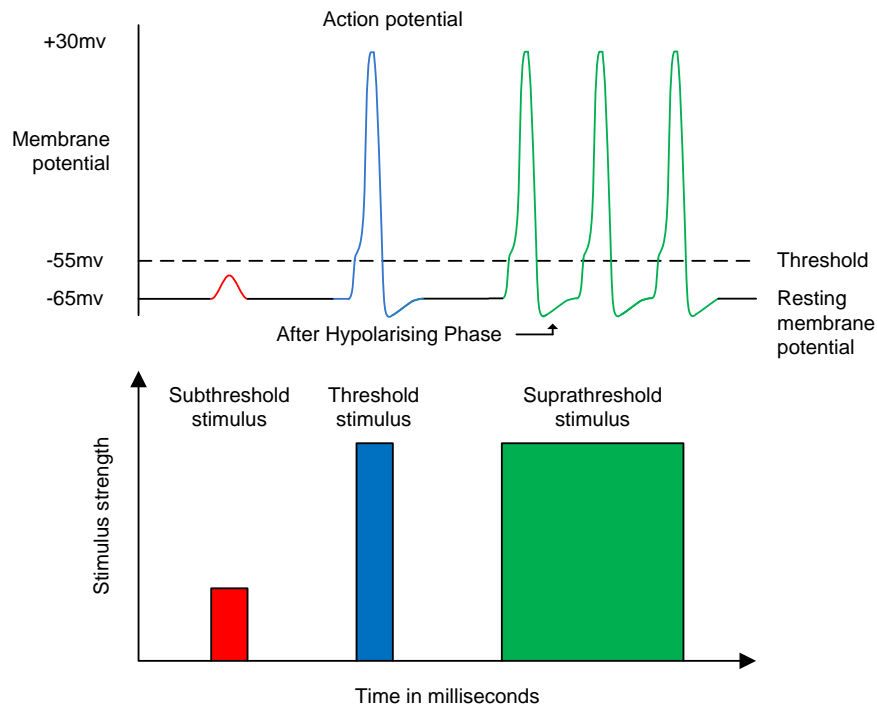
This is a basic overview of an extremely complex process. Fundamental components of this overview will now be discussed so as to provide an insight into theories and concepts relevant to this research.

### *2.1.1 Neurons*

The fundamental building block of the nervous system is the neuron. Neurons are electrically excitable cells that process and transmit information through electrical and chemical signals. Although they differ in size, function and number of connections, all consist of three main parts: a cell body, dendrites and an axon.

Neurons communicate to each other through synapses. Synapses are gaps between neurons in which nerve impulses cannot conduct. Synapses allow information to be filtered and integrated. In response to a nerve impulse, a pre-synaptic neuron will release a neurotransmitter which diffuses across the synaptic gap and binds to receptors of a post-synaptic neuron. The post-synaptic neuron will then respond by generating a graded electrical potential (a localised change in the electrochemistry of the nerve membrane) known as a Post Synaptic Potential (PSP). If a membrane threshold potential is reached by either one or a number of summated PSPs, an action potential is generated. An action potential is a self-regenerating wave of chemical activity that allows neurons to carry signals over long distances. Stimuli exceeding the threshold will produce action potentials of the same magnitude as threshold stimuli. Whilst the threshold is exceeded action potentials will continue to be generated following an After Hypolarising Phase (AHP) of the action potential (Figure 2-1). The AHP is a period (typically 1.0-4.0ms) in which the membrane potential of the neuron briefly becomes more negative than its normal resting level below threshold [26]. Hence, a larger stimulus than normal would be needed in order to cause a second action potential during the AHP. The normal direction of travel by an action potential along a neuron is known as orthodromic conduction. Conduction in the opposite direction to this is known as antidromic.

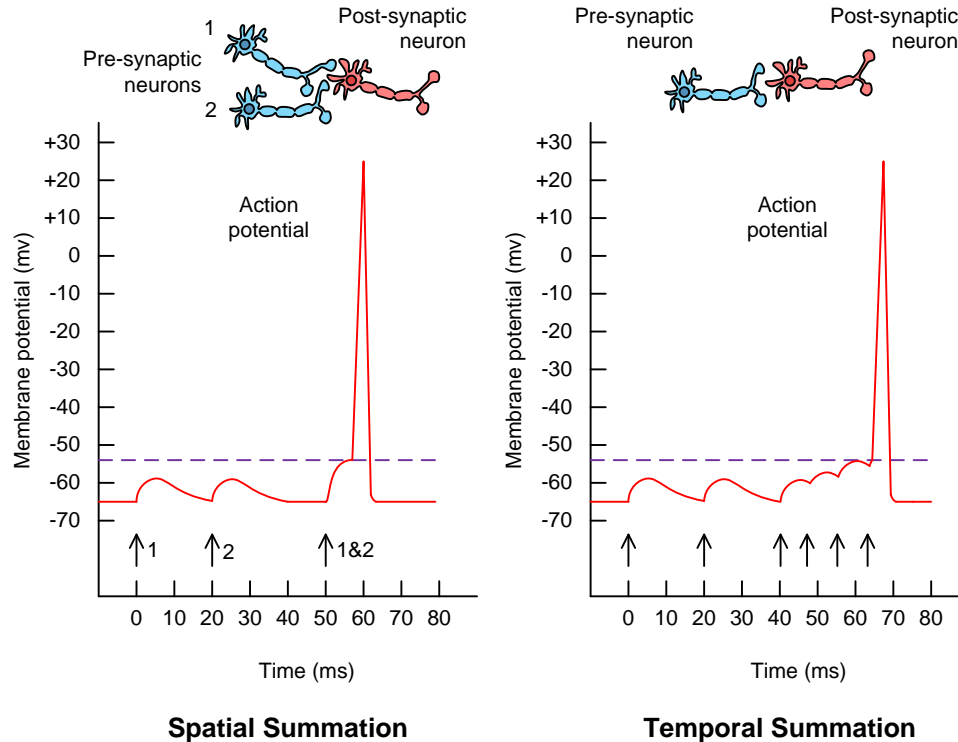




**Figure 2-1: Stimulus strength and action potential propagation**

*Arrows indicate excitatory post synaptic potentials. Depiction based upon Tortora, Grabowski, 2003 [26]*

Neurotransmitters can be excitatory or inhibitory. Excitatory neurotransmitters cause an Excitatory Post Synaptic Potential (EPSP) in the post synaptic neuron which brings its membrane potential closer to threshold, where a low intensity stimulus is required to excite the neuron. Inhibitory neurotransmitters generate an Inhibitory Post Synaptic Potential (IPSP) in the post-synaptic neuron which it brings its membrane potential further from threshold, where a high intensity stimulus is required to excite the neuron. Each neuron may have many synaptic connections with different neurons and hence these neurotransmitters will summate. Post synaptic potential can summate by two methods acting in parallel: temporal and spatial summation (Figure 2-2). Spatial summation is the summation of PSPs in response to stimuli that occur at different locations in the membrane i.e. summation due to simultaneous neurotransmitter release by several pre-synaptic neurons. Temporal summation is the summation of PSPs in response to stimuli that occur at different times i.e. summation of neurotransmitter due to repeated rapid neurotransmitter release by a single pre-synaptic neuron. A typical EPSP or IPSP lasts 15ms and hence a second release of neurotransmitter must occur from either this or another pre-synaptic neuron within this time in order for summation to occur. The combined effect of these two methods of summation influence whether and what neurons fire action potentials.



**Figure 2-2: Depiction of spatial and temporal summation**

*Depiction based upon Tortora, Grabowski, 2003 [26]*

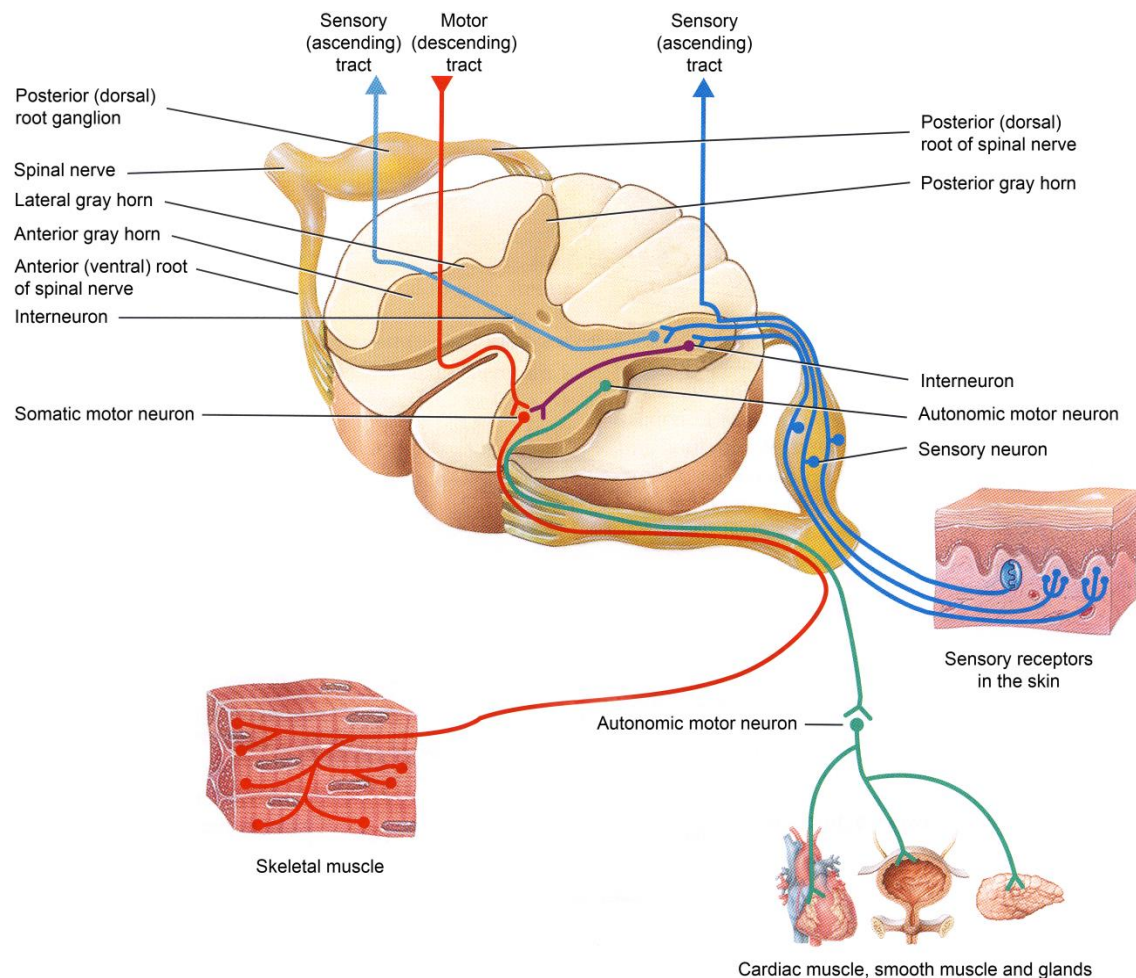
Chemical synapses do not share the bidirectional transmission property of conduction along neurons. However whilst an antidromic action potential arriving at a post synaptic neuron will not directly induce electrical changes in the pre-synaptic neuron, it is theorised that the strength of the synapse can be influenced. Hebb proposed that modifiable synapses would be strengthened if pre-synaptic firing coincided with, or was shortly followed by, post synaptic discharge [27]. It follows from this theory that the function and structure of synapses have the ability of change over time as the CNS continuously adapts to its efficient use. The ability of this dynamic system to receive both spatial and temporal input hence makes the CNS extremely powerful in the control and learning of human movement.

### 2.1.2 The spinal cord

A key function of the spinal cord is in the propagation of nerve impulses and integration of information. Billions of neurons form the grey and white matter of the cord giving its transverse cross section a distinctive butterfly or H shape (Figure 2-3).

White matter is primarily composed of distinct bundles of myelinated neuron axons (see section 2.1.3) which route information up and down the spinal cord. These bundles are

known as tracts and are distinguished by neurons within them which have a common origin or destination and carry similar information. The central grey matter of the spinal cord receives and integrates incoming and outgoing information, routing sensory or motor stimuli in order to coordinate a response. It is a very complex system, with each neuron typically receiving summative input from 100 to 10,000 chemical synapses. The grey matter is subdivided into regions called horns. The ventral (anterior) gray horns contain somatic  $\alpha$ -motor neurons that supply skeletal muscles. The dorsal (posterior) gray horns contain cell bodies and axons of interneurons of incoming sensory neurons. Interneurons are neurons which integrate information from sensory neurons through chemical synapses and elicit motor responses by exciting or inhibiting appropriate motor neurons. They can interact with motor neurons at the same spinal segment, across the cord to contra-lateral motor neurons or to other spinal levels. They enable movements to be coordinated within a limb, with proximal or distal activity of a limb or with movements of the contra-lateral limb. Descending inputs from the brain can modulate the excitability of interneurons, turning on and off reflex pathways for example (section 2.2.6) or allowing conscious voluntary control to dominate movement.



**Figure 2-3: Spinal cord transection indicating processing of sensory and motor output**

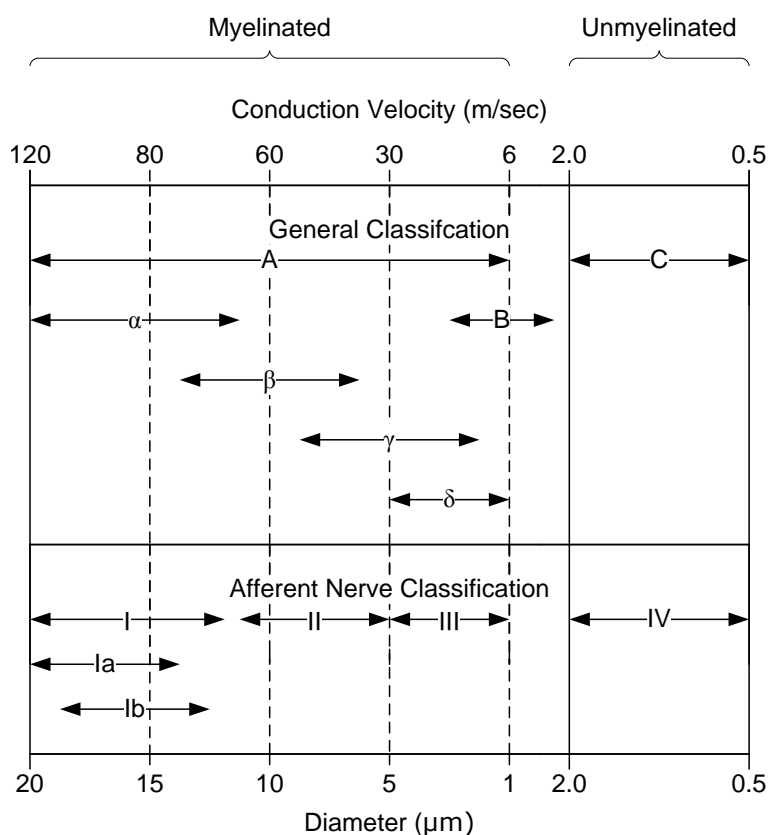
Modified from Tortora, Grabowski, 2003 [26]. Reproduced with permission of John Wiley & Sons, Inc.

### 2.1.3 Peripheral nerves

Nerves are long slender bundles of neuron axons which conduct electro-chemical nerve impulses. Most neuron axons are covered in a multi-layered lipid and protein covering (myelinated) which insulates the neuron and increases conduction velocity by the action potential effectively ‘hopping’ quickly from gaps or nodes in the myelination along the neuron. Whilst most sensory and motor neurons are myelinated, some slow autonomic ones are unmyelinated. Axons can be divided into three major size groups: large myelinated, medium myelinated and small unmyelinated. The conduction velocity of a neuron correlates to both its diameter and degree of myelination. Individual nerve fibres are typically classified in two ways [28]. The first depends on the axon diameter and categorises nerves into A, B or C. The A group is further classified into subgroups  $\alpha$ ,  $\beta$ ,  $\gamma$  and  $\delta$ . The second system proposed by Lloyd [29] classifies afferent nerve fibres

from muscles into four groups (I-IV) primarily on the basis of conduction velocity, but also origin and function. Figure 2-4 summarises the properties of these different classifications which will be used throughout this thesis.

Spinal nerves originate or terminate in the spinal cord and connect the CNS to sensory receptors, muscle glands, etc. in the rest of the body to form the PNS. A typical spinal nerve has two connections to the spinal cord: a posterior root and an anterior root (Figure 2-3). They are mixed nerves as the posterior nerve contains sensory (afferent) axons and the anterior nerve motor (efferent) axons. Most mixed nerves also contain afferent nerve fibres that convey pain and temperature signals to the autonomic nervous system.



**Figure 2-4: Peripheral nerve classification**

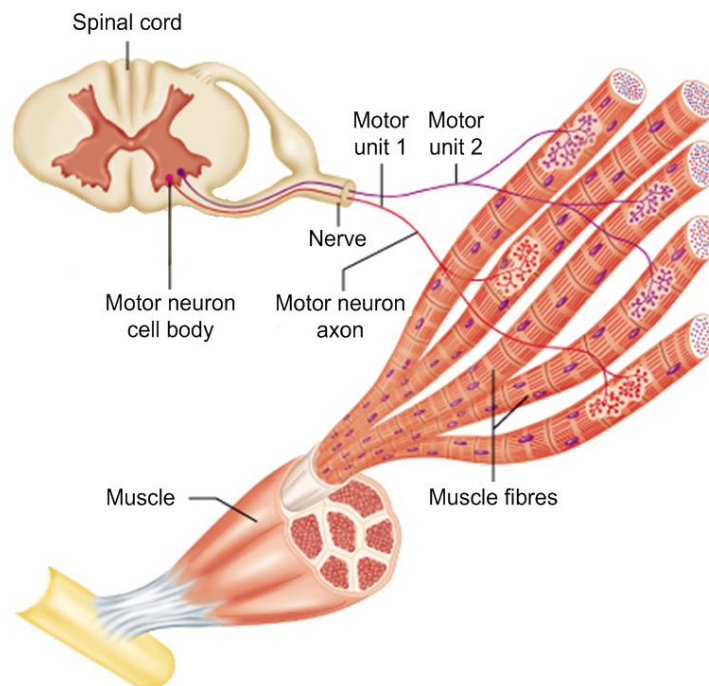
*Figures of conduction velocity and diameter based upon collectively published figures [28-30]*

#### 2.1.4 The motor unit

Following the axon of each somatic motor neuron distally, it branches a few millimetres before reaching the muscle and forms neuromuscular junctions with a number of muscle fibres (e.g. 10-3000) to create what is referred to as a motor unit (Figure 2-5). A motor

unit comprises of the motor neuron and all the muscle fibres that it forms neuromuscular junctions (innervates) with.

The muscle fibres of a motor unit will be typically dispersed throughout the muscle rather than clustered together. When an  $\alpha$ -motor neuron is activated all the muscle fibres of the motor unit contract in unison. At the neuromuscular junction there is a chemical synapse (section 2.1.1) which the motor neuron action potential cannot conduct across. The arrival of the action potential at the end plate of the  $\alpha$ -motor neuron causes a neurotransmitter called Acetylcholine (Ach) to be briefly released which crosses the synapse and binds to the motor end plate of the muscle fibre the other side. This causes a muscle action potential to flow which then initiates the contraction of the muscle fibre. The effect of Ach binding only lasts briefly as it is rapidly broken down (typically  $<0.5\text{ms}$  [31]) by an enzyme reaction. If another nerve impulse reaches the end bulb more Ach will be released and the process continues. Depending on the number and frequency of which motor units are recruited, muscle tension can be appropriately controlled for the desired function [26].



**Figure 2-5: Organisation of skeletal muscle with two motor units identified**

*Depiction based upon Marieb, 2001 [32]*

## 2.2 The Control, Function and Anatomy of Muscle

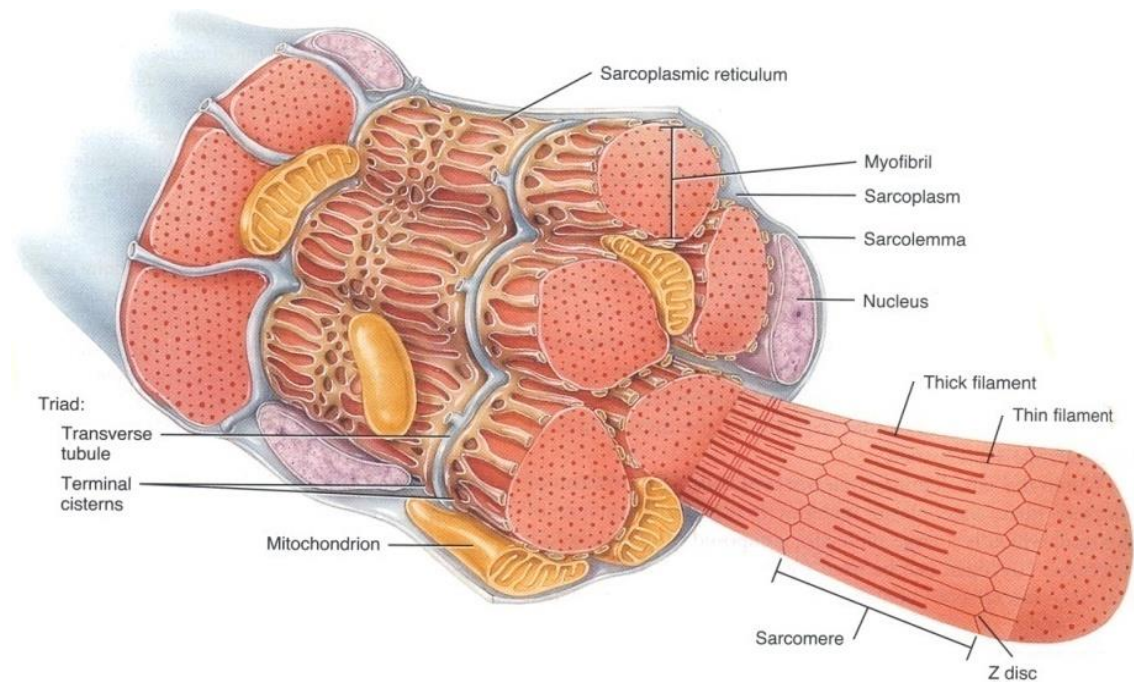
Having introduced the fundamental pathway of nervous control from the brain to muscle, details of the muscle anatomy and function and how it feeds back information to the CNS so as to enable coordination of movement will now be discussed.

### 2.2.1 *Muscle fibres*

Skeletal muscle is formed of muscle cells more commonly referred to as muscle fibres. These muscle fibres generally range from 10 to 100µm in diameter and from a few milli-meters to a number of centimetres in length. At birth, muscle fibre loses its ability to undergo cell division. Omitting significant muscular damage, the number of fibres remains fixed throughout one's lifetime. Physical ability is not fixed throughout life however, as the size and type of muscle fibres is able to change with age and usage.

The nuclei of skeletal muscle fibres are located beneath a plasma membrane of the muscle cell known as the sarcolemma (Figure 2-6). Thousands of small tunnels known as transverse tubules enable muscle action potentials which reach the sarcolemma to pass from the surface towards the fibre centre. This ensures each action potential excites throughout the muscle fibre at the same instance. Within the sarcolemma is the sarcoplasm, the cytoplasm of the muscle fibre. Sarcoplasm contains a substantial amount of glycogen which can be used to synthesise Adenosine TriPhosphate (ATP), a molecule used to store and release energy to power muscular contractions. It also contains a protein only found in muscle called myoglobin. Myoglobin binds oxygen molecules together which can be used by mitochondria for the production of ATP, this will be referred to again when distinguishing different types of muscle fibre (section 2.2.2). The sarcoplasm is filled with long thread like (~2µm diameter) structures which extend the entire length of the muscle fibre. These are myofibrils and are innate to the contractile function of the muscle. Each myofibril is encircled by a membranous sac called the sarcoplasmic reticulum. Dilated end sacs of the sarcoplasmic reticulum butt against transverse tubules from both sides. In a relaxed muscle fibre the sarcoplasmic reticulum stores calcium ions ( $\text{Ca}^{2+}$ ). Release of  $\text{Ca}^{2+}$  from the sarcoplasmic reticulum triggers muscle contractions and will be discussed further during the actual excitation-contraction cycle.

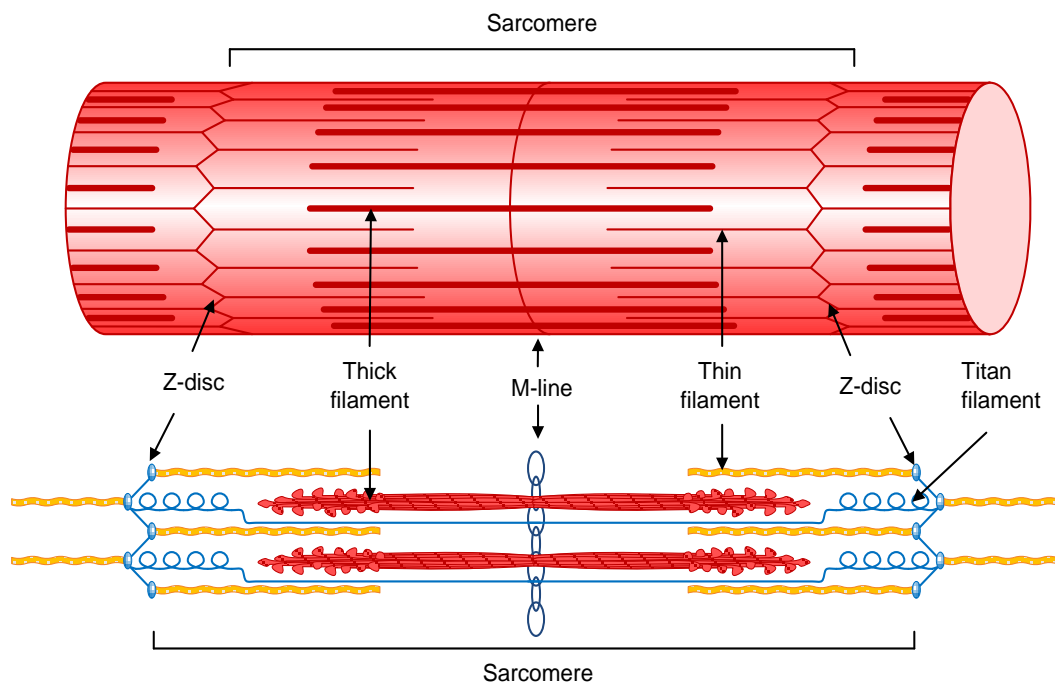




**Figure 2-6: Cross section of skeletal muscle fibre**

*Modified from Tortora, Grabowski, 2003 [26]. Reproduced with permission of John Wiley & Sons, Inc.*

Myofibrils are formed of thin and thick filaments which are involved in the contraction process. Filaments do not extend the entire length of myofibrils but are instead arranged in compartments called sarcomeres (Figure 2-7). Sarcomeres are the basic functional units of myofibrils and are separated from each other by narrow, plate-shaped regions of dense protein material called Z-discs.

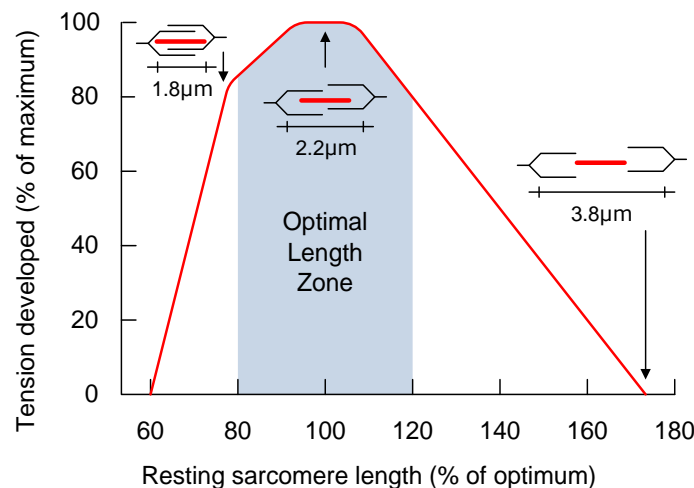


**Figure 2-7: Cross section of a muscle filament and sarcomere**

*Depiction based upon Tortora, Grabowski, 2003 [26]*



Depending on whether the muscle is contracted, relaxed or stretched, the thick and thin elements overlap by different amounts thus influencing the number of actin-binding sites available for cross-bridge changes. This accounts for differences in the maximum amount of tension that can be produced at different resting lengths of the sarcomere and hence muscle (Figure 2-8).



**Figure 2-8: Length-tension relationship of skeletal muscle**

*Depiction based upon results of Gordon et al. [33]*

The main components in thick and thin filaments are the contractile proteins myosin and actin respectively. These proteins push or pull cellular structures to achieve movement by converting the chemical energy in ATP to force. Thick filaments are collections of myosin molecules. Each myosin molecule is shaped like two golf clubs twisted together with the stem pointing towards the centre, or M-line, of the sarcomere. Thin filaments are anchored at one end to Z-discs and are predominantly formed of actin molecules. Each actin molecule has a myosin binding site where a myosin head can attach. In a relaxed muscle, myosin is blocked from binding to actin by strands of tropomyosin covering the myosin binding sites. The tropomyosin is held in place by troponin molecules.

When a muscle action potential propagates along the sarcolemma and into the transverse tubules it causes high concentrations of  $\text{Ca}^{2+}$  to be released by the sarcoplasmic reticulum into the cytosol around the thick and thin filaments. The released  $\text{Ca}^{2+}$  combines with troponin and causes it to change shape. This conformational change moves the tropomyosin away from the myosin binding sites on the actin and begins the muscular contraction cycle. The myosin heads include an ATP-binding site and ATPase, an enzyme which hydrolyses ATP into Adenosine DiPhosphate (ADP). This reaction reorients and energises the myosin head such that it is able to bind and

form cross bridges with the actin of the thin filaments. Once formed, the power stroke occurs as the myosin head rotates and stem flexes, sliding the thin filament past the thick filament towards the M-line. As the thin filaments slide inward the Z-discs move closer together and the sarcomere becomes shorter. This in turn causes the muscle fibre and hence muscle as a whole to shorten. At the end of the power stroke the myosin head remains attached to the actin until another ATP molecule is present for it to attach to. When the myosin head binds to another ATP molecule it detaches from actin and the cycle is ready to repeat. The cycle continues as long as ATP (energy) is available and the  $\text{Ca}^{2+}$  level near the thin filament is sufficiently high to bind with troponin.

It is the increase in  $\text{Ca}^{2+}$  concentration in the cytosol which starts a muscle contraction. Accordingly, a decrease stops it. Hence the sarcoplasmic reticulum also contains  $\text{Ca}^{2+}$  active transport pumps that use ATP to constantly move  $\text{Ca}^{2+}$  from the cytosol into the sarcoplasmic reticulum. Whilst muscle action potentials propagate through the transverse tubules,  $\text{Ca}^{2+}$  flows into the cytosol faster than it can be pumped out continuing the contraction cycle. Once motor action potentials cease, the  $\text{Ca}^{2+}$  concentration in the cytosol decreases due to the pumps, the tropomyosin blocks the myosin binding sites of the actin and the contraction cycle stops.

### 2.2.2 *Types of skeletal muscle*

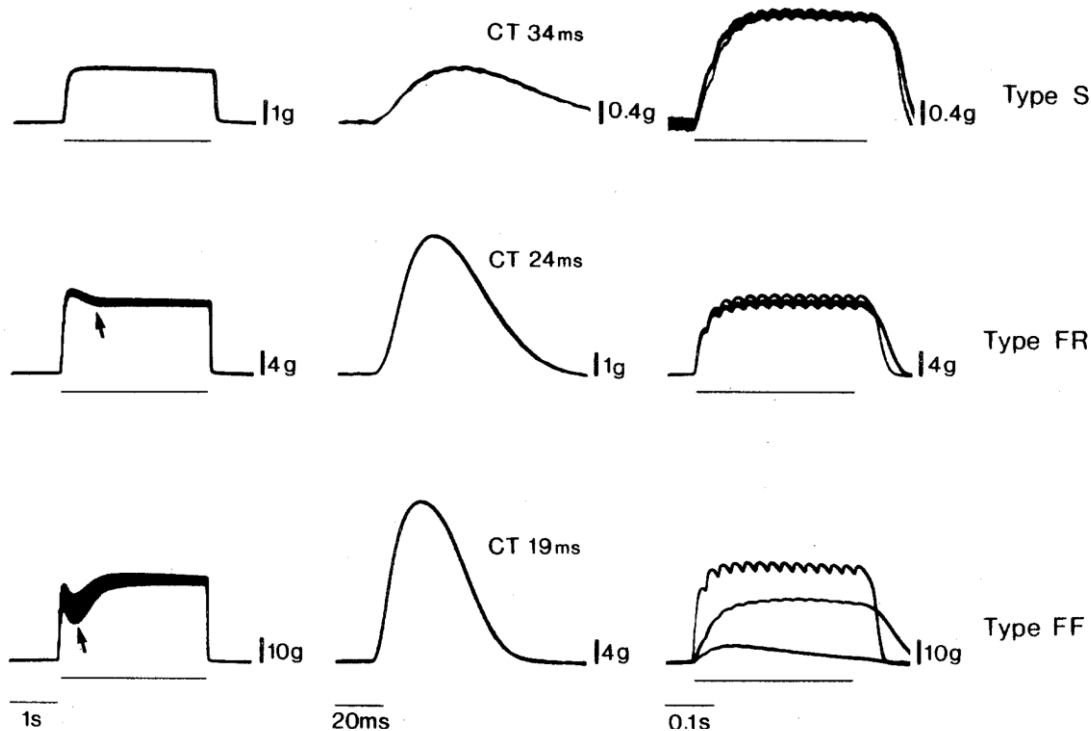
Muscle fibres are not all alike in composition and function and differ in the rate at which they can split ATP molecules (affecting speed and strength of contraction) and the type of enzymatic process they use to synthesize ATP (affecting fatigue resistance). Based upon these structural and functional differences, three types of fibre have been classified and their typical contraction characteristics are depicted in Figure 2-9:

- Slow (type S or I) fibres are smallest in diameter and produce only small amounts of force. They have large amounts of myoglobin and mitochondria enabling them to generate ATP quickly. ATP is hydrolysed slowly by myosin heads and hence they have a slow speed of contraction. They are fatigue resistant and are capable of prolonged, sustained contraction such as those involved when maintaining posture and for aerobic, endurance activities such as long distance running.
- Fast fatigue Resistant (type FR or IIa) fibres also contain large amounts of myoglobin and have good fatigue resistance. Their myosin heads hydrolyse

ATP 3-5 times faster than type I fibres and hence have a faster contraction time.

- Fast fatigable (type FF or IIb) fibres are largest in diameter and contain the most myofibrils. They generate very powerful contractions quickly but hydrolyse ATP rapidly. Hence they are adapted for intense anaerobic movements of short duration such as power lifting.

Some muscles are of predominantly one type of muscle fibre, most contain a mixture however. In this way the total range of operation of a muscle is extended beyond that of any single unit type. For example, the soleus which is used throughout standing or walking is typically composed of slow twitch fibres. The gastrocnemius however, which is used for sudden but brief contractions such as running or jumping, is predominantly composed of fast fibre types. Although the total number of muscle fibres is established at birth, the type of each fibre can change throughout life in response to factors such as exercise or inactivity [34].



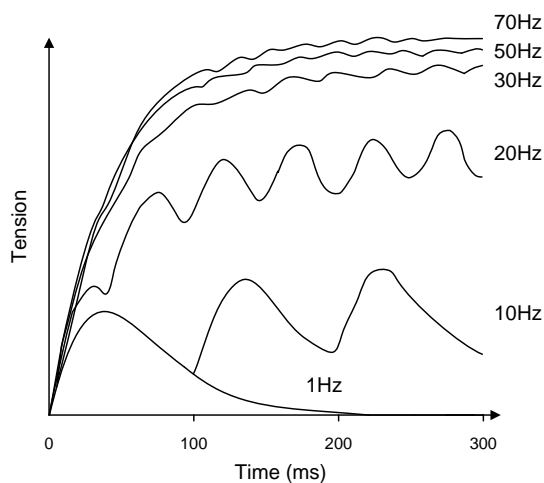
**Figure 2-9: Physiological identification of motor unit types**

Each row illustrates isometric tension (grams) recorded at the cat peroneus tertius muscle tendon due to particular types of motor unit. Each column indicates the response to 40Hz tetanus, twitch and fatigue tests. Arrows indicate 'sag' associated with FR and FF motor units during tetanus stimulation in which the initial contraction twitch gives an unfused tetani (see section 2.2.3 for explanation). Three superimposed records of the 1<sup>st</sup>, 60<sup>th</sup> and 120<sup>th</sup> tetanus are included during the fatigue test. Note different calibration marks for each motor unit type. (modified from Jami et al., 1982, Figure 1 [35], with kind permission from Springer Science and Business Media)

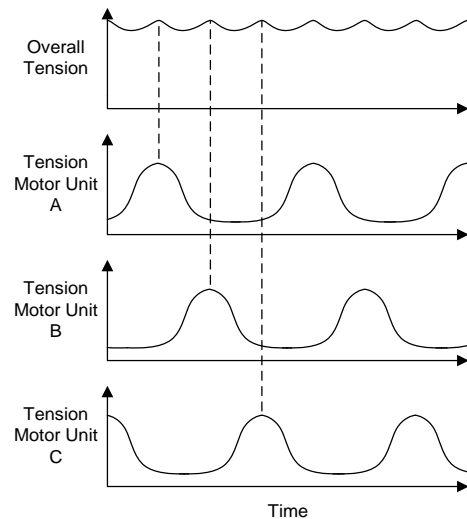
Each muscle fibre has a single neuromuscular junction and those innervated within a common motor unit are of the same fibre type. The size, metabolism and functional properties of muscle fibres are matched to the  $\alpha$ -motor neuron that innervates them. That is, small diameter  $\alpha$ -motor neurons innervate slow twitch muscle fibres, and large diameter  $\alpha$ -motor neurons innervate fast twitch muscle fibres

### 2.2.3 Activation of skeletal muscle

The response of a skeletal muscle to a single nerve impulse is the twitch response and differs between muscles. If more than one impulse is given at an interval which is less than the contraction time of the muscle, the force produced by each impulse summates. A fused tetanus is produced when the force fluctuations to each individual impulse can no longer be distinguished. As indicated in Figure 2-10, contractions of motor units are fused at approximately 30Hz and above.



**Figure 2-10: Typically observed relation between stimuli frequency and tension**  
Depiction based upon Baker et al. [1]



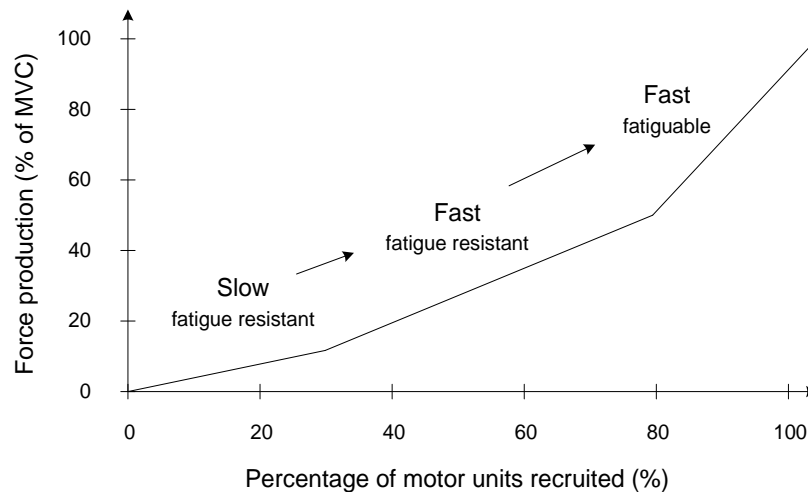
**Figure 2-11: Depiction of tension summation amongst motor units**  
Depiction based upon Baker et al. [1]

Most voluntary contractions activate motor units asynchronously. The firing rate of individual motor units can be well below the frequency where the tension it provides summates (approximately 30Hz) yet a smooth controlled movement is still produced. This is due to the asynchronous summation of force between motor units. Whilst some are contracting others are relaxing (Figure 2-11). This pattern delays muscle fatigue and permits smooth controlled contractions.

During a sustained contraction the activation rates of motor units are continuously modulated by the CNS to optimise force. At the start of a rapid contraction, motor units may fire at frequencies of 150Hz or more for the first two or three impulses in order for twitch forces to rapidly develop in generating large forces [8-11]. This is akin to a naturally occurring high frequency doublet stimulus and will be discussed further in section 4.4.1. Firing rates gradually decline throughout the rest of the contraction to rates as low as 20Hz. The surprising feature of this decline is that it is not accompanied by a drop in muscle force. During fatigue there is a change in the mechanical properties of motor units and the relaxation time of single motor unit twitches increase [36]. Due to this increase in twitch time, the motor neuron activation rate needed to produce a fused tetanus declines [37] (Figure 2-9). It is hypothesised that this decrease in motor unit firing frequency serves to forestall fatigue by optimising the force output of motor units whilst also protecting against conduction failure at the neuromuscular junction due to prolonged high discharge rates. This characteristic is termed “Muscle Wisdom” [38, 39] and is thought to stem from reflex pathways within the spinal cord [40]. This highlights the intelligence of the CNS to optimally control and utilise muscle function. There are two conditions when motor units are not activated asynchronously: during very powerful contractions and in the presence of fatigue. A technique known as cross correlation can be used to assess this [41]. If the discharge of two motor units of the same muscle was unrelated, recording their electrical activity and plotting the relative time between discharges would indicate equal temporal discharge probability. In reality there is often a small peak at time zero indicating that they activate in synchrony. This is explained in that each motor unit’s motor neuron receives a common synaptic input which brings them towards threshold at the same time.

#### *2.2.4 Motor unit recruitment order during voluntary contractions*

In order to make best use of the properties of the different muscle fibre types, motor units are recruited in a specific order depending on the requirements of the task being performed. Henneman and colleagues postulated that in all types of contraction the order in which a motor unit was recruited depended solely on the size of its motor neuron axon [42]. Therefore if a weak contraction is required, slow twitch fibres which are suited to long lasting weak contractions are recruited, but if greater force is required fast fatigue resistant followed by fast fatigable fibres are recruited (Figure 2-12).



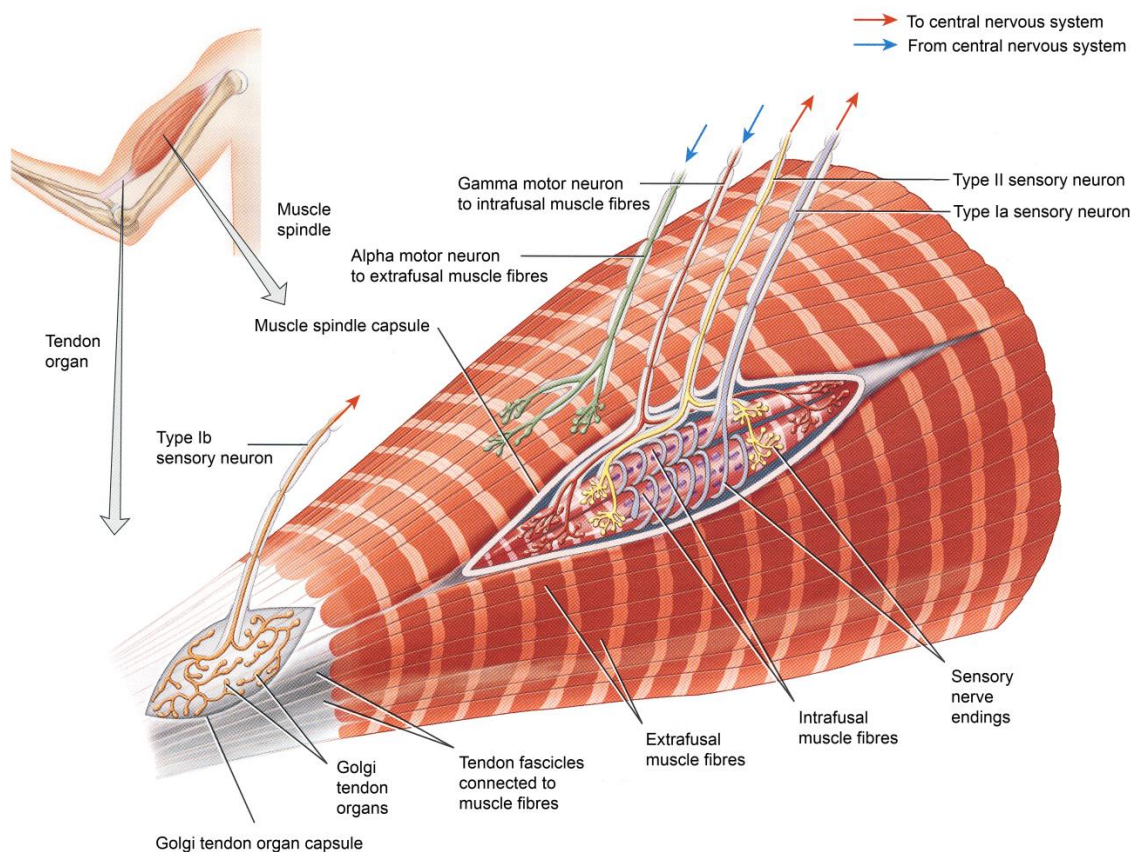
**Figure 2-12: Motor unit recruitment order trend during voluntary skeletal muscle activation**

As described by Henneman *et al.* [42], based upon graphical depiction by Gregory & Bickel 2005 [43] (MVC = maximal voluntary contraction)

Although the voluntary recruitment order of Figure 2-12 is widely supported through observed findings, a detailed explanation continues to be debated [43]. The most widely accepted hypothesis of the Henneman recruitment order is based upon the assumption that a given input to an  $\alpha$ -motor neuronal pool evokes the same synaptic current in all cells. It is also assumed that the passive electrical properties and hence resistance per unit area (resistivity) of cell membrane is constant and independent of  $\alpha$ -motor neuron size. Increasing the axon diameter, and hence cell surface area, can be thought analogous to adding resistors in parallel between the interior and exterior of the cell. It therefore follows that the input resistance of a large  $\alpha$ -motor neurons are small compared to that of small  $\alpha$ -motor neurons. Hence if the synaptic current is the same, small  $\alpha$ -motor neurons with large input resistances will be depolarized to a greater extent than larger  $\alpha$ -motor neurons. If the threshold for action potential generation is the same in all  $\alpha$ -motor neurons then smaller ones will fire action potentials before larger ones. This explanation continues to be disputed, largely based on the assumption of equal synaptic currents. A more comprehensive review and basis for the assumption is provided by Rothwell [44].

### 2.2.5 The muscle spindle and golgi tendon organ

In coordinating movement the CNS requires information regarding limb position and movement. Skeletal and muscular proprioceptors (mechanoreceptors), embedded within muscles and tendons detect internal stimuli within the body and inform the CNS of such instances as when muscles are contracted, the amount of tension in tendons and the position and movement of joints. Exteroceptors detect external stimuli such as touch and heat. There are three different types of mechanoreceptors: these sense muscle length, muscle length and speed and muscle tension respectively. The first two are located within an encapsulated sensory receptor termed a muscle spindle which is interspersed within the belly of skeletal muscles as shown by Figure 2-13.



**Figure 2-13: Muscle spindle and golgi tendon organ**

Modified from Tortora, Grabowski, 2003 [26]. Reproduced with permission of John Wiley & Sons, Inc.

Each muscle spindle consists of several slowly adapting sensory nerve endings termed primary and secondary endings which wrap around or connect to specialised muscle fibres called intrafusal muscle fibres (as oppose to extrafusal muscle fibres; normal contractile skeletal muscle). Primary spindle endings (large type Ia afferent) are sensitive to both muscle stretch (muscle length change) and rate of change of muscle stretch (speed of muscle length change). Secondary spindle endings (type II afferent) are sensitive to just muscle stretch. All muscle spindles have type Ia afferents, but not all type II afferents. In addition to their sensory neurons they contain motor neurons called gamma ( $\gamma$ ) motor neurons. These adjust the tension in a muscle spindle to variations in length of the muscle; this keeps the intrafusal muscle fibres taut and maintains sensitivity of the primary and secondary endings to stretching of the muscle. Additionally ~20% of efferent innervations of muscle spindles are from branches of  $\alpha$ -motor neurons known as beta ( $\beta$ ) motor neurons. As the firing frequency of a  $\gamma$ -motor neuron increases the muscle spindle becomes more sensitive to stretching in its mid-region; enabling the nervous system to maintain an optimal range for signalling changes in muscles independent of their actual length. In general,  $\gamma$ -motor neuron activity follows  $\alpha$ - (and hence  $\beta$ -) motor neuron activity. However this is not so in instances when a muscle is required to contract whilst lengthening (eccentrically contract). For example, the tibialis anterior eccentrically contracts during early stance to prevent foot slap. Increasing sensitivity about the intrafusal fibres mid-point whilst the muscle is lengthened would be detrimental to the functional movement being completed.

The principal role of the muscle spindle is in providing sensory information to a feedback loop maintaining muscle length. Increasing the length of the muscle increases the number of action potentials in the Ia and II afferent neurones. These afferents enter the dorsal root of the spinal cord and form a monosynaptic (i.e. not via an interneuron) connection to the  $\alpha$ -motor neuron which innervates the same muscle. As the muscle is stretched, the muscle activity is increased, returning the muscle to its original length. This is the stretch reflex and its use and function is described along with other reflexes in section 2.2.6 which follows.

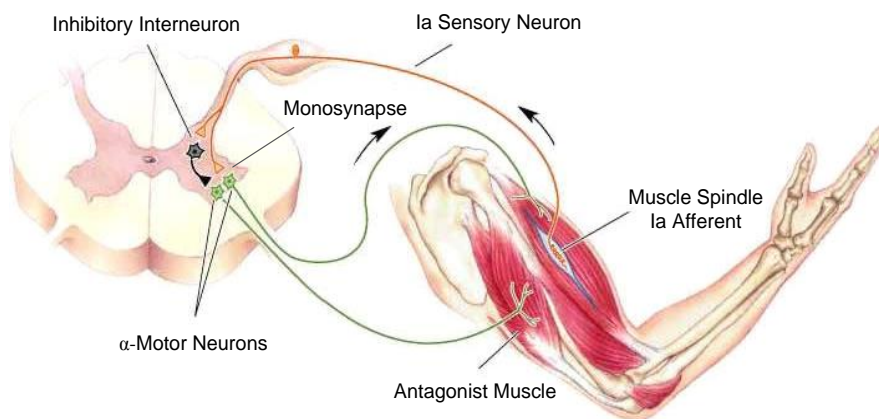
The third type of receptor responds to changes in muscle tension and are termed golgi tendon organs. They are located at the junction between muscle fibres and tendon and when tension in the muscle forms their afferent nerve endings are compressed and excited (Figure 2-13). Golgi tendon organs have a slightly smaller diameter (type Ib afferent Figure 2-4) afferent nerve than the primary spindle endings.



### 2.2.6 Spinal reflexes

Reflexes are fast, involuntary coordinated patterns of muscle activation and relaxation elicited by peripheral stimuli which are used throughout movement. Basic components of a spinal reflex arc are a sensory receptor, a sensory neuron, an integration centre with one or more synapses in the CNS, an  $\alpha$ -motor neuron and an effector. Somatic spinal reflexes include the stretch, tendon, flexor withdrawal and crossed extensor reflexes [26].

The most simplistic form of motor control is the monosynaptic spinal reflex from Ia afferents to  $\alpha$ -motor neurons where integration is considered to be completely regulated within the spinal cord. The ipsilateral stretch reflex introduced in section 2.2.5 can be generally thought of as a monosynaptic reflex and counteracts a muscle stretch by contracting the stretched muscle (Figure 2-14).



**Figure 2-14: Stretch and reciprocal inhibition reflexes**

*Modified from Bear, Connors, Paradiso 2001 [45]. Reproduced with permission of Lippincott Williams.*

At the same time the reciprocal inhibition reflex will also be activated in order to relax the antagonistic muscle that opposes the stretch reflex contraction. This is classed as a polysynaptic reflex as it involves more than one synapse within the spinal cord. The afferent sensory neuron detecting the stretch, as well as activating the monosynaptic stretch reflex, branches in the spinal cord and synapses with an inhibitory interneuron which synapses and inhibits an  $\alpha$ -motor neuron that would normally excite the antagonist muscle (Figure 2-14). Reciprocal inhibition prevents conflict between opposing muscles and is vital when coordinating movement [26].

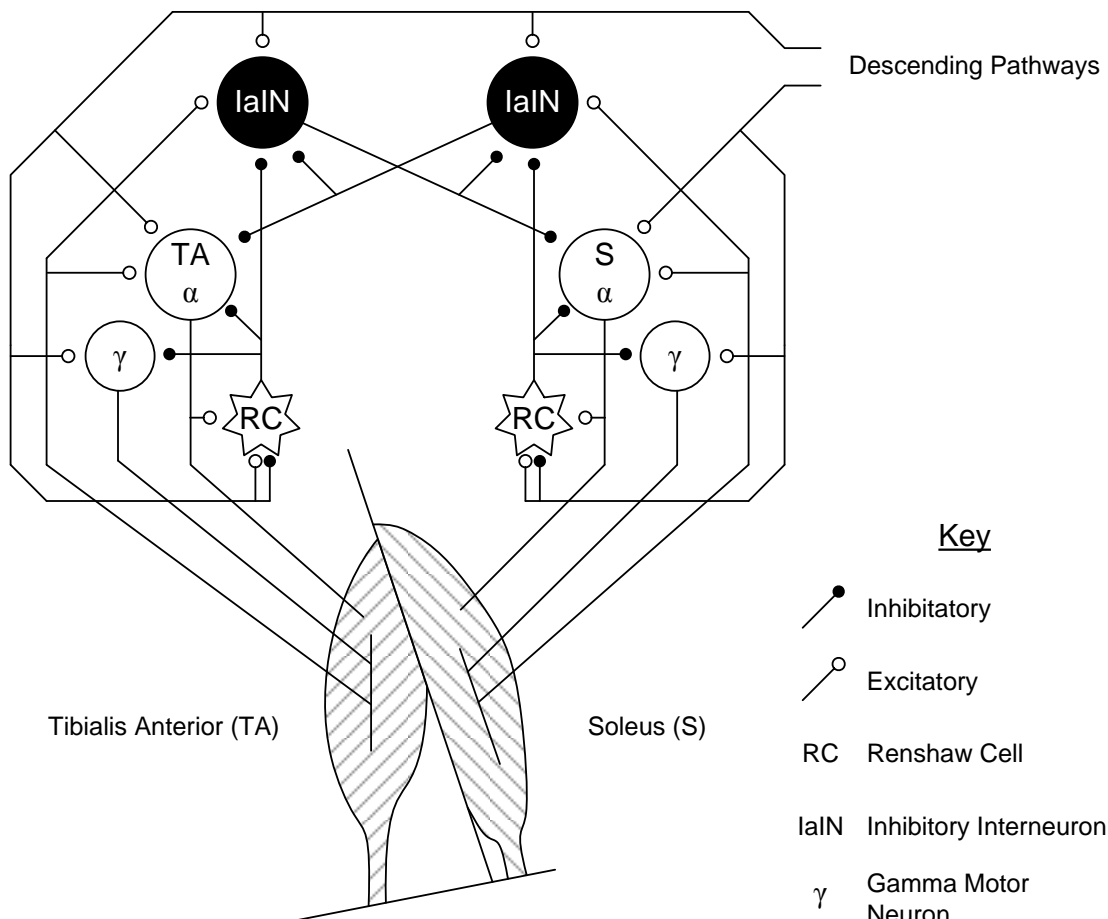
There are many more reflexes such as pain reflexes which protect the body from harm. The flexor withdrawal reflex is an inter-segmental reflex which activates interneurons at different spinal cord segments so as to provide hip, knee and ankle flexion. An example of its function would be when inadvertently stepping on a sharp object to quickly withdraw weight from the painful stimulus. It also provokes a crossed extensor reflex which again operates at inter-segmental levels so as to activate extensor muscles in the contra-lateral lower limb to shift weight on to this side whilst maintaining balance.

Some reflexes are inborn, others are learned or acquired. Reflexes are used when coordinating walking and circumvent decisions from higher levels (e.g. brain) such that it can be completed without conscious effort whilst enabling a sudden response should a sharp object be stepped upon for example. As authors such as Wolpaw *et al.* demonstrate, it is possible to condition reflexes thus demonstrating versatile adaptability of the spinal cord [46].

#### 2.2.7 Renshaw cells

Renshaw cells are spinal interneurons which are activated by collaterals of  $\alpha$ -motor neuron axons. They inhibit the  $\alpha$ -motor neuron from which they receive their input, thus reducing the sensitivity of the  $\alpha$ -motor neuron to further excitatory input (Figure 2-15). This effect is termed recurrent inhibition and although its function is still debated some authors describe this as 'enhancing the contrast' within the motor neuron pool [47, 48]. Renshaw cells are also paired to the  $\gamma$ -motor neuron and Ia inhibitory interneurons that mediate reciprocal inhibition of antagonist motor neurons. Thus Renshaw cells provide negative feedback on agonist  $\alpha$ -motor neurons and facilitate antagonist motor neurons [49]. Like other spinal interneurons they are influenced by descending motor pathways as demonstrated by electrophysiological changes in inhibition effects observed during voluntary or postural movements [50].

Total muscle force depends upon the number of motor units activated, the firing rate of those motor units and the type of muscle fibres they innervate. It is also theorised that when very large, very sudden forces are required, Renshaw cells inhibit smaller motor units thus ensuring that only units required for the activity are active, and those motor units which would be redundant during an activity do not fire unnecessarily [51].



**Figure 2-15: Renshaw cells and recurrent inhibition of the lower limb**

*Renshaw Cells provide negative feedback on their  $\alpha$ -motor neuron partner and the Ia inhibitory interneuron mediating reciprocal inhibition of the antagonist muscle. Depiction based upon Barnes, Johnson 2008 [49] and Enoka 2008 [52].*

This chapter has given a background to unimpaired motor function, which permits the explanation of investigations and results in following chapters. It is crucially important to note however that the motor function described is that of unimpaired physiology. The motor function of an individual with UMN dysfunction can differ from this unimpaired model at many levels. Although the clinical presentation of UMN dysfunction on motor control can vary considerably, common effects will now be briefly discussed such that factors pertaining to this intended patient group can be introduced when discussing the use of electrical stimulation in Chapter 4.

## Chapter 3 Effect of Upper Motor Neuron Injury on Neuromuscular Control

It is intended for the outcomes of this research to enhance the benefits gained from using FES by people who have sustained an UMN injury. An UMN injury is one affecting the brain or spinal cord and can result in altered volitional movement control. Conditions involving UMN impairment include stroke, spinal cord injury, cerebral palsy, multiple sclerosis, hereditary spastic paraplegia and Parkinson's disease.

### 3.1 Upper motor neuron syndrome and spasticity

The term 'upper motor neuron syndrome' refers to the collective motor control changes that occur in skeletal muscle following an UMN lesion. The clinical features of UMN syndrome can be divided into two broad groups (Table 3-1). Negative and positive phenomena are generally associated with either reduced or additional motor activity respectively.

Positive Phenomenon	Negative Phenomenon
<ul style="list-style-type: none"> <li>• Increased tendon reflexes</li> <li>• Clonus</li> <li>• Positive Babinski sign</li> <li>• Spasticity (a velocity dependent increase in resistance to passive movement)</li> <li>• Dyssynergic patterns of co-contraction during movement</li> <li>• Associated reactions and other dyssynergic stereotypical spastic dystonia</li> </ul>	<ul style="list-style-type: none"> <li>• Muscle weakness</li> <li>• Loss of dexterity</li> <li>• Fatigability</li> </ul>

*Table 3-1: 'Positive' and 'Negative' phenomena of upper motor neuron syndrome*

*Table reproduced from Barnes et al. [53]*

With immobility, soft tissues surrounding the muscle including tendons, ligaments, and joints themselves can also develop changes resulting in decreased compliance affecting Range Of Movement (ROM) and function.

Spasticity is a common but not inevitable feature of UMN syndrome (a positive phenomenon) that can cause profound disability through complex neurophysiological impairment. For a comprehensive explanation of the pathophysiology of spasticity, the reader is recommended to Sheean [54]. To date, a commonly quoted definition of spasticity is that given by Lance [55]:

*“a motor disorder that is characterised by a velocity dependent increase in the tonic stretch reflex with exaggerated tendon reflexes, resulting from the hyper-excitability of the stretch reflex, as one component of the upper motor neurone syndrome”*

*Lance, 1980*

Lance’s definition denotes that spasticity is a pure motor disorder that exclusively results from hyper excitability of the stretch reflex. In 2005 a multi-centred European Union funded research project entitled Support Programme for Assembly of database for Spasticity Measurement (SPASM), identified a need to update the definition of spasticity to accurately reflect more recent research findings and clinical interpretations. The group proposed the following definition of spasticity [56]:

*“disordered sensori-motor control, resulting from an upper motor neurone lesion, presenting as intermittent or sustained involuntary activation of muscles”*

*Burridge et al.2005*

This redefines spasticity as a generic term which describes the entire range of positive signs and symptoms of UMN syndrome. It excludes negative features and pure biomechanical changes in soft tissues and joints which are associated with immobility. This revised definition from the SPASM project also reflects that spasticity is a sensory as well as motor disorder and does not result purely from the stretch reflex.

Aspects of the negative and positive phenomena of UMN syndrome will now be further discussed with relevance to this research.

### *3.1.1 Negative phenomena of UMN syndrome*

Following a UMN injury there will generally be a reduction in physical mobility associated with impairment or absence of voluntary muscle activation. This decrease in motor activity characterises the negative phenomena of UMN syndrome. Muscles which are no longer receiving “typical” efferent control generally develop fast fatigable twitch properties [34, 57]. Although as outlined in section 2.2.2, such fast twitch fibres characteristically develop large amounts of force, after UMN injury they waste due to inactivity. As their metabolic demand reduces, muscle bulk and blood supply also reduce. This leads to a reduction in maximum force production and fatigue resistance which contributes to a loss of movement dexterity.

### *3.1.2 Positive phenomena of UMN syndrome*

Positive features of UMN refer to an imbalance of supraspinal inhibitory and excitatory inputs which produce a state of net disinhibition and hyper-excitability of the spinal reflexes. This is often characterised by hyper-excitability of the stretch reflex, loss of normal reciprocal inhibition and abnormal co-activation between agonists and antagonist muscles. These consequences can result in abnormally increased muscle tone known as hypertonia. Clinically, increased flexor tone in the upper limb and increased extensor tone in the lower limb are often noted. Soft tissue changes associated with immobility, can arise from muscle being maintained in shortened position due to such hypertonia. Therefore during rehabilitation post UMN injury, good posture, activity and regular muscle stretching is encouraged in order to maintain ROM and prevent contractures.

For a patient with UMN syndrome a troublesome positive phenomenon can be clonus caused by hyper-excitability reflexes. Clonus is a series of involuntary, rhythmic, muscular contractions and relaxations which can occur spontaneously or more commonly in response to, often slight, muscle stretch. Ankle clonus can impede safe mobilisation by causing the toes to catch the ground during the swing phase of gait.

Other more painful extensor and flexor spasms can be a feature of UMN syndrome. These can occur spontaneously or in response to mild sensory stimulation due to hyper excitable reflexes and involve multiple joints. For example in the lower limb an extensor spasm may involve hip and knee extension with plantarflexion and inversion of the foot.

Many of the positive phenomena of UMN syndrome occur at rest but may be exacerbated by movement. During dynamic conditions, abnormal co-contraction of agonist and antagonist muscles can disrupt normal smooth movements causing spastic dystonia. Involuntary unnecessary activation of muscle remote from those engaged in a task can occur. Such associated reactions can interfere with balance and function.

### 3.2 Assessment of Spasticity

There are many methods of attempting to quantify spasticity that were examined by the SPASM project [58-60] and will now be summarised. Clinical methods tend to involve manual, uncontrolled perturbations that are subjective and at best provide semi-quantitative data. Electrophysiological measurement of abnormal motor function can be used to assess spasticity however this can provide limited assessment of the complex positive phenomenon described. Due to the reflex mediated nature of spasticity presentation, an electrically elicited reflex known as the H-reflex can be used to assess it [61] (discussed in section 4.1.2). In Voerman *et al's*. [60] review of the H-reflex and other neurophysiological assessments of spasticity, it was concluded that the methods used are sensitive to a considerable number of experimental conditions and are characterized by a moderate reliability and sensitivity. Correlations with other spasticity assessment parameters are moderate to poor and it is recommended that combined neurophysiological – biomechanical assessments of spasticity are completed during active, functional movements.

### 3.3 Summary

As discussed within Chapter 2, there are many processes and factors affecting motor control and hence force production. An UMN injury will often cause both soft tissue and neurophysiological changes affecting both sensory and motor systems. Collectively this represents a delicate balance of complex inter-dependencies. In the instance of UMN injury, a pronounced effect on processes at many levels is the cause of the variety of unique clinical presentations amongst UMN patients.

## Chapter 4 Electrical Stimulation

Electrical stimulation is used extensively in modern healthcare during diagnostic investigations, therapy and rehabilitation. In accordance with the focus of this research, a brief overview of its diagnostic, therapeutic and clinical use will first be summarised.

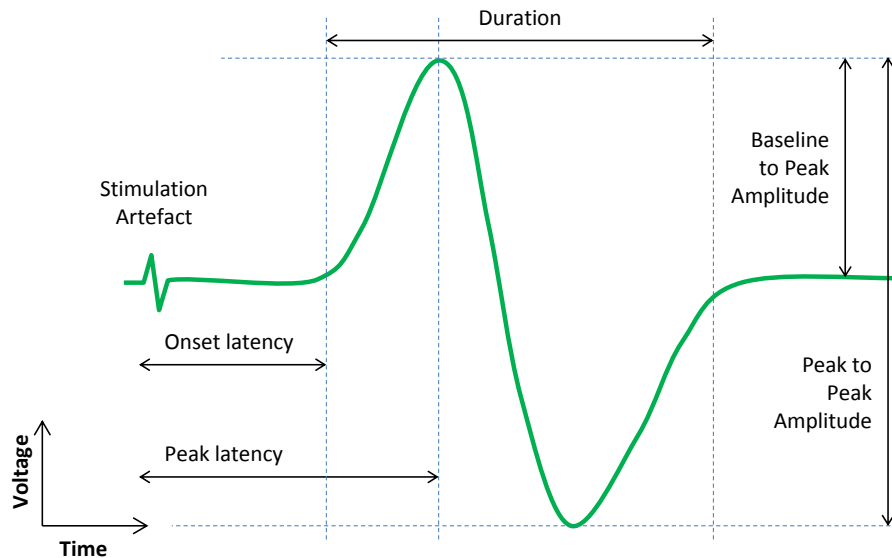
### 4.1 Electrical Stimulation for Diagnostic Investigation

Different pathological processes result in changes in the speed and efficiency of sensory and motor nerve conduction. A nerve conduction study is a collection of electro-diagnostic tests which can be used to assess neurological function. Three nerve conduction tests relevant to this research will now be discussed.

#### *4.1.1 Motor nerve conduction study*

A motor nerve conduction study applies single supramaximal electrical stimulation pulses to a peripheral motor nerve and records Electromyography (EMG) from the muscle it innervates. The size and latency of the resulting EMG response to each pulse is used to assess the function of the nerve. Parameters describing the resulting Compound Muscle Action Potential (CMAP) or M-wave, are indicated in Figure 4-1. Onset latency represents the conduction along the fastest (widest diameter) myelinated axons, whereas peak latency represents conduction along the majority of the axons.





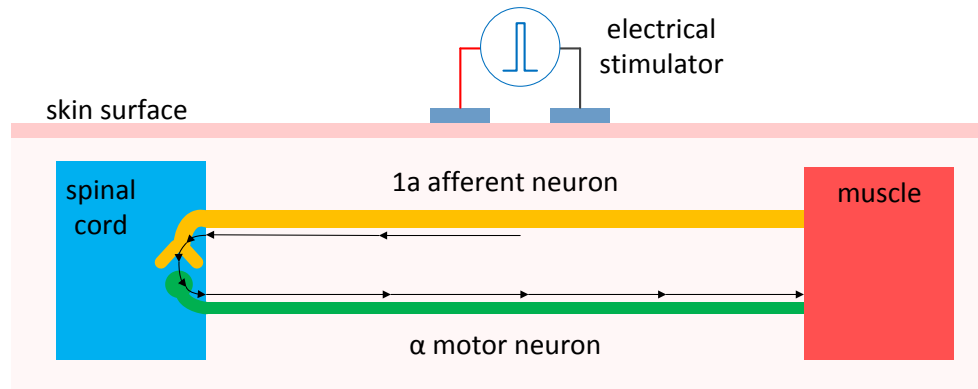
**Figure 4-1: Compound Muscle Action Potential waveform parameters**

Following the direct muscle response (compound muscle action potential or M-wave), late responses may be recorded. The increased latency of these components is associated with their conduction pathway. Two late responses relevant to this study are now discussed.

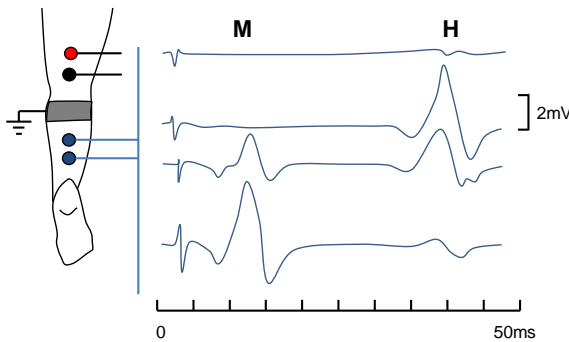
#### 4.1.2 H-reflex testing

The H-reflex is a fundamental neurophysiology test used to assess the excitability of spinal reflexes. As such, it can be used as quantitative spasticity assessment tool [61]. Due to an inverse relationship between axon diameter and electrical stimulus threshold for activation, large Ia afferent nerves can be artificially activated at a lower intensity than smaller diameter  $\alpha$ -motor neurons (Figure 2-4). EMG recorded from a muscle innervated by the peripheral nerve can show a reflex response due to such a sub-motor threshold stimulus. The response will have a latency associated with the afferent conduction from stimulation site to the spinal cord, synaptic transmission across the spinal cord, efferent conduction to the muscle and synaptic transmission across the neuromuscular junction (Figure 4-2).

As the intensity of the stimulus is increased sufficiently,  $\alpha$ -motor neuron axons are activated and a direct muscle response (M-wave) is elicited. At high intensities the H-wave is abolished due to antidromic motor conduction rendering the  $\alpha$ -motor neuron in its refractory period to the reflex (Figure 4-3). Figure 4-4 shows a characteristic plot of H- and M-wave amplitudes to stimulation intensity.

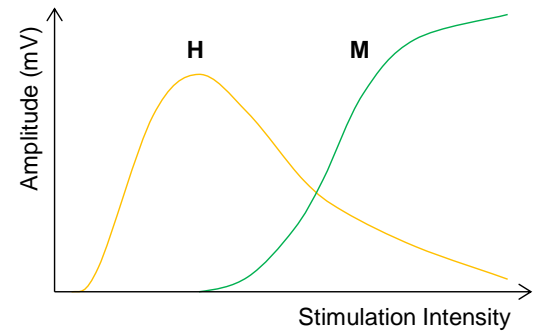


**Figure 4-2: Depiction of H-wave mechanism**



**Figure 4-3: Evoked potentials with increasing pulse amplitude of medial popliteal nerve.**

*Depiction based upon [62]*



**Figure 4-4: Typical H- and M-wave recruitment curves**

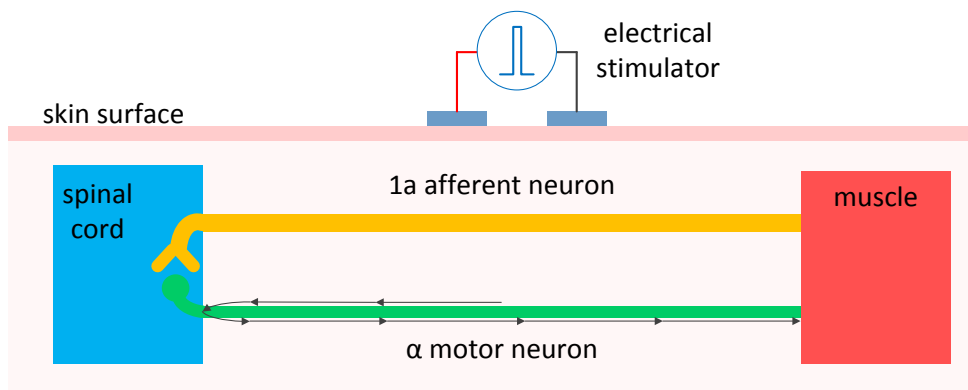
*Depiction based upon [62]*

If two or more stimuli are applied to a nerve within the order of a few seconds the direct muscle response (M-wave) and the reflex response (H-wave) will demonstrate different behaviours. Successive M-wave responses will be very similar. The H-reflex following the second stimuli will generally be of smaller amplitude than the first however. This difference is thought to be due to the properties of the central synapse that is part of the H-reflex arc but not the M-response [63]. The depression of the H-response has been termed post-activation depression and can last a number of seconds [64, 65].

H-reflex amplitude is generally elevated in patients with spasticity due to hyper-excitability of stretch reflexes following Ia afferent activation. Measurement of the H-reflex can be influenced by a number of factors besides motor neuron pool excitability and post activation depression. Voerman *et al.* [61] provides a review of such factors including amongst others, stimulus repetition [66] and duration [67] and limb position. In a practical example of this, Schneider *et al.* [68] demonstrated its task dependent nature throughout the gait cycle. Despite such influences, factors affecting the reflex can generally be controlled such that the H-reflex has been shown to be sufficiently reproducible during diagnostic investigations [69].

### 4.1.3 F-response testing

F-wave studies apply supramaximal intensity stimuli to an  $\alpha$ -motor neuron whilst recording EMG from a muscle supplied by it. A response with a similar latency of the H-reflex can be seen in some muscles however unlike the H-reflex, this response does not lessen with increasing stimulus intensity or frequency. This response is termed the F-wave and is caused by antidromic  $\alpha$ -motor neuron conduction. Due to the time course of membrane depolarisation at the cell body of the anterior horn motor cell, the membrane recovers from its refractory period in time to respond to its continuing depolarisation. In effect the F-wave is reflected back such that it has a latency slightly shorter ( $\sim 0.5\text{ms}$ ) than the H-reflex (section 4.1.2) due to the lack of synaptic delay at the spinal cord. Whilst the F-wave is not a reflex, per se, in that it results from conduction of action potentials only within the stimulated nerve, within literature it is commonly referred to as a reflex component and this convention is adopted within this thesis.



**Figure 4-5: Depiction of F-wave mechanism**

Diagnostically F-waves are of use when assessing nerve root neuropathies (radiculopathy) due to their occurrence only when the antidromic action potential has conducted along the proximal nerve segment and has been reflected at the anterior horn cell. F-wave amplitude has been proposed as a factor for measuring changes in motor neuron excitability and hence spasticity [70, 71]. When a mild voluntary contraction (10-30% maximal voluntary contraction of the muscle) is performed larger F-waves are noted. It is thought that the descending input may excite the membrane, facilitating antidromic conduction of the soma dendrite thereby increasing the probability of a recurrent response. These mild muscle contraction effects are reported to be less consistent with F-waves compared to H-waves [72].

Table 4-1 summarises properties of H- and F-waves which are relevance to this research when identifying the mechanism of EMG late responses.

Name	Reflex Component	
	H-wave	F-wave
Nature	Monosynaptic reflex	Antidromic stimulation of $\alpha$ -motor neuron
Afferent pathway	Ia afferent	$\alpha$ -motor neuron
Efferent pathway	$\alpha$ -motor neuron	$\alpha$ -motor neuron
Stimulus intensity	Submaximal	Supramaximal
Effect of increasing stimulus	Inhibition	Facilitation
Amplitude	5-100% of M-wave	5% of M-wave
Morphology	Stable	Variable
Motor unit in recruitment with respect to M-wave	Different	Same
Persistence	Persistent	Variable

**Table 4-1: H- and F-wave properties [73]**

## 4.2 Electrical Stimulation for Rehabilitation

The use of electrical stimulation for therapeutic or functional use predates its diagnostic use. Short periods of stimulation are typically applied in a cyclic or activity dependent manner in order to provide a therapeutic or functional benefit to the user.

### 4.2.1 Transcutaneous electrical nerve stimulation

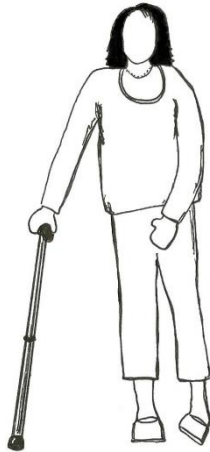
Transcutaneous Electrical Nerve Stimulation (TENS) applies therapeutic electrical stimulation generally at sub-motor threshold intensities. It is predominantly used in pain relief and hypotheses for its successful action include restoration of afferent input, inhibition of hyper-excitability afferent neurons and pre-synaptic inhibition within the dorsal horn of the spinal cord [74].

#### 4.2.2 *Functional electrical stimulation*

Functional Electrical Stimulation (FES) applies faradic electrical stimulation to innervated nerves in order to produce a functional movement in muscles paralysed by UMN injury. Faradic stimulation is generally regarded as stimulation which applies pulses of less than 1.0ms in duration and at frequencies below 100Hz [1].

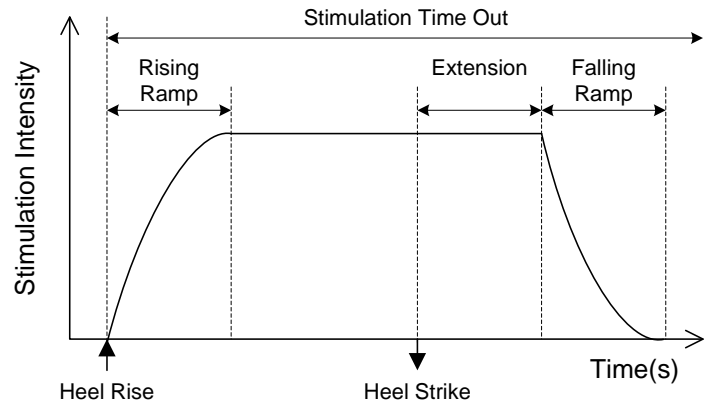
Stimulation can be transcutaneously applied using skin surface electrodes or percutaneously through implanted electrodes. The depolarisation of a nerve depends on the strength of the applied electrical stimulus and the duration for which it is applied. Each stimulation pulse of sufficient intensity generates action potentials in  $\alpha$ -motor neuron axons in close proximity to the electrodes. The orthodromic conduction of action potentials is followed by a momentary synchronous contraction in muscle fibres of the excited motor unit. Due to the synchronous nature of artificial activation, the stimulation frequency must be sufficiently high to produce a smooth tetanic response (Figure 2-10). Stimulating at higher frequencies increases the rate of torque production however results in more rapid muscle fatigue. In order to balance such factors practical FES systems typically apply stimulation between 20 and 50Hz.

FES has a number of applications such as FES rowing, FES cycling, upper limb neuroprosthesis and gait correction systems. In the example of dropped foot correction (Figure 4-6), stimulation is applied to the common peroneal nerve to provide dorsiflexion with moderate eversion during the swing phase of gait. Stimulation is typically timed using a footswitch placed underneath the heel of the affected side. So as not to provoke a stretch reflex of the calf muscles, stimulation is ramped on following heel rise. At heel strike an extension period of stimulation is applied to mimic eccentric activity of the dorsiflexors thus preventing foot slap due to the natural moment formed about the ankle. Following the extension period, stimulation is ramped off (Figure 4-7).



**Figure 4-6: Depiction of dropped foot following stroke**

*Original artwork Wilkinson I, 2012*



**Figure 4-7: Trapezoidal stimulation envelope of ODFSIII dropped foot stimulator**

In addition to direct recruitment of motor nerves, afferent stimuli due to FES can be used to evoke an inter-segmental reflex response which may aid in providing a functional movement. For example, in the correction of dropped foot, stimulation applied to the common peroneal nerve can evoke a withdrawal reflex which can reinforce the required muscle contraction in addition to providing additional knee and hip flexion (section 2.2.6) [75, 76]. Clinically this is often used to greatest effect when applying stimulation to the common peroneal nerve above the popliteal fossa. It appears that stimulating the nerve more proximally, where additional afferent input has joined it, a greater withdrawal reflex response can be gained as compared to other configurations stimulating more distally.

Whilst the detailed neurophysiological response to long-term electrical stimulation is poorly understood [77], clinically spasticity can be reduced through FES for dropped foot correction [78, 79]. As described in Chapter 3, spasticity (SPASM definition [56]) refers to a collection of symptoms which result from the disruption to complex and interdependent UMN systems. As such, the mechanism of spasticity reduction by use of FES is not fully understood, however restoration of more normal muscle activation patterns, and/or muscle strengthening are thought responsible.

### 4.3 Neuromuscular Response to Electrical Stimulation

Having introduced clinical uses of electrical stimulation, properties of the body's response to such stimulation will now be discussed with relevance to this research.

#### 4.3.1 *Response to antidromic activation of motor neurons*

The concept of antidromic conduction was introduced in section 2.1.1. It is not a mechanism naturally utilised by the nervous system and hence when observed, commonly results from artificial magnetic or electrical stimulation. In response to a high intensity antidromic  $\alpha$ -motor neuron action potential an F-wave as described in section 4.1.3 can be generated. It has been reported that antidromic impulses in motor axons can reduce the excitability of  $\alpha$ -motor neurons projecting into the same or synergistic muscles through the activation of Renshaw Cells [20] (section 2.2.7).

#### 4.3.2 *Nerve activation order during surface stimulation*

Neurophysiological studies have indicated that large diameter axons are more easily excited than smaller diameter axons by an extracellular current stimuli [80, 81]. This is also confirmed by the established H-reflex test (section 4.1.2). In order to bring a point along a nerve axon to threshold during transcutaneous stimulation, sufficient extracellular current must pass across the cell membrane into the axon and then out again. For any given axon, the majority of stimulation current bypasses it, moving instead through other axons or the low resistant pathway provided by extracellular fluid. It follows that axons into which current can most easily enter are depolarised most and have the lowest threshold for extracellular current activation. Since a greater fraction of total extracellular current will flow through axons with a large cross sectional area those that innervate fast twitch fibres will be activated at a lower extracellular current intensity than smaller axons innervating slow twitch muscle fibres. This preferential recruitment of larger motor units prior to smaller ones amounts to a reversal of the efficient Henneman size principle described in section 2.2.4 [42, 82]. Coupled with the synchronous activation order during electrical stimulation (section 2.2.3) this recruitment order reversal is thought significant to the rapid rate of fatigue experienced during artificial muscle stimulation rather than voluntary excitation by the CNS.

A number of research publications and review articles have however suggested motor unit recruitment order during transcutaneous electrical stimulation is not as consistent as this and may be non-selective [43, 83]. Gregory and Bickel [43] outline a conjecture that rather than a reversal of the Henneman size principle, transcutaneous electrical stimulation causes non-selective activation of motor units. The authors however do not discuss the afferent effect of stimulation and activation of motor neurons via spinal reflexes. Due to the increased size of the Ia afferent neurons it is reasonable, and widely acknowledged through H-reflex studies, that these afferents will be stimulated at a lower threshold than  $\alpha$ -motor neurons. If the afferent stimuli of electrical stimulation cause reflex responses then these will follow the Henneman size principle [84]. If direct motor activation by electrical stimulation marks a complete reversal of this, then it is this author's view that in combination with reflex responses, the net summated effect would appear that of a non-selective recruitment order.

#### *4.3.3 Muscle fatigue and functional electrical stimulation*

Muscle fatigue has been described as a transient decrement in the force generating ability of a muscle due to recent contractions [36]. It is a complex culmination of a number of processes which principally act within muscle fibres. In a review by Barry and Enoka [85], the authors conclude that to date it has not been possible to develop a comprehensive model of muscle fatigue as the prevailing mechanism that impairs muscle performance varies with the characteristics of the task that is being completed. Factors known to be involved are inadequate release of  $\text{Ca}^{2+}$  ions from the sarcoplasmic reticulum resulting in a decline in  $\text{Ca}^{2+}$  concentration in the sarcoplasm [86], insufficient oxygen for use by mitochondria in ATP production, depletion of glycogen and other nutrients, build up of lactic acid and ADP and failure of action potentials in the motor neuron to release acetylcholine. Before a combination of these changes at the muscle fibre level occur, an individual may experience feelings of fatigue. This response is termed central fatigue and is generated by changes in the CNS. Although the exact mechanism is unknown it may be a protective mechanism to stop an individual causing damage through excessive activation of muscles once fatigued.

Central fatigue is not generally considered when discussing fatigue due to FES as muscle is activated via the peripheral motor nerves, thus bypassing the CNS. The rate of muscle fatigue during FES induced muscle activation is higher than that of a



voluntary contraction for a number of reasons as outlined in earlier sections. Stokes and Cooper provide a comprehensive review of these [87]. Principal factors are the spatially fixed, synchronous activation of a subset of neurons within the motor neuron bundle in a manner markedly different from unimpaired pathology (section 2.2.3). These high levels of fatigue have been found to limit the clinical effectiveness of FES and many studies continue to investigate methods of reducing this. In addition to the innate differences in muscle activation, clinical users of FES will generally have a conversion towards fast fatigable muscle fibres resulting in an increased rate of muscular fatigue following their UMN dysfunction (section 3.1.1).

#### *4.3.4 Post tetanic potentiation due to electrical stimulation*

Post Tetanic Potentiation (PTP) is the enhancement of muscular force elicited by previous muscle activation. This is opposed to fatigue, which eventually follows PTP and is the depression of force due to previous activation. PTP can occur in both the central and peripheral nervous systems following repetitive electrical stimulation. Centrally, PTP at the Ia synapse within the spinal cord has been shown to facilitate enhancement of excitatory post-synaptic potentials of motor neurons [88]. Peripherally PTP of muscle fibres is attributed to an increase in myosin light chain phosphorylation following electrical stimulation which causes conformational changes in the myosin head to a more favourable position for cross-bridge binding. It also makes actin and myosin more sensitive to  $\text{Ca}^{2+}$ . PTP is primarily observed in fast twitch (type IIa and II) muscle fibres [89] such as would be expected in chronically paralysed muscle. The degree of both central and peripheral potentiation has been shown to depend on the stimulation frequency as well as history and varies between subjects [90].

#### *4.3.5 Adaptive response of skeletal muscle to electrical stimulation*

Electrical stimulation has drawn interest when used to maintain muscle bulk and transform muscle fibre types. Converse to inactivity, chronic low frequency stimulation causes muscle to undergo a series of changes from fast to slow fibre properties [91]. Salmons and colleagues postulate that even the relatively infrequent and intermittent stimulation of a dropped foot stimulator user is enough to cause this translation [92]. The same authors investigated stimulation pattern dependences on induced muscle

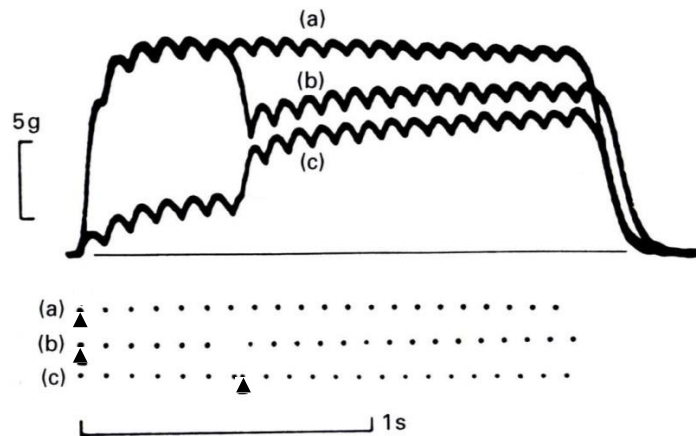
changes by comparing continuous 2.5Hz stimulation to the same amount of net stimulation applied in triplets with inter-pulse intervals of 6 and 12ms, delivered every 1.2 seconds, over 12 weeks. In the rabbit this indicated that although shortening velocity and fatigue resistance are driven by aggregate impulse activity, changes in muscle bulk show distinct pattern dependence. As will be discussed next in section 4.4, such a pattern of stimulation is a key topic of this research and is generally shown to elicit a larger force than the same amount of net stimulation equally spaced over the same time window. Force generation is thought to be a powerful stimulus to protein synthesis and difference in the preservation of muscle bulk could be attributed to enhancement of this [93].

#### 4.4 The ‘Catch-like’ Effect of Electrical Stimulation

The force developed by a muscle during electrical stimulation depends upon many factors. In addition to those discussed previously, the pattern or spacing of the applied electrical stimulation affects force production.

##### 4.4.1 *Overview of the catch-like effect*

In 1970 Burke *et al.* reported a ‘catch-like’ property of muscle in which force augmentation was produced by the inclusion of an initial, high-frequency burst of two or more pulses at the start of a sub-tetanic low-frequency train of stimulation [7]. A 10ms initial doublet electrical stimulus was shown to provide sudden non-linear summation of force that was accompanied by an enhanced level of force that could be maintained by low frequency stimulation (Figure 4-8). Similar discharge patterns have been reported in motor units during voluntary contractions and may be a strategy employed to develop sudden torques when muscles are fatigued [8-11].



**Figure 4-8: Tension responses of cat medial gastrocnemius, slow motor unit [7]**

Upper three traces (a, b & c): isometric force measured in grams, plotted against time.

Lower three corresponding traces: stimulation timing - ▲ = 10ms doublet, • = 82ms spaced single pulse.

Each train contains 22 stimuli and depicts effects of timing changes in doublet application.

Trace (a): sudden increase in torque due to initial 10ms doublet (▲) at start of train.

Elevated tension maintained by constant 12.2Hz (82ms period) stimulation.

Trace (b): as (a) until drop in tension when interval after 7<sup>th</sup> stimuli is lengthened to 117ms.

Trace (c): gradual increase in tension with 12.2Hz stimulation until moderate increase in tension seen when 26ms doublet applied at 7<sup>th</sup> & 8<sup>th</sup> pulse.

This catch-like effect has drawn interest when assessing its use for FES applications. Neuromuscular factors such as level of fatigue [94, 95], prior muscle activation [96, 97], fibre-type composition [98-100], contraction type [101] and muscle length [102, 103] have been shown to affect the extent of force augmentation due to the effect. Additionally timing [104, 105] and intensity [106] characteristics of the stimulation applied have been shown to influence the effect. With this said however, such catch-like inducing stimulation trains have been consistently shown to enhance both isometric and non-isometric muscle force, especially when muscles are fatigued when compared to constant frequency stimulation of comparable frequency [12].

#### 4.4.2 Mechanisms of the catch-like effect

The catch-like property was originally demonstrated in single, denervated mammalian motor units [7]. This complete transection of the motor unit from the spinal cord removes the potential presence of spinal reflex effects. Hence as defined, the catch-like effect is an inherent property of skeletal muscle. The mechanism of the effect remains unclear but the two primary mechanisms that have been proposed are increased  $\text{Ca}^{2+}$  concentration within the sarcoplasmic reticulum of muscle fibres and increased stiffness

of the series elastic elements [107-110]. Studies which have sought to confirm these hypotheses have not been conclusive and suggest other mechanisms in addition to these should also be considered [111-113].

If to be utilised clinically, catch-like stimulation would be applied to patients with intact lower motor neuron systems. Only Karu *et al.* [17] appear to have measured surface EMG recordings with the intact human lower motor neuron system whilst catch-like stimulation is applied. The authors conclude that enhanced torque is due solely to the inherent muscle effect and is not due to the recruitment of additional motor units. This is based upon comparing the EMG response from single to doublet pulses at different intensities and indicating a linear summation in EMG activity accompanied by a disproportionate increase in torque i.e. the inference that the same motor units are activated and hence additional torque must be inherent within the muscle. Although suggestive this is not conclusive however. The stimulation artefact of the amplifier used appears to have lasted approximately 50ms, infringing on the resulting EMG muscle activity due to stimulation. Additionally EMG cannot be directly correlated to force produced, in part due to lack of a distinction between slow and fast muscle fibre type activation [114].

#### 4.4.3 *Use of catch-like stimulation with UMN injury patients*

The catch-like effect appears a largely experimental finding which to date is yet to be knowingly utilised within a clinical application [115]. A minority of studies investigate its use with intended UMN injury patients and report mixed findings [13-19]. Some of these differences can be explained by protocol and inclusion/exclusion criteria. For example, some UMN injury patients had received no prior conditioning treatment and the effects of spasticity may confound investigation. Authors agree however that the pathological effect of UMN injury appears to affect mechanisms responsible for the catch-like effect [12].

With the many complex systems associated with movement, coupled with an UMN injury affecting one or many of these, numerous speculations regarding these mixed findings could be made. In essence, assuming the explanations of the catch-like effect given in section 4.4.2 are correct, factors affecting these may be present in muscle following UMN injury. For example there may be changes in  $\text{Ca}^{2+}$  dynamics or  $\text{Ca}^{2+}$  sensitivity within muscle. Equally a reduction in tendon stiffness has been reported in

paralysed muscles [112]. If stretching of the muscle series elastic elements by the first pulse of a doublet (indicative of catch-like stimulation) enables the second pulse to act upon a less compliant system then a decrease in stiffness may explain the mixed results. Speculating, spasticity (section 3.1) may improve the effect through an increase in series resistance, conversely a hyper-excitability stretch reflex may oppose the response.

#### 4.4.4 *Effects of potentiation on the catch-like effect*

Burke *et al.* first reported force augmentation due to the catch-like effect reducing in a potentiated muscle [97]. The linear decrease in force augmentation due to catch-like stimulation to amount of potentiation reported by Ding *et al.* in the human quadriceps muscle is thought to be explained by the proposed similar mechanisms of  $\text{Ca}^{2+}$  sensitivity shared by these phenomena [96]. In effect the author concludes little further advantage is provided by the catch-like effect in a potentiated muscle as the shared mechanisms of force enhancement have already been utilised by peripheral potentiation.

#### 4.4.5 *Effects of muscle type on the catch-like effect*

Force augmentation has been shown in both slow and fast fibre types [7, 100, 116], however muscle training using chronic low frequency stimulation to convert fast to slow fibre types has been shown to abolish it in a large animal (porcine) model [99]. The authors conclude that the loss of force enhancement due to the catch-like effect in chronically stimulated muscles suggests a link between the catch-like effect and the intracellular changes brought about through chronic electrical stimulation affecting muscle activation.

#### 4.4.6 *Effects of fatigue on the catch-like effect*

Catch-like stimulation has consistently provided greater peak forces and force-time integrals in fatigued muscles compared to constant frequency stimulation [17, 100, 113, 117-120]. Fatigue causes a number of changes within skeletal muscle including, but not limited to, a decrease in sarcoplasmic  $\text{Ca}^{2+}$  concentration [86] and a decrease in sensitivity to  $\text{Ca}^{2+}$  [121]. These factors reduce the maximum rate of development and level of force when stimulated with constant frequency stimulation. Catch-like

stimulation appears to prevent this decline, potentially overcoming these deficits by the increase in  $\text{Ca}^{2+}$  and stiffness mechanisms thought responsible for the effect.

Studies comparing catch-like inducing stimulation trains with constant frequency trains to produce similar force-time integrals have suggested reduced rates of muscle fatigue when using catch-like stimulation patterns [39, 117, 118]. Recent studies have also however shown repetitive activation with catch-like inducing trains provide greater fatigue than repetitive activation with constant frequency stimulation of the same number of pulses [120, 122]. This increased rate of fatigue during the catch-like stimulation may be due to the increased force produced during the fatigue protocol. Supportive of this supposition, Abbate *et al.* conclude that catch-like stimulation applied to fast muscle fibres of the rat was associated with an increase in performance accompanied by an according increase in energy expenditure resulting in no difference in efficiency [123].

#### 4.4.7 Effect of muscle length on catch-like effect

Although the majority of studies investigating the catch-like effect assess isometric torque at optimal muscle resting length, catch-like stimulation has been shown to provide greatest force augmentation at short rather than long muscle lengths [102, 103]. This is consistent with the mechanisms of increased stiffness of the series elastic components, at short muscle length the first pulse will have more muscle slack to take up thus producing greater augmentation when the second pulse of a doublet is applied.

### 4.5 Central Nervous System Components of Motor Control during FES

There appears a tendency for solely motor effects to be considered during the use of FES as it is this which is often the primary intention of the intervention. However in addition to direct motor unit recruitment, an accompanying afferent signal is applied to the spinal cord along with antidromic conduction along  $\alpha$ -motor neurons [20]. Reviewing FES literature, many studies appear to overlook this, only considering direct motor effects of electrical stimulation. With reference to the overview given in Chapter 2, the human body is a tremendously complex system and the assumption that stimulation has only an orthodromic motor effect would appear an oversight.

#### 4.5.1 *Afferent effect of stimulation on motor response*

At present Mela *et al.* appear the only authors to have investigated the contribution of secondary reflex activity (either H- or F-waves) to the force elicited by a muscle stimulated by a single pulse during a functional movement [124]. Reflex mediated activity was found to be accountable for moments in the order of 10-15% during twitch stimulation of a group of six unimpaired participants. Although a small unimpaired participant group, this study indicated the need to consider such components when ascertaining the effects of FES.

Collins *et al.* have reported torques larger than expected from direct motor axon activation alone, when applying wide pulse-width, high frequency stimulation either continuously or in two seconds bursts to muscles of the lower limb. Such increased torques were present when applied to people with complete spinal cord injury [21, 22] or healthy sleeping individuals but not when a nerve block was applied proximal to the stimulation site [21, 23]. The additional torque has been attributed to being of central nervous system origin, being initiated by evoked sensory volleys that provide excitatory input to neurons in the spinal cord. Enhanced H- and M-wave components and observations of additional spontaneous  $\alpha$ -motor neuron action potentials suggest the additional torque was not generated due to post tetanic potentiation (section 4.3.4). The authors propose that the sensory volley generates persistent inward currents, referred to as plateau potentials which produce self-sustained  $\alpha$ -motor neuron discharge [21].

Optimizing stimulation parameters to further recruit afferents using wide pulse-width stimuli (0.5–1.0ms) [67] has been shown to elicit both significant ‘central’ (due to spinal reflex mechanisms) and ‘peripheral’ components (due to direct motor unit recruitment) of force and has drawn interest as it has the potential to have a number of benefits regarding fatigue and muscle training [125]. Akin to voluntary movement,  $\alpha$ -motor neurons activated by reflex pathways will follow the more efficient Henneman size principle [42]. Electrically elicited contractions which make use of a greater proportion of fatigue resistant fibres would be expected to reduce the rapid onset of fatigue that often develops. Activating muscles in a way more akin to a natural contraction may also have ramifications on muscle training effects [126].

As Collins *et al.* have shown how to turn on these central components of force [24], they have also investigated how to turn them off. This is needed if such techniques are to be used to control functional movements. It is also of particular interest when

considering use with UMN injury patients with over-active spastic muscles. For example, many UMN injury patients with a dropped foot experience over activity of the calf muscles. This over activity stems from net disinhibition of spinal reflexes due to spasticity. If stimulation can be tailored such that it has an increased inhibitory effect on these spastic muscles then the functional response to stimulation may be improved. Although the stimulation trains applied by Collins *et al.* are applied over a number of seconds it is conceivable that a high frequency doublet of stimulation (indicative of catch-like stimulation) at the start of a train of stimulation may have a similar effect. If this were so, recovering spinal reflexes may contribute to some of the torque enhancement of previous catch-like stimulation studies [25].

#### 4.5.2 Antidromic effect of catch-like stimulation on $\alpha$ -motor neurons

Doublet stimuli have been shown to abolish the F-wave response due to the collision of the first F-wave with the second antidromic action potential [127]. Although of potential use during diagnostic stimulation investigation, due to the high intensity generally required to evoke this effect it is thought unlikely to be seen during clinical FES.

Mrowczyński *et al.* investigate the effects of antidromic conduction due to doublet (5-10ms spacing) stimulation applied to the sciatic nerve of the rat. Significant changes in the After-Hyperpolarising Phase (AHP) of  $\alpha$ -motor neurons were noted as compared to the effect of single stimulation pulses. Doublets increased the depth and duration of AHP. As mentioned in section 2.1.1, the AHP represents a period of reduced excitability of the  $\alpha$ -motor neuron. The minimum repetitive discharge rates are inversely proportional to the AHP duration. This result implies slowing of the  $\alpha$ -motor neuron firing rate following the effects of an antidromic doublet and may be a separate process or be linked to excitation of Renshaw cells coupled to  $\alpha$ -motor neurons.

This also supports reports by Crenna that the simultaneous discharge of Renshaw cells due to an antidromic stimulation pulse can produce a short 20-30ms period of  $\alpha$ -motor neuron inhibition in which it is unlikely to be responsive to undesired reflex effects [20]. The excitatory or inhibitory nature of Renshaw cells is known to vary and their function does not appear to be extensively documented or understood [128].



This chapter has introduced the use of electrical stimulation for diagnostic, therapeutic and rehabilitation interventions. Following the focused overview of neurophysiologic systems involved in the control of unimpaired and UMN impaired motor control described in Chapter 2, a discussion of the effects of stimulation on such systems is given. This discussion raises a number of theories and questions which continue to be advanced by current research. The following chapter will draw upon some of these findings in formulating investigations designed to further the understanding of key principles of FES as well as advancing the potential clinical use of catch-like effect stimulation.

## **Chapter 5   Research Hypothesis & Study Design**

A comprehensive background to current properties and theories of unimpaired and UMN impaired motor control and the use of electrical stimulation was given in Chapters 2, 3 and 4 respectively. As outlined, there are many complex interdependencies between the described processes, with the understanding of many continuing to be furthered. As such, to attempt to combine these and logically distil a meaningful theoretical explanation of the clinical effects catch-like stimulation may have, is subject to many sensitive and confounding factors. In contrast, solely using clinical observations or outcome measures obtained with catch-like stimulation provides limited grounds to contribute to understanding of the mechanisms responsible for the effect. Such understanding is required if it is to be most effectively utilised within a patient population in the future.

This research has sought to use current theory and background from literature to inform and aid the clinical use of FES. A structured research approach has been developed to answer three research questions which assess the neurophysiologic effects of stimulation in unimpaired and impaired participant groups. Investigation of the research questions have relevance to how and whether, catch-like stimulation may be effectively used clinically whilst also furthering understanding of the neurophysiological response to electrical stimulation.

The posed research questions are presented with an accompanying overview of their justification and investigation methods. Whilst the overview of the investigation strategy remains broad in this chapter, a detailed and structured protocol is provided in Chapter 8.

## 5.1 Formulation of Research Question 1

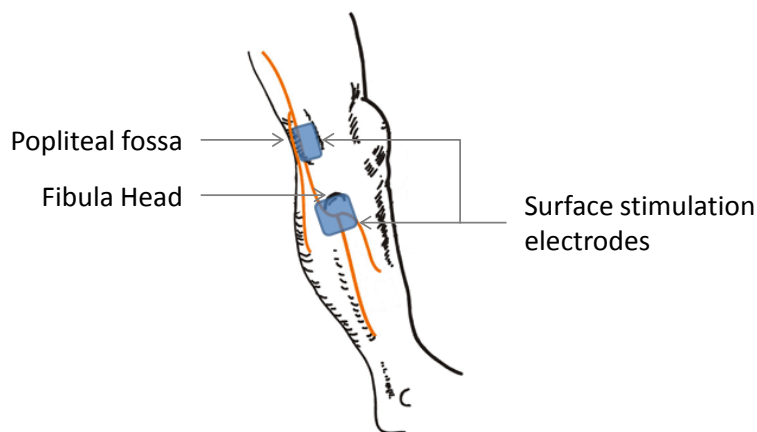
*How significant are reflexes to conventional and catch-like stimulation?*

### **Research Question 1**

#### *5.1.1 Justification of research question 1*

In order to investigate the significance of spinal reflexes on muscle activation during the application of catch-like stimulation it is first necessary to establish their effects during the use of conventional stimulation through assessment of Research Question 1. Use of the term conventional stimulation within this chapter refers to stimulation of one or more pulses evenly separated by a period between 20 and 50ms.

Following a review of literature, it is the author's opinion that there has been a tendency for the motor rather than sensory effects of electrical stimulation to be reported. This is somewhat counter to the author's experience of FES applied clinically during dropped foot correction. Clinicians of the National Clinical FES Centre routinely seek to utilise the withdrawal reflex in order to promote additional hip and knee flexion during the swing phase of gait in order to foot clearance. This is completed through stimulation of the common peroneal nerve as it passes posterior of the fibula head and medial of the popliteal fossa as shown in Figure 5-1. It is the groups' supposition that greater afferent input has joined the common peroneal nerve more proximally thus prompting the greater withdrawal reflex. Whilst commonly administered and accepted by clinicians the mechanism does not appear to have been quantified or investigated when used in this manner.



**Figure 5-1: 'Popliteal fossa' electrode positions for dropped foot correction**  
*Common peroneal nerve indicated in orange. Modified from [76]*

Burridge *et al.* [129] who completed a randomised controlled trial assessing the single channel Odstock Dropped Foot Stimulator (ODFS), noted the immediate effect of FES on the tibialis anterior and peroneal muscles was to “*bring the ankle into greater dorsiflexion as the foot left the ground and facilitate a flexor withdrawal response in which flexion occurred at both hip and knee joint*” (pp208-209).

Thrasher and Popovic [130] note in their review of FES walking systems that by the principle of stimulating the peroneal nerve, all will partially utilise the withdrawal reflex, with a key benefit of this being the ability to activate hip flexor muscles which would otherwise not be possible through surface stimulation. Kim *et al.* [131] appear amongst the few authors to have sought to quantify the withdrawal reflex contribution when using FES for of gait assistance. In a group of spinal cord injury patients (n=6) they report initial kinematic conditions at toe-off influence the reflex component with a significant linear relationship between the reflex moment and hip angle ( $p < 0.05$ ).

As discussed in section 4.5.1, Mela *et al.* [124] investigated the contribution of antidromic motor and orthodromic sensory activation of the common peroneal nerve to resulting ankle dorsiflexion torque. In an unimpaired group (n=6) these reflex components (F- and H-waves), which followed direct motor activation (M-wave) due to single stimulation pulses, accounted for 10-15% of recorded ankle dorsiflexion moment. This reasonably substantial component of muscle activation may have implications for muscle fibre type activation depending upon its mechanism i.e. H- or F-wave. As discussed in section 3.3.2, H-reflex mediated muscle activation will follow the Henneman size principle [70]. If motor activation by M- and F-wave responses to electrical stimulation mark a complete reversal of this efficient order, then when in combination with a notable H-wave component the net summated effect would appear that of a non-selective recruitment order.

If Mela *et al.*'s study was to be repeated with UMN injury participants then the altered spinal reflex sensitivity associated with spasticity (section 3.1) would be expected to affect findings. It is this group who are the intended recipients of electrical stimulation and therefore further investigation with unimpaired and impaired individuals is required if findings are to contribute to theoretical debate whilst also supporting and developing clinical use. Research Question 1 therefore assesses the reflex effect of conventional stimulation in both unimpaired and impaired participant groups.

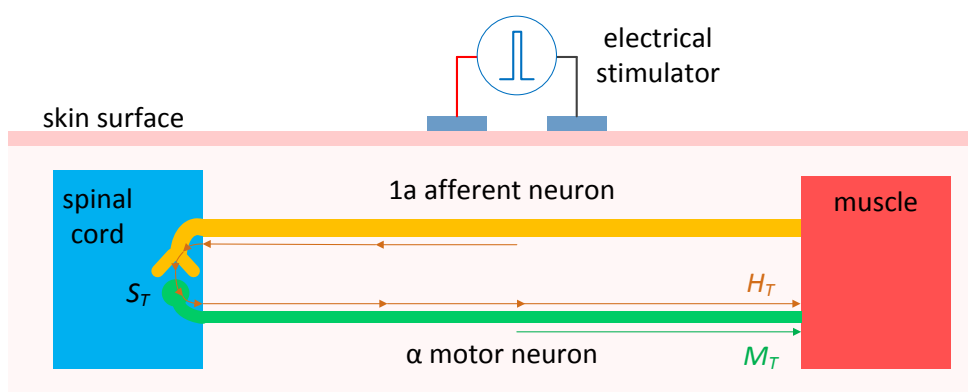
Improved understanding of the reflex effect of stimulation may aid more effective clinical use of conventional stimulation. If such findings are considered with respect to

catch-like stimulation, they pose the question of whether differences noted between this and conventional stimulation could partly be accounted for by differences in reflex activity. Without a conclusive explanation of the catch-like effect [111-113], Research Questions 2 and 3 further explore this concept.

### 5.1.2 Investigation of research question 1

Electromyography synchronised to transcutaneously applied electrical stimulation was the primary outcome measure selected during the investigation of Research Question 1. Correlation of EMG activity features with the application of stimulation would enable inferences regarding the neurophysiological activation pathway to be made. Single stimulation pulses (twitch response) and bursts of stimulation would allow assessment of the immediate neurophysiological differences in response as well as changes over the duration of a typical functional movement caused by tetanus stimulation.

Typical conduction velocities of afferent and efferent nerves are well characterised through clinical neurophysiological testing (Figure 2-4). Figure 5-2 depicts the application of a single electrical stimulation pulse midway between spinal cord and muscle. Accounting for known latencies in this system, Equation 5-1 and Equation 5-2 describe the expected latency of the resulting direct motor (M-wave) and spinal reflex mediated (H-wave) component of EMG activity recorded at the muscle being stimulated.



**Figure 5-2: Latency identification of direct (M-wave) and spinal reflex mediated (H-wave) motor activation**

$$M_T = \frac{\text{Distal Motor NCD}}{\text{Motor NCS}} + \text{Neuromus SD}$$

**Equation 5-1: M-wave latency calculation***(values used for example of dropped foot correction shown in brackets)*

<i>Distal Motor NCD</i>	=	<i>Motor Nerve Conduction Distance</i>	<i>(0.15m)</i>
<i>Motor NCS</i>	=	<i>Motor Nerve Conduction Speed</i>	<i>(40ms<sup>-1</sup>)</i>
<i>Neuromus SD</i>	=	<i>Neuromuscular Junction Synaptic Delay</i>	<i>(0.5ms)</i>
<i>M<sub>T</sub></i>	=	<i>M-wave onset latency</i>	<i>(4.25ms)</i>

$$H_T = \frac{\text{Afferent NCD}}{\text{Afferent NCS}} + \text{Central SD} + \frac{\text{Motor NCD}}{\text{Motor NCS}} + \text{Neuromus SD}$$

**Equation 5-2: H-wave latency calculation***(values used for example of dropped foot correction shown in brackets)*

<i>Afferent NCD</i>	=	<i>Afferent Nerve Conduction Distance</i>	<i>(0.95m)</i>
<i>Afferent NCS</i>	=	<i>Afferent Nerve Conduction Speed</i>	<i>(40ms<sup>-1</sup>)</i>
<i>Central SD</i>	=	<i>Central Synaptic Delay</i>	<i>(1.0ms)</i>
<i>Motor NCD</i>	=	<i>Motor Nerve Conduction Distance (spine to muscle)</i>	<i>(0.95m)</i>
<i>Motor NCS</i>	=	<i>Motor Nerve Conduction Speed</i>	<i>(40ms<sup>-1</sup>)</i>
<i>Neuromus SD</i>	=	<i>Neuromuscular Junction Synaptic Delay</i>	<i>(0.5ms)</i>
<i>H<sub>T</sub></i>	=	<i>H-wave onset latency</i>	<i>(29.0ms)</i>

Equation 5-1 and Equation 5-2 can be used when calculating typical M- and H-wave onset latencies (Figure 4-1) of the tibialis anterior EMG waveform when applying stimulation for dropped foot correction (Figure 5-1). Using the example values provided, these onset latencies evaluate to 4.25ms and 29.0ms respectively. Onset latency represents conduction along the faster axons of the  $\alpha$ -motor neuron and hence values of peak latency will be slightly larger. Equation 5-1 and Equation 5-2 can be used to infer the activation pathway of resulting EMG activity features based upon observed onset latencies. Based upon these example calculations, an EMG amplifier capable of peak to peak M-wave amplitude measurement would need to be able to record EMG features within a typical peak latency time of 10ms following dropped foot correction stimulation.

In addition to assessing spinal mediated reflex activation of an excitatory nature, EMG measurements can also assess inhibitory activation. Excitatory reflex activity can be characterised by an increase in EMG activity at a latency suggestive of spinal reflex mediation (e.g.  $\geq H_T$  latency). Inhibitory reflex activity can be characterised by a reduction in EMG activity of an already active muscle at a latency suggestive of spinal reflex mediation (e.g.  $\geq H_T$  latency).

As discussed in sections 4.1.2 and 4.1.3, reflex components can be affected by a number of different factors (e.g. voluntary effort, afferent input, joint angle). Whilst this multifactorial nature complicates its controlled investigation, such factors will inevitably vary throughout gait. Therefore an investigational approach which sought to permit theoretical investigation along with that expected to be seen in a clinical setting was adopted. A series of investigations were proposed in which different factors were controlled in turn thereby seeking to assess the effect of each. Whilst this may be effective from a theoretical basis, findings may not be indicative of the clinical application. Assessment of EMG during dropped foot stimulation was therefore also incorporated within the study design.

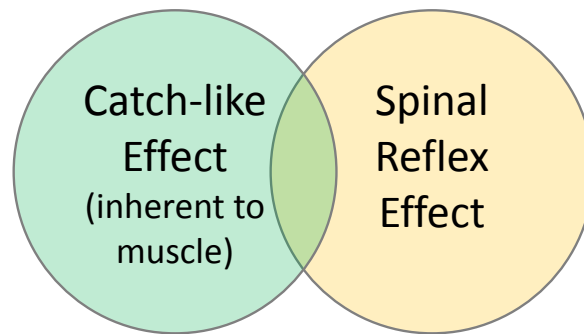
## 5.2 Formulation of Research Question 2

*Is increased torque commonly observed when utilising catch-like stimulation caused, in part, by enhanced excitatory spinal reflex components which activate additional muscle fibres to those activated by direct  $\alpha$ -motor neuron excitement?*

### **Research Question 2**

#### 5.2.1 Justification of research question 2

The catch-like property was originally demonstrated in single, denervated mammalian motor units and as such is defined as an inherent property of skeletal muscle [7]. By the definition of a patients' suitability for FES they must have an intact lower motor system. Although potentially of altered function due to spasticity, they will have an intact spinal reflex pathway. This research investigates the presence and effect of spinal reflex components in addition to that of the catch-like effect inherent to muscle (Figure 5-3). Over recent years the work of Collin's *et al.* has focused attention towards the spinal reflex response during FES [25, 125]. Possibly due to the original demonstration and definition of the catch-like effect in denervated muscle, the response of spinal reflexes to the use of 'catch-like inducing' trains of stimulation does not appear to have been pursued.



**Figure 5-3: Venn diagram of hypothesised motor control influences to FES**

*Common component hypothesised to be observed during human investigation.*

The findings of Mela *et al.* [124] have relevance to catch-like stimulation in addition to conventional constant frequency stimulation. Although investigations using catch-like trains typically assess dynamic torque responses over hundreds of milli-seconds, and the results of Collins *et al.* [25] also discussed in section 4.5.1 are of an elevation in torque over a number of seconds, it raises the question of whether torque enhancements seen in previous catch-like stimulation studies are partly due to spinal reflex components. For example, during investigations into the use of catch-like inducing stimulation patterns Binder-Macleod *et al.* have reported using relatively long stimulation pulse-widths of 600 $\mu$ s which could be considered preferable for spinal reflex excitation [67].

Although it is known that following a stimulation pulse the H-reflex is inhibited (section 4.4.1) it is not known how doublet stimuli spaced by a time comparable to the duration of a typical EPSP or IPSP present at a synapse ( $\sim 15$ ms) will effect post activation depression. Challenges of achieving such performance with current measurement instrumentation may be partly responsible for limited reports of such investigations.

With instrumentation permitting identification of muscle activation through either direct motor or spinal mediated responses, further evidence can be contributed to the on-going debate regarding recruitment order during transcutaneous electrical stimulation.

As discussed in section 3.5.1,  $\alpha$ -motor neurons activated by spinal reflex pathways will follow the Henneman size principle of natural muscle activation [42]. If catch-like stimulation had an increased excitatory spinal reflex effect then muscle fibres activated by this component would follow this more efficient natural recruitment order. This would be advantageous as increased activation of slow twitch muscle fibres would reduce the rate of muscle fatigue associated with artificial electrical stimulation. Indeed this difference in muscle fibre recruitment may provide some explanation of favourable findings of reduced rates of muscle fatigue when adopting catch-like stimulation [39, 117, 118].



### 5.2.2 *Investigation of research question 2*

Completing H-reflex tests (section 4.1.2) about the lower limb using both single conventional and catch-like stimuli would enable the presence of increased spinal reflex components due to the catch-like effect to be assessed.

In a similar fashion to the investigation of Research Question 1, the use of single doublet stimuli and bursts of these would enable investigation of the instantaneous effects as well as those over a sustained contraction. The latency of resulting EMG activity would also enable inference of pathways causing the activation when assessed at varying muscle length, tension, effort etc.

As discussed in section 4.3.2, without a consensus on the  $\alpha$ -motor neuron recruitment order of surface stimulation it is difficult to offer an explanation of how and whether recruitment is different using catch-like stimulation. As noted in section 5.1.2, applying single conventional or catch-like stimulation pulses also enables the physical twitch of the limb due to stimulation to be assessed and may provide information regarding muscle fibre recruitment order.

## 5.3 Formulation of Research Question 3

*Do the use of doublet stimuli have an enhanced reciprocal inhibition effect on an active antagonist muscle; thus in part explaining the enhancement in torque commonly observed when utilising catch-like stimulation?*

### **Research Question 3**

#### 5.3.1 *Justification of research question 3*

One suggested mechanism by which FES can reduce spasticity (section 4.2.2) is reciprocal inhibition [78]. Extending the justification of Research Question 2, enhanced movement torque observed when using catch-like stimulation in participants with an intact lower motor neuron system could be due to a reduction in opposing rather than supporting force. In the presence of UMN syndrome this could be through an enhanced inhibition effect of an overactive antagonist muscle rather than excitatory effects on the agonist. Research question 3 was therefore developed to assess this possibility.

### 5.3.2 *Investigation of research question 3*

As explained when discussing the concept of graded potentials (section 2.1.1) and synaptic connections within the spinal cord (section 2.1.2), an inhibitory effect would take place in the form of inhibitory neurotransmitters at synaptic junctions within the spinal cord. Demonstration of this non-invasively can be inferred through activity reduction of an already active muscle within a time period consistent with spinal inhibition. Therefore in an unimpaired participant an opposing voluntary contraction would need to be present when electrical stimulation is applied. For the investigation of research question 3 this would be attained through asking unimpaired participants to complete a voluntary, functional movement known to utilise the antagonist muscle of interest whilst doublet stimuli are applied. Dorsiflexing and plantarflexing the foot in time to a visual sinusoidal indicator of angle was utilised for this purpose.

In participants of impaired UMN function, the same could be completed if sufficient voluntary control was present. If not and in the presence of hypertonia, it may be possible to observe continual firing of overactive antagonist muscles and a reduction in this EMG activity when stimulation is applied. By the nature of spasticity, this inappropriate activation may not be seen at rest and hence assessment during walking was also incorporated into the study design.

## 5.4 Investigation of Research Questions

Research Questions 1-3 were formed in light of critical review of literature and clinical observations. In order to meaningfully investigate them, a structured approach addressing factors thought to affect them was developed. A discussion of such aspects prior to formulation of the investigational systems core requirements and fundamental research protocol is now given.

### 5.4.1 *Choice of participant population*

This research sought to inform clinical use of conventional and catch-like electrical stimulation with patients who had sustained an UMN injury. However, as described in Chapter 3, factors such as spasticity, muscle weakness or muscle fibre type changes associated with the UMN injury may in some cases, mask or complicate interpretation of findings. Therefore the posed research questions would also be investigated with an

unimpaired participant population primarily recruited from the Clinical Science and Engineering Department at Salisbury District Hospital. This department operates alongside the National Clinical FES Centre.

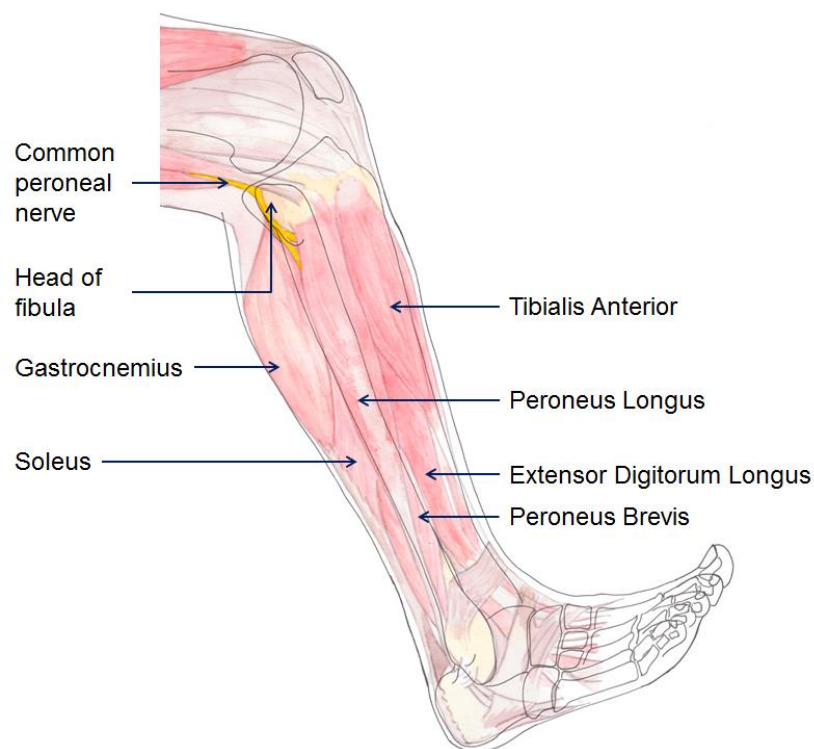
Completion of this research within the National Clinical FES Centre placed it amongst a large population of patients who had had a stroke and were existing users of FES for the correction of dropped foot from which to recruit from. These participants would have already been assessed against the contraindications of FES as part of receiving their FES treatment. Issues such as excessive muscle tone or specifics in electrode positioning would hence have been addressed through their clinical care. Whilst this represented a specialised subset of UMN injury patients it avoids some of the issues that may have contributed to the mixed findings discussed in section 4.4.3. Potential patient participants would be selected partly on locality to minimise travel requirements or otherwise investigations arranged such that they followed scheduled review appointments.

The conditioning of impaired participants to FES may have caused some training or habituation. Crone *et al.* [132], investigated disynaptic 1a reciprocal inhibition of the soleus H-reflex in healthy controls ( $n=74$ ) and in patients with multiple sclerosis ( $n=34$ ). Disynaptic 1a reciprocal inhibition was exhibited by the healthy participants but was rarely observed in the patient group. Of the patients who took part in the study, four were regular users of dropped foot stimulation. In these patients a pronounced inhibition response comparable to the healthy participants was seen. The sub-group did not differ in their degree of spasticity or any other clinical parameter. The authors suggested that regular activation of peripheral nerves is of importance for maintenance of activity in spinal pathways and these patients had received this through their use of FES for dropped foot correction.

#### 5.4.2 *Choice of muscle groups*

Whilst the use of conventional or catch-like stimulation is not limited to providing the contractions of any particular superficial muscle or group, its functional application is most prevalent in gait rehabilitation systems. As this research wished to assess the use of catch-like stimulation with a view to its future functional use, stimulation was applied in functional manner as oppose to targeting a single muscle acting alone.

In 2009 the UK NICE issued interventional procedures guidance for use of surface and implantable FES dropped foot correction systems following UMN injury. Presently the most common clinical application of FES appears to be in this manner for the correction for dropped foot. It is hence in the lower limb and in order to provide ankle dorsiflexion with moderate eversion that stimulation was investigated during this study. Figure 5-4 indicates the lower limb anatomy with a description of the function and insertion of principle muscles. EMG was collected from lower limb agonist and antagonist muscles: tibialis anterior and soleus respectively. The soleus was selected as opposed to the medial or lateral gastrocnemius muscles of the calf as these are weak knee flexors [133] and may be activated by the withdrawal reflex, thereby complicating interpretation of results. The agonist – antagonist pairing between tibialis anterior and soleus muscles is relevant to dropped foot correction and was utilised when investigating Research Question 3.



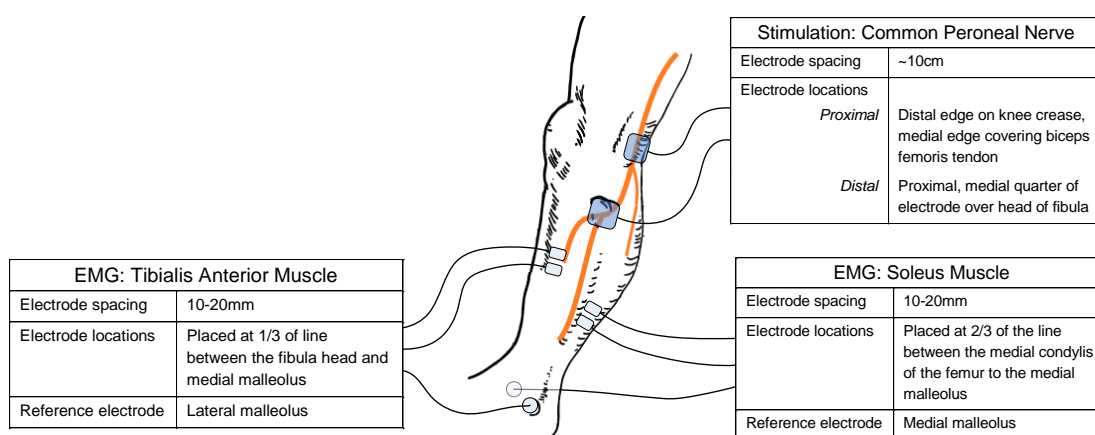
**Figure 5-4: Anatomy of lower limb**

*Original artwork Wilkinson I, 2012*

#### 5.4.3 Electrical stimulation and electromyography

In order to answer Research Questions 1 – 3 a means of applying either conventional or catch-like stimulation and identifying and measuring the direct motor (M-wave) and reflex components (e.g. H-wave, F-wave) was required.

When applying electrical stimulation, hypoallergenic 5cm x 5cm stimulation electrodes would be used and positioned as used clinically in the treatment of dropped foot with FES. Stimulation would be applied to the common peroneal nerve as it passes posterior of the fibula head and medial of the popliteal fossa as shown in Figure 5-5. Due to inherent variation amongst individuals', slight modification of these positions would be required for some participants in order to provide dorsiflexion with mild eversion of the foot appropriate for dropped foot correction. Adjustments to electrode positions were made based upon knowledge of the underlying anatomy and clinical experience of positioning for effective dropped foot correction.



**Figure 5-5: Stimulation and EMG recording electrodes positions**

Relative representation of common peroneal nerve position shown in orange.

EMG electrode positioning based upon SENIAM recommendations [134].

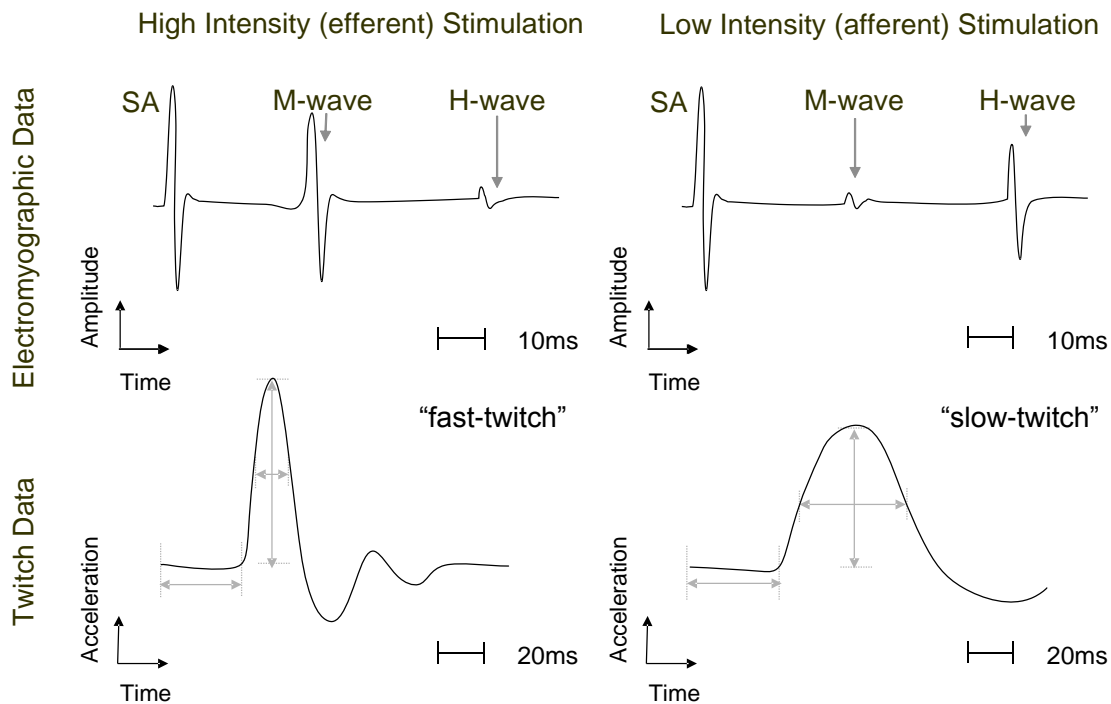
The EMG amplifier was required to recover from the large transients of stimulation within a time period comparable to the expected M-wave peak latency in order to permit identification and measurement of this feature. The ability to observe EMG directly after the application of a stimulation pulse may enable a more conclusive result either supporting or contrasting the observations of Karu *et al.* [17] regarding the mechanisms of the catch-like effect (section 4.4.2). Although a common requirement of diagnostic neurophysiology equipment (section 4.1), circuitry permitting the continuous measurement of EMG following the application of an electrical stimulation pulse appears to be infrequently reported [135-137]. The inability to record such bio-potentials in the presence of stimulation artefact may account for the lack of research in this area. Without access to a suitable commercially available system, original development of a portable EMG amplifier with this functionality was required during the study.

The Surface ElectroMyoGraphy for the Non-Invasive Assessment of Muscles (SENIAM) project was a European Union, Biomedical Health and Research Program (BIOMED II) funded project, active between 1996 and 1999. The project developed European recommendations for sensors and sensor placement procedures and signal processing methods for surface EMG [134]. These recommendations would be utilised throughout this research when specifying instrumentation performance, acquiring surface EMG and analysing resulting waveforms.

#### 5.4.4 *Kinetic twitch data*

Whilst formulating the research questions it was speculated whether motor neuron recruitment order and hence muscle fibre type activation could be inferred by correlating EMG measurement with kinetic twitch data.

Without a firm consensus on the  $\alpha$ -motor neuron recruitment order of surface stimulation it is difficult to offer an explanation of how and whether recruitment is different using catch-like stimulation. Hence investigation of Research Question 2 would potentially allow assessment of recruitment order using both single and doublet stimulation pulses. A number of methods of classifying muscle fibre types are reported in literature however there is no universally accepted method to assess usage during a particular action [138]. A previously reported non-invasive method suitable during surface stimulation is to infer muscle fibre recruitment by correlating kinetic twitch response (Figure 2-9) to M-wave and spinal reflex components [84, 139]. Although unable to provide a quantitative measure of muscle fibre types activated, it is a non-invasive test intended to provide initial data suggestive of fundamental differences in recruitment. In order to assess twitch response, two 3-degree-of-freedom accelerometers were affixed to the lower limb under test and acceleration recorded concurrently with EMG data. In order to attempt this, a number of outcome measures describing the resulting acceleration twitch response would be correlated to the resulting EMG activity in order to infer changes in muscle activation due to supposed changes in M- and H-wave amplitudes (Figure 5-6).



**Figure 5-6: Example of muscle fibre type activation inference from M- and H-waves**

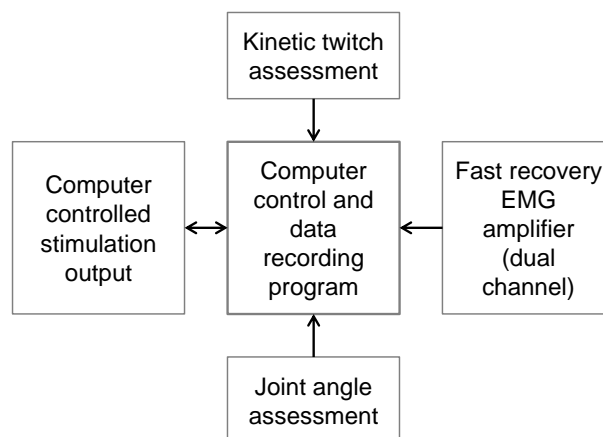
*Hypothetical kinetic twitch data shown.*

*Inference of activation through analysis of variables characterising twitch i.e. peak acceleration, acceleration-time integral, twitch start time, twitch time, time to peak acceleration.*

*(SA = Stimulation Artefact)*

## 5.5 Formulation of Investigational System Requirements

Having defined research questions and established how they would be practically investigated, an overview of the required investigation system could be formed. Figure 5-7 provides a block diagram describing components of the envisaged investigational setup and the basic interactions of the system.



**Figure 5-7: Block diagram investigational system requirements**

In order to enable the research questions to be investigated in the manner described, there was a high degree of interaction between the systems of Figure 5-7. Where commercial systems providing the required control or functionality were not available, in-house hardware and software was developed. A functional specification for each of the modules of Figure 5-7 was detailed and is now summarised.

#### *5.5.1 Data control and recording software*

The software control system at the core of Figure 5-7 would enable master control and coordination of all data at a single interface. It would guide both the investigator and participant through the research protocol. Due to this and its necessity to interface to custom and commercial hardware systems, a custom software would be developed by the author.

It was required to control and coordinate data acquisition through the interfaced hardware. During phases of the research protocol where variables such as joint angle were varied it would implement the triggering algorithm which would control when stimulation was applied and hence measurements recorded. There would be the potential to record large amounts of data and hence the system needed to be able to complete basic data processing before saving data in a format suitable for offline analysis. Visual display of data during collection was necessary in order to be able to identify when stimulation or measurement parameters needed to be adjusted.

#### *5.5.2 Computer controlled stimulation output*

The computer controlled stimulation output was required to apply conventional and catch-like stimulation of varying intensity, timing and repetition (i.e. twitch or burst stimulation). It needed to function in a safe and effective manner with all applied parts electrically isolated from mains connection. All stimulation settings would be computer controlled so that whilst full manual control through a software interface would be possible, stimulation settings could be automatically configured depending upon the selected phase of the research protocol. This would reduce the time required to complete the research protocol whilst also removing potential investigator error through incorrect stimulation configuration. Two way computer control would also enable the stimulation output to confirm its status or stimulation settings prior to application.



Rather than develop a custom stimulation output stage design, elements of an existing output design which has been demonstrated to be safe, effective and with low instances of skin irritations would be used. The stimulation output had to be able to apply stimulation over a comparable intensity range to that used for dropped foot correction. The CE marked Odstock III Dropped Foot Stimulator (ODFSIII)<sup>1</sup> can apply 0-350 $\mu$ s pulse-width stimulation of 0-100mA amplitude into a 1k $\Omega$  load (electrode skin model), 40 times per second. The computer controlled stimulation output would therefore need to be capable of producing stimulation of comparable frequency and intensity to this when applying conventional and catch-like stimulation.

In order to permit the measurement of EMG shortly after the application of a stimulation pulse, measures to minimise stimulation artefact would be implemented. Therefore the combined characteristics of the stimulation output and input properties of the fast recovery EMG amplifier would be considered in unison.

In order to keep the investigation as similar to clinical practice as possible the same Platinum PAL 5cm x 5cm electrodes were selected for use, thereby maintaining compatibility with existing electrode leads and plug/sockets.

As it is wished for ability to use the stimulator during functional tasks, its size and enclosure was to be minimised in order to maintain a portable battery powered system that could be worn on the belt or lower limb.

To permit measurements (i.e. EMG, physical twitch) to be correlated to the application of stimulation, an optically isolated synchronisation signal would be provided by the computer controlled stimulation output interfaced to the data acquisition system.

### 5.5.3 *Fast recovery electromyography amplifier*

This two channel device would permit investigation of agonist and antagonist muscle activation of the lower limb and would provide the primary outcome measure of this research. In order to allow identification and measurement of direct motor and reflex components following stimulation, its output had to be able to recover from the large artefact caused by a stimulation pulse in a time comparable to at least the typical M-wave peak latency (Equation 5-1, e.g. 10ms). As noted when describing the requirements of the computer controlled stimulation output, this would be accomplished through design of the EMG amplifier in light of the characteristics of the stimulation

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<sup>1</sup> Odstock Medical Limited, Salisbury, England. [www.odstockmedical.com](http://www.odstockmedical.com)

output. Other performance requirements of the EMG system would follow those of the SENIAM guidelines [140]. Due to applied electrical connection to the user, all applied parts would be electrically isolated from mains. In the same manner as the computer controlled stimulation output, the system would be used during functional tasks and therefore would be a portable battery operated system that could be worn on a belt or the limb under investigation during walking. A low battery indicator was specified such that intensity of applied stimulation was known to remain consistent provided the low indicator was not lit.

Regarding usage, silver-silver chloride (Ag-AgCl) disposable tab electrodes would be used and positioned as recommended by the SENIAM guidelines [140].

#### *5.5.4 Joint angle control and assessment*

Joint angle is known to affect reflex excitability [141] therefore during investigation of the research questions this was either restricted or varied in a controlled manner during specific phases of the investigation.

When wishing to control joint angle, a safe and effective passive system to secure a participants ankle joint at plantigrade was required. Whilst being comfortable and effective in this requirement it still had to permit the attachment measurement instrumentation to the participant. It needed to be suitable for use during right or left foot investigations with adjustments to enable use with patients of different size and strength.

When varying joint angle, a system was required for the purposes of triggering stimulation and assessment of ROM. Such a system which permitted dynamic joint angle assessment would be combined with custom software for this intended function.

#### *5.5.5 Kinetic twitch measurement*

Measurement of kinetic twitch would be an exploratory measurement that may permit inference of muscle fibre type activation. The measurement system itself would be of negligible mass compared to the participants' limb and worn upon it such that it experienced the same physical movement as the limb. Three axis accelerometers were specified such that the resulting acceleration could be calculated regardless of mounting orientation.

This chapter began with a review of key publications that, in combination with clinical observations, inform the broad research hypothesis of the study. Improved understanding of the reflex effects of conventional electrical stimulation may aid its effective clinical use. Such investigation permits comparison when assessing the hypothesis that excitatory or inhibitory reflex effects partially account for force enhancement when utilising catch-like stimulation with participants of intact lower motor neuron function. Three research questions evaluate this hypothesis through the investigation of direct and reflex motor effects of both conventional and catch-like stimulation in participants with unimpaired and impaired UMN function. For each research question, justification and details of their investigation are given. Following an outline of broad study design decisions, the requirements of an investigation setup is described prior to its detailed realisation within Chapter 6.

## **Chapter 6    Development of Investigational Setup**

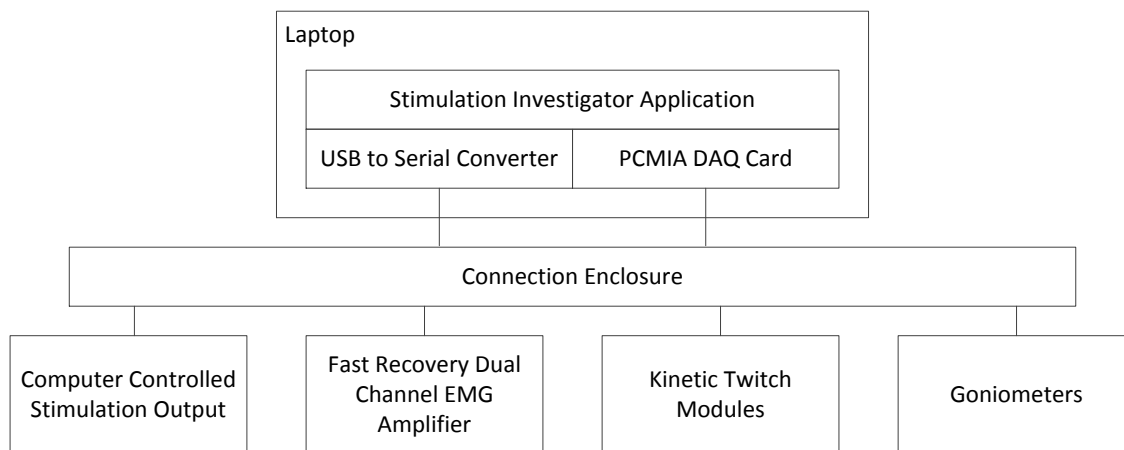
An overview of the investigational setup required to investigate the posed research questions was provided in Chapter 5. This chapter begins by reviewing the overall system topology before expanding upon its realisation. Existing, commercially available systems and tools were identified for use where possible. In the absence of these, custom systems were developed in order to realise the required functionality. The design, development, testing and refinement of such systems are documented such that meaningful results can be assured when interpreting data. Whilst in-house development of systems required substantial development efforts, the completed system provided a flexible research setup tailored to its application. The development process also provided comprehensive understanding and ownership of performance of constituent modules in order to ensure meaningful interpretation of gathered data.

A complete functioning system is presented at the end of this chapter. All system modules were tested and calibrated individually and collectively. Initial exploratory data collected with the developed system is presented in Chapter 7. Following collection and analysis of such data, minor refinements to the investigational system were made and these are incorporated and described within this chapter.

## 6.1 System Overview

During investigation of the research hypothesis a large amount of data would need to be carefully coordinated and collected. A custom software system was implemented in order to reside over and control all other systems. This software application would operate from a laptop computer and lead the investigator and participant through the series of planned investigations. It would automate configuration of hardware between tests thereby minimising time requirements, removing potential user configuration error and ensuring smooth progression of investigation sessions.

In order to permit measurements of joint angle, physical twitch and EMG synchronised to the application of stimulation, there would need to be control and coordination between the different hardware modules. In a similar manner to software control all at one level, all hardware would be connected to a 'Connection Enclosure' which would act as a single hub for the system (Figure 6-1). This permitted control and/or monitoring of all signals by the Data Acquisition (DAQ) whilst aiding organisation and minimisation of connections between hardware modules.



**Figure 6-1: Overview of investigational setup organisation**

Hardware modules were identified or developed individually and where appropriate tested in unison e.g. computer controlled stimulation output and fast recovery dual channel EMG amplifier. Software development of the Stimulation Investigator application continued throughout and was updated as additional modules were realised. In light of this development sequence, the design and developed details of each of these hardware modules is now discussed before that of the Stimulation Investigator software application.

## 6.2 Computer Controlled Stimulation Output

### 6.2.1 Overview

In order to investigate stimulation pulse intensity and spacing effects on resulting muscle contractions, precise control over applied stimulation was required. Both individual and bursts of conventional and catch-like stimulation would be used to investigate the research questions and therefore the stimulation output had to be capable of applying these.

A review of computer controlled electrical stimulators for research applications was made. Of those identified the majority of these were systems developed for one off research applications and therefore had not gained CE mark certification required for commercial sale within the European Union. The Hasomed, RehabStim<sup>2</sup> was the only identified computer controlled, CE marked stimulator which appeared capable of applying conventional and catch-like stimulation. Such a system would require additional funding to that available to the study. Development of interface hardware would also still be required in order to enable footswitch triggering and synchronisation signals with other instrumentation.

The author had the necessary knowledge, experience and tools required to develop a custom system that would permit investigation of the posed research questions. In view of no commercially available systems being identified that did not requiring further modification, an in-house development method was selected.

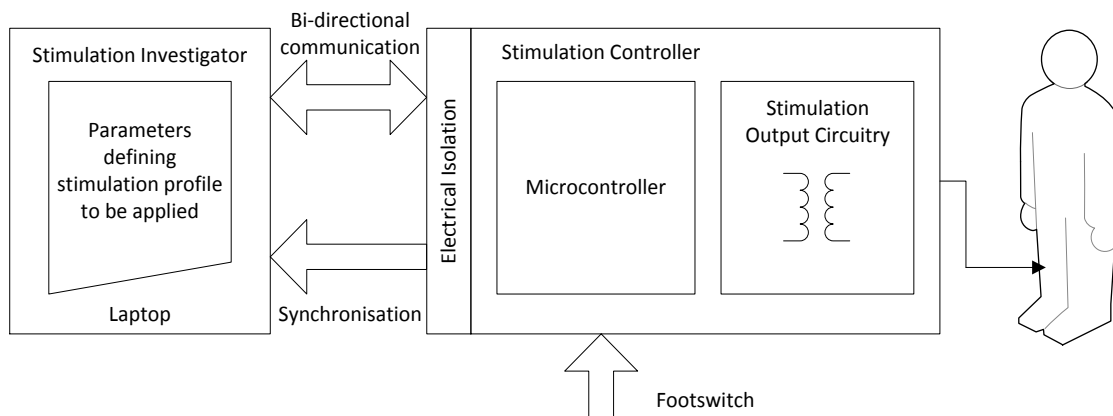
Using a laptop computer as a real-time controller to trigger a stimulation output to apply a pulse was initially contemplated. Initial investigations however identified difficulties in attaining adequate timing precision. Such difficulties were exacerbated by the need to consider other background software processes that placed additional demands on processor time.

In order to avoid timing precision limitations associated with the interfaced computer, a hardware system based upon a dedicated microprocessor capable of accurately reproducing a stimulation profile defined by parameters was implemented. This method permitted descriptions of stimulation profiles to be effectively pre-loaded, using a non-time-critical communication method. Such a method permitted all data to be easily

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<sup>2</sup> HASOMED GmbH, Magdeburg, Germany. [www.hasomed.de/en](http://www.hasomed.de/en),

communicated digitally over an optically isolated serial link. This communication link was bi-directional and therefore was used to incorporate acknowledgment of correct data transfer before allowing signalling to actually apply the described stimulation profile. Figure 6-1 provides an overview to the system. The computer controlled stimulation output received a footswitch input in order to enable the application of stimulation to be timed to the gait cycle during functional investigations. An electrically isolated synchronisation signal commenced data acquisition by the DAQ when stimulation was applied.

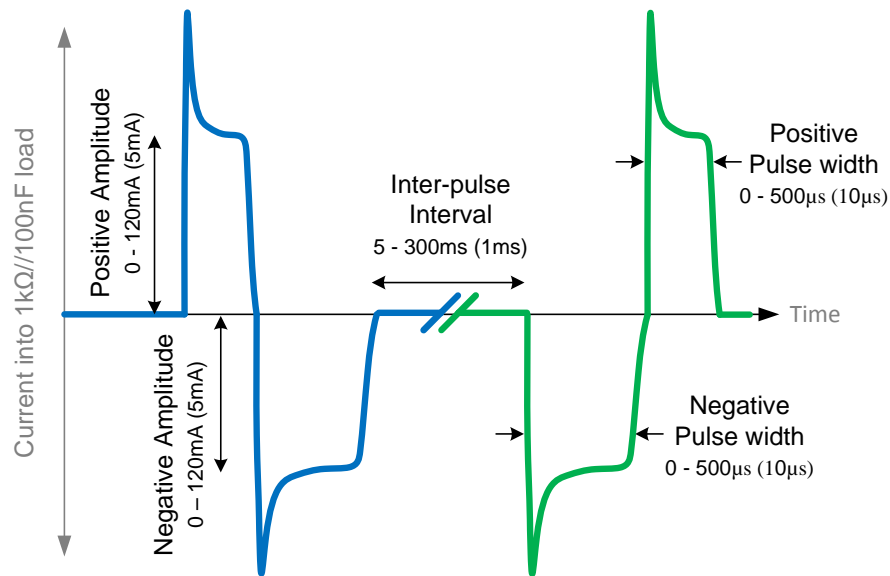


**Figure 6-2: Computer controlled stimulation output overview**

The design, implementation and refinement of this system is now discussed in detail.

### 6.2.2 Design and development

Parameters necessary to describe either conventional or catch-like pulses of stimulation of monophasic or biphasic polarity as depicted in Figure 6-3 were specified based upon stimulation settings used clinically and collected from literature. The ability to describe two independent stimulation pulses was implemented in order to enable future investigation of doublets comprised of dissimilar pulses. With the ability to repeat each of these pulses a specified number of times, two distinct bursts of stimulation could be delivered.



**Figure 6-3: Stimulation parameters defining applied conventional or catch-like stimulation**

*Choice of single (blue) or doublet (blue + green) pulse provided, doublet pulse shown.*

*Pulses can be monophasic or biphasic with the initial polarity of each pulse controlled.*

*Value in (brackets) indicates smallest incremental change permitted by software.*

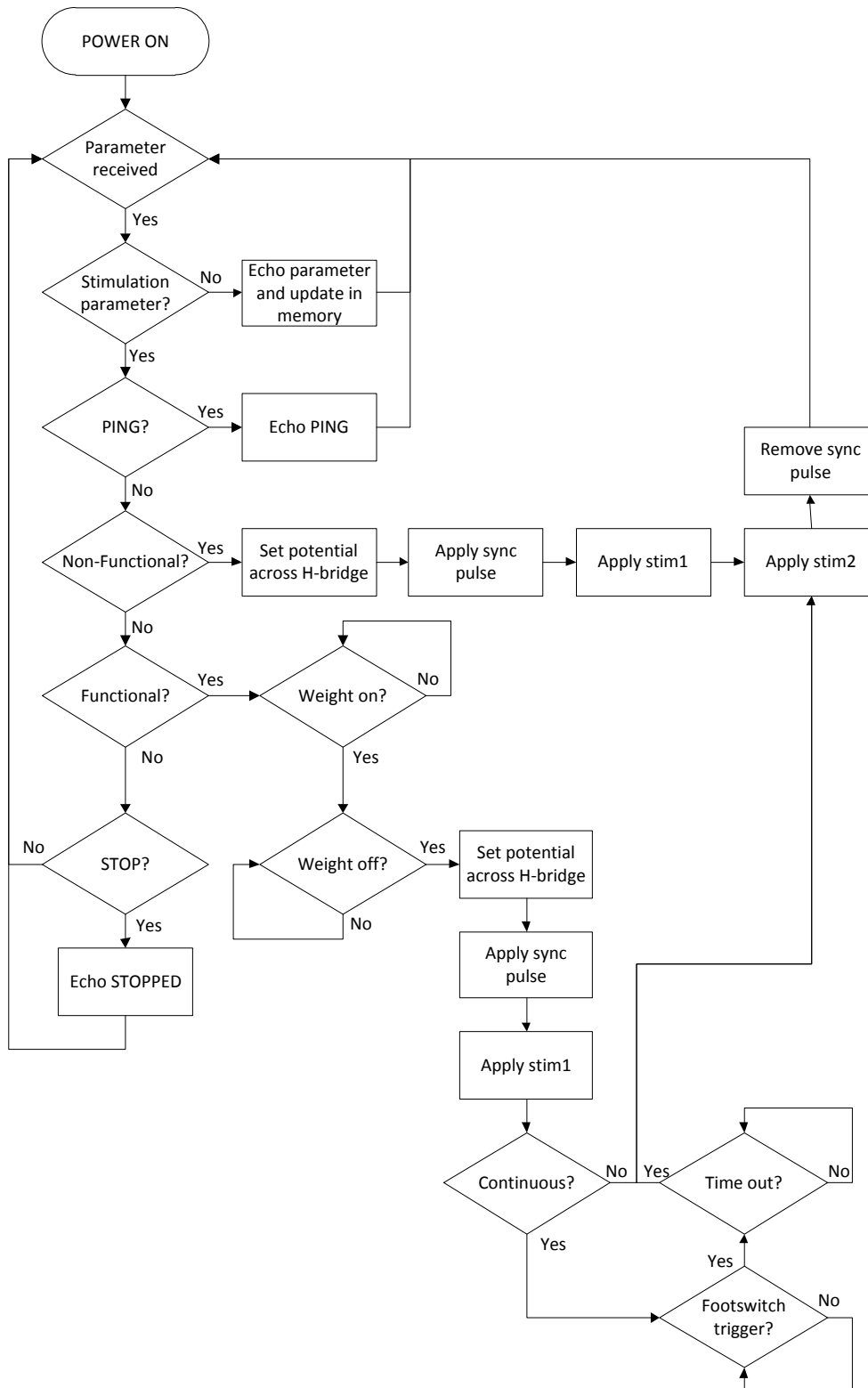
A serial interface was adopted due to ease of interfacing and implementing with developed hardware and software systems. A Prolific PL-2303 USB to Serial converter<sup>3</sup> was incorporated within the 'connection enclosure box' (Figure 6-1). In order to ensure electrical safety when using the stimulator, this interface was electrically isolated from potentially mains powered equipment. Sufficient voltage potential was rectified and smoothed from the 'request to send' and 'data terminal ready' lines of the serial interface to power an opto-isolator. This design permitted a bidirectional optically isolated serial link without need for a separate battery powered supply.

A digital microcontroller with hardware support for serial communications was used to receive and acknowledge these commands. A design based around a Peripheral Interface Controller (PIC) executing a program written in C language was designed and developed. A Microchip 18F2525 PIC was selected due to its hardware features, the ability to compile and program it using descriptions written in C language and the availability of development tools. C code describing the flow diagram of Figure 6-4 was implemented. When in idle mode and not applying stimulation, the controller monitors the serial interface for updates to stimulation parameters. If a parameter is received the appropriate program branch is executed before returning to the idle state.

<sup>3</sup> Prolific Technology Inc, Taiwan. [www.prolific.com.tw/eng/](http://www.prolific.com.tw/eng/)



Where appropriate, use of function calls within the code aided software organisation and development. For example, such functions are called singularly or within finite duration loops during the application of twitch or burst stimulation profiles respectively. Table 6-1 defines stimulation parameters conveyed across the serial port interface.



**Figure 6-4:** Flow diagram describing operation of stimulation output microcontroller routine

Name	Description	Value	Increments	No. 8 bit words
DELAY	Delay in milli-seconds between falling edge of sync signal and stimulation pulse.	0-255ms	1ms	1
POSPW *	Pulse-width in $\mu$ s of positive pulse.	0-500 $\mu$ s	10 $\mu$ s	2
NEGPW *	Pulse-width in $\mu$ s of negative pulse	0-500 $\mu$ s	10 $\mu$ s	2
POSAMP *	Value governing current amplitude of positive pulse.	0-120mA	5mA	1
NEGAMP *	Value governing current amplitude of negative pulse.	0120mA	5mA	1
POSNEG *	TRUE if positive pulse leads negative.	255 or 0	TRUE / FALSE	1
SINGDOUB	TRUE if doublet pulse.	255 or 0	TRUE / FALSE	1
PERIOD1	Time in milli-seconds between repetitions of either single or doublet pulses.	5-300ms	5ms	1
DOUBSPAC	Time in milli-seconds between first and second pulse of a doublet stimuli.	5-300ms	1ms	1
PNUM	Number of pulses forming stimulation sequence (1 for twitch tests)	0-255	1	1
FSWITCH	TRUE if subsequent stimulation is to be triggered from footswitch input.	255 or 0	TRUE / FALSE	1
PING	Used to check stimulator if connected and functioning.	-	-	-
STIM	Instructs stimulator to apply stimulation sequence as defined by above variables.	-	-	-

**Table 6-1: Computer controlled stimulation output control variables**

\* Parameters are defined for pulse 1 and pulse 2. Conventional stimulation formed solely of pulse 1. Doublet stimulation formed of pulse 1 and pulse 2.

The stimulation output circuitry utilised the pulsed transformer output method of the CE marked Odstock III Dropped Foot Stimulator (ODFSIII<sup>4</sup>). This audio transformer has a secondary winding resistive impedance that approximately matches the typical skin electrode contact resistance (1.0k $\Omega$ ) [142], thereby efficiently coupling stimulation to a user. The ODFSIII demonstrates use of this transformer in a current step up configuration to efficiently applying faradic stimulation from a battery powered, body worn device such that users tolerate the system well and do not experience significant instances of skin irritation [143]. Momentarily switching a 9.0V signal (PP3 power source) across the transformer primary windings can produce current pulses of 120mA into a 1.0k $\Omega$  test load. This method presents an inherently safe form of applying

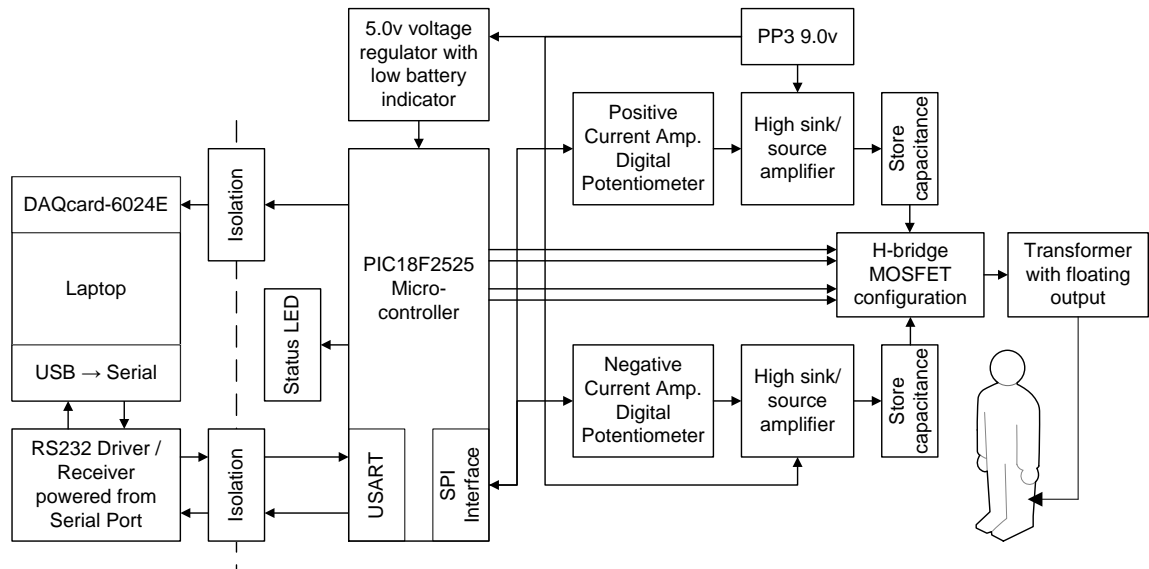
<sup>4</sup> Odstock Medical Limited, Salisbury, England. [www.odstockmedical.com](http://www.odstockmedical.com)

stimulation as a prolonged DC pulse applied to the transformer will cause it to saturate or fail whilst maintaining isolation of the user throughout.

An H-bridge arrangement as commonly used in motor control, permitted positive and negative stimulation pulses to be applied by varying the current flow direction through the transformers primary windings. Positive and negative pulse-width was controlled by the duration that each arm of the H-bridge was switched. Stimulation pulse amplitude was varied by controlling the voltage potential that would momentarily be switched across the primary windings of the transformer. Digital potentiometers interfaced to the microcontroller and controlled by POSAMP and NEGAMP parameters, controlled the input potential to a low output impedance voltage amplifiers. The output of these amplifiers sunk and sourced current to large store capacitors placed in parallel with the primary winding of the transformer during switching. When the H-bridge permits current flow through the primary windings of the transformer, these amplifiers in combination with the store capacitor, attempt to source constant current between the stimulation electrodes for the duration of the pulse.

During functional investigations, the application of stimulation would be timed to the gait cycle. Either individual conventional or catch-like stimuli applied at heel rise or a stimulation burst throughout swing and into stance, as typically applied by dropped foot stimulators, would be applied. A tracking comparator circuit design as used within the ODFSIII, was utilised to provide a digital signal corresponding to whether a connected footswitch had weight applied across it consistent with stance. As reflected in the flow diagram of Figure 6-4, this signal would be used to time the application of stimulation. Should the system fail to detect heel strike once triggered, a time out function ensured stimulation could not be indefinitely applied to the user.

Figure 6-5 shows the constituent elements of the computer controlled stimulation outputs and how they are interfaced in order to achieve the functionality described. For future use it should be noted that this system can be used as a stand-alone system from a computer with a USB or serial communications port able to convey the control parameters of Table 6-1.



**Figure 6-5: Block diagram of computer controlled stimulation output**

The following description of operation accompanies the final circuit schematic provided in Figure 6-6.

Use of a low power RS232 line driver/receiver with automatic power shutdown (U1-MAX3223) enables it to derive power from the ‘request to send’ and ‘data terminal ready’ lines of the serial communication terminal. The send and receive lines are optically isolated (OI2-P901V and OI3-P901V) before interfacing the microcontroller’s (U2-PIC18F2525) USART terminals. Using this serial interface, a simple alphabetical code informs the microcontroller which of the twelve possible stimulation parameters the following 8- or 16-bit transmission controls. The microcontroller echoes the commands and values which are displayed on the graphical user interface of the Stimulation Investigator program (section 6.7) and logs them within the measurement output file. A look-up table conveys calibrated values to the digital potentiometers for each 5mA step of positive and negative current amplitude using a Serial Peripheral Interface (SPI) bus protocol to a dual package of 100kΩ digital potentiometers (U3-MCP42100). A low drop out linear regulator (U5-MAX883) provides a steady 5.0V voltage level to power the microcontroller and potentiometers and indicates a low battery indicator below a 6.8V battery potential. The outputs of the potentiometers control the positive and negative stimulation pulse amplitudes and are derived from the regulated 5.0V line, hence being stable irrespective of battery terminal potential variations. Two non-inverting amplifiers amplify and buffer the potentiometer outputs to provide two potentials from which to switch the primary windings of the transformer

(TX1) across in order to provide positive or negative stimulation pulses. A dual op-amp package (U4A, U4B-L272) was sourced due to the large sink/source output capabilities of each non-inverting amplifier op-amp. This enabled charge or discharge of the 330 $\mu$ F store capacitors (C10, C12) to within 10% of the maximum change in stimulation amplitude within the minimum doublet pulse spacing of 5.0ms. Four switching lines from the microcontroller (RA0, RA1, RB3, RB4) control the PMOS and NMOS H-bridge, governing the pulse-width and polarity of the applied stimulation pulses. The potential across each 330 $\mu$ F store capacitor governs the positive (C10) and negative (C12) pulse current amplitude respectively. To minimise the risk of skin irritation, fly-back diodes (D1, D2) enable residual back potentials across the primary coil windings of the transformer following stimulation to be discharged to ground. During exploratory data collection a small residual discharging potential was noted across the primary windings of the transformer. The switching sequence of the H-bridge following a stimulation pulse was modified such that the two ends of the primary windings were held at ground. This removed this residual potential and appeared to further reduce any remaining stimulation artefact seen by the fast recover EMG amplifier of section 6.3. The microcontroller also provides (RA2) a 20 $\mu$ s optical isolated (OI1-P901V) synchronisation pulse sufficient to trigger commencement of data acquisition by the DAQcard (Figure 6-5).

The tracking comparator footswitch input can be described as a non-inverting Schmitt trigger with a 10 $\mu$ F low leakage capacitor (C13), connected between the feedback connection and ground so as to provide a delay in the switching points. If a sufficiently large and fast change in the potential across the footswitch is detected, the output (U4) may be toggled. R28 prevents the potential divider voltage from dropping too low such that the current through R31 becomes greater than that through R30. R29 placed in parallel with the connected footswitch improves sensitivity at the lower resistive range of the footswitch (deviations from weight on to weight off the footswitch).

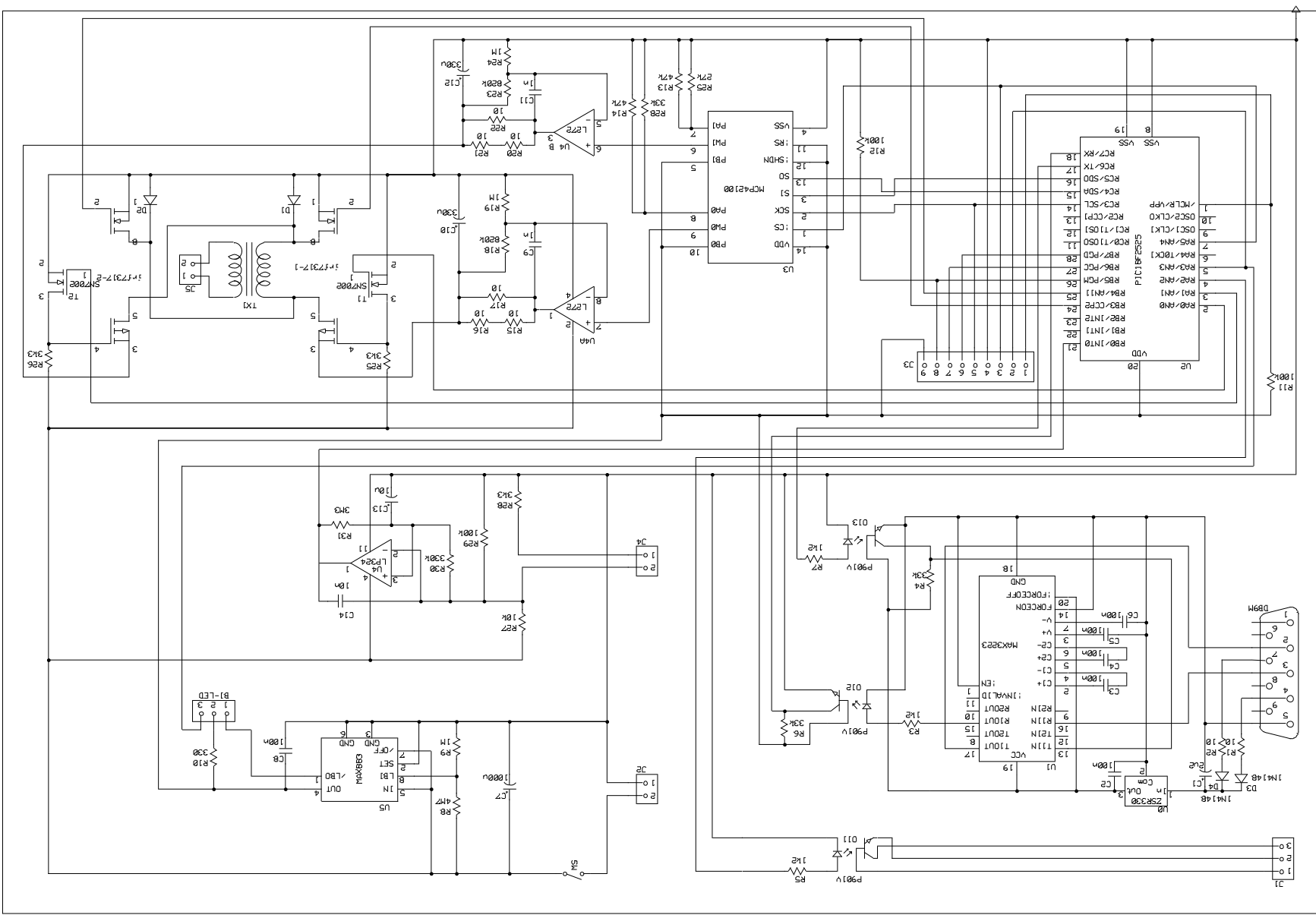


Figure 6-6: Computer controlled stimulation output circuit schematic

A custom double sided Printed Circuit Board (PCB) was designed and developed in-house using shareware CAD tools<sup>5</sup>. Once populated and tested it was housed in a body worn Acrylonitrile Butadiene Styrene (ABS) plastic case with belt clip enabling the system to be worn either around the waist or in a pouch on the lower leg (Figure 6-27).

### 6.2.3 Calibration and testing

The amplitude of stimulation pulses was calibrated by measuring the output across a standard  $1.0\text{k}\Omega//100\text{nF}$  parallel test load which mimics the skin electrode model [142]. The 8-bit value of each potentiometer wiper which produced stimulation pulse amplitudes of 5mA increments between 0 and 120mA was recorded. These values were used within a look up table by the Stimulation Investigator application in order to permit control of pulse amplitude to within this precision.

Following amplitude calibration, the full range of remaining parameters of Table 6-1 were also assessed into a  $1.0\text{k}\Omega//100\text{nF}$  parallel test load. The physiological effect of the stimulator output was confirmed on the author. The system consumed 241mW when powered and not applying stimulation.

## 6.3 Dual Channel Electromyography Amplifier

### 6.3.1 Overview

In order to investigate muscle activation following the transcutaneous application of electrical stimulation, an EMG amplifier was required to accurately convey myoelectric signals from muscles shortly after a stimulation pulse. A dual channel amplifier was required in order to permit the reciprocal nature of agonist - antagonist muscle pair activity to be assessed in the lower limb.

The computer controlled stimulation output of section 6.2 would apply stimuli where potentials of up to 120V may be seen between the stimulation electrodes. Although this would be largely seen as a common mode signal, the superimposed component of interest would be in the order of  $10^4$  times less in magnitude and hence could easily be masked by artefact. The amplifier's output therefore needed be able to quickly recover following the large transients caused by the application of electrical stimulation,

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<sup>5</sup> ExpressPCB version 6.14. [www.expresspcb.com](http://www.expresspcb.com)

enabling identification and measurement of activity of muscle fibres activated by individual electrical stimulation pulses. Significant technical challenge would be in recovering from this artefact in sufficient time such that the resulting muscle activity could be recorded.

In developing the specification for the amplifier, recommendations for surface EMG amplifier requirements, signal processing methods, sensors and sensor placement procedures were consulted from the SENIAM project [140].

A literature review of EMG systems used in the presence of the electrical stimuli was made. As previously described (section 4.1), few technical publications of systems permitting the continuous instantaneous measurement of EMG following the application of an electrical stimulation pulse appear to be reported in literature [135-137]. Of commercial systems only the Cambridge Equipment Design (CED)<sup>6</sup> 1902 input clamp option was identified. This system utilises a sample and hold concept in which the potential at the amplifier inputs, immediately prior to the application of stimulation, is sampled and held for a finite time until the artefact has passed at which point the inputs are switched back to the live recording [144]. Whilst this avoids gross saturation of the amplifier due to the artefact, it still introduces a step change when switching from the held potential to the live potential [145]. The settling time will be a function of the recovery time set by the lower corner frequency of the EMG amplifiers pass band. The optimal time to 'hold' the amplifier input and avoid saturation will vary between individuals due to the magnitude and properties of the artefact seen with the adopted setup. If used during this research, attempts to set the sample and hold time to a value suitable for all users would have to be made. Therefore, neither this commercial system nor the sample and hold method it employed, were pursued further due to the inherent step response artefact following a fixed sample and hold time.

Without a commercially available system it was decided to design and develop a custom system. This would give ownership of performance and enable the system to be tailored to the characteristics of the computer controlled stimulation source of section 6.2.

Due to the applied nature of the system, the user would need to be electrically isolated from any potentially mains operated equipment e.g. laptop computer. The system needed to be compact and wearable so as to permit use with agonist and antagonist muscles during functional investigations i.e. walking.

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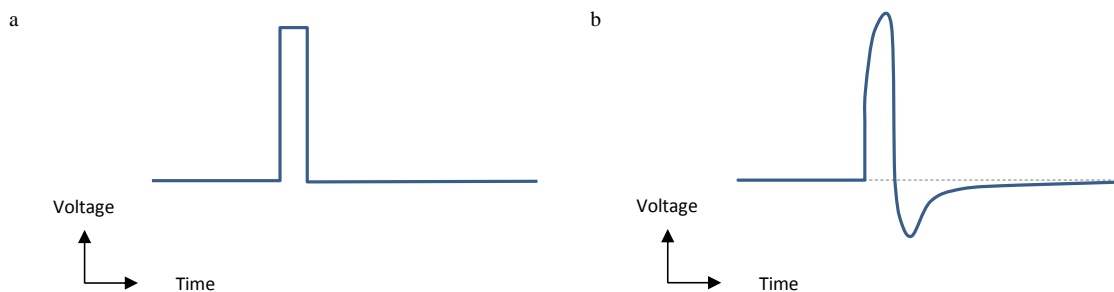
<sup>6</sup> Cambridge Electronic Design Limited, Cambridge, England. [www.ced.co.uk](http://www.ced.co.uk)



### 6.3.2 Design and development

A design proposed by Thorsen [137] was identified during literature review which appeared to meet the requirements of the intended application. The design utilised two feedback loops to provide artefact suppression and fast DC offset. In effect an amplifier in which the filter time constant could be temporarily changed whilst a threshold was exceeded had been realised.

Thorsen's design was simulated using OrCAD Capture CIS, release 15.7<sup>7</sup> so as to aid understanding prior to realising the system in hardware. Initial component values were based upon those reported and those used in simulation to achieve the described performance. Upon testing the amplifier with the computer controlled stimulation output of section 6.2, the output did not appear as expected. Comparison of the simulation results to those measured in the laboratory indicated the reason was due to different characteristics of the applied stimulation pulse. Thorsen's design assumed the monophasic stimulation pulse of Figure 6-7<sup>a</sup>. Whilst a close likening can be achieved by stimulation output designs the same author has since published [146], this is not the characteristic profile achieved by the adopted pulsed transformer method described earlier. The computer controlled stimulation output of section 6.2 produced a pulse akin to that shown in Figure 6-7<sup>b</sup> in which following negative overshoot, the potential asymptotically returned to baseline. Clinically this is considered advantageous as an element of net charge balance is achieved which is thought to be accountable for lower instances of skin irritations with respect to purely monophasic stimulation. If the assumption is made that the stimulation artefact present at the recording electrode is an attenuated version of either Figure 6-7<sup>a</sup> or <sup>b</sup> then the significance of their different characteristic becomes evident when a large gain is applied.



**Figure 6-7: Voltage potential at stimulation electrodes**

<sup>a</sup> Depiction of a purely monophasic pulse as reported by Thorsen [137].

<sup>b</sup> Depiction of a pulsed transformer pulse as applied by computer controlled stimulation output (section 6.2)

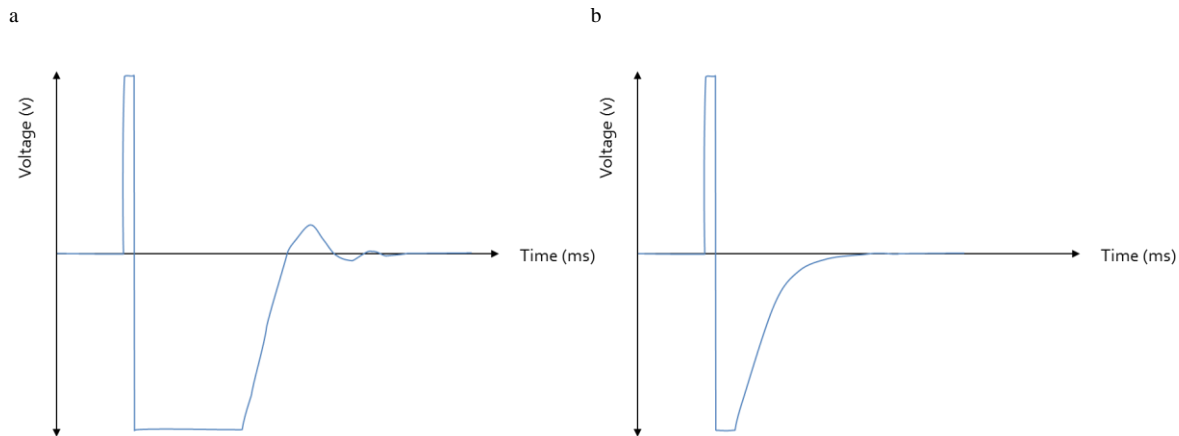
<sup>7</sup> Cadence Design Systems. [www.cadence.com](http://www.cadence.com)

For a purely monophasic stimulation pulse, the duration of saturation of an initial gain stage will be that of the pulse-width. Considering the stimulation pulse produced by the pulsed transformer output, the gain stage will first saturate during the pulse-width and then also in the opposite direction during the resulting overshoot.

Thorsen's design relied upon the saturation period of the pre-amplifier being comparable to just the pulse-width of the stimulation pulse. The design used a capacitor (C1, Figure 3 of [137]) within the feedback loop of the current switch to prevent its activation during application of the stimulation pulse. Due to the saturation period being short with respect to the time constant of the high pass filter (8Hz), there would be minimal change in the high pass filter output following the pre-amplifier returning from saturation, thus minimising stimulation artefact.

In response to stimulation by a pulsed transformer stimulation pulse, the overshoot of the stimulation artefact tail caused the current switch to act following the delay introduced by the described capacitor. Following deactivation of the current switch, the amplifiers output would recovered from saturation in a time period consistent with the 8Hz high pass filter. Under these conditions the design provided little benefit to that of just a preamplifier and high pass filter acting alone (Figure 6-8<sup>a</sup>). To be of useful function, the application required the current switch to quickly act and disengage to aid recovery from both the stimulation pulse itself and the resulting overshoot. The capacitor of Thorsen's design was therefore removed such that the current switch activated without delay whenever a disturbance larger than the expected EMG signal was detected on the output of the preceding pre-amplifier. In the presence of the pulsed transformer pulse of Figure 6-7<sup>b</sup>, this would be first during the pulse itself and then in the opposite direction during the overshoot. The current switch would stay engaged until the output returned from saturation to below the switching threshold at which point the high pass filter would be re-engaged. The switching threshold of the current switch was reduced from approximately  $\pm 600\text{mV}$  used by Thorsen to  $\pm 200\text{mv}$ . This was completed in order to utilise the linear amplifier range of the isolation amplifier that would follow it whilst also reducing the level at which the switch would disengage and the potential from which the slow high pass filter would have to recover from. Diode clamps limited the input to the high pass filter whilst the current switch was engaged, thereby minimising recovery artefact. By increasing the corner frequency of this filter from 8.0Hz to 20Hz it was comparable to the artefact tail. This further improved the amplifiers response to a pulsed transformer stimulation pulse as recovery was faster and

generally avoided overshoot. The high pass filter corner frequency was not increased further as this would have begun to compromising the signal pass band. The developed system could be described as an intelligent blanking filter in which the system is blanked for the optimal length of time. By the two feedback loops acting on the same integrator (capacitor) the filters are smoothly reengaged rather than a step change akin to the sample and hold method described earlier (Figure 6-8<sup>b</sup>).

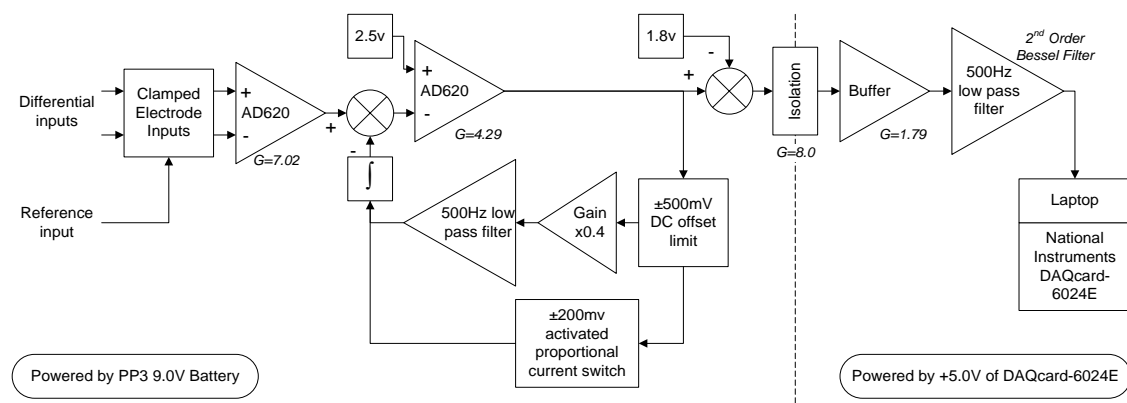


**Figure 6-8: Depiction of amplifier output following pulsed transformer stimulation pulse**

<sup>a</sup> Depiction of conventional amplifier output

<sup>b</sup> Depiction of implemented amplifier output based upon modified Thorsen design

A block diagram of the developed system which utilised concepts of Thorsen's design is shown in Figure 6-9.



**Figure 6-9: EMG system block diagram**

Dashed line indicated optical isolation between patient connected instrumentation (left) and mains powered instrumentation/equipment (right)

G= gain of amplifier stage

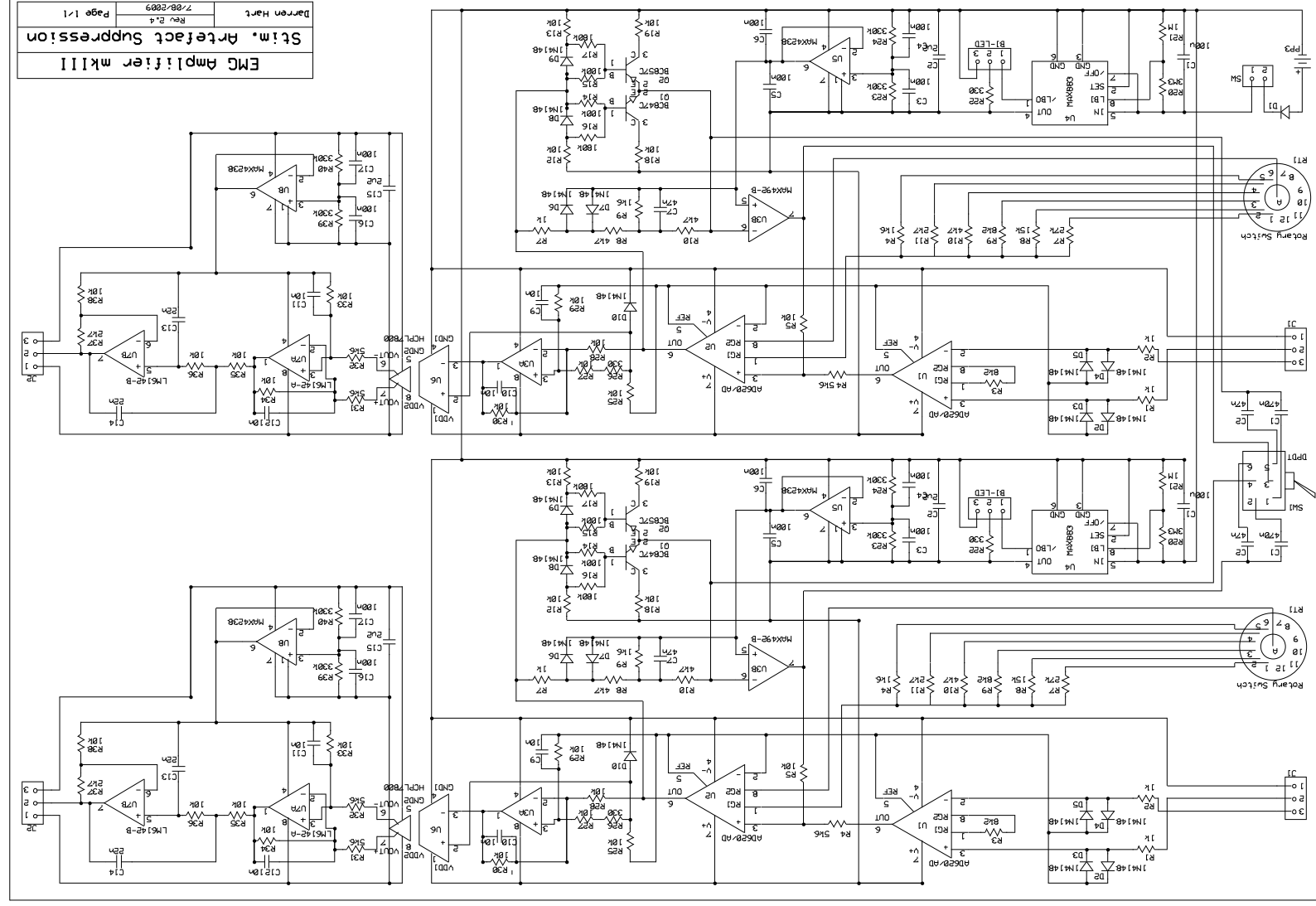
The gain and frequency response was initially selected so as to display EMG signals of 10.0mV or less over a range of 20-500Hz without saturating the output. To aid understanding of performance and optimal design the system was simulated using OrCAD Capture CIS, release 15.7. This approach significantly facilitated the efficient design of the amplifier and enabled the response to stimulation prior to PCB development to be assessed.

The following description of operation accompanies channel 1 of the realised dual channel fast recovery EMG amplifier circuit schematic provided in Figure 6-10.

The two differential signal inputs are clamped to within  $\pm 0.6V$  of the reference lead potential to protect the first instrumentation amplifier (U1-AD620) input. The gain of this instrumentation amplifier should be large to improve its common mode rejection ratio, but not so large to cause it to saturate due to DC offsets. Thus R3 sets the gain to 7.02 enabling a DC offset of  $\pm 128mV$  to be compensated for by the output of the feedback path op-amp (U3B-MAX492). R4 and R5 are a compromise between minimal signal attenuation and maximal offset compensation range due to the limited output swing of the first instrumentation amplifier (U1-AD620). The isolation amplifier (U6-HCPL7800) has a linear input range of  $\pm 200mV$ . The second instrumentation amplifier (U2-AD620) has a gain set between 2.8 and 31.9 by R6-R11 which sets the maximum input EMG amplitude that can be reproduced at the output to 15.6mV to 1.39mV respectively. Both instrumentation amplifiers quickly recover from saturation and are fundamental to the amplifiers dynamic performance. Through careful biasing (R11-R16) an offset of more than  $\pm 200mV$  causes the NPN or PNP transistor to switch, quickly charging or discharging C9 thus recovering the output from sudden, or present at switch on, offsets. During operation when large differential inputs (e.g. stimulation artefact) are not causing activation of this recover path, a band pass filter with corner frequencies between 20Hz and 500Hz is formed by R8-R11 and C8 and C7 respectively. R8-R11 also limit the maximum compensation rate of the output of U3B when the artefact recovery system is activated. The differential amplifier (U3A) which follows the second instrumentation amplifier (U2-AD620) shifts its resting output to a level of 0.6V in order for the isolation amplifier (U6-HCPL7800) to operate effectively. The differential amplifier (U7A-LM6142) following the isolation amplifier applies gain and power amplification of the signal. A 2<sup>nd</sup> order anti-aliasing Bessel filter (U7B-LM6142) with a corner frequency of 500Hz follows and is selected due to its favourable phase response. A low drop out linear regulator (U4-MAX883) provides a steady 5.0V

voltage level to power the patient connected side of the amplifier. A low battery indicator alerts the investigator when the battery potential falls to 5.8V or less. Two op-amp voltage followers (U5-MAX4238 patient side, U8-MAX4238 mains side) provide steady split rail levels of 2.5V which are able to sink and source current.

A custom double sided PCB was designed and developed in-house using the same tools and methods as utilised when realising the computer controlled stimulation output. Once populated and tested two of these boards were housed in a body worn ABS plastic case with belt clip enabling the system to be worn either around the waist or in a pouch around the lower leg (Figure 6-27). Power consumption of the two EMG channels was measured at 400mW during normal operation.



### 6.3.3 Calibration and testing

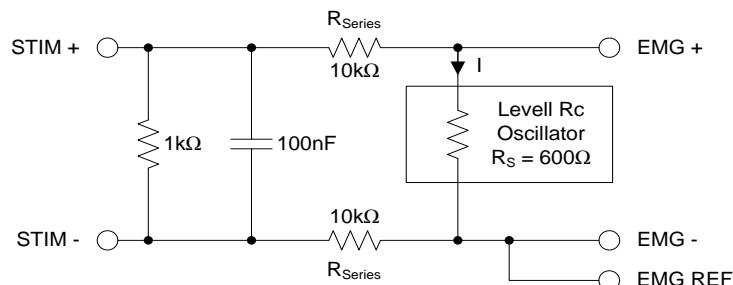
The setup of Figure 6-11 was used to mimic conditions during intended operation. A Levell RC Oscillator Type TG200D<sup>8</sup> floating signal generator applied a sinusoid across the amplifier inputs over the typical frequency (20-500Hz) and amplitude ( $\leq 10\text{mV}$ ) typical of surface EMG [147]. In developing this test setup, stimulation applied to the authors lower leg was used to estimate the series resistance of skin between the stimulation and EMG electrodes. Stimulation was applied above the tibialis anterior muscle belly using hypoallergenic neuro-stimulation electrodes (Nidd Valley Medical<sup>9</sup>, Platinum blue PALs 5cm x 5cm, ref: 901220). EMG collected using disposable EMG electrodes (ViaSys Healthcare<sup>10</sup>, ref: 019-435300) placed in between these stimulation electrodes, enabled the component of the stimulation amplitude appearing across the amplifiers inputs to be measured using a floating (battery powered) oscilloscope. Applying a 100mA amplitude, 400 $\mu\text{s}$  pulse-width stimuli, a 96.8V amplitude pulse was seen across the stimulation electrodes and a 2.52V component across the EMG amplifier input. Series resistance between the stimulation terminals and EMG input leads would model this voltage drop. In this configuration the current that stimulation would cause to flow across the 600 $\Omega$  output impedance of the RC oscillator would be given by Equation 6-1. The series resistance required for this to occur could then also be calculated (Equation 6-2). Adopting nearest preferred values, two 10k $\Omega$  resistors were selected as shown in Figure 6-11.

$$I = \frac{2.52}{600} = 4.2\text{mA}$$

**Equation 6-1: Calculation of RC oscillator current**

$$R_{\text{Series}} = \frac{1}{2} \times \frac{96.8 - 2.52}{4.2 \times 10^{-3}}$$

$$R_{\text{Series}} = 11.2\text{k}\Omega$$



**Figure 6-11: Stimulation output calibration and test setup**

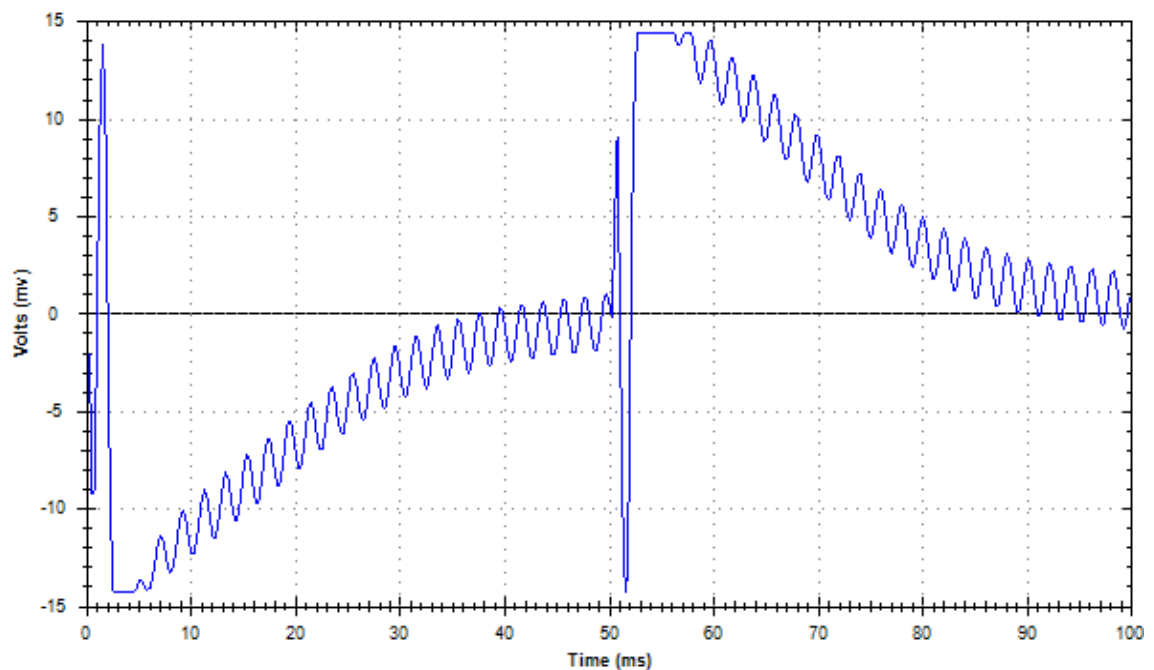
**Equation 6-2: Calculation of series skin model resistance**

<sup>8</sup> Levell Electronics Ltd, Hertfordshire, England

<sup>9</sup> Nidd Valley Medical Limited, Harrogate, England. [www.niddvalleymedical.co.uk](http://www.niddvalleymedical.co.uk).

<sup>10</sup> ViaSys Healthcare, Surrey, England. [www.viasyshealthcare.com](http://www.viasyshealthcare.com)

The parallel impedance formed by these two series resistances and the RC oscillator were sufficiently high so as not to significantly reduce the  $1.0\text{k}\Omega$  resistive impedance seen by the stimulation output. Stimulation evaluating the full range of stimulation parameters was applied in conjunction with a  $500\text{Hz}$   $2.0\text{mV}$  sinusoid (EMG mimic) across the test load to assess the amplifiers recovery time. Even in the presence of maximal monophasic (non-charge balanced pulse) the output was able to recover within approximately  $8.0\text{ms}$  as indicated in the example of Figure 6-12. Based upon earlier calculations (section 5.1.2) this would be sufficient to enable M-wave amplitude at peak latency to be identified and assessed.

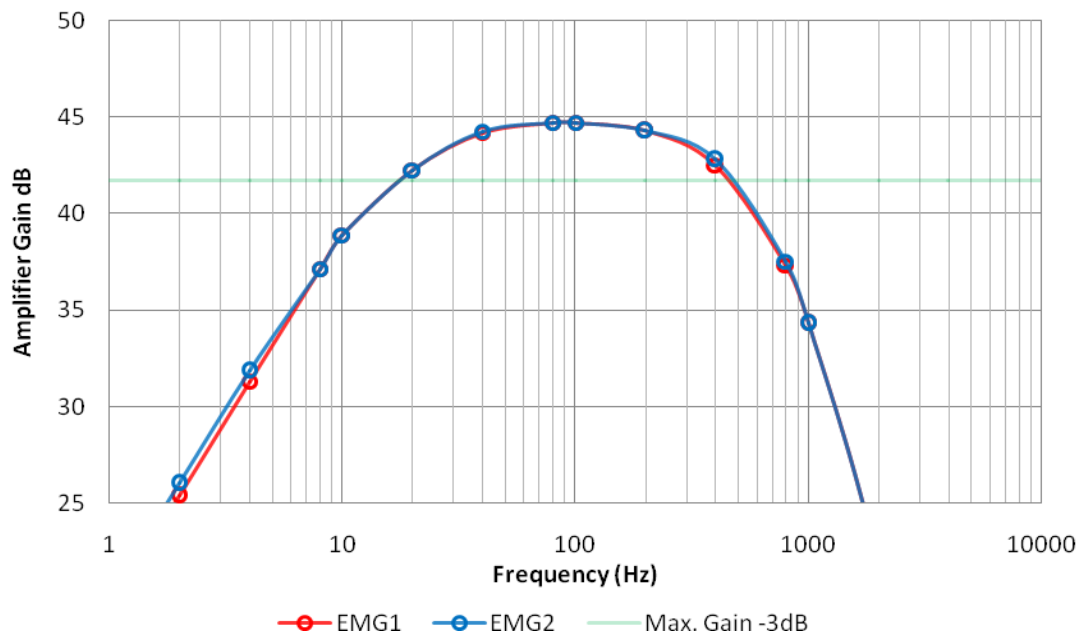


**Figure 6-12: Recorded EMG amplifier output response following maximal stimulation**

*Output recovers within approximately  $8.0\text{ms}$  when applying  $100\text{mA}$  amplitude,  $500\mu\text{s}$  pulse-width positive and negative monophasic pulses at  $0\text{ms}$  and  $25.0\text{ms}$  respectively.*

Consistent performance between both channels of the amplifier was confirmed and the differential input switched so as to ensure no distortion due to input polarity. Figure 6-13 provides the systems frequency response to a  $5.0\text{mV}$  amplitude sinusoid and indicates the measured  $18\text{-}490\text{Hz}$  frequency range when the overall system gain was set to 190 ( $45.6\text{dB}$ ).

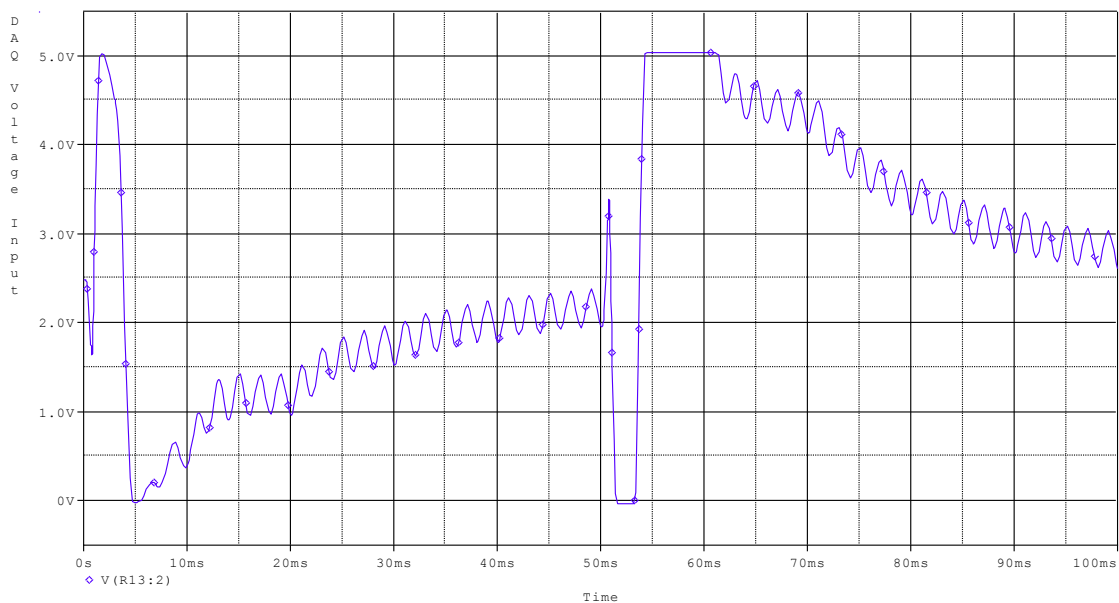




**Figure 6-13: Recorded frequency response of dual channel EMG amplifier**

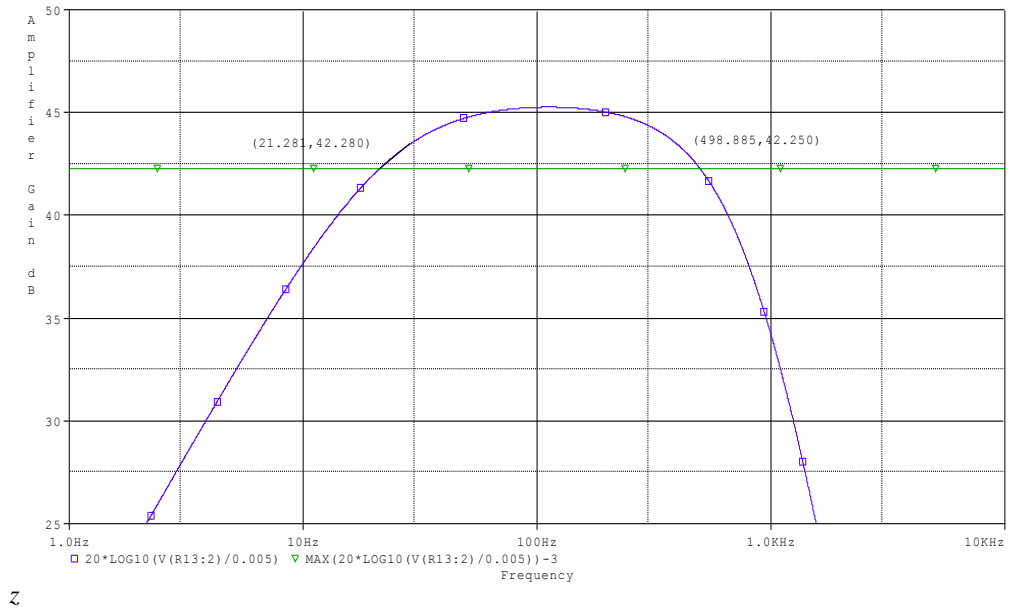
Setup of Figure 6-11 used with 5.0mV amplitude sinusoid over 1-4000Hz. -3dB points at 18 & 490Hz.

Throughout testing actual circuit performance was assessed and compared to that of OrCAD PSPICE simulation results. With reference to Figure 6-12 and Figure 6-13, good correlation was seen from both transient and frequency responses between simulation results and those recorded from the realised system (Figure 6-14 and Figure 6-15).



**Figure 6-14: Simulated EMG amplifier output response following maximal stimulation**

Results gained using OrCAD PSPICE v15.7



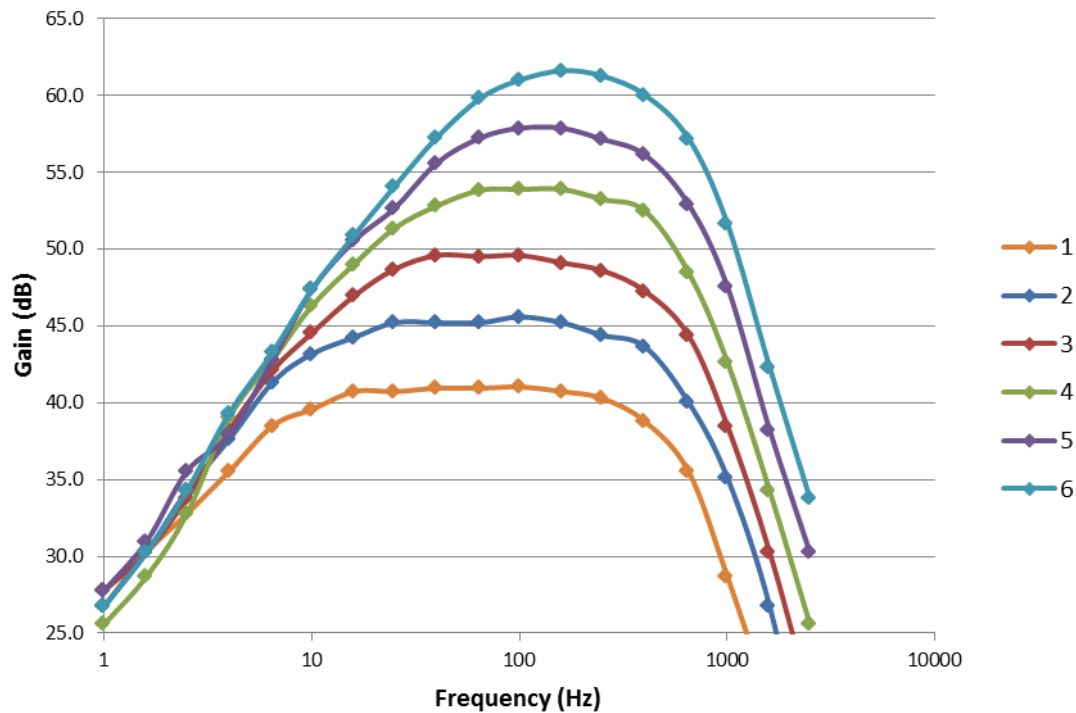
**Figure 6-15: Simulated Frequency response of EMG amplifier**

Setup of Figure 6-11 used with 5.0mV amplitude sinusoid over 1-4000Hz. -3dB points at 21.2 & 499Hz. Results gained using OrCAD PSPICE v15.7

Following initial exploratory data collection it was found that the magnitude of EMG and hence peak M-wave amplitude varied considerably across different participants. Peak M-wave amplitudes varied between approximately 0.5mV and 50mV. Whilst an initial fixed gain EMG amplifier design avoided saturation at large magnitudes, it resulted in poor signal to noise ratio when recording the lower magnitude. In order to prevent this occurrence the ability to select different gain settings was incorporated.

Due to the systems design the addition of a selectable gain stage was not straightforward however. It was not wished to vary the gain of the first instrumentation amplifier as this was currently set to maximise common mode rejection whilst avoiding saturation due the negative overshoot. The following artefact suppression feedback system was configured to present the EMG recovered from the artefact tail over a fixed input range matched to the properties of the isolation amplifier. It was therefore not wished to vary gain stages following this as the artefact suppression systems function would be compromised. The most appropriate stage for which to introduce variable gain was the second instrumentation amplifier (Figure 6-10 U2-AD620). The principal drawback of this approach was that as this amplifier was part of a negative feedback loop the frequency response was a function of the this amplifier. Although it is not generally wished for the pass band of an EMG amplifier to vary with gain settings it would not pose a significant problem in this instance. Gain settings would be set at the

start of the testing with an individual and not varied. Comparisons would generally be within participant, with any cross comparisons amongst participants made using ratiometric values. The frequency response at each gain stage was assessed and calibration factors added to software such the same amplitude was reported at 200Hz (Figure 6-16).



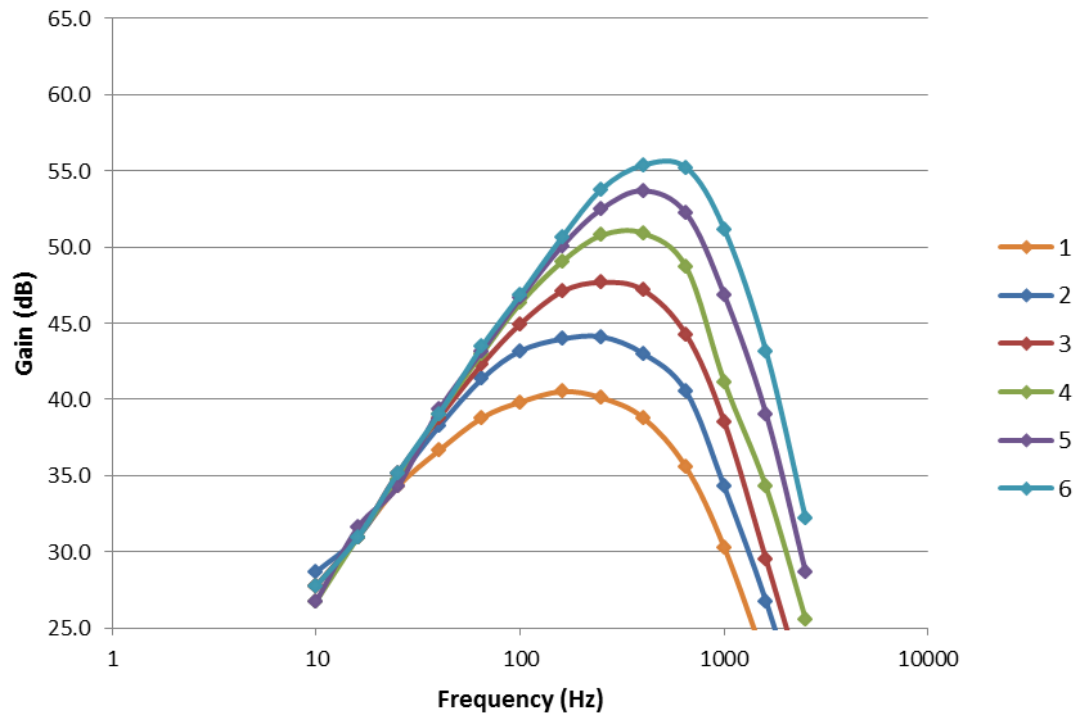
**Figure 6-16: Frequency response at full pass band setting at different gain settings**

*Note, increase in high pass filter corner frequency with increasing gain*

*Gain stage number (Gain/Gain(dB))*

Following testing on the author it was noted that remaining stimulation artefact dropped considerably as the distance between the stimulation and recording electrodes was increased. It was therefore noted that for participants of shorter height and hence leg length, the separation between the electrodes may remain small compared to other participants. Variation in anatomy and electrode placements could also result in a small distance between stimulation and recording electrodes. It appeared conceivable that difficulties of recording EMG due to remaining stimulation artefact could still possibly be encountered in some participants due to such factors. As a precaution to this the ability to switch the amplifiers frequency response to a higher proportion of the EMG signal band was implemented. This was realised using a double-pole-double-throw switch in order to reduce the store capacitor by a factor of 10 thus increasing the high

pass corner frequency by 10. The frequency response when switched to this higher signal band was recorded at each gain setting and is shown in Figure 6-17. Calibration factors were derived and implemented in software such that the mid band gain for high or full frequency range settings were equal.



**Figure 6-17: Frequency response at higher frequency pass band setting at different gain stages**

As in Figure 6-16, increase in high pass filter corner frequency with increasing gain  
Gain stage number (Gain/Gain(dB))

During data collection, stimulation artefact did not prevent identification and measurement of the M-wave of unimpaired or impaired participants. Hence although implemented this higher frequency option was not utilised during practical measurement.

Table 6-2 summaries the gain and frequency response of the fast recover EMG amplifier at different gain and frequency pass band settings.

Gain Setting	Standard Frequency Setting			High Pass Frequency Setting		
	Av (dB)	FL (Hz)	FU (Hz)	Av(dB)	FL (Hz)	FU (Hz)
1	41.4	6	459	40.5	50	499
2	45.6	9	474	44.2	63	590
3	49.8	15	460	47.7	96	614
4	53.9	23	501	51.0	135	687
5	58.0	36	499	53.6	184	749
6	61.6	53	527	55.4	210	895

**Table 6-2: Gain and frequency response summary at different amplifier settings**

*Av* = Voltage gain

*FL* = Lower (high pass filter) -3dB corner frequency

*FU* = Upper (low pass filter) -3dB corner frequency

Mains interference could not generally be noted on the EMG amplifier outputs partly due to the large common mode rejection ratio of the first instrumentation amplifier. On infrequent occasions during exploratory data collection, mains interference of up to 500 $\mu$ V was noted however. On such occasions measures such as switching off of fluorescent room lighting and avoidance of loops in the EMG electrode leads provided minor reduction in this noise component. In an attempt to resolve this issue an earth bonding strap as used commonly used during computer or electronics repair to avoid electrostatic discharge was procured. These devices typically have a 50k $\Omega$  series resistance incorporated into them to limit discharge current. In this instance there was no need to limit the flow of leakage current to ground and hence this series resistance was removed. The modified earth bonding strap was connected to an unmodified standard earth bonding UK plug adaptor with electrical connection solely to the ground conductor (Figure 6-18). During investigations the strap was placed around the contralateral ankle to the leg being studied. Although mains interference was reduced further it still remained present at times. During early data collection the source of mains interference was identified. EMG measurements had often been collected when the author or participant was supine on a clinic plinth with electronic height control. If the control unit of the plinth was powered during data collection mains interference was present on resulting EMG traces. It was thought that the coils of the height adjustment motor were energised under such conditions and this causing the interference. All further measurements were completed with the plinth disconnected from its mains supply and no further problems were encountered. As good practice, the earth bonding strap was still used during investigations.



*Figure 6-18: Modified earth bonding strap with unmodified earth bonding UK plug*

## 6.4 Kinetic Twitch Modules

### 6.4.1 Overview

A system to quantify the physical twitch of the lower limb following individual conventional or catch-like twitch stimuli was required to make inferences about resulting rate of development and magnitude of torque. The measurement method should not influence the resulting movement. A multi-moment chair system capable of the isometric measurement of 14 lower limb joint moments [148] was initially considered, however physical constraint of the ankle joint would affect proprioceptive and muscle spindle inputs, detracting from typical natural voluntary movement. Light weight wearable Xsens<sup>11</sup> orientation sensors were considered due to their negligible mass not noticeably affecting resulting movement. Upon investigation the hardware of the available instrumentation had insufficient frequency response for the fast dynamics of a muscle twitch however. These sensors utilise a sensor fusion algorithm to combine inertial data with magnetic heading data to form orientation [149]. Measurement of solely acceleration provides a pseudo measure of resulting torque which would enable quantification of muscle twitch whilst maintaining the benefits of a wearable non-invasive system. Two three-axis accelerometers of sufficient full-scale range and frequency response were selected to quantify the twitch movement of the foot and shank upon the application of stimulation.

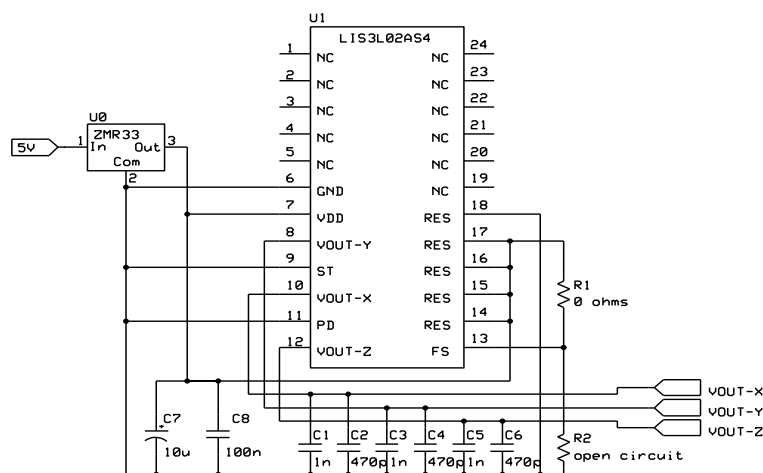
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<sup>11</sup> XSens Technologies, Enschede, The Netherlands. [www.xsens.com](http://www.xsens.com).

### 6.4.2 Design and development

STMicro<sup>12</sup> LIS3L02AS4 three degree of freedom accelerometers were sourced and configured to provide a voltage input to the DAQ representing acceleration in each axis. These accelerometers were available in a surface mount PCB package lending them to in house development. A full-scale range of  $\pm 6g$  with a 0.5mg resolution of over 100Hz bandwidth was considered ample to record the dynamics of the lower limb.

Power was delivered to these units from the +5.0V line of the DAQ via a 3.3V voltage regulator to the accelerometers. The units were packaged in ABS plastic cases. Electrical isolation was not required as there would be no directly connected patient parts. Appropriate capacitor values (1n47F) provided an anti-aliasing corner frequency of approximately 1.0kHz well above the frequency components of expected muscle twitches. A custom PCB implemented the circuit schematic of Figure 6-19. The final packaged system can be seen in use in Figure 6-27 at the end of this Chapter.



**Figure 6-19: Kinetic twitch unit circuit schematic**

### 6.4.3 Calibration and testing

Acceleration in each axis was conveyed to the DAQ by three voltage potentials. The ‘zero g’ voltage level and sensitivity of each is specified to within  $\pm 10\%$ . In order to provide accurate comparisons between trials the system would require calibration to determine these two unknowns for each axis. A method of taking six static measurements with just gravity acting would provide six equations expressing the resulting magnitude of acceleration being equal to  $g = 9.807 \text{ ms}^{-2}$  which could be solved

<sup>12</sup> STMicroelectronics. [www.st.com](http://www.st.com)

for the six unknowns. Each accelerometer was reversed within each plane (i.e. applying  $g$  and then  $-g$ ) to avoid ill-conditioning when solving the six equations for six unknowns. The Microsoft Solver add-in for Microsoft Excel<sup>13</sup> was used to resolve these as depicted in Figure 6-20. This add-in uses a Generalized Reduced Gradient (GRG2) Algorithm to vary cell values in order for a specified expression to be evaluated true. The offset and sensitivity values ( $R_x$ ,  $R_y$ ,  $R_z$  and  $A_x$ ,  $A_y$ ,  $A_z$ , respectively) shown in Figure 6-20 for the proximal and distal sensors were incorporated within data processing routines of the Stimulation Investigator application.

	A	B	C	D	E	F	G	H	I	J	K
		<b>x Calibrate</b>			<b>y Calibrate</b>			<b>z Calibrate</b>			
1											
2		Proximal	Distal		Proximal	Distal		Proximal	Distal		When at the rest the magnitude of the resulting acceleration will be equal to $g = 9.807\text{ms}^{-2}$ . The six equations below can be solved by evaluating the six sets of measurements made when reversing each accelerometer in each plane to avoid ill-conditioning.
3	x	2.414	2.364		1.754	1.736		1.765	1.715		
4	y	1.758	1.694		2.367	2.329		1.716	1.706		
5	z	1.707	1.805		1.727	1.774		2.385	2.419		
6											
7	x	1.089	1.081		1.747	1.703		1.739	1.732		Measurements made with DAQcard 6024E averaged 10 times over 1.0s window
8	y	1.691	1.671		1.083	1.033		1.741	1.670		
9	z	1.731	1.758		1.719	1.798		1.042	1.137		$ xyz  = \sqrt{A_x \times (V_x - R_x)^2 + A_y \times (V_y - R_y)^2 + A_z \times (V_z - R_z)^2}$
10											
11					Offset			Sensitivity			
12			$g$	$R_x$	$R_y$	$R_z$	$A_x$	$A_y$	$A_z$		<b>Equations of B13 - B18</b>
13	Proximal	9.807	9.807	1.751	1.725	1.713	14.779	15.273	14.598		$\sqrt{G13 \times (B3 - D13)^2 + H13 \times (B4 - E13)^2 + I13 \times (B5 - F13)^2}$
14		9.807									$\sqrt{G13 \times (B7 - D13)^2 + H13 \times (B8 - E13)^2 + I13 \times (B9 - F13)^2}$
15		9.807									$\sqrt{G13 \times (E3 - D13)^2 + H13 \times (E4 - E13)^2 + I13 \times (E5 - F13)^2}$
16		9.807									$\sqrt{G13 \times (E7 - D13)^2 + H13 \times (E8 - E13)^2 + I13 \times (E9 - F13)^2}$
17		9.807									$\sqrt{G13 \times (H3 - D13)^2 + H13 \times (H4 - E13)^2 + I13 \times (H5 - F13)^2}$
18		9.807									$\sqrt{G13 \times (H7 - D13)^2 + H13 \times (H8 - E13)^2 + I13 \times (H9 - F13)^2}$
19					Offset			Sensitivity			
20			$g$	$R_x$	$R_y$	$R_z$	$A_x$	$A_y$	$A_z$		<b>Equations of B21 - B26</b>
21	Distal	9.807	9.807	1.723	1.681	1.778	15.274	15.125	15.291		$\sqrt{G21 \times (C3 - D21)^2 + H21 \times (C4 - E21)^2 + I21 \times (C5 - F21)^2}$
22		9.807									$\sqrt{G21 \times (C7 - D21)^2 + H21 \times (C8 - E21)^2 + I21 \times (C9 - F21)^2}$
23		9.807									$\sqrt{G21 \times (F3 - D21)^2 + H21 \times (F4 - E21)^2 + I21 \times (F5 - F21)^2}$
24		9.807									$\sqrt{G21 \times (F7 - D21)^2 + H21 \times (F8 - E21)^2 + I21 \times (F9 - F21)^2}$
25		9.807									$\sqrt{G21 \times (I3 - D21)^2 + H21 \times (I4 - E21)^2 + I21 \times (I5 - F21)^2}$
26		9.807									$\sqrt{G21 \times (I7 - D21)^2 + H21 \times (I8 - E21)^2 + I21 \times (I9 - F21)^2}$

Figure 6-20: Determination of accelerometer coefficients using Microsoft Solver method

## 6.5 Isometric Ankle Bracket

### 6.5.1 Overview

A passive ankle support constraining a participants ankle to plantigrade (or as near as achievable) was required during isometric investigations. It needed to permit attachment of the computer controlled stimulation output, EMG amplifier and kinetic twitch measurement modules whilst remaining comfortable during use.

<sup>13</sup> Microsoft Corporation. [www.microsoft.com/excel](http://www.microsoft.com/excel)



Commercially available fixed Ankle Foot Orthotics (AFOs) were considered and trialled however in general these secured the joint through contact against the posterior or anterior surfaces of the lower leg. Such a constraint method was not practical whilst collecting surface EMG from tibialis anterior and soleus muscles. Issues of size and left or right usage also required an appropriate selection of these to be acquired.

It was felt that the most effective system would be to develop a custom ankle bracket designed specifically for use alongside the clinic plinth used during the study. The participant's weight on the clinic plinth would be utilised to constrain the bracket between plinth and wall. Designed appropriately, this would provide a sturdy supporting bracket able to permit measurement during isometric ankle joint conditions.

### *6.5.2 Design and development*

A timber framed design with removable foot blocks was developed to meet the requirements of the ankle bracket (Figure 6-21). Padded Velcro strapping was used to secure a participant's foot within the block across the dorsal forefoot and ankle. The foot block was suitable for either left or right use and could be secured to a number of predefined heights along the brackets surface. Attachment of the forefoot part of the foot block could be controlled over an ark thereby permitting external rotation of the lower limb should the participant not be able to position their foot parallel to their midline. The laminate finish of the brackets surface and the ABS foot blocks aided cleaning and disinfection between uses.

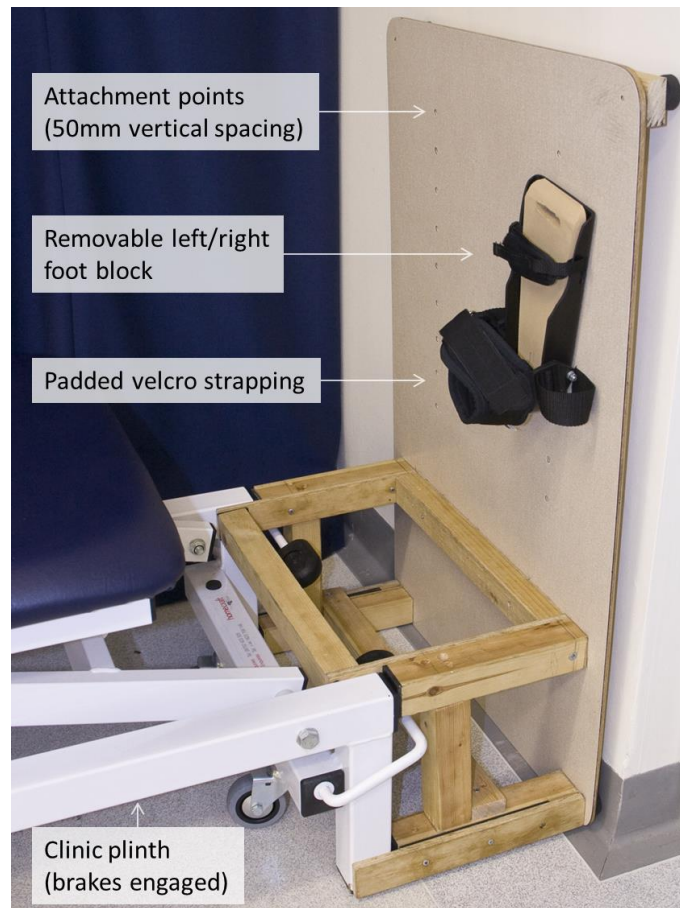
## **6.6 Electro-Goniometer**

### *6.6.1 Overview*

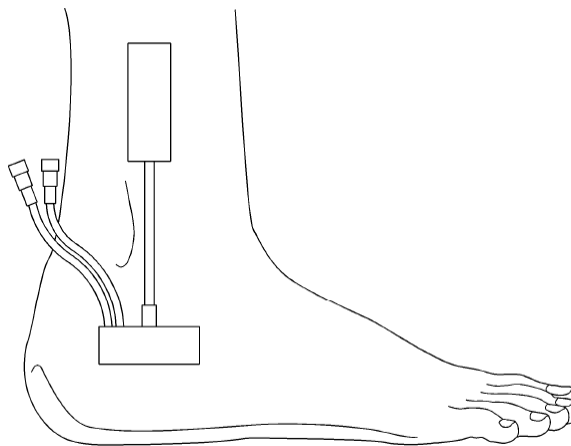
During isotonic investigations a method to trigger the application of stimulation from ankle flexion/extension angle was required. Within the Clinical Science and Engineering Department a goniometer system (Biometrics Ltd<sup>14</sup>) was available for use. The system included a two axis SG110/A goniometer intended for use when measuring dorsiflexion/plantarflexion and inversion/eversion of the ankle joint as indicated in Figure 6-22.

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<sup>14</sup> BioMetrics Ltd, Newport, England. [www.biometricsltd.com](http://www.biometricsltd.com)



**Figure 6-21: Isometric ankle bracket**



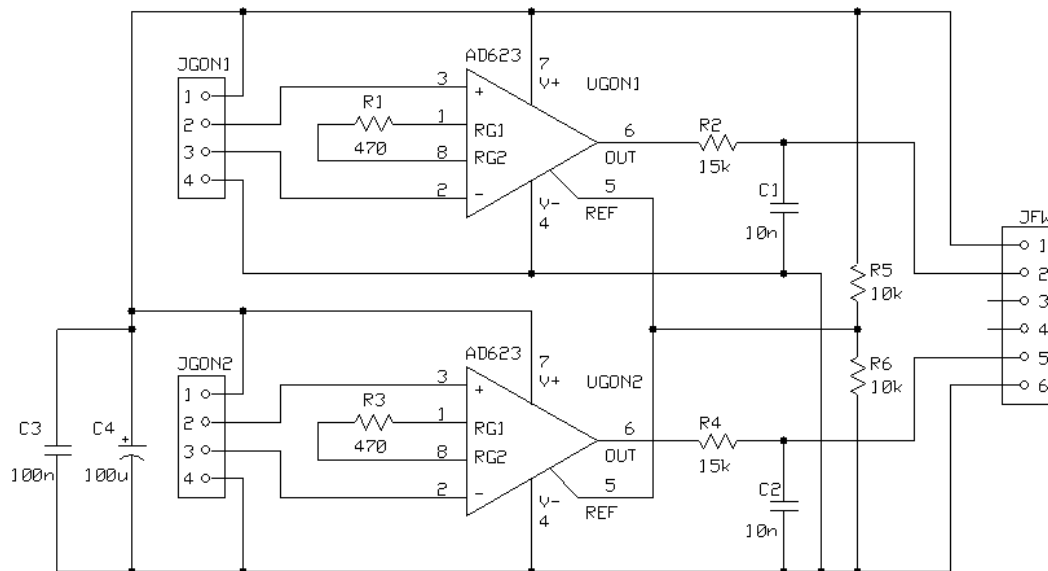
**Figure 6-22: Ankle goniometer used for assessment of ankle ROM<sup>14</sup>**

Each axis of the goniometer was a Wheatstone bridge in which the resistance of each potentiometer arm varied with the angle between goniometer arms. The Biometrics system included hardware which provided amplification, filtering and data acquisition functions. This proprietary interface hardware was not used during the study as interfacing to the Stimulation Investigator application would have significantly

increased the complexity of its implementation. Instead a basic instrumentation amplifier circuit was constructed such that an analogue potential, proportional to the angle of the goniometer arms, could be acquired by the DAQ used to acquire EMG and accelerometer waveforms.

### 6.6.2 Design and development

The two channel amplifier of Figure 6-23 was developed and tested. R1 and R3 set the gain of the instrumentation amplifiers to 214. This gain was selected in order to provide a signal between 0.5V and 4.5V at the amplifier output when the goniometer was varied between  $\pm 90$  degrees of neutral. Over this range the manufacturer quotes the SG110/A to be accurate within  $\pm 2$  degrees. R2-C1 and R4-C2 are 1.0kHz anti-aliasing filters. R5 and R6 provide a 2.5V reference potential on which the amplifier output rests.



**Figure 6-23: Two channel goniometer amplifier**

The circuit was packaged in a compact plastic ABS case with integrated belt clip. This meant that the amplifier could be positioned within 50cm's of the goniometer thus minimising cable length and susceptibility to electrical interference.

In order to calibrate the output of the amplifier a protractor was used to vary the angle between goniometer arms in 5 degree increments in each axis. The voltage output of each amplifier was recorded and a linear trend line fitted when plotted against protractor angle. The gradient and offset of the trend line for each amplifier was defined within the Stimulation Investigator source code such the analogue potential could be converted into angular deviation from neutral in both axes of the goniometer.

## 6.7 Stimulation Investigator Application

### 6.7.1 *Functional specification*

A software system able to control hardware, coordinate, display and export collected data was required. It would graphically lead the investigator and participant through the series of planned investigations through automating configuration of hardware and collection of data between sub-tests. For issues of portability and hardware compatibility it would operate from a laptop computer running a current Microsoft Windows operating system.

During early mock-ups of the system it was soon noted that a key requirement of the software system would be to facilitate the efficient configuration and collection of data so as to not be overly demanding on participant's time whilst ensuring all relevant data was collected without a trial being missed or incorrectly configured. Each investigational session would involve the repetition of a number of applications of stimulation each assessing variation in a different parameter or condition. The research protocol would therefore be realised within the functionality of the software.

Within the research protocol it was realised that reflex activity could be modulated by a participant's voluntary effort. In seeking to control this, participants would be instructed to complete various supporting or opposing movements during different applications of stimulation. In order to convey such instructions to participants, a dual display system was specified so as to permit distinction between information intended for the investigator and information intended for the participant.

All stimulation parameters would be set and controlled through the investigator's graphical user interface and be communicated and echoed by the stimulation controller. Upon an instruction to apply stimulation a synchronisation signal would be given to commence the synchronous data collection of EMG (section 6.3) and accelerometer data (section 6.4) following the application of stimulation (section 6.2). Scaled acquired data should be displayed throughout collection thereby giving an indication of actual values and variation. The ability to average data between trials would improve signal to noise ratio in the presence of random noise whilst indicating a measure of variation to aid data interpretation ( $\pm$  standard deviation). Expandable 'Test EMG' and 'Test XYZ' windows would display voltage-time plots as measured by the DAQ system

corresponding to these system outputs. These features were incorporated for use when identifying correct EMG electrode placements and system calibration.

The participant form would provide prompts and feedback as identified in the research protocol (Chapter 8). Each phase of the investigation would have an associated form displayed to the participant. In effect commands would be passed between the investigator and participant form providing notification of system events.

### 6.7.2 *Design and development*

Although for such a specific application there would not be a commercially available software system, commercially available software tools could be made use of to develop such a system. A software language which permitted an appropriate balance between high and low level control when interfacing hardware and graphically displaying information was required. Through prior experience of software development in C, Microsoft Visual C# was identified as an appropriate language for the outlined software development task. A Microsoft C# self-study was consulted and completed in order to gain the necessary skills to develop the software system [150]. An open source graph plotting class (Zedgraph<sup>15</sup>) was also identified and used whenever graphically displaying data.

The Clinical Science and Engineering department was in possession of a National Instruments<sup>16</sup> data acquisition card (DAQcard-6024E) which was suitable for use with laptops with an available PCMCIA slot. This card met the requirements of the data acquisition task, being able to simultaneously acquire data from multiple analogue channels to 14-bit precision at frequencies well above two times that of the highest signal frequencies of interest when analysing surface EMG. The National Instruments DAQmx family of products is supported by the Microsoft .Net development framework and hence the DAQcard-6024E could be controlled through C#. This had the additional benefit that the code developed would be compatible with alternative DAQmx compatible devices that shared the same hardware features. Within C# there was support for accessing the computers serial ports when interfacing to the computer controlled stimulation output of section 6.2.

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<sup>15</sup> <http://zedgraph.sourceforge.net/>

<sup>16</sup> National Instruments Corporation (UK) Ltd, Berkshire, England. [uk.ni.com](http://uk.ni.com).

The system was built up in logical steps from initial data capture through to synchronised collection, display and storage. Substantial amendments to program structure or function were marked by a major version change number with minor ones a subsequent number. Such context specific flexibility was of great use following initial exploratory data collection.

Software development was completed in parallel to protocol development. From an early stage the protocol was based upon participants attending a single investigational session in which a series of tests designed to investigate the posed research questions would be completed. The development of this protocol is discussed in Chapter 8. Following initial exploratory data collection from the author, the investigation session could be described by six principal phases. Each phase would comprise of a number of sub-tests in which different variables and or conditions were assessed. Quickly a large amount of data would be produced and hence careful consideration was given to how this would be stored and analysed.

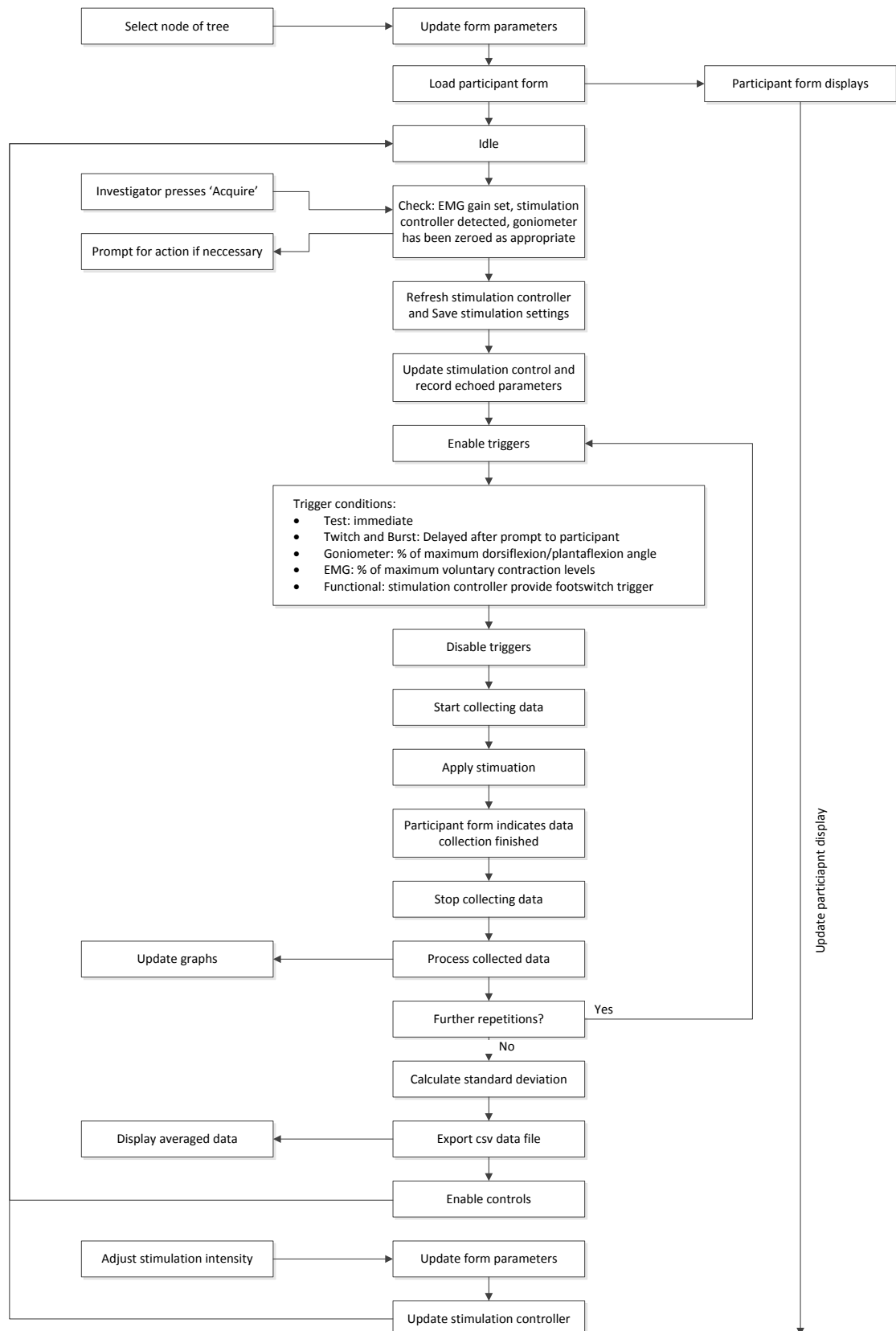
Organising the acquisition, storage and retrieval of data from these tests within a tree structure appeared logical. The root is represented by the participant themselves in the form of a unique anonymous code. At the next level are 6 nodes relating to the 6 phases of the research protocol. Within each of these are then sub phases investigating properties such as with and without effort or at different angles of ankle dorsiflexion through different sub-tests. Each of these individual conditions or sub-tests are generally formed of four repetitions completed at 25%, 50%, 75% and 100% of stimulation intensity as would be setup for use clinically. Data from these trials are stored within folders which mirrors this tree structure. Within the investigator's form of the Stimulation Investigator application, the centre point would be this tree structure. When a trial is completed the associated node of the tree changes to a green tick indicator. When all the children of a parent node are completed the parent node also changes to a green tick indicator and the node collapses to indicate its completion. This enables the investigator to clearly see when a sub-phase of the research protocol is completed. The graphical depiction of the tree structure in use can be seen on the Stimulation Investigator screenshot of Figure 6-25.

When a node of the tree is clicked upon and a trial selected, the stimulation controller and DAQ are appropriately configured for this trial. In between trials the investigator selects the appropriate stimulation intensity before clicking 'Acquire' as indicated in Figure 6-25. Data is automatically saved within this tree structure following a sub-test

being completed. This automatic data storage removes the risk of lost data due to the investigator forgetting to manually save a sub-test. Once a sub-test is complete a '1' appears next to it. This number increments if and when it is repeated. This therefore minimises both setup error and the requirements of the participant's time.

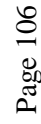
The flow diagram of Figure 6-24 describes the function of the Stimulation Investigator application. A screenshot of it in use is also shown in Figure 6-25.

When investigator and participant are ready, a sub-test is initiated when the investigator clicks the 'Acquire button'. The resulting data files are automatically saved as Comma Separated Value (CSV) files suitable for analysis by commercial system (e.g. Microsoft Excel) as well as the custom stimulation analysis system of section 6.8. The header section of the file contains information detailing the sub-test such as the stimulation and acquisition settings. The CSV filename is automatically incremented and saved to the appropriate folder within the tree structure corresponding to the sub-test.



**Figure 6-24: Flow diagram of Stimulation Investigator operation**





## 6.8 Stimulation Analysis Software

### 6.8.1 *Overview*

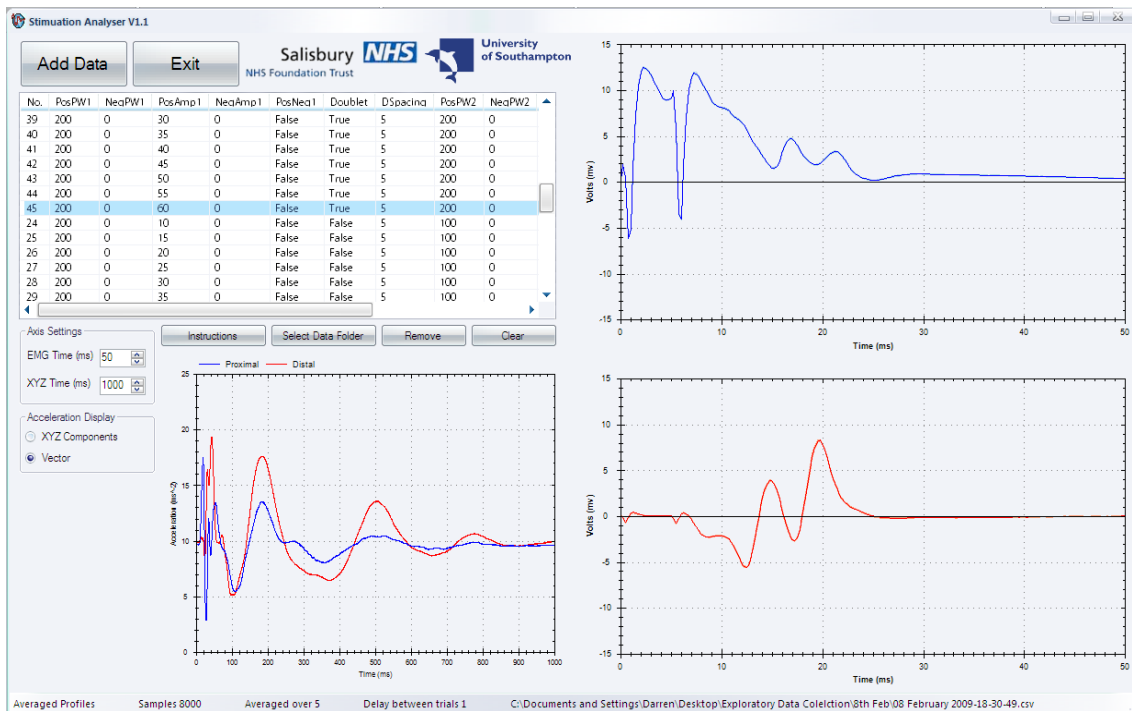
Amassed data from the described software and instrumentation would require analysis. During development and exploratory data collection a means to quickly review and easily compare data trials was required.

Although commercial data analysis programs such as Microsoft Excel could be used for this purpose, at this stage it presented as a laborious process, requiring complex macros and significant computing power. It was wished to have a simple application which could load and instantly switch between and compare data from different experiments. It was hence decided to develop a custom ‘Stimulation Analysis’ application to load multiple data sets such that comparison and analysis of trials could be efficiently completed.

### 6.8.2 *Design and development*

A Microsoft C# application presented as a relatively straightforward progression having developed the Stimulation Investigator application of section 6.7. The user first selected a root folder for which all the amassed data from a participant has been stored. The CSV files were then loaded and the stimulation parameters pertaining to the trial displayed in tabular format. This enabled columns to be sorted, thereby arranging trials by parameter values. Selecting a data trial row updated graphical displays utilising the same Zedgraph graph plotting classes as in the Stimulation Investigator application. These displays also indicated the EMG and accelerometer readings such that cursor readings from points of interest could be noted for subsequent analysis.

A screenshot of the system in use whilst analysing exploratory data from the author is shown in Figure 6-26.



**Figure 6-26: Screenshot of Stimulation Analyser application**

The Simulation Analyser application was used during exploratory data collection however once the research protocol was developed it was decided that the ability to utilise finer control and more tools was advantageous. At this stage a Microsoft Excel analysis system was developed. The time taken to set up and fully analyse a single individual was significant however this was then used as a template with which to easily reapply the analysis to other participant datasets. The approach to data analysis is described in Chapter 9.

## 6.9 Developed Investigational Instrumentation

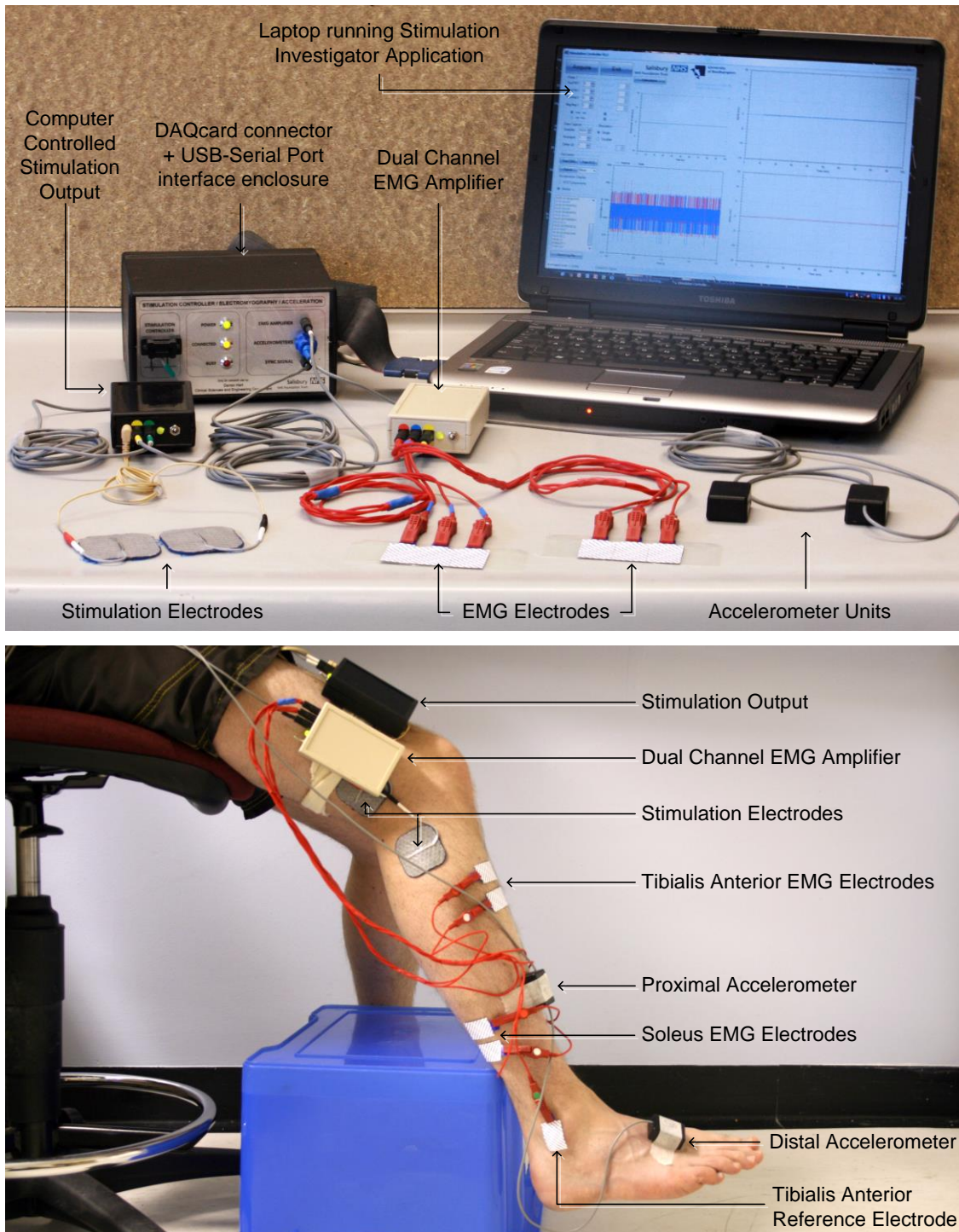
The developed software and instrumentation was designed and developed exclusively for clinical investigation of the research hypothesis of Chapter 5. As it was to be used to investigate a physiological process it would be classed as a Medical Device by the Medical Device Directive (93/42/EEC) [151]. In accordance with Bulletin 18 of the Medicines and Health Care Products Regulatory Agency (MHRA) CE marking of such a system was not required when it was not being sold and used purely for research without a view to commercialisation.

All instrumentation was designed by the author to the essential requirements of the Medical Device Directive. Chartered engineers within and external to the supervision

team reviewed design documentation and confirmed safe and effective operation. An electrical safety test relevant to a class IIa, type BF medical device was completed by the Medical Electronics department at Salisbury District Hospital on the whole system (Appendix A). The developed instrumentation was intended and used only by the author during investigation of the research hypothesis and was clearly labelled “exclusively for clinical investigation”. A risk assessment of use of the system was completed and is included in Appendix B.

## 6.10 Summary of Investigational System

The design and development of systems to realise the investigation system topology presented at the beginning of the chapter (Figure 6-1) has been presented. Novel electronic and software engineering development has created an investigational setup which enables investigation of the posed research questions. Systems crucial to this success were the fast recovery dual channel EMG amplifier and the computer controlled stimulation output. A design concept for an artefact suppression fast recovery EMG amplifier proposed by Thorsen [137] was extensively reconfigured in order for it to successfully function with a stimulation output design used clinically. Re-design of the feedback loops within the design produced an optimal sample and hold system with smooth reengagement of the output trace. The computer controlled stimulation output permits comprehensive control over stimulation parameters such that a wide array of possible parameters can be applied. Although such development represented significant challenge and design complexity, the realised system is simple to use whilst allowing comprehensive control over investigation parameters. Through an integration of software and hardware the investigator and participant is guided through the research protocol with automated setup and recording of measurements. The completed system is shown prior to exploratory data collection in Figure 6-27 when on its own and when in use.



**Figure 6-27: Investigational setup instrumentation**

*EMG amplifier shown prior to addition of selectable gain and high frequency pass band controls*

*Top: system shown connected to laptop computer running Stimulation Investigator application*

*Bottom: system shown in use during exploratory data collection*

As discussed within the introduction to this Chapter, initial exploratory data collection aided refinement of the investigational setup described. The next Chapter discusses initial use of the investigational setup during exploratory data collection which informed these refinements and aided development of the research protocol.



## **Chapter 7 Initial Exploratory Data Collection**

During development of the investigational system discussed in Chapter 6, simulation and testing into passive loads confirmed compliance with theoretical performance requirements. Whilst of use, such tests assumed the theoretical requirements adequately accounted for the variation that would be encountered amongst groups of unimpaired and impaired participants. Additionally, by the very nature of passive loads, no physiological responses as would be used to investigate the research questions were recorded. It was therefore wished to use the developed investigational setup to collect initial exploratory data from the author, indicative of that which would be collected during formal investigations. Such testing was not intended to form part of the structured investigation of the research questions but would aid development of the research protocol whilst also indicating any necessary instrumentation or software refinements.

Developed instrumentation had been designed to the essential requirements of IEC60601-1 and had been overseen by a supervision team comprising of chartered engineers and registered Clinical Scientists. It was felt that the rights, safety, dignity and well-being of members of the immediate supervision team would not be compromised by initial exploratory testing amongst an individual of the group prior to ethical approval. In order to utilise developed instrumentation for the structured investigation of the research questions posed in Chapter 5, evidence of appropriate safety measures in addition to ethical approval would be required before testing with other human participants.

Seven ‘exploratory investigations’ were completed each assessing aspects of the, as then, envisaged research protocol. A description of each of the exploratory investigations follows. Where data trends or aspects relevant to the research protocol design were noted, these are described within the summary at the end of each

exploratory investigation. Further refinement of the investigational setup and the research protocol were completed in parallel to these exploratory investigations and this has been described within Chapter 6 and Chapter 8 respectively.

## 7.1 Exploratory Investigation 1:

### Conventional and Catch-like Stimuli H-Reflex Tests

Following development and testing of functioning versions of the computer controlled stimulation output, the dual channel EMG amplifier and Stimulation Investigator application of Chapter 6, a series of basic H-reflex tests were conducted upon the author. The instrumentation setup followed that described in section 4.1.2 using both single conventional and catch-like stimulation pulses whilst recording kinetic twitch of the lower limb (accelerometer data). Such a test with an individual not known to deviate from normal neurophysiological function assessed the developed systems intended performance in addition to providing data typical of that sought during investigation of Research Question 1, page 52. The data obtained also permitted calculation of nerve conduction speed and identification of M- and H-wave features of the resulting EMG whilst demonstrating system performance. Completion of such an exploratory test also provided a useful indication of time requirements when developing the protocol design.

#### 7.1.1 *Exploratory investigation 1: Setup*

In light of the discussion of section 4.1.2, measures were taken to control factors known to influence H-reflex testing. Data collection was completed with the first author comfortably seated and relaxed with his right leg, flexed at the hip, partially flexed at the knee and resting with the calf on a cushioned plinth. Skin was prepared and electrodes positioned as recommended by the SENIAM guidelines [140] and shown in Figure 5-5. The negative stimulation electrode of the monophasic pulse was positioned distally over the common peroneal nerve as it passes below the fibula head to mimic the polarity of stimulation commonly applied during dropped foot correction. Pulse-width was held constant at 200 $\mu$ s whilst current amplitude of the applied monophasic stimulation pulse was increased from the level of sensory perception (10mA) to the threshold of pain (60mA) experienced by the author. Data was acquired at 4000Hz for

two seconds following the application of stimulation with a delay of one second between trials. Neglecting computing time of the Stimulation Investigator application, stimulation was applied at 0.3Hz. Data was averaged over five trials in order to reduce the effects of noise and random variation. Current was increased for a single conventional stimulus and then a 5.0ms spaced doublet. From setting up of instrumentation to taking off, data collection over six trials lasted approximately 30 minutes.

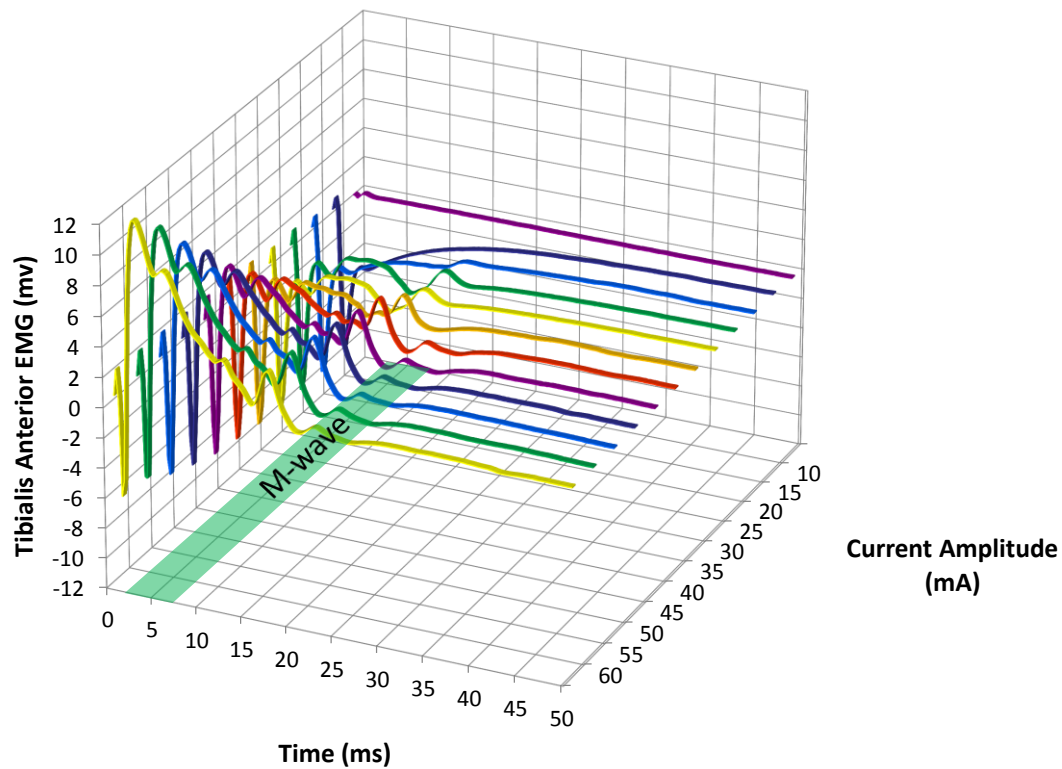
### *7.1.2 Exploratory investigation 1: Conventional stimuli results*

Data from each trial was exported in a CSV format and visually analysed using the Stimulation Analyser application of section 6.8. Mean EMG across repetitions was computed for each current amplitude and plotted on three-dimensional axes using SigmaPlot<sup>17</sup>. Mean tibialis anterior and soleus EMG plots in response to 200µs pulse-width single stimuli are shown respectively in Figure 7-1 and Figure 7-2. There appeared no meaningful EMG activity beyond 50ms and hence data is plotted up until this time.

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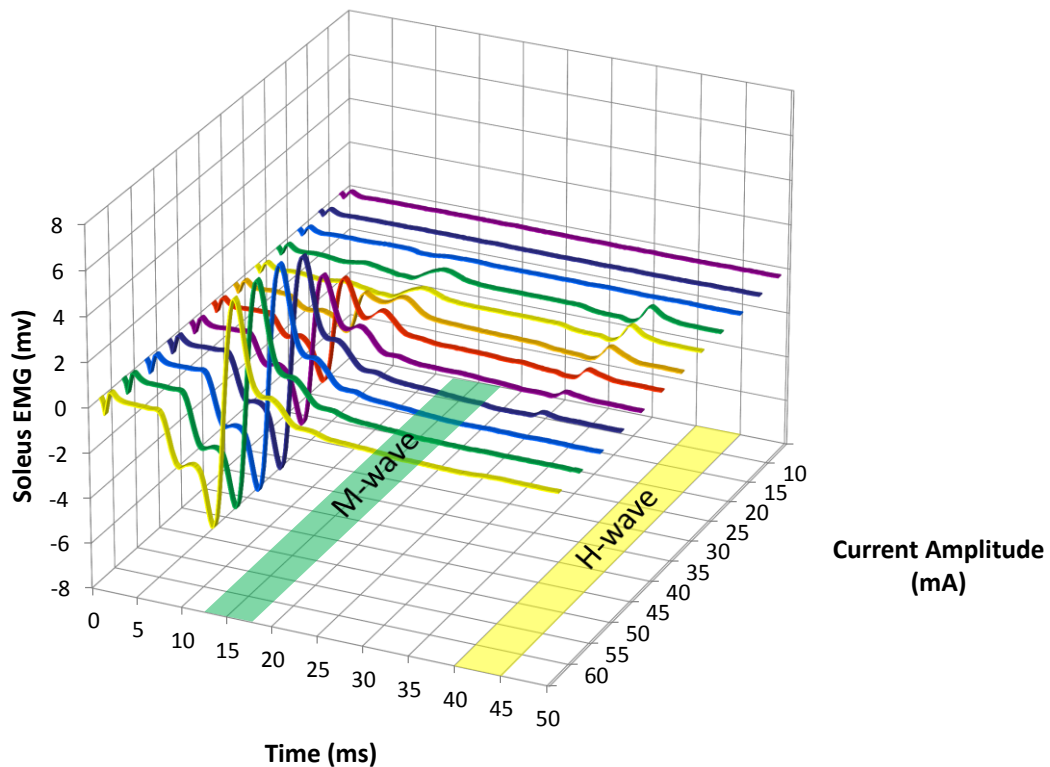
<sup>17</sup>Systat Software Inc. [www.sigmaplot.com](http://www.sigmaplot.com)





**Figure 7-1: Tibialis anterior EMG responses following 200 $\mu$ s pulse-width stimuli**

Data averaged over 5 trials. Superimposed stimulation artefact present over approximately first 20ms.



**Figure 7-2: Soleus EMG responses following 200 $\mu$ s pulse-width stimuli**

Data averaged over 5 trials. Peaks in M- and H- wave amplitude seen at 15.00 and 42.25ms respectively.

### 7.1.3 Exploratory investigation 1: Conventional stimuli discussion

Whilst it was the intent of the adopted stimulation electrode positioning to primarily activate the tibialis anterior, what appeared the onset of M-and H-wave peaks at 6.5ms and 40.5ms respectively were identified over the range of mean soleus EMG responses. This was unexpected as the soleus should be relaxed so as to avoid co-contraction as the tibialis anterior is activated. It appeared that in addition to the common peroneal nerve the author's tibial nerve had been excited thus provoking soleus activation.

#### Stimulation Artefact

Notable artefact following the applied single stimulation pulse was seen on the mean tibialis anterior EMG responses (Figure 7-1). At low current stimulation intensities the artefact recovery circuitry of the EMG amplifier was only engaged in response to the actual stimulation pulse rather than the artefact tail. At higher stimulation intensities the overshoot of the applied stimulation pulse and resulting artefact, caused the artefact recovery circuitry to be immediately re-engaged. This accounts for the change from approximately -12mV to +12mV in output level at which the artefact recovery appears to commence over the 10-60mA range of tested current amplitudes.

The stimulation artefact present on the averaged soleus EMG responses (Figure 7-2) was substantially less than the tibialis anterior, the most probable cause of this appeared to be the increased distance between stimulation and EMG recording electrodes.

#### Nerve Conduction Speed and M- and H- Wave Identification

The author's soleus M-wave was used to calculate an estimate of tibial nerve  $\alpha$ -motor conduction speed. Assuming no significant difference between conduction speed of the tibial nerve and the deep branch of the common peroneal nerve [152], an estimate of the tibialis anterior M-wave onset following the applied stimuli was also made. The distance from the centre of the negative stimulation electrode to the midpoint between the soleus EMG recording electrodes was 0.24 metres. The onset of M-wave activity appears at 6.5ms. Assuming a delay at the neuromuscular junction of 0.5ms [31], the nerve conduction speed was evaluated to  $40.0\text{ms}^{-1}$  (Equation 5-1). This was possibly a little slow however it remains comparable to figures reported for normal subjects (Shehab *et al.*  $46.1\text{ms}^{-1} \pm 3.3$  (n=21) [152], Metso *et al.*  $57.7\text{ms}^{-1} \pm 3.31$  (n=5) [153], Shefner *et al.*  $52.4\text{ms}^{-1}$  (n=10) [154]). Using this conduction speed over the 0.12m

distance between the negative stimulation electrode and midpoint of the tibialis anterior EMG recording electrodes provided an estimate of M-wave onset time of 3.5ms. In Figure 7-1 the tibialis anterior M-wave appears to be superimposed on to the steep stimulation artefact recovery curve. When EMG recording site and stimulation site are in such close proximity, M-wave identification is challenging due to the large stimulation artefact recovery tail.

The collected data was also used to form an estimate of the Ia afferent tibial nerve conduction speed. Peripheral nerves related to the control and functions of the lower limb distal to the knee, descend from levels L4, L5 and S1 of the spinal cord. These levels are approximately in line with the navel and hence an estimate of the conduction distance of Ia afferent nerves during an H-reflex test could be made. The approximate nerve pathway distance from the negative stimulation electrode to the navel of the author was 0.77m. Utilising the earlier values of synaptic delay and motor nerve conduction speed, Equation 7-1 provided an estimate for the afferent nerve conduction speed.

$$H_T = \frac{\text{Afferent NCD}}{\text{Afferent NCS}} + \text{Central SD} + \frac{\text{Motor NCD}}{\text{Motor NCS}} + \text{Neuromus SD}$$

<i>Afferent NCD</i>	=	<i>Afferent Nerve Conduction Distance</i>
<i>Afferent NCS</i>	=	<i>Afferent Nerve Conduction Speed</i>
<i>Central SD</i>	=	<i>Central Synaptic Delay</i>
<i>Motor NCD</i>	=	<i>Motor Nerve Conduction Distance</i>
<i>Motor NCS</i>	=	<i>Motor Nerve Conduction Speed</i>
<i>Neuromus SD</i>	=	<i>Neuromuscular Junction Synaptic Delay</i>
<i>H<sub>T</sub></i>	=	<i>H-wave onset latency</i>

*Evaluating...*

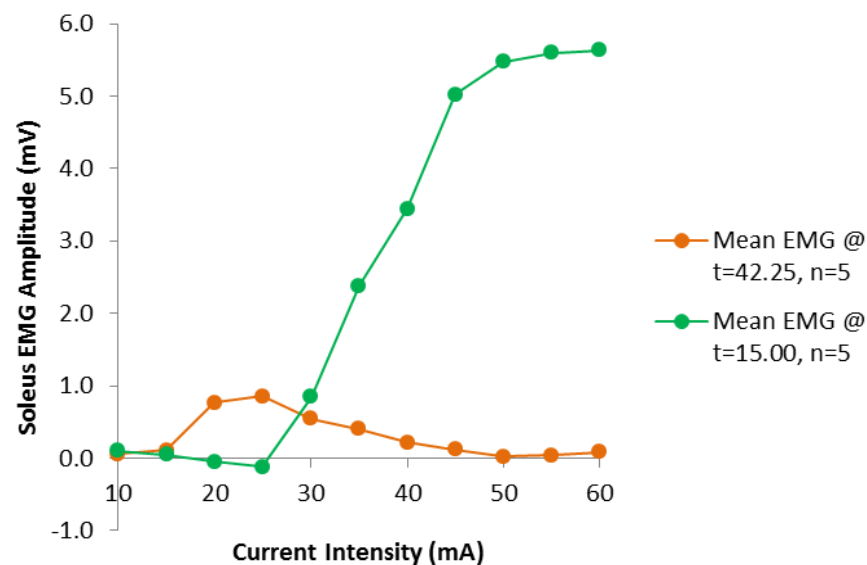
$$\frac{0.77}{\text{Afferent NCS}} + (2 \times 0.5 \times 10^{-3}) + \frac{0.77 + 0.24}{40.0} + 0.5 \times 10^{-3} = 40.5 \times 10^{-3}$$

$$\text{Afferent NCS} = \frac{0.77}{13.75 \times 10^{-2}} = 56.0\text{ms}^{-1}$$

***Equation 7-1: Estimation of Ia afferent tibial nerve conduction speed from exploratory data***

The calculated value of afferent nerve conduction speed was within the ranges reported by other similar studies conducted with unimpaired subjects (Shehab *et al.* 48.7ms ± 6.0 (n=21) [152], Metso *et al.* 63.4ms ± 3.34 (n=5) [153], Shefner *et al.* 57.6ms (n=10) [154]).

The observed soleus activity was characteristic of reported H-reflex responses (section 4.1.2). The conclusion that observed peaks of activity observed at 42.0ms were H- as opposed to F-waves was supported by their tendency to decrease in magnitude with increasing stimulation intensity and hence M-wave amplitude. Plots of averaged soleus EMG amplitude at times corresponding to peak M- and H-wave activity against the increasing current intensity produced the characteristic plots of Figure 7-3.

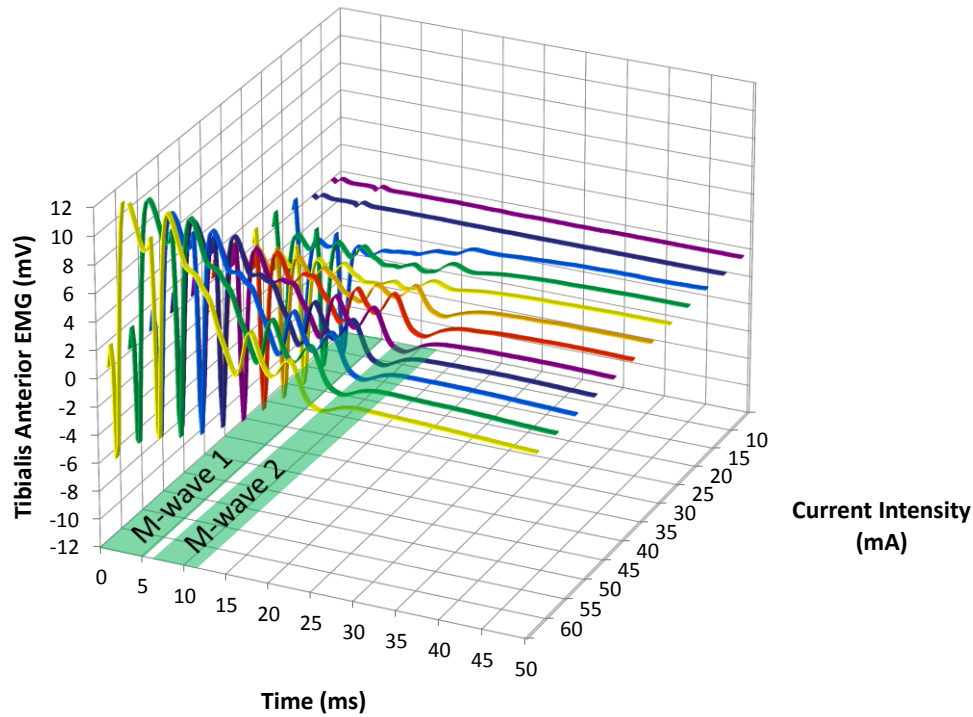


**Figure 7-3: Soleus M and H-wave amplitude versus stimulation current intensity**

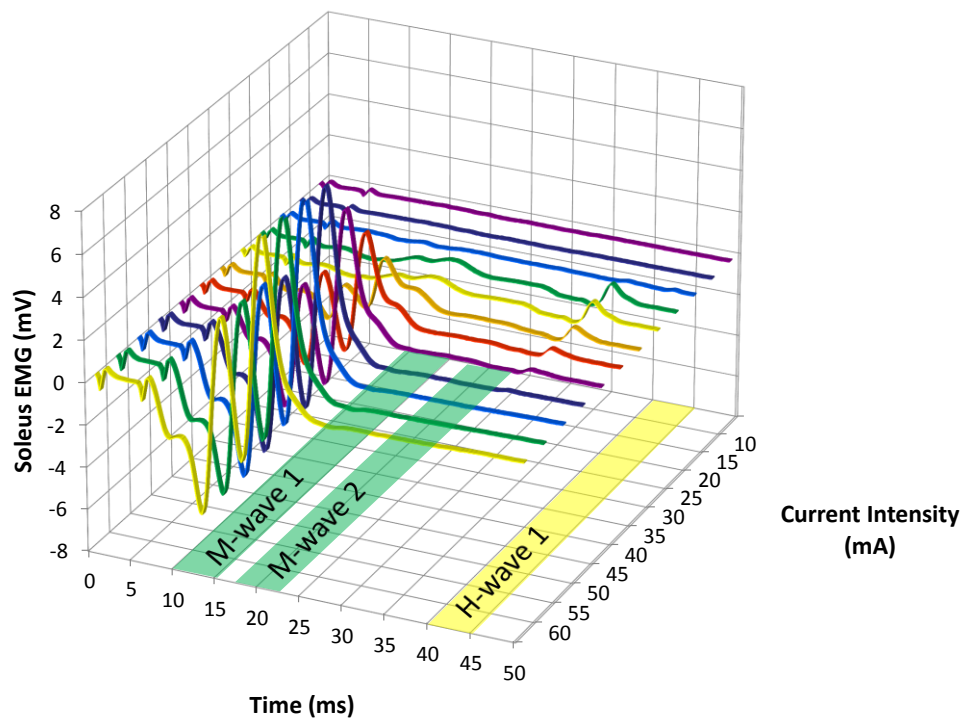
*Legend indicates time at which mean EMG output correlates to maximum perceived M- or H wave peak.*

#### 7.1.4 Exploratory investigation 1: Catch-like stimuli results

Similar 3D plots of averaged tibialis anterior and soleus EMG plots in response to 200 $\mu$ s pulse-width, 5.0ms spaced catch-like stimuli are shown respectively in Figure 7-4 and Figure 7-5. Again, there appeared no meaningful EMG activity beyond 50ms and hence data is plotted up until this time.



**Figure 7-4:** *Tibialis anterior EMG responses following 200 $\mu$ s pulse-width 5.0ms catch-like stimuli*  
*Data averaged over 5 trials.*



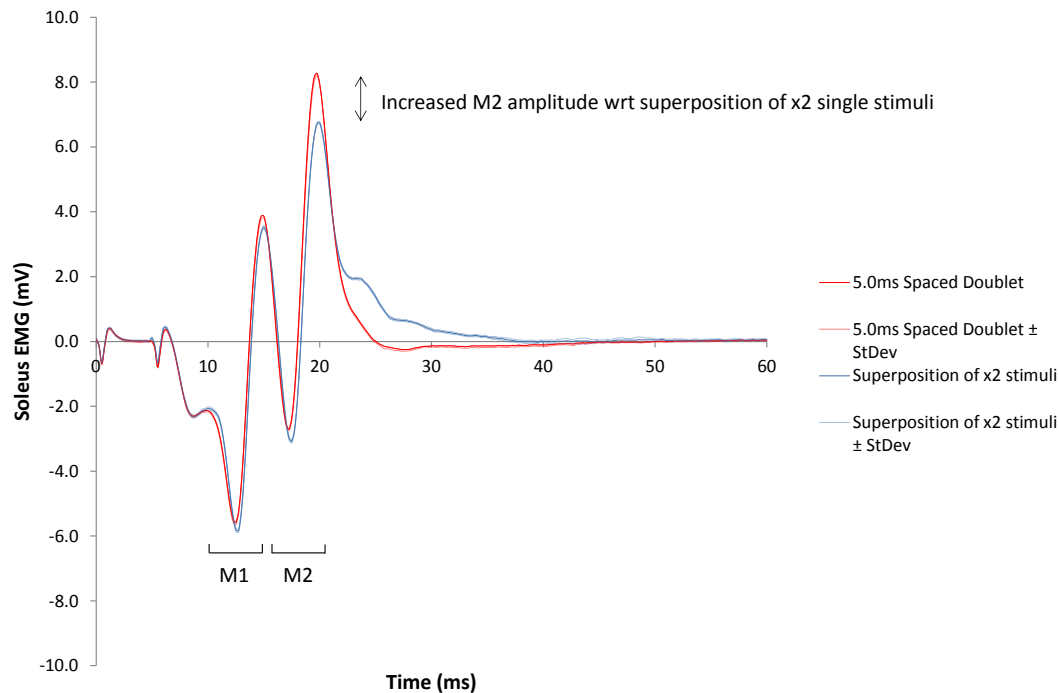
**Figure 7-5:** *Soleus EMG responses following 200 $\mu$ s pulse-width 5.0ms catch-like stimuli*  
*Data averaged over 5 trials. Super-position of M-waves due to each stimuli of the doublet.*  
*Single H-wave correlates to first stimuli, second stimuli does not appear to evoke a second H-wave.*

### 7.1.5 *Exploratory investigation 1: Catch-like stimuli discussion*

Both the tibialis anterior and soleus EMG responses were predictably subject to similar stimulation artefact to those of the single stimuli responses of Figure 7-1. The peak tibialis anterior EMG activity seen at 16.0ms remained and was followed by a second at 21.0ms, presumably resulting from the second 5.0ms spaced pulse.

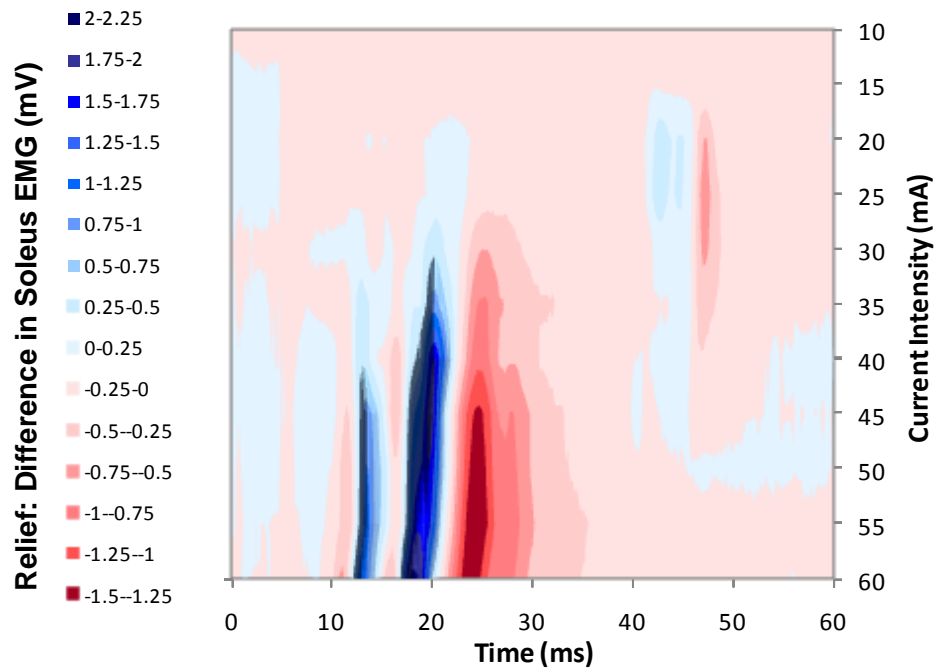
The soleus mean EMG responses following a 5.0ms doublet of Figure 7-5 showed similar features to the single stimuli response of Figure 7-2. Akin to the single stimulation pulse response, a peak M-wave amplitude was seen at 15.0ms correlating to the first pulse of the doublet. A second M-wave also appeared summated upon this 5.0ms later (20.0ms) correlating to the second stimulation pulse of the doublet. At lower current intensities an H-wave still appeared present at the same current intensity (20-35mA) and importantly time as during the single stimulation pulse trials. Unlike with the M-waves, no second H-wave was seen 5.0ms after this. The authors collected data suggested the second stimulation pulse of a doublet did not elicit an H-wave.

Comparison of peaks between the two M-waves of the soleus doublet was complicated due to their apparent super-position. This can be more clearly seen when viewing the 2D plot of the 200 $\mu$ s pulse-width doublet recorded at 60mA seen in Figure 7-6. Rather than attempt to identify the onset and amplitude of each M-wave of the doublet response, a comparison to that which could be expected by a linear super-position of two single stimuli responses delayed by the same 5.0ms doublet spacing was made. This is also shown at 60mA stimulation intensity (Figure 7-6) and suggests enhanced peak amplitude of the second M-wave at 20ms.



**Figure 7-6: Doublet response and algebraic summation of two single pulse responses spaced by 5.0ms**  
 All stimuli of 200 $\mu$ s pulse-width, 60mA amplitude. Mean soleus EMG calculated over 5 repetitions.

To assess whether this was an effect seen over the range of tested current intensities, such analysis was repeated at these current amplitudes. This data is presented in Figure 7-7 as a surface relief plot of the difference in EMG amplitude between the observed doublet response and the super-position of two appropriately delayed single responses of the same current intensity. The enhanced second M-wave peak can be seen by the positive bands (blue shading) seen at current intensities of 30-60mA at 20ms. A lack of second H-wave due to the second pulse of the doublet can be seen by the negative bands (red shading) seen at current intensities of 15-40mA at approximately 47ms. The region of negative banding (red shading) at current intensities of 30-60mA between 20-30ms may have the net effect of little difference in area under the EMG response curves. Conversely it may be an artefact due to assumed equivalence of linear super-position of two single responses to the measured doublet response.



**Figure 7-7: Surface plot of  $\Delta$ (doublet response and delayed super-position of two single responses)**

Blue shading indicates higher than expected doublet EMG activity, red shading less.

Legend indicates bands of difference in averaged EMG output.

At low currents the difference can be seen due to no H-wave. At high currents there is a peak at approximately 20ms where the amplitude of the second M-wave is greater than that of the super-position of two M-waves from a single response.

The plateau of the M-wave magnitude seen in the soleus EMG response of Figure 7-3 at high stimulation intensities is typical of that found in the literature and is thought to represent the response of the entire  $\alpha$ -motor neuron bundle to maximal stimulation [52, 63]. If a proportional correlation between EMG and muscle activity is assumed then at maximum M-wave all motor units are recruited. The additional super-position of the second M-wave of the doublet seen in Figure 7-7 would contraindicate this however and suggest additional motor units are activated by the second stimulus. This infers even when stimulating at the threshold of pain not all neurons of the  $\alpha$ -motor neuron bundle are depolarised and a greater magnitude of M-wave could be achieved by a doublet. This is counterintuitive and hence raises a more fundamental question –what does the EMG signal actually reflect? Thorough explanation of this appears to be largely overlooked in most texts. As discussed in Chapter 2, electrical activity linked with a number of processes involved during a muscle contraction can produce a net current flow within the sensing volume of the EMG electrodes. Hence it would appear logical



to deduce the net recorded current flow (M-wave) is comprised of the following components:

- Pre-synaptic neuron end plate potentials.
- Post-synaptic end plate potentials of muscle membranes near the muscle motor point.
- Depolarisation waves along transverse tubules into muscle fibre interiors.
- Depolarisation waves along the muscle membrane surface of fibres.
- Muscle fibre action potentials of fibres of the excited motor units.

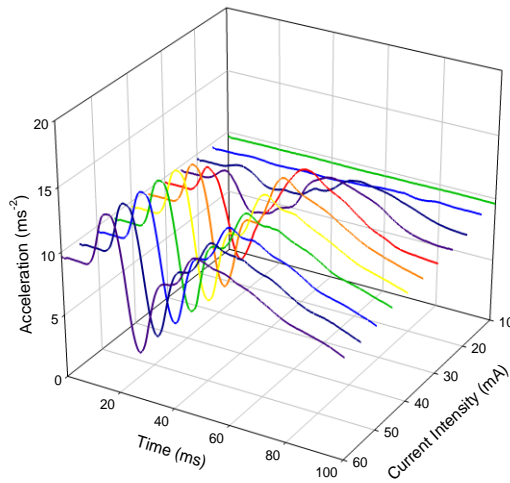
The actual muscle fibre action potentials will be caused by the flow of  $\text{Ca}^{2+}$  across the muscle membrane into the sarcoplasm. The heightened peak of the second pulse of a doublet may actually indicate an increase in  $\text{Ca}^{2+}$  release rather than the activation of additional muscle fibres. If this were so it would support previous hypotheses that enhanced  $\text{Ca}^{2+}$  release is responsible for the catch-like effect (section 4.4.2).

### **Accelerometers**

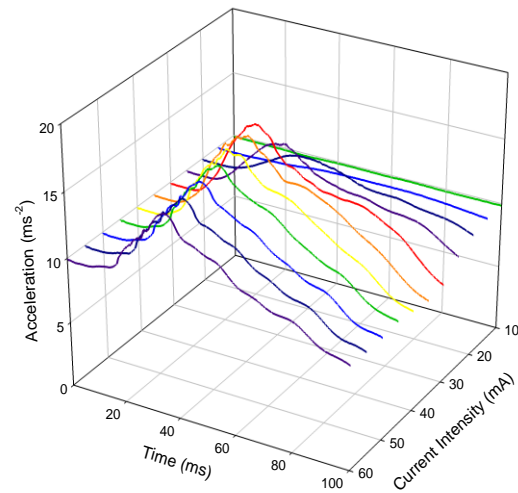
Muscle twitch data obtained from the proximal and distal accelerometers positioned on the surface of the tibialis anterior and dorsal aspect of the forefoot were collected during twitch experiments. The magnitude of the averaged resultant accelerations recorded from the proximal and distal units when applying single and doublet stimuli over increasing current intensity are shown in Figure 7-8 and Figure 7-9 respectively.

It appeared a reasonable supposition that the initial disturbance following the application of stimulation provides data of greatest use in assessing changes in muscle fibre activation. Appropriate selection of the time axis in these plots (100ms) indicated the physical twitch shows reasonable temporal similarity to the twitch contraction times of individual muscle fibres shown in Figure 2-9. As described in section 5.4.4, it was intended to calculate parameters such as peak to peak acceleration, rise time, twitch duration etc. when analysing accelerometer data.

Single Stimuli: Proximal Resultant Acceleration Magnitude

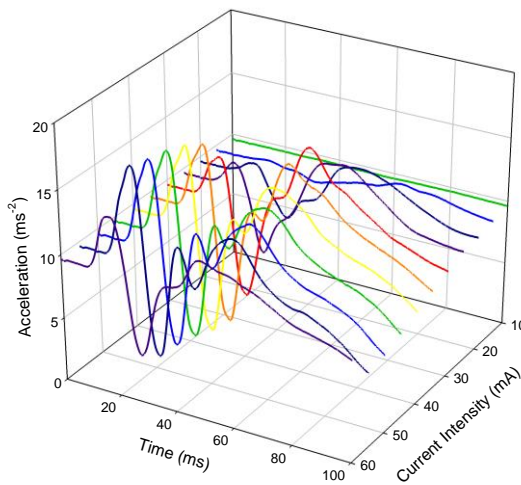


Single Stimuli: Distal Resultant Acceleration Magnitude

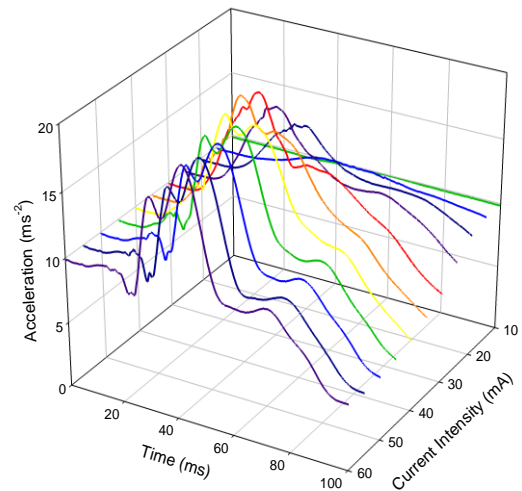


**Figure 7-8: Proximal (lower leg) and distal (forefoot) acceleration following conventional twitch**  
 Resultant acceleration displayed over first 100ms to indicate initial disturbance caused by muscle twitch.

Doublet Stimuli: Proximal Resultant Acceleration Magnitude



Doublet Stimuli: Distal Resultant Acceleration Magnitude



**Figure 7-9: Proximal (lower leg) and distal (forefoot) acceleration following catch-like twitch**  
 Resultant acceleration displayed over first 100ms to indicate initial disturbance caused by muscle twitch

### 7.1.6 *Exploratory investigation 1: Outcomes*

This first experiment provided encouraging results regarding investigation of the research hypothesis whilst also constructively identifying a number of refinements to be made to the developed investigational setup.

The substantial stimulation artefact present on tibialis anterior EMG responses complicated data interpretation to the extent that analysis was limited. Further reduction of this artefact component was sought through a number of modifications to instrumentation as well as its setup and usage. The hardware modifications described in Chapter 6 were made and principally included:

- Re-biasing of filtering values to improve recovery from stimulation artefact.
- Addition of pre-set EMG amplifier gain controls at the time of filter re-biasing.
- Reduction of residual voltage potential across primary coils of stimulation transformer through shorting primary coil to ground in between stimulation pulses.
- Addition of a high frequency EMG amplification component only setting.
- Addition of earth bonding strap (section 6.3.3)

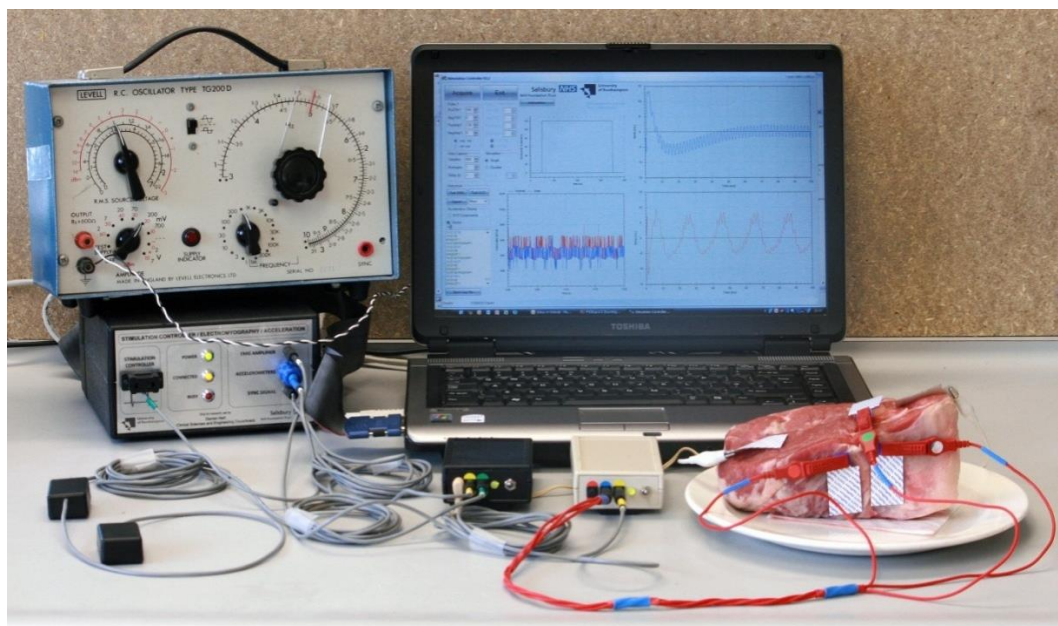
Regarding usage, it was found the substantial stimulation artefact experienced during Exploratory Investigation 1 could be reduced through improved skin preparation and slightly more distal placement of stimulation electrodes. Use of a steret 70% isopropyl alcohol swab to clean and lightly abrade the skin over which EMG electrodes were to be placed was introduced. Although what was considered the SENIAM tibialis anterior EMG electrode placements had been followed during exploratory investigation 1, upon closer inspection it appeared a slightly proximal placement had been used which had exacerbated the stimulation artefact difficulties.

Although the combination of instrumentation and setup changes would not remove the stimulation artefact, they were effective in reducing it to an acceptable level. The reduction in this can be seen in the EMG responses gained during subsequent exploratory investigations as shown in Figure 7-13 and Figure 7-15

Reviewing the conventional single stimuli tibialis anterior EMG responses, the consistent peak at 16.0ms appeared to be too late to be an M-wave but too fast to be an H-wave. Whilst it may have been additional activation via slower conducting Ib orthodromic afferent activation, there was no evidence to support this. It was therefore

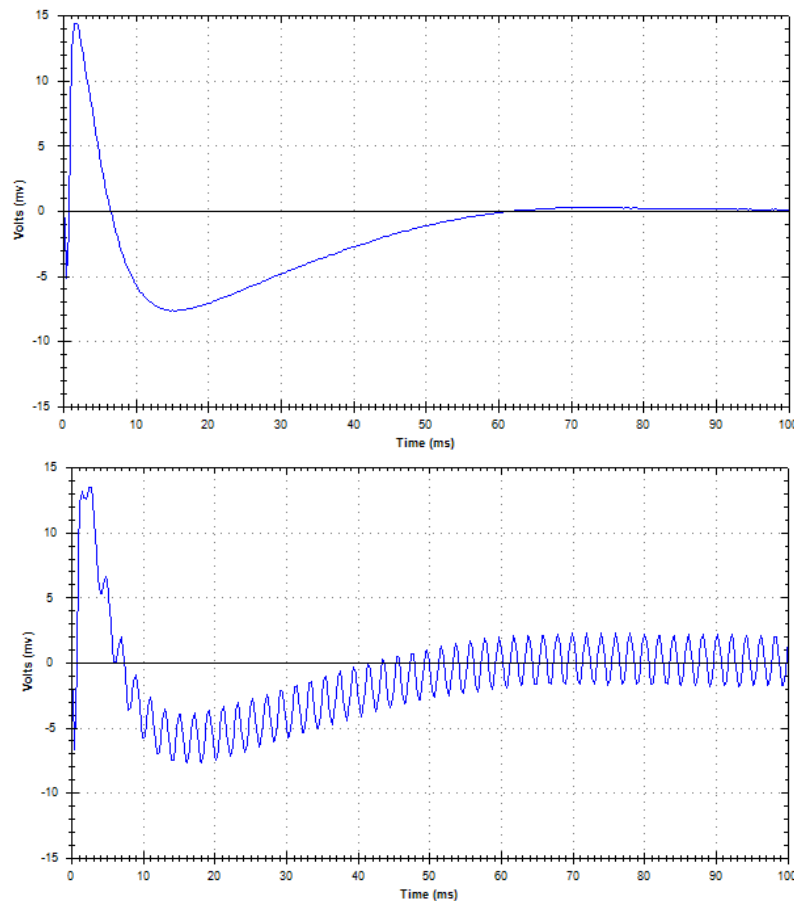
a plausible concern that this could have been an artefact response. Although a theoretical justification for such an artefact effect could not be reasoned and circuit simulation had not been suggestive of this, testing of the stimulation output with tissue devoid of neurophysiological activity provided definitive investigation of this. A leg of lamb prepared as typically sold by a butcher, was acquired for which to investigate the innate EMG artefact recorded following the application of stimulation. Due to its prepared state, stimulation was applied to the fascia rather than skin surface and hence was likely to represent a worst case scenario.

Stimulation was applied to one side of the piece of meat and EMG recorded from the opposite. The reference electrode was affixed centrally to the cut flesh. Applying stimulation over the full range of current intensities only the artefact similar to that seen with the  $1.0\text{k}\Omega/100\text{nF}$  test load was recorded. Using a floating signal generator (Levell RC TG200D) a  $100\text{mV}_{\text{RMS}}$  sinusoid was applied on the opposite side to the centrally affixed EMG reference electrode to mimic a flow of current within the sensing volume of the EMG electrodes. This was displayed uniformly attenuated and superimposed on top of the previously recorded artefact. This result indicated the system functioned as intended on a neurophysiological inactive flesh model and did not give cause to suggest peaks in activity seen from the first author were due to system artefact. The investigational setup and output waveforms of this experiment are provided in Figure 7-10 and Figure 7-11 respectively.



**Figure 7-10: Investigational setup during recovery from stimulation artefact assessment**

*EMG amplifier shown prior to addition of selectable gain and high frequency pass band controls*



*Response showing artefact curves. Overshoot beyond 0V suggests inductance or recovery too fast for 20Hz DC removal to track.*

*Response with 100mV<sub>RMS</sub> sinusoid applied to centre of lamb leg mimicking voluntary EMG. Sinusoid is superimposed on artefact curve.*

**Figure 7-11: Fast recovery EMG amplifier response following recovery from stimulation artefact**

## 7.2 Exploratory Investigation 2:

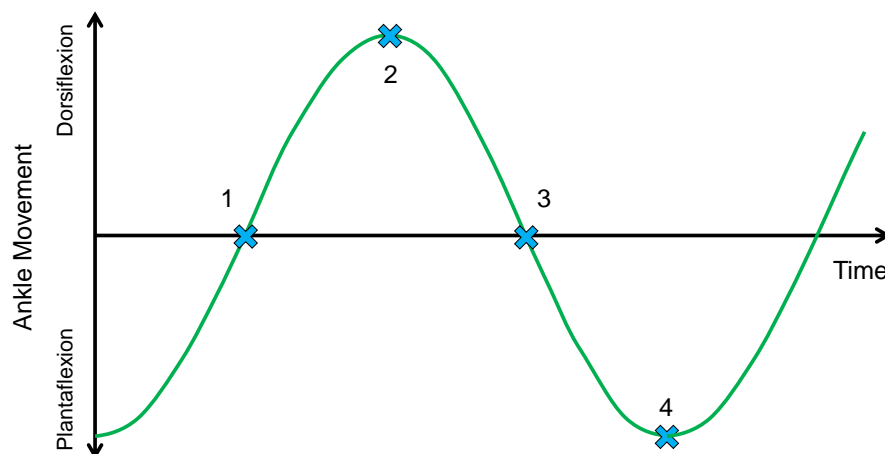
### Conventional Twitch & Isotonic Movement

During repetitions of the earlier conventional and doublet stimuli twitch tests of Exploratory Investigation 1, it was noted that both the M-wave and reflex components of the tibialis anterior and soleus appeared to vary when completed in combination with a voluntary movement. Whilst it was expected for reflex components (sections 4.1.2 and 4.1.3) to vary with muscle length and voluntary effort, a change in M-wave amplitude was not. Such observations suggested the EMG response to orthodromic motor activation from surface stimulation was dependent upon the muscle length at which stimulation was applied. The effect of muscle length on the response to conventional and catch-like stimulation had not been considered in reference to the research questions up until this point. It was therefore wished to further assess the effect of muscle length on M-wave amplitude in order to determine whether this should be accounted for in the protocol design. This would be completed through application of stimulation during a dynamic isotonic movement. An isotonic movement is one in

which muscle length varies whilst muscle tension remains constant. A practical approximation to this at the ankle would be if the foot was dorsiflexed and plantarflexed in a harmonic motion against gravity when free from constraint.

### 7.2.1 Exploratory investigation 2: Setup

The same investigation setup but with the refinements described following exploratory investigation 1, was used by the author. In addition, an electronic metronome with a period of three seconds was used to aid in consistently mimicking the smooth cyclical dorsiflexion and plantarflexion ankle movement depicted in Figure 7-12. A single conventional twitch stimulus was then manually triggered by a button click by the author at the four labelled trigger points. Although this manual triggering method resulted in some variation of joint angle at which stimulation was applied, this was completed five times at each point and the mean EMG response computed. In doing so, voluntary EMG superimposed upon the activity caused by the application of stimulation was attenuated.



**Figure 7-12: Intended ankle movement during twitch tests**

<sup>1</sup> Passing through neutral from plantarflexion to dorsiflexion ( $0^\circ$  sinusoidal tracking signal)

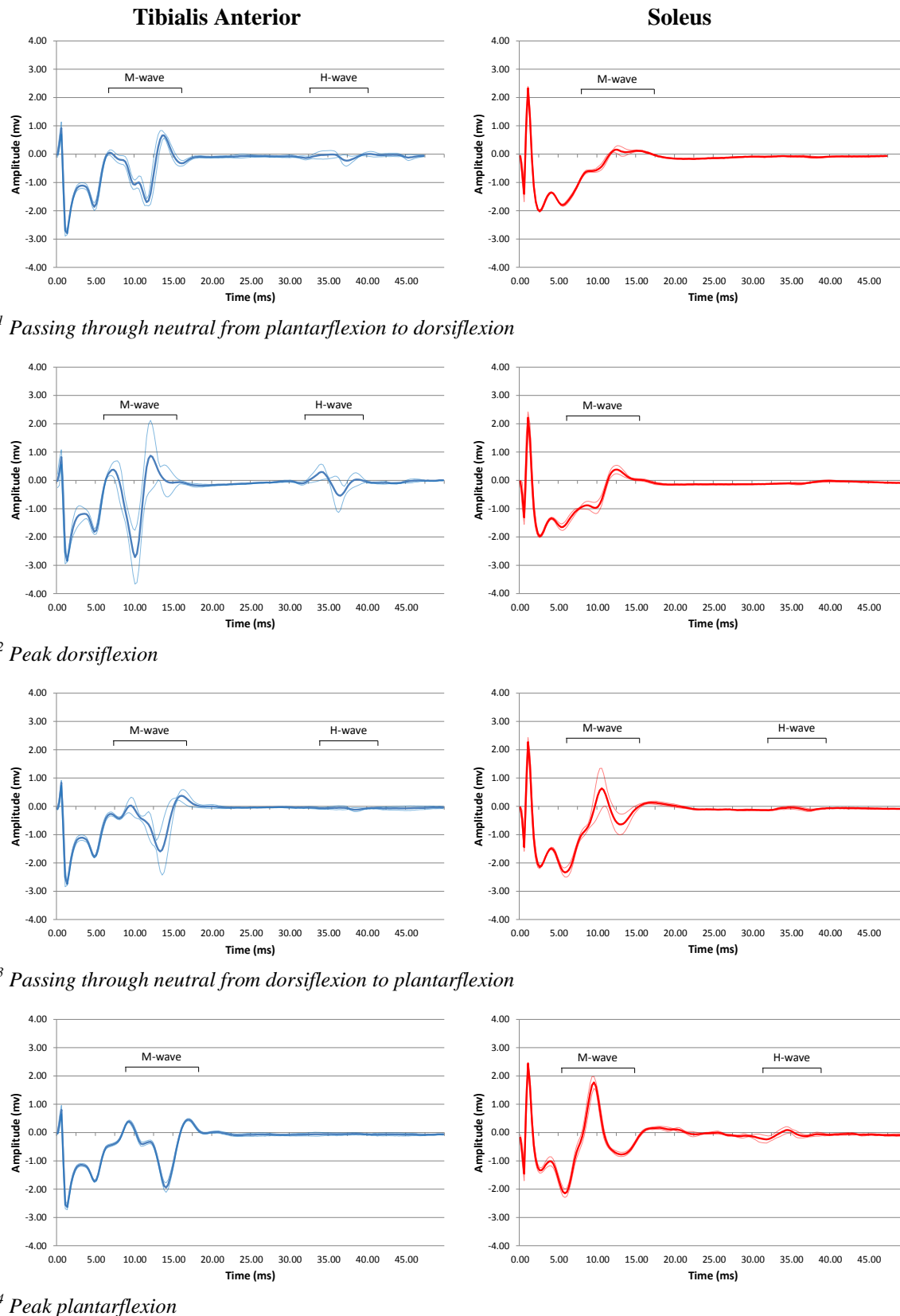
<sup>2</sup> Peak dorsiflexion ( $90^\circ$  sinusoidal tracking signal)

<sup>3</sup> Passing through neutral from dorsiflexion to plantarflexion ( $180^\circ$  sinusoidal tracking signal)

<sup>4</sup> Peak plantarflexion ( $270^\circ$  sinusoidal tracking signal)

### 7.2.2 Exploratory investigation 2: Results

Figure 7-13 displays the mean tibialis anterior and soleus EMG responses collected whilst completing the voluntary ankle movement depicted in Figure 7-12. Note the successful reduction in stimulation artefact following the measures described in section 7.1.6 when compared to Figure 7-1.



**Figure 7-13: Tibialis anterior and soleus EMG responses at varying ankle joint angles**

Number descriptions refer to point within the cyclical movement depicted in Figure 7-12

Mean EMG calculated over 5 repetitions. Watermarked lines indicate  $\pm 1$  standard deviation from mean.

Identification of what was thought to be M- and H-wave features labelled.

### 7.2.3 *Exploratory investigation 2: Discussion*

The data collected supported observed trends noted in M-wave and reflex components when combining voluntary ankle movements and twitch stimulation.

The largest peak to peak M-wave amplitude occurred at peak dorsiflexion in the tibialis anterior and peak plantarflexion in the soleus. It was not possible to conclude whether this correlation was with shortened muscle length and/or voluntary effort. The apparent increase in peak to peak M-wave amplitude did not appear to be caused by electrode contact changes as the stimulation artefact remained consistent in addition to the reflex component varying. This observation was further investigated in exploratory investigations 3 and 4.

In addition to the trend in peak to peak M-wave amplitude it was noticed that the latency of the M-wave appeared to vary for both the tibialis anterior and soleus with ankle angle.

For both muscles, the M-wave latency appeared slightly reduced at the angles corresponding with greater peak to peak M-wave amplitude. Nerve conduction speed is not expected to vary with voluntary effort or muscle length. If this assumption is made, the distance over which the orthodromic  $\alpha$ -motor neuron action potential travelled in these instances must have been reduced. This would infer the nerve either has an elastic component or the point along the nerve at which it is depolarised by stimulation varies. Reflex components observed at points 1 and 2 in the tibialis anterior and 3 and 4 in the soleus (Figure 7-12) were thought to be of H-wave origin due to their magnitude and facilitation with voluntary effort. Without assessing the influence of stimulation intensity upon their magnitude there remained some uncertainty as to whether these could be F-waves.

### 7.2.4 *Exploratory investigation 2: Outcomes*

It was not possible to differentiate between voluntary effort and muscle length during the isotonic contraction used during Exploratory Investigation 2. A principal outcome was therefore to support the completion of isometric as well as isotonic tests within the research protocol. An isometric contraction is one in which the muscle length does not change. Comparison of findings between isotonic and isometric conditions may enable



the effects of voluntary effort and muscle length to be differentiated through the control of muscle length. Passive and active movement tests would also be incorporated into the research protocol to aid this differentiation.

In order to permit this, consistent methods of triggering the application of stimulation during each of these types of active tests required development. Although use of a metronome and manual triggering of stimulation appeared successful during isotonic investigations with the author, more variable results may have been obtained amongst a mixed group of participants less familiar with the study. The electro-goniometer system described in section 6.6 was therefore developed and interfaced with the investigational setup in order to provide the ability to trigger stimulation from joint angle. This also allowed assessment of ankle joint angle throughout investigations.

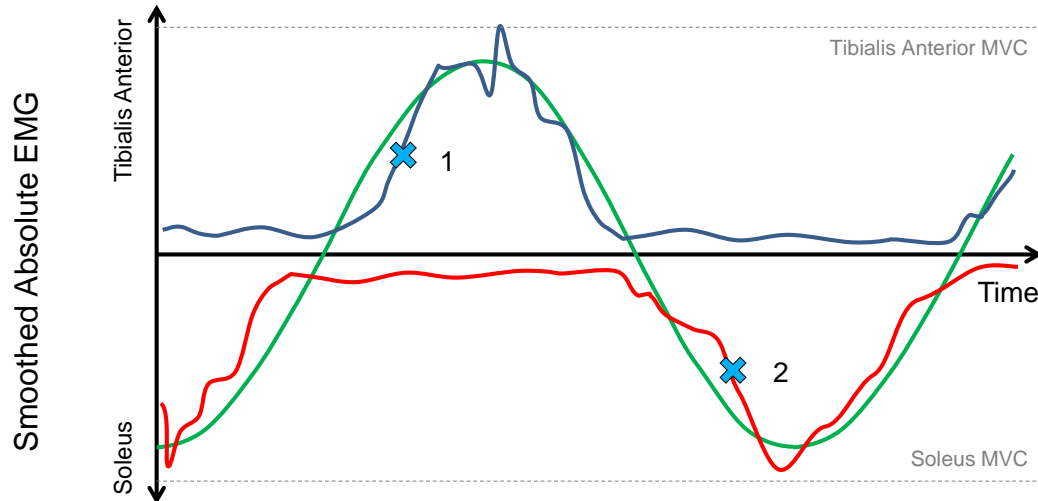
### 7.3 Exploratory Investigation 3:

#### Conventional and Catch-like Twitch applied during Isometric Conditions

Exploratory Investigation 2 supported incorporation of isometric test conditions with the research protocol in order to control muscle length whilst assessing the effects of voluntary effort. Exploratory Investigation 3 assessed and refined this method whilst collecting initial data from the author.

##### *7.3.1 Exploratory investigation 3: Setup*

In order to synchronise the application of stimulation with voluntary effort, stimulation would be triggered from tibialis anterior and soleus absolute EMG during isometric conditions. A display similar to that shown in Figure 7-14 indicated easily interpretable tibialis anterior and soleus EMG activity levels whilst attempting to dorsiflex or plantarflex against the immovable ankle bracket of section 6.5. A sinusoid of three second period was provided to aid the author when attempting to modulate the displayed absolute EMG activity in synchrony with it.



**Figure 7-14: Approximate voluntary smoothed absolute EMG during twitch tests**

Note, smoothed absolute soleus EMG inverted on y-axis

<sup>1</sup> 50% of tibialis anterior maximum voluntary contraction trigger point

<sup>2</sup> 50% of soleus maximum voluntary contraction trigger point

In order to provide both the author and participant with a measure of EMG that could be easily interpreted and modulated with effort against the sinusoid, absolute EMG with a mean moving average filter was displayed (Equation 7-2). Whilst reflecting the number of motor units active, their size, and firing rates [155], mean absolute EMG level was also less computationally demanding than root mean squared value and thus could more easily be realised by the Stimulation Investigator application. During theoretical and experimental comparisons between mean absolute and root mean squared EMG filtering methods when seeking to estimate amplitude, Clancy *et al.* [156] concluded that mean absolute EMG activity was superior. This was due to EMG being more closely approximated to a Laplacian rather than Gaussian distribution which the former is more closely approximated to by mean absolute EMG value.

$$EMG_{ABS}(t) = \frac{1}{N} \sum_{t-N}^t Abs(EMG_{RAW}(t))$$

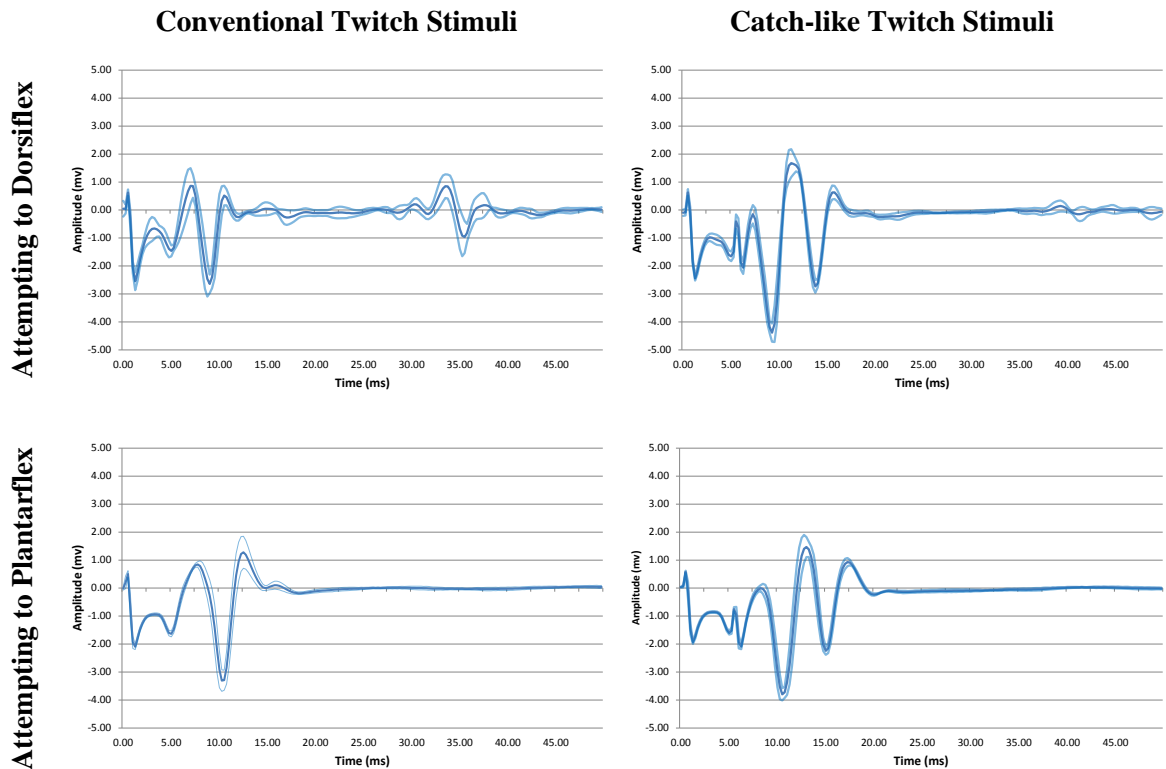
**Equation 7-2: Calculation of smoothed absolute EMG ( $EMG_{ABS}$ ) from raw EMG ( $EMG_{RAW}$ )**

An averaging window of 250ms was selected based upon SENIAM guidance recommendations [134]. When plotted against a rolling time axis this window provided a mean absolute EMG trace that was responsive to movement and could be quickly be increased with sustained effort. The 250ms time delay introduced by the averaging window was considered negligible when viewing the trace upon the participant display of the Stimulation Investigator application. The triggering system logged peak  $EMG_{ABS}$  value and displayed the continuous value of  $EMG_{ABS}$  as a percentage of this. A trigger level of 50% was found to avoid miss-triggering and required a moderate rather than maximal contraction to activate. Once triggered, the system would not be triggered until data collection had finished and  $EMG_{ABS}$  had returned to below the trigger threshold.

The Stimulation Investigator application was also modified to continuously compute  $EMG_{ABS}$  without a smoothing window. This would be used when attempting to assess the inhibition effects of conventional and catch-like stimulation through analysis of mean absolute values of EMG.

### 7.3.2 *Exploratory investigation 3: Results*

The mean raw EMG response following five repetitions of twitch stimuli was calculated and recorded. In this manner, temporally stochastic voluntary EMG would be attenuated, effectively cancelling out the voluntary component and maintaining the response due to stimulation. Only tibialis anterior EMG responses are shown in Figure 7-15 in order to illustrate the outcome of this investigation. Note the increased variation between mean EMG response and plus and minus one standard deviation variations due to voluntary activation of the tibialis anterior when attempting to dorsiflex.



**Figure 7-15: Tibialis anterior EMG response during isometric testing with ankle at plantigrade**

### 7.3.3 Exploratory investigation 3: Discussion

For M-waves resulting from both conventional and catch-like twitches, peak to peak amplitude remained similar when attempting to dorsiflex as well as plantarflex. In light of the findings of Exploratory Investigation 2 this suggests the variation noted in M-wave amplitude was due to muscle length effects rather than voluntary effort.

The tibialis anterior reflex activity was only present when attempting to dorsiflex and not plantarflex. It was therefore thought to be an H-wave due this facilitation with voluntary effort. This observation reasserted the need to assess the effects of voluntary effort within the protocol design and was relevant to all three research questions. This investigation did not investigate the influence of muscle length on reflex components in the absence of voluntary effort.

### 7.3.4 Exploratory investigation 3: Outcomes

This investigation successfully demonstrated and aided refinement of an isometric phase of the envisaged protocol design. A suitable method of triggering the application of stimulation based upon voluntary EMG activity was developed and tested. Data

collected using this method would permit further investigation of the posed research questions.

In order to trigger stimulation during isometric conditions, some voluntary control of the lower limb was required. In impaired participants the isometric investigations would be omitted if unable to trigger stimulation via EMG. For those with some voluntary control however, the ability to adjust the sensitivity of the triggering system was provided. Investigator control of the EMG<sub>ABS</sub> mean moving averaging window between 50ms and 1000ms was included, with a default value of 250ms. In a similar manner, control of the percentage of maximum voluntary contraction threshold that stimulation was triggered at was provided between 30% and 70%, with the default value being 50%.

## 7.4 Exploratory Investigation 4:

### Burst of Conventional Stimulation

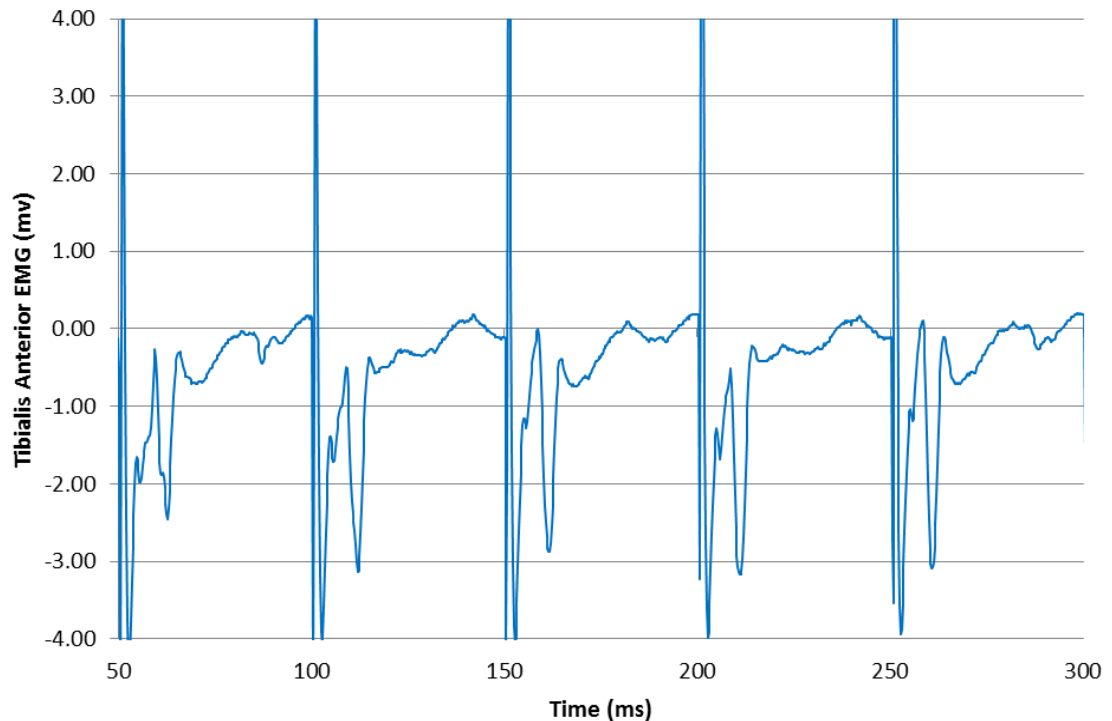
Up until this point in the exploratory investigations, only the response to conventional and catch-like twitch stimuli had been assessed. Exploratory Investigation 4 assessed the response to a burst of 50ms period stimulation in order to ensure no adverse summative stimulation artefact effects were encountered. It was also wished to investigate whether direct motor and reflex component characteristics varied over such a burst, and if so, was this influenced by combination with voluntary movement.

#### 7.4.1 *Exploratory investigation 4: Setup*

The author's tibialis anterior and soleus EMG responses to the application of a burst of conventional stimulation were assessed using the same instrumentation setup as Exploratory Investigation 2. As it was wished to assess M- and H-wave changes with movement, the Biometrics goniometer system was used to record ankle joint angle (section 6.6). The stimulation burst comprised of 40 pulses of 200 $\mu$ s pulse-width, 50mA current amplitude and 50ms stimulation period. These stimulation parameters were typical of that needed for the author to produce dorsiflexion with moderate eversion as suitable for dropped foot correction. At the same time the author attempted to smoothly dorsiflex and plantarflex the foot under investigation in synchrony to a sinusoid of 3 seconds period, similar to that depicted earlier in Figure 7-12.

### 7.4.2 Exploratory investigation 4: Results

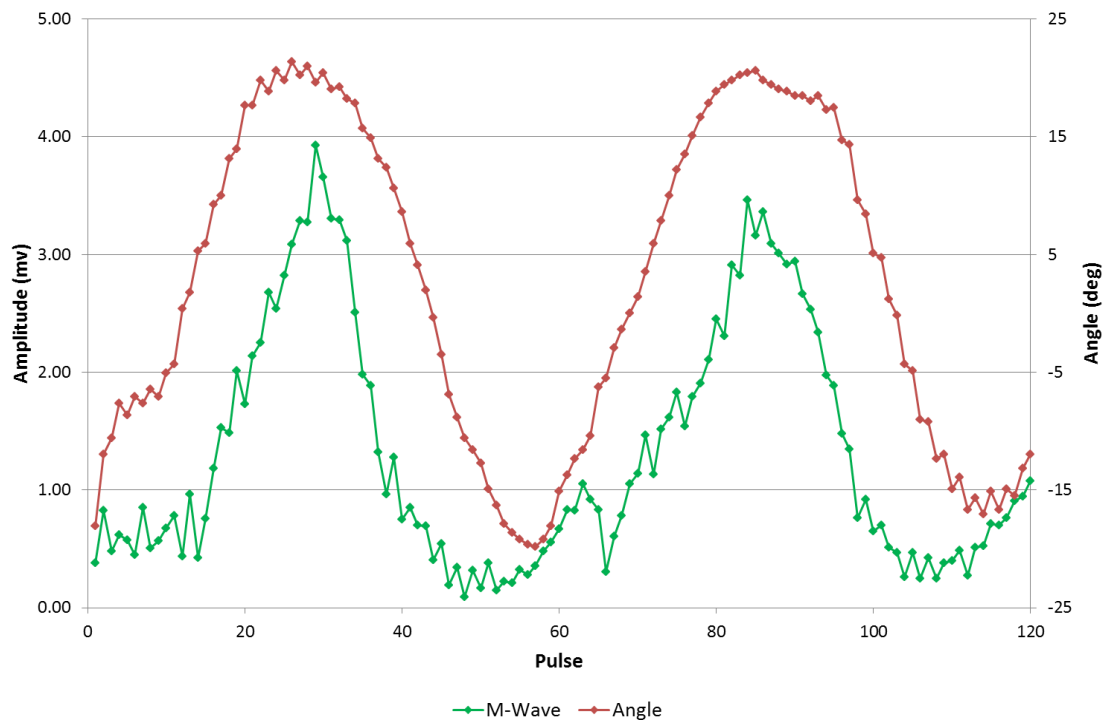
Figure 7-16 displays the tibialis anterior EMG response to the first five stimuli of such a stimulation burst applied to the author when relaxed.



**Figure 7-16: Author's tibialis anterior EMG response to burst of conventional stimulation**

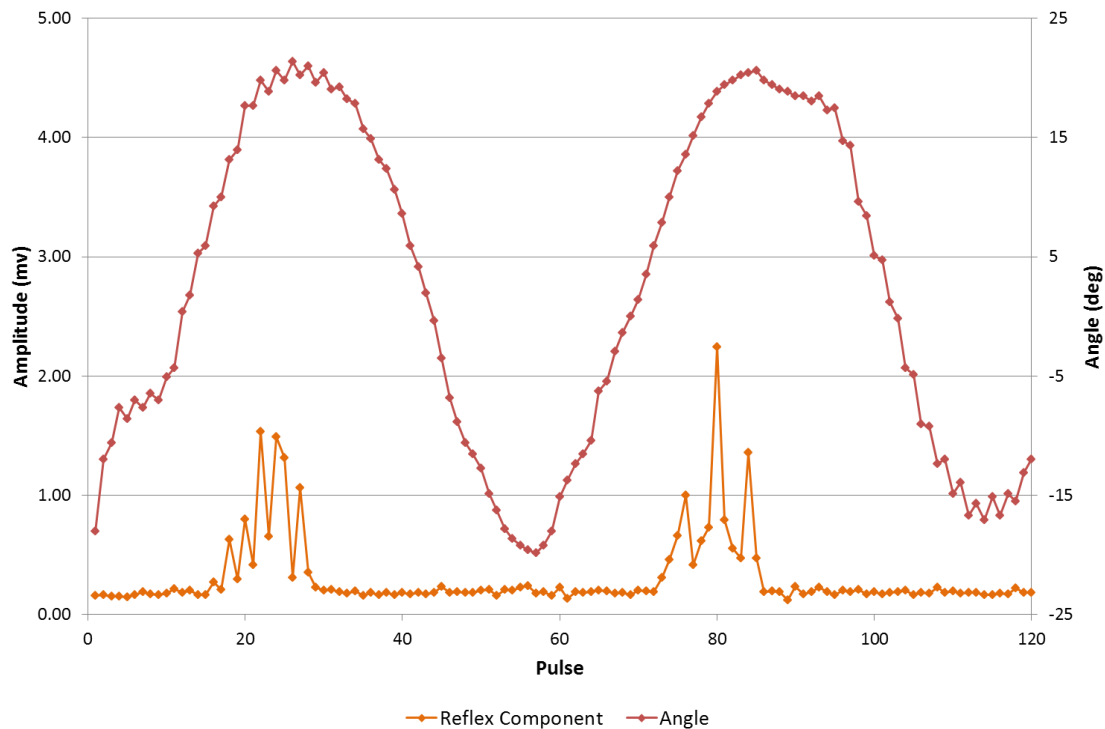
*Five stimuli applied over 250ms shown*

EMG responses were first reviewed and visually compared using the Stimulation Analyser application (section 6.8). Following this, data was exported in CSV format to Microsoft Excel. A Microsoft Visual Basic macro was created to compute peak to peak amplitude values of M-wave and reflex components following each stimulation pulse. This macro reported the maximum and minimum values over a defined time window (M-wave: 5-15ms, H- or F-wave: 35-45ms). Figure 7-19 displays an example of the points identified and subsequently used to derive peak to peak M-wave and reflex component amplitude. The peak to peak M-wave amplitude following each of the 40 stimulation pulses is plotted in Figure 7-17 with the ankle joint angle plotted on the secondary y-axis. Similar analysis was completed for reflex components and is shown in Figure 7-18.



**Figure 7-17: Author's M-wave and ankle angle movement during conventional burst stimulation**

*Positive angle: dorsiflexion, negative plantarflexion*



**Figure 7-18: Author's reflex component and ankle movement during conventional burst stimulation**

*Positive angle: dorsiflexion, negative plantarflexion*

### 7.4.3 *Exploratory investigation 4: Discussion*

The response of an individual conventional stimulus within a burst as indicated in Figure 7-16, is largely that of the single twitch repeated. For both the tibialis anterior and soleus EMG responses the artefact recovery tail diminished prior to the subsequent pulse within the burst and there was no adverse summation of stimulation artefact effects.

Following each stimulation pulse, a clearly identifiable tibialis anterior M-wave was observed. This had an onset latency of between 5ms and 15ms which was typical of that noted during Exploratory Investigations 2 and 3. In a similar manner to that noted during Exploratory Investigation 2, the tibialis anterior M-wave amplitude appeared to increase with ankle flexion angle.

In keeping with earlier findings, what appeared an H-wave wave was seen during periods of the burst between 35ms and 45ms following the application of each stimuli. Unlike the M-wave, the H-waves polarity differed between instances however this may be expected due to the activation of slightly different motor units by the reflex pathway. The H-wave could be varied by attempting to “work with” or facilitate the movement that stimulation was causing. This was evident by its presence at angles correlating to dorsiflexion of the foot.

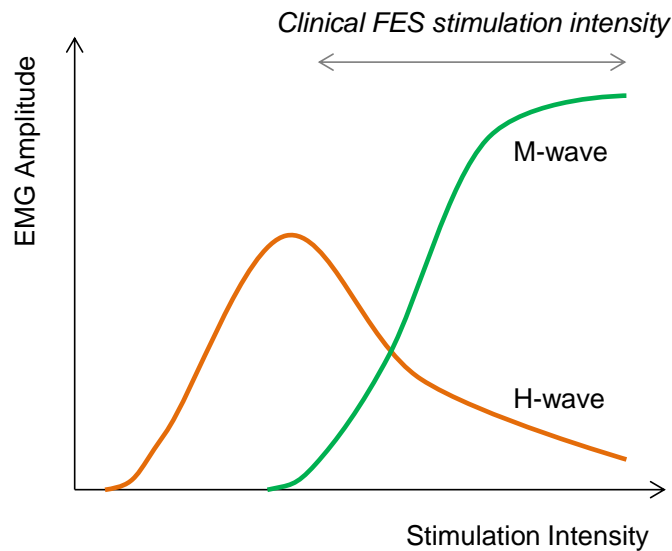
Whilst on first inspection of Figure 7-17 there appears reasonable correlation between peak to peak M-wave amplitude and joint angle, the M-wave trace appeared slightly saw tooth rather than sinusoidal. There appeared a more gradual increase in peak to peak M-wave amplitude during ankle dorsiflexion compared to the sudden reduction when plantarflexed.

Theory dictates that as stimulation intensity and M-wave amplitude increases, H-waves are annihilated by antidromic motor activity (section 4.1.2). As indicated by Figure 7-19, it is not known at what magnitude of stimulation intensity (x-axis) is generally associated with clinical FES.

If an assumption is made that FES is applied in the stimulation intensity range indicated in Figure 7-19, then an increase in H-wave is accompanied by a decrease in M-wave of similar magnitude. For the purposes of discussion, the summation of M-and H-wave amplitude is assumed to be a constant over the stimulation intensity indicated in Figure 7-19 i.e. an increase in M-wave is accompanied by an equivalent decrease in H-wave amplitude. Following this assumption, Figure 7-20 provides the summated response of

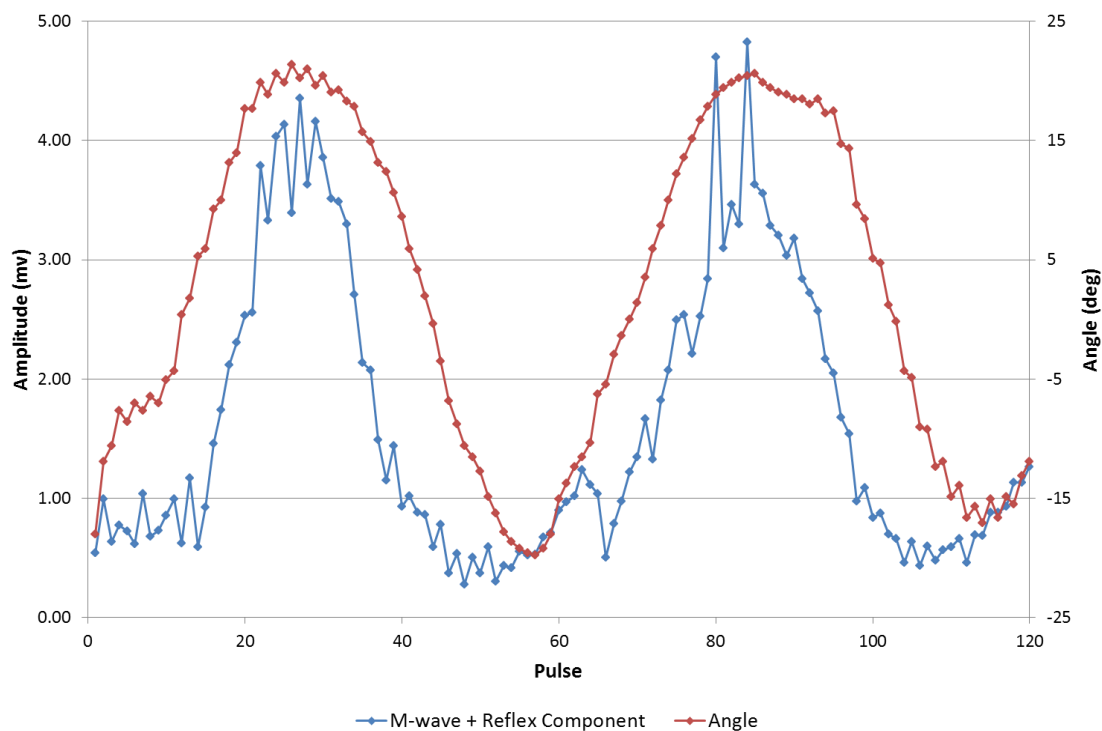


M- and H-wave. Note the improved agreement between ankle joint angle and summated EMG response compared to the slightly saw-tooth M-wave plot of Figure 7-17. This improved correlation appears to support the above assumption whilst demonstrating the modulation of M-wave amplitude with joint angle.



**Figure 7-19: M- and H-wave characteristic plot when considered in light of clinical FES use**

*Note, H-wave characteristics will be subject to excitability/inhibition effects.*



**Figure 7-20: Summation of author's M- and H- wave amplitude alongside ankle joint angle during voluntary movement and conventional burst stimulation**

#### 7.4.4 *Exploratory investigation 4: Outcomes*

The successful measurement and analysis of the author's EMG following individual stimuli of a burst of stimulation demonstrated the investigational setup's ability to function as intended for the proposed study. Exploratory Investigation 4 also indicated that joint angle and effort could, and should, be assessed during the application of bursts of conventional and catch-like stimulation within the research protocol.

When a voluntary movement was applied alongside a burst of stimulation it was noted that the author's M-wave and H-wave components varied. Whilst tibialis anterior M-wave amplitude appeared to show direct correlation with ankle angle, the H-wave was only present as the author initiated dorsiflexion.

Effort would affect the interneurons and either facilitate or inhibit generation of an H-wave. Whilst in the case of the author, this data supported the conclusion that muscle length affects M-wave amplitude, it still did not provide information regarding the exact mechanism behind this. As previously noted, due to the mechanism of the M-wave it was not expected to vary with joint angle or voluntary effort when constant intensity stimulation was applied. Renshaw cells would vary the ease of which  $\alpha$ -motor neuron axons would be activated by descending input at the spinal cord. The same effect was not expected to be present mid-way along the  $\alpha$ -motor neuron bundle when activated by electrical stimulation. The variation in M-wave amplitude with joint angle appeared to signal that either less of the  $\alpha$ -motor neuron bundle was being activated when the foot was in an extended position or the EMG activity that was being recorded was less. The apparent reduction in M-wave with increased H-wave amplitude suggested a reduction in effective stimulation intensity at the nerve. However being unable to identify how much of the H-wave was due to facilitation and how much due to a reduction in antidromic motor activity prevented a firm conclusion.

Three theories were formed which could account for this:

1. Relative movement between surface stimulation electrodes and the common peroneal nerve, causes variation in electric field strength at the nerve and hence motor unit activation during a contraction.
2. At shortened muscle lengths a greater proportion of muscle fibres appearing within the sensing volume of the surface EMG electrodes and hence a larger EMG signal being recorded.

3. Changes in cross-sectional area of muscle, or reduction in muscle surface to EMG electrode distance, increases the magnitude of surface EMG signal during contraction of the muscle.

Initial investigations into each of these were conducted. Brief explanations of each of these three hypotheses including the acquired data and how this informed the finding are discussed in exploratory investigations 5, 6 and 7 respectively.

## 7.5 Exploratory Investigation 5:

### Movement between stimulation source & common peroneal nerve

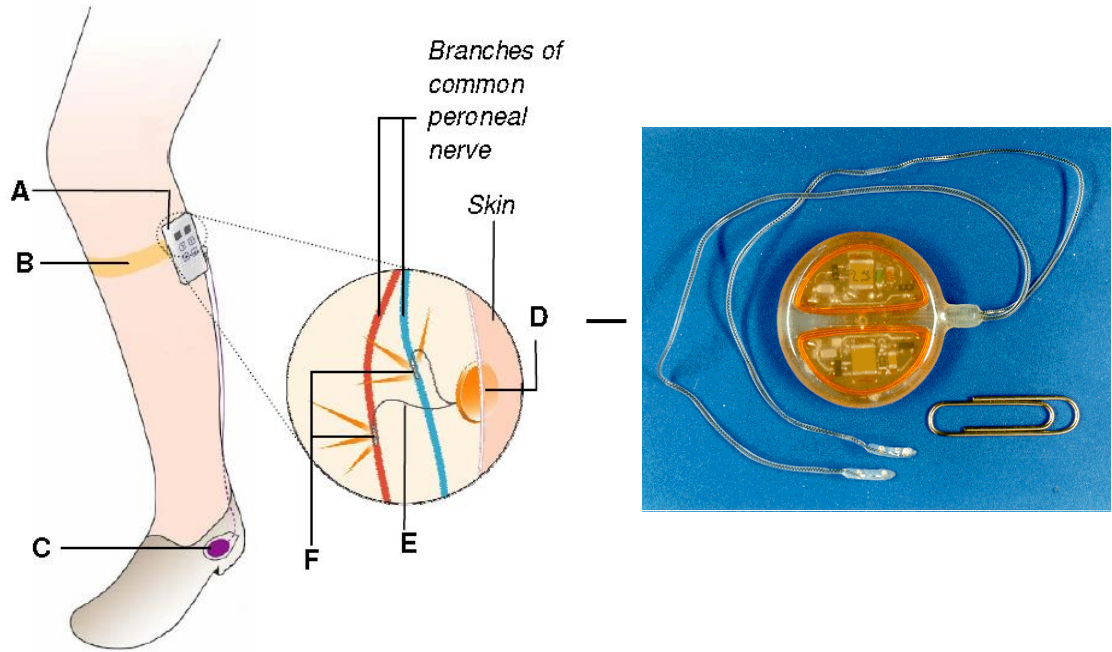
Whilst considering the possibility of nerve movement relative to the stimulation electrodes, the author was made aware of video footage appearing to support this during surgery to implant a dropped foot stimulator known as a STIMuSTEP<sup>18</sup>. During this procedure a video recording of the surgical procedure was made for training purposes. Replaying the footage at the time instance that a burst of test stimulation was applied to the exposed common peroneal nerve, appeared to indicate nerve movement in response to the resulting muscle contraction. Such relative movement between the nerve and the skin surface may partly account for the variation seen in M-wave amplitude when combined with a voluntary movement.

#### 7.5.1 *Exploratory investigation 5: Setup*

The STIMuSTEP system comprises of an implantable two channel stimulator (Figure 7-21) and an external control box. General anaesthetic is used when implanting the stimulator under the lateral side of the affected leg, distal to the knee. The electrodes are impaled and sutured underneath the epineurium of the deep and superficial branches of the common peroneal nerve. Through setting appropriate stimulation levels between these two channels, ankle dorsiflexion with moderate eversion can be produced during the swing phase of gait when timed using a footswitch. The transmitter is positioned over the receiver and power introduced via an inductive link (Figure 7-21).

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<sup>18</sup> Finetech Medical Ltd, Hertfordshire, England. [www.finetech-medical.co.uk](http://www.finetech-medical.co.uk).



**Figure 7-21: STIMuSTEP when used for dropped foot correction**

*External controller (A) positioned over site of Implant Receiver (D) using Leg Strap (B). The implant receiver applies stimulation via flexible silicon encapsulated cables (E) to epineuron electrodes (F) impaled on the deep and superficial branches of the common peroneal nerve. Footswitch (C) is placed under the heel of effected leg<sup>18</sup>.*

### 7.5.2 Exploratory investigation 5: Results

During the implant procedure, stimulation is applied whilst the implant site is open in order to ensure the correct electrode positions. On this occasion the leg was supported such that the ankle was suspended in mid-air whilst the transmitter was brought into proximity with the implant as a test burst of stimulation was applied. The nerve appeared to ‘pull-in’ as if being tightened and hence moving slightly deeper from the skin surface. Whilst this was a clinical observation and the handheld video recording was not specifically intended for this purpose, frame stills allow this instance to be documented and assessed. Frame stills captured immediately prior to and mid-way through the burst of stimulation being applied are shown in Figure 7-22 and Figure 7-23 respectively. Adobe Photoshop CS3<sup>19</sup> was used to align the static objects within these frames such that just the movement of the nerve could be assessed. The yellow indicators of Figure 7-23 indicate the nerve movement between frames using an edge of a tethered suture as a reference. The nerve appeared to move by a distance comparable to the width of the electrode assembly which was 2.75mm.

<sup>19</sup> Adobe Systems Software Ireland Ltd. [www.adobe.com/uk](http://www.adobe.com/uk)



**Figure 7-22: STIMuSTEP implant electrodes sutured to common peroneal nerve: no stimulation**



**Figure 7-23: STIMuSTEP implant electrodes sutured to common peroneal nerve: stimulation applied**

*Yellow arrows indicate movement of nerve relative to Figure 7-22.*

### 7.5.3 Exploratory investigation 5: Discussion

Whilst of somewhat limited interpretation, this analysis indicated that in the case shown the common peroneal nerve appeared to move by approximately 2 to 3mm when a stimulation burst was applied. Although exactly how the electric field set up by the stimulation electrodes varies underneath the skin surface does not appear to be well understood, the displacement of this movement is comparable to the diameter of the nerve itself and may provide an explanation of why M-wave appeared to vary with movement in the author. In this scenario the surrounding subcutaneous fat has been peeled back and therefore the effect may be exacerbated without this tissue surrounding and hence supporting the nerve.

This was an intriguing observation that the author is not aware to have been discussed or reported in literature previously. If characteristic of the wider population's typical physiological response, it has ramifications if attempting to control surface applied FES contractions by modulating stimulation intensity to mimic natural EMG firing patterns. A further development of this investigation would be to assess the EMG response to conventional surface stimulation and that applied with the STIMuSTEP system. As the STIMuSTEP system uses tethered electrodes it should not be influenced by the nerve

movement and hence the M-wave amplitude should remain constant. This is possible as a surface stimulator can still be used in the presence of a STIMuSTEP implant with no additional risk to patient or implant. Changes in M-wave amplitude may then be correlated to limb movement and the effect characterised in that individual.

#### *7.5.4 Exploratory investigation 5: Outcomes*

Although this did not substantially influence the research protocol design it helped to further investigate and provide possible explanations of trends observed during earlier exploratory investigations.

### **7.6 Exploratory Investigation 6**

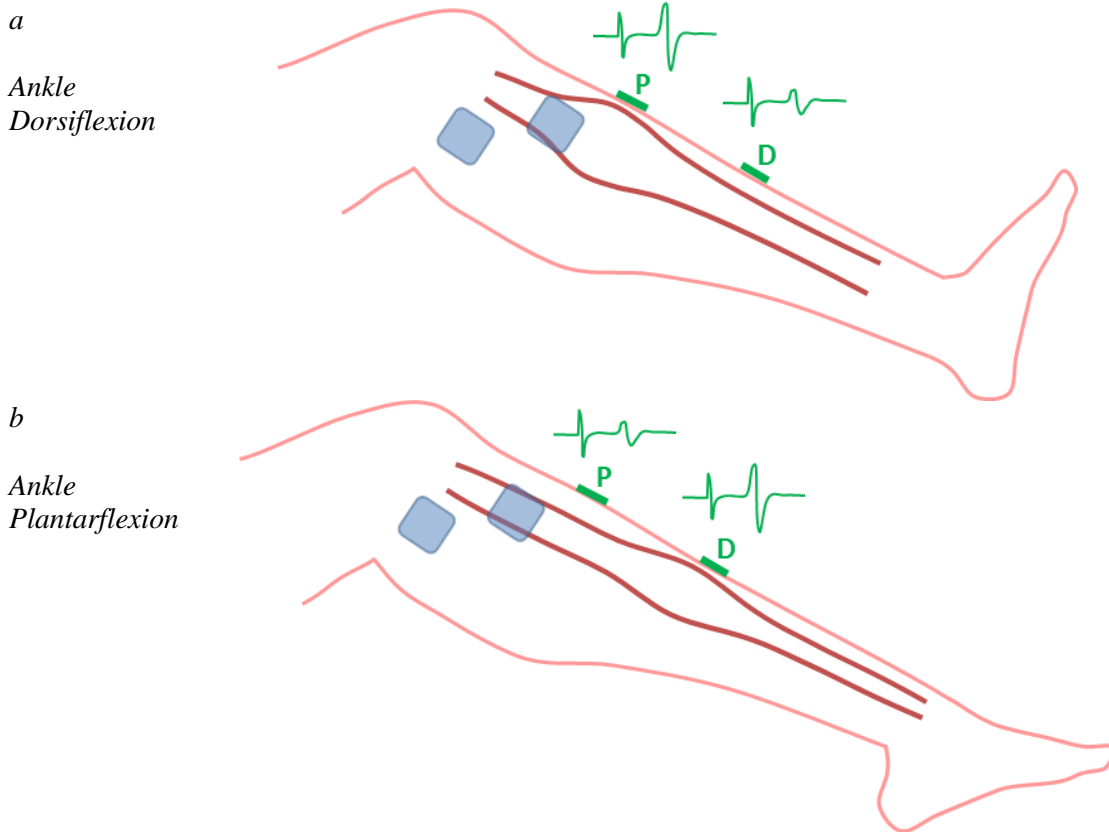
#### **Lateral Movement between Motor Point & EMG Electrodes**

When considering the physiological mechanism responsible for EMG as partially discussed in section 7.1.5, it was conceivable that the M-wave amplitudes sensitivity to muscle length was due to relative movement between the muscle and the EMG recording electrodes.

The hypothesis behind this possible effect is depicted in Figure 7-24. To simplify the explanation, an assumption is made that the greatest EMG activity is present over the motor point of the muscle and that the motor points moves relative to the EMG electrodes when the foot is flexed or extended. As shown in Figure 7-24<sup>a</sup>, when in a flexed position the tibialis anterior motor point will be more proximal and when extended, more distal (Figure 7-24<sup>b</sup>). Depending upon the EMG electrode placements relative to the motor point the amplitude will either increase or decrease depending upon whether the motor point is closer or further away during a movement.

#### *7.6.1 Exploratory investigation 6: Setup*

Eight EMG electrodes of 10mm width were placed in 5mm intervals along the length of the tibialis anterior as shown in Figure 7-25. A burst of conventional stimulation was applied in combination with a cyclical voluntary ankle movement as described in Exploratory Investigation 4 (section 7.4.1). This was repeated seven times, each time recording the EMG response from a pair of adjacent EMG electrodes.



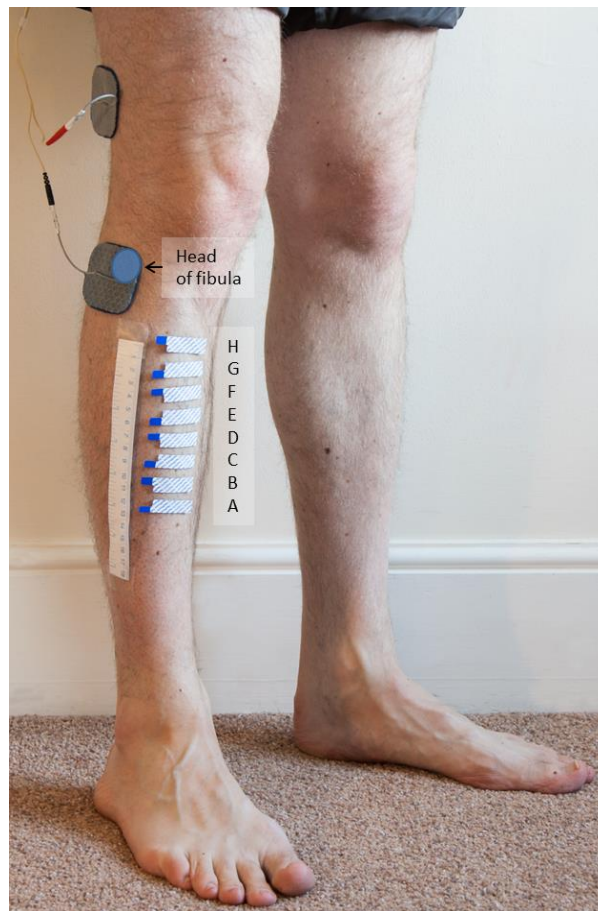
**Figure 7-24: Relative movement between muscle and EMG recording electrodes**

*PAL stimulation electrodes shown in blue.*

*EMG electrodes shown in green: P=Proximal, D=Distal.*

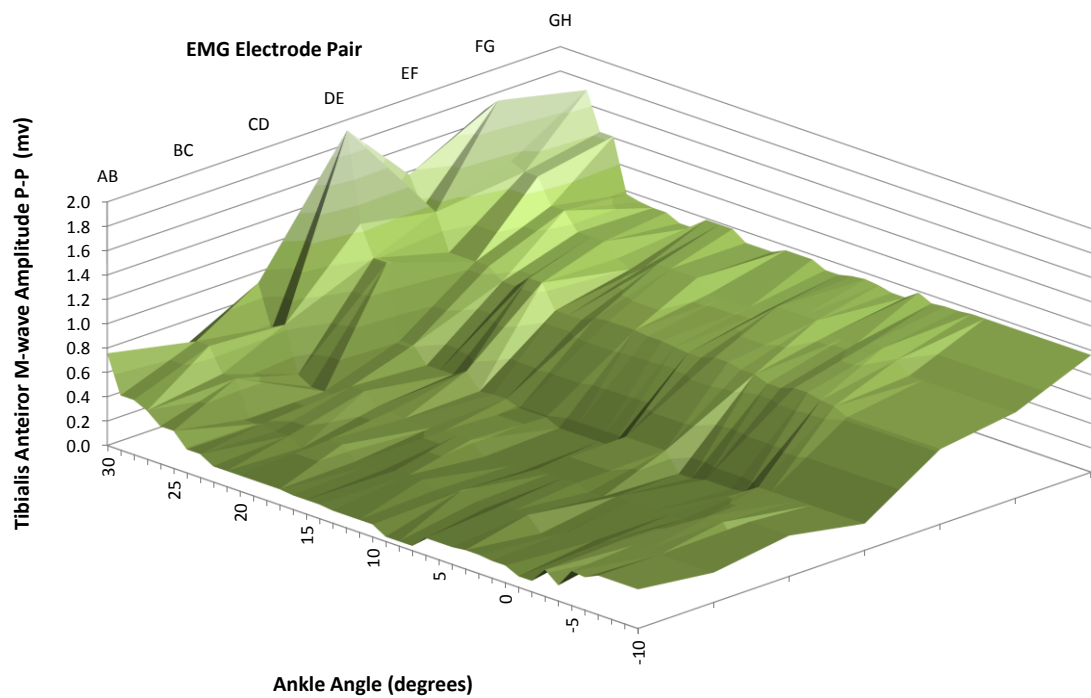
### 7.6.2 Exploratory investigation 6: Results

Using the method described in exploratory investigation 4 (section 7.4.2), the peak to peak amplitude of the M-wave following each stimulation pulse was measured. A look-up function was then used to tabulate the peak to peak M-wave amplitude recorded at one degree steps over the performed voluntary movement. This permitted the contour plot of Figure 7-26 to be produced, displaying the M-wave amplitude trend at each EMG electrode pair on a common ankle angle axis.



**Figure 7-25: EMG electrode positions used during exploratory investigation 6**

*Reference EMG electrode placed on medial malleolus of right ankle*



**Figure 7-26: Tibialis anterior M-wave contour plot: electrode pair, ankle angle**

*Electrode pairs as indicated in Figure 7-25 e.g. AB= EMG recorded between electrodes A and B*



### 7.6.3 *Exploratory investigation 6: Discussion*

The EMG electrode pair GH was most proximal and hence in closest proximity to the stimulation electrodes. It had the greatest stimulation artefact present on the tibialis anterior EMG responses. In the contour plot of Figure 7-26, this can be seen by the elevated peak to peak amplitude observed across the range of ankle angles for electrode pair GH. This is due to the M-wave appearing artificially high due to its super-position on the stimulation artefact recovery curve. It is not until distal EMG electrode pair DE that M-wave measurement by the EMG amplifier was not affected by this artefact. Electrode pair DE was closest to the electrode position suggested by the SENIAM guidance and adopted during all other exploratory investigations. The largest peak to peak M-wave amplitude was recorded from this electrode pair and supported the SENIAM guidance.

For all electrode pairs the largest peak to peak M-wave amplitude was seen at shortened muscle lengths when the author's foot was in a dorsiflexed position. This negates the hypothesis put forward in Figure 7-24, suggesting the observed M-wave amplitude variations with muscle length have not been due to relative lateral movement between the motor point and EMG electrodes.

### 7.6.4 *Exploratory investigation 6: Outcomes*

Exploratory Investigation 6 suggested lateral movement between the tibialis anterior motor point and EMG recording electrodes were not accountable for M-wave variation with joint angle noted in earlier exploratory investigations completed upon the author. Although this investigation did not substantially influence the research protocol design, it provided counter evidence to an explanation of the trends in M-wave amplitude seen in earlier exploratory investigations.

Regarding EMG measurement, it was encouraging to demonstrate that the largest and tibialis anterior EMG response without notable stimulation artefact was from the electrode pair placed closest to that recommended by the SENIAM guidance. Measurements also suggested that EMG electrodes could be placed slightly more distal (e.g. pair CD) in order to further minimise stimulation artefact whilst and still successfully recording tibialis anterior EMG.

## 7.7 Exploratory Investigation 7:

### Muscle Fibres within Sensing Volume of EMG Electrodes

Exploratory Investigation 6 had indicated relative lateral movement between the motor point and EMG recording electrodes was not responsible for changes in M-wave amplitude. Continuing to question exactly what is represented by the EMG signal, it was considered whether the increased M-wave amplitude was due to the increase in cross sectional area of a muscle when tensed and at a shortened length. In effect this amounted to a larger number of muscle fibres being grouped within the sensing volume of the EMG electrodes.

#### 7.7.1 *Exploratory investigation 7: Setup*

In order to investigate the above hypothesis a portable ultrasound machine was used to provide approximate cross-sectional area measurements of the tibialis anterior directly underneath the adopted SENIAM electrode placements when tensed with the foot in a dorsiflexed position and when relaxed with the foot in a plantarflexed position under gravity. The author sat on a clinic plinth with leg suspended as previously used in Exploratory Investigations 1, 2, 3 and 4.

A Dynamic Imaging<sup>20</sup> C\MCII ultrasound machine with and B-mode fan head was used. A scale marker was placed on screen so as to aid subsequent spatial measurements. A digital SLR camera positioned on a tripod and activated by a remote shutter cable was used to acquire screenshots of the ultrasound machine display.

An anatomy textbook [157] with cross-sectional views and descriptions of function of lower leg musculature was used to identify muscles, specifically the tibialis anterior.

#### 7.7.2 *Exploratory investigation 7: Results*

The acquired screenshots were processed within Adobe Photoshop CS3. Using the ultrasound machines onscreen measurement display as a scale indicator, measurements of circumference and cross sectional area of the tibialis anterior could be made when in tensed and relaxed conditions. These screenshots with the cross sectional area measurements indicated are shown in Figure 7-27.

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<sup>20</sup> Dynamic Imaging Ltd., Livingston, United Kingdom.

### 7.7.3 Exploratory investigation 7: Discussion

The large increase in tibialis anterior cross sectional area in its active compared to relaxed state may explain the variations in M-wave amplitude seen in earlier exploratory investigations. The author had little subcutaneous fat between skin surface and muscle and hence this effect may be more notable in this instance compared to others.

### 7.7.4 Exploratory investigation 7: Outcomes

The findings of this investigation supported the hypothesis put forward to explain the variation in M-wave amplitude with muscle length. It also further supported the use of isometric tests within the protocol design in order to control muscle length and hence attempt to restrict changes in cross sectional muscle area.



*Tibialis anterior relaxed,  
foot plantarflexed*

*Area = 504mm<sup>2</sup>*

*Perimeter = 99mm*



*Tibialis anterior active, foot  
dorsiflexed*

*Area = 700mm<sup>2</sup>*

*Perimeter = 111mm*

**Figure 7-27: Ultrasound images: cross section of tibialis anterior at motor point**

*Tibialis anterior highlighted in red*

## 7.8 Reflection on Initial Exploratory Data Collection

The preliminary aim of initial exploratory data collection was to assess system performance and to gain indicative experimental data to aid effective protocol design. It also presented as an opportunity to complete exploratory analysis on such preliminary data from the author. An ordered discussion of these aspects will now be provided.

### *7.8.1 Discussion of system performance during exploratory data collection*

Exploratory Investigation 1 prompted refinement of the stimulation output stage and EMG amplifier in order to further minimise stimulation artefact and permit identification and measurement of tibialis anterior M-wave following stimulation of the common peroneal nerve. Following these refinements, the developed system enabled collection of data to demonstrate investigation of the posed research questions. The systems functional objective was confirmed whilst identifying minor refinements which would ease investigation and analysis prior to using the developed system during clinical investigation.

### *7.8.2 Discussion of collected exploratory data*

The preliminary data collected from the author during exploratory investigation 1 showed encouraging likeness to published findings. Although limited data from a single individual, it also permitted initial assessment of previously unpublished effects of catch-like stimulation on EMG.

The ability to easily arrange, compare and step through collected data using the Stimulation Analyser application enabled visual identification of what appeared M- and H-wave of the soleus data EMG data. Although suggestive of unintended depolarisation of the tibial nerve, it was encouraging to record a well-documented, characteristic response. Analysis of the acquired exploratory data (section 7.1.2) provided estimates of motor and sensory nerve conduction speeds comparable to those reported in literature [152-154].

Following application of conventional and catch-like stimuli during repetitive voluntary dorsiflexion and plantarflexion of the author's foot, exploratory investigation 2 supported the inclusion of isotonic and isometric conditions as part of the research

protocol. Conventional and catch-like twitch stimuli were applied under isometric conditions during Exploratory Investigation 3 and suggested earlier observed variations in M-wave amplitude were due to muscle length rather than voluntary effort effects. The reflex components identified when attempting to dorsiflex and plantarflex during isotonic (Figure 7-13 <sup>2+3</sup>) and isometric conditions (Figure 7-15) appeared similar and supported their modulation by voluntary effort.

During Exploratory Investigation 4 bursts of conventional and catch-like stimulation, rather than individual stimuli, were applied during repetitive voluntary dorsiflexion and plantarflexion of the author's foot. This provided further information with which to assess the effects of muscle length and voluntary effort on M-wave and reflex component variation.

Three hypotheses were formed for the explanation of observed M-wave amplitude variation with muscle length. Each of these were the subject of an exploratory investigation to support or refute them. Of these the following two hypotheses were supported:

1. Relative movement between surface stimulation electrodes and the common peroneal nerve, causes changes in electric field strength at the nerve and hence motor unit activation during a contraction.
2. Changes in cross-sectional area of the muscle or reduction in muscle surface to EMG electrodes distance, increases the magnitude of surface EMG signal during contraction of the muscle.

Regarding the proposed research questions of Chapter 5, the absence of a second reflex component to the second stimulus of the doublet opposes the hypothesis which forms Research Question 2, page 56. If of H-wave origin, its absence may have been due to the noted period of post activation depression linked to the time for the central synapses membrane to be restored [64, 65]. The catch-like effect is most clearly observed when an initial high frequency doublet is followed by subtetanic frequency stimulation; such subtetanic frequency stimulation may provide sufficient time for the H-wave to recover.

## **Chapter 8    Research Protocol**

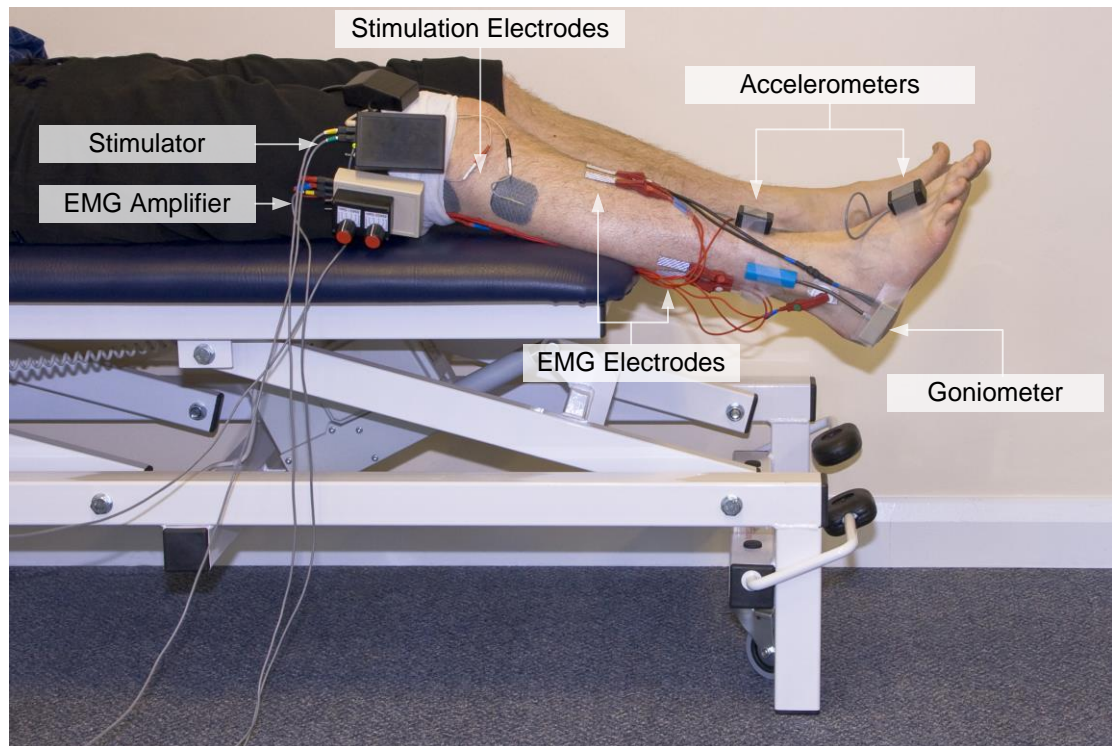
The collection and analysis of exploratory data described in Chapter 7 aided refinement of the research protocol prior to seeking approval to complete investigations with unimpaired and impaired participants. This chapter begins with an overview of the study design which enabled investigation of three research questions posed in Chapter 5. In order to investigate these, a single investigational session comprising of six phases was developed. The design and structure of these phases and how they sought to specifically investigate different aspects of the research hypothesis are discussed in detail. Table 8-2 summaries the completed sub-tests and provides a means of referencing completed sub-tests using a numerical code during subsequent chapters of this thesis. The chapter concludes by detailing broad research governance and recruitment aspects of the study.

## 8.1 Study Design

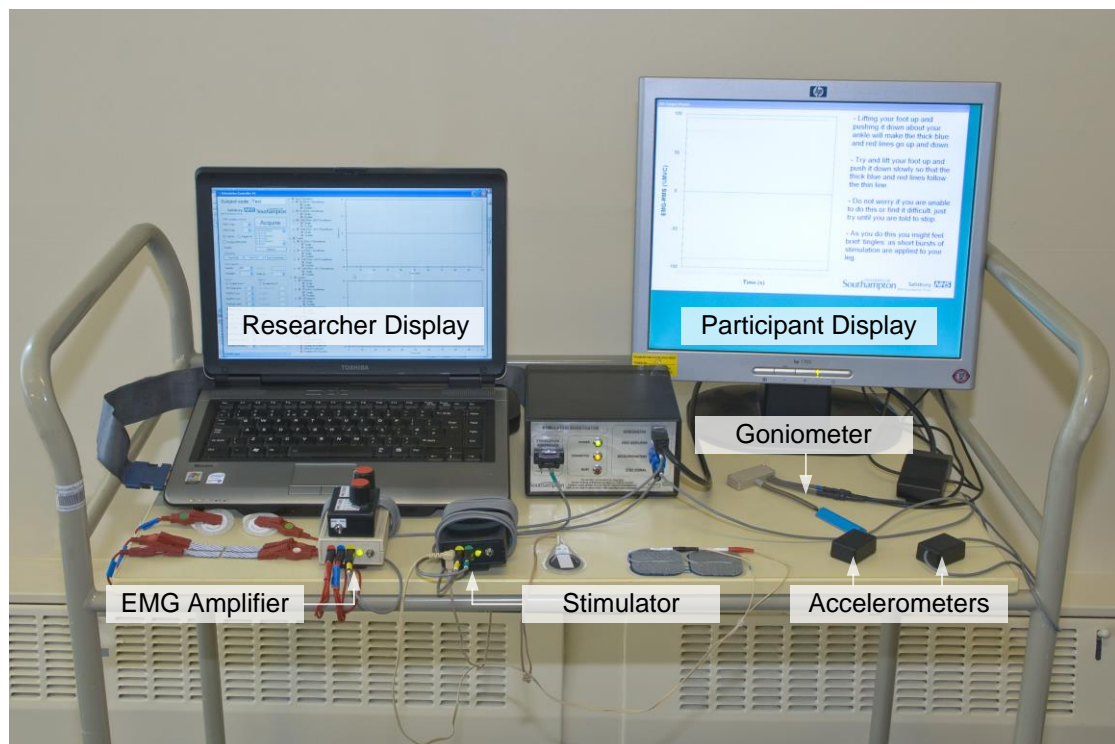
### 8.1.1 Overview

Whilst it was the intention of this research to inform future clinical use of conventional and catch-like electrical stimulation when used with patients who have sustained a UMN injury, it was also wished to investigate the posed research questions with unimpaired individuals. Through evaluating the research hypothesis in these two groups, comparison of the findings may further characterise the effects of UMN on the response to electrical stimulation and muscle activation. As discussed in Chapter 3, factors such as excessive spasticity, muscle weakness or muscle fibre type changes associated with UMN injury may, in some cases, mask or complicate interpretation of results. Investigating the posed research questions amongst unimpaired participants would seek to mitigate such confounding factors from observations amongst this group.

During the investigational session, six investigation phases would seek to assess or control different factors relevant to the research questions of Chapter 5. Figure 8-1 displays the developed instrumentation setup in use permitting measurement of EMG and muscle twitch following stimulation. Figure 8-2 displays the mobile investigational system as stored and transported during investigations.



**Figure 8-1:** Participant worn instrumentation as used during research protocol



**Figure 8-2:** Investigational system on wheeled trolley as used during research protocol



### 8.1.2 *Study recruitment*

Unimpaired participants were recruited from the Clinical Science and Engineering department at Salisbury District Hospital and the School of Electronics and Computer Science at the University of Southampton. Impaired participants were recruited from those being seen at the National Clinical FES centre. In recruiting existing users of FES, impaired participants had already been assessed against the contraindications and were familiar with the sensation and principles of stimulation. The research hypothesis could be applied to a number of UMN injury groups which benefit from FES i.e. stroke, incomplete spinal cord injury, multiple sclerosis. Due to the small recruitment numbers of this exploratory study, it was decided to only recruit impaired participants who had had a stroke in order to avoid potential subgroup effects due to different conditions. As seen at the National Clinical FES Centre, this chronic patient group is typically stable in condition and less prone to sudden fatigue compared to other patient groups such as those affected by multiple sclerosis. As noted in Chapter 3 when discussing the effects of UMN syndrome, differences in response may exist between these groups associated with the properties of the condition.

During design of the research protocol the following group sizes were selected in order to provide exploratory data to investigate the research hypothesis:

- 10 unimpaired participants
- 10 participants who have sustained a stroke.

The selected sample size was considered sufficient for group effects to be identified whilst providing a reasonably small standard deviation. Descriptive statistics (i.e. mean, standard deviation) would be used during data analysis when performing group comparisons with non-parametric analysis techniques.

In order to permit the feasibility of the research protocol to be assessed, two participants from each of the unimpaired and impaired groups completed the study before further recruitment. Although not expected, should this have identified necessary amendments to the research protocol, these could have been communicated to the ethics committee and academic sponsors before data from the remaining sixteen planned participants was collected.

### 8.1.3 Inclusions and exclusion criteria

The inclusion and exclusion criteria that was used during recruitment was based upon that used by the National Clinical FES Centre when assessing patients for FES treatment. Whilst impaired participants would have been assessed against this criteria, a number of points remain relevant to unimpaired participants. Additional criteria was added reflecting the functional requirements involved with aspects of the investigational session and the wish to avoid co-morbidities which could complicate data interpretation.

	<b><i>Inclusion Criteria</i></b>
1	For impaired participants: chronic (more than 6 months) UMN injury patients who have a dropped foot due to stroke and are currently using a single channel FES device.
2	For unimpaired participants: male participants with no history of UMN injury/condition.
3	Able to tolerate the sensation FES transcutaneously applied to the common peroneal nerve at the popliteal fossa.
4	No known neurophysiologic conditions affecting the lower motor neuron system.
5	Medically stable.
6	Able to understand and follow simple instructions.
7	Able to walk at least 10 metres with and without the stimulator.
8	Able to independently transfer to and from clinic plinth.
9	Intact skin condition of lower limb such that necessary electrodes and sensors can be placed using adhesive tape.
10	Over the age of 18.
11	Does not rely on use of any other orthotic device in conjunction with FES for dropped foot correction (innersoles not included).
	<b><i>Exclusion Criteria</i></b>
1	Allergic to plastic material or micropore tape.
2	Contra-indications to FES (already applied for participants using FES).
3	Poor skin condition.
4	Pregnancy (the effects of FES on the unborn child is unknown).
5	Pacemaker users.
6	Poorly controlled epilepsy.
7	Fixed ankle contracture on side to be tested.
8	Type I diabetes.

**Table 8-1: Research participant inclusion and exclusion criteria**

#### 8.1.4 *Investigation session*

Participants were required to attend a single investigation session which lasted no longer than 90 minutes. This took place within one of the clinic rooms of the National Clinical Functional Electrical Stimulation Centre, Salisbury District Hospital. For impaired participants this was arranged for the same day shortly after their next scheduled review appointment. Following discussion of any questions or concerns between the participant and author, informed written consent (Appendix C) was taken and the participant allocated a unique anonymous code. The author completed a 'Participant Study Form' (Appendix D) noting whether the participants left or right leg was under investigation. Unless otherwise requested the dominant leg of unimpaired participants was utilised.

Participants were asked to remove their socks and shoes and either change into shorts or roll their trousers up to approximately 10cm above their knee. They were then asked to transfer on to or sit on the clinic plinth with the height of the plinth varied appropriately prior to this. With assistance if required, participants transferred into a supine position such that their lower leg, midway down their calf, was suspended over the end of the clinic plinth (Figure 8-1). The clinic plinth was positioned with one side against a wall such that the risk of falling was minimised. A goniometer was affixed using micropore tape to the lateral side of the participant's ankle (Figure 8-1). The two accelerometers units were also attached by the same method to the mid-point of the anterior aspect of the tibia anterior and the dorsal aspect of the foot. Use of Urisleeve elasticated bandages (single use) helped contain and support all the wires and sensors around the participants lower leg (not shown). Once all instrumentation had been attached, the author verbally checked that the participant remained comfortable and the attached instrumentation (i.e. wires/sensors/Urisleeve) was not applying excessive pressure to surfaces of the lower leg.

Throughout phases 1 – 5 of the study the participant was asked to remain relaxed and observe the 'participant display' monitor positioned on the wheeled trolley such that they could comfortably and clearly view it (Figure 8-2). Instructions displayed on the participant display (font size  $\geq 20$  point) were also verbally conveyed by the author.

## 8.2 Investigation Protocol Development

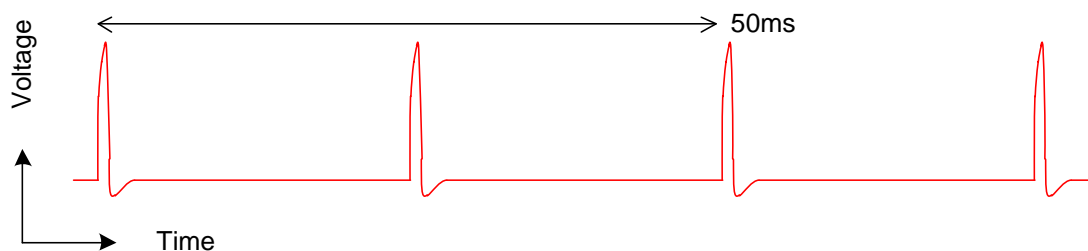
The exploratory data collection of Chapter 7 provided an indication of the time and motivational requirements (on behalf of a participant), needed to complete envisaged investigations. During development the protocol was retested on the author and supervision team such that further feedback and refinement could be made. The purpose and design of these six phases is now discussed in detail. When referring to individual sub-tests, numerical codes beginning with phase number followed by the node within the tree structure are used. Table 8-2 summarises the function and order of these sub-tests and the reader is encouraged to familiarise themselves with this table in order to aid clarity of later Chapters. The research protocol detailing the setup and completion of the investigational session which was followed during the study is included in Appendix E.

### 8.2.1 *Phase 1*

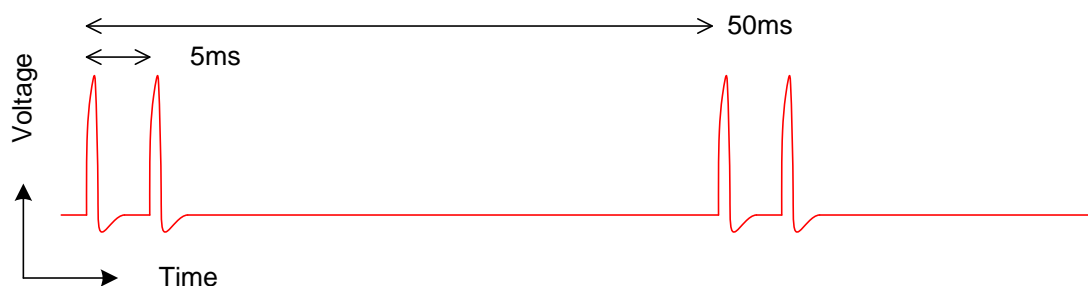
Phase 1 was designed to confirm effective set up of electrodes and instrumentation prior to data collection. Its primary aim was to set appropriate stimulation intensities and EMG amplifier gains such that reflex responses could be identified following the production of an artificial motor response by electrical stimulation.

Participants were asked to lay supine with their leg under investigation partially suspended over the end of the clinic plinth. With their leg extended, instrumentation would be affixed prior to collection of data. Instrumentation to permit measurement of tibialis anterior and soleus EMG activity was setup first. The author manually identified EMG electrode placements using a measuring tape and palpation of the lower limb in accordance with the SENIAM guidelines [57]. Skin condition at the stimulation electrode sites was checked in order to ensure skin integrity i.e. no perceived susceptibility to skin irritation. Skin at the EMG recording electrodes sites was cleaned using alcohol wipes (Sterets: isopropyl alcohol 70%). If required, excessive hair was trimmed with an electric trimmer. Following placement of silver-silver chloride EMG electrodes (Ag-AgCl), micropore tape and urisleeve elasticated bandaging was used to secure them in place and prevent gradual loss of adhesion due to movement/gravity. The gain of the EMG amplifier was reduced to the lowest setting labelled 1 (41dB). The earth bonding strap of Figure 6-18 was affixed around the lower leg in an attempt

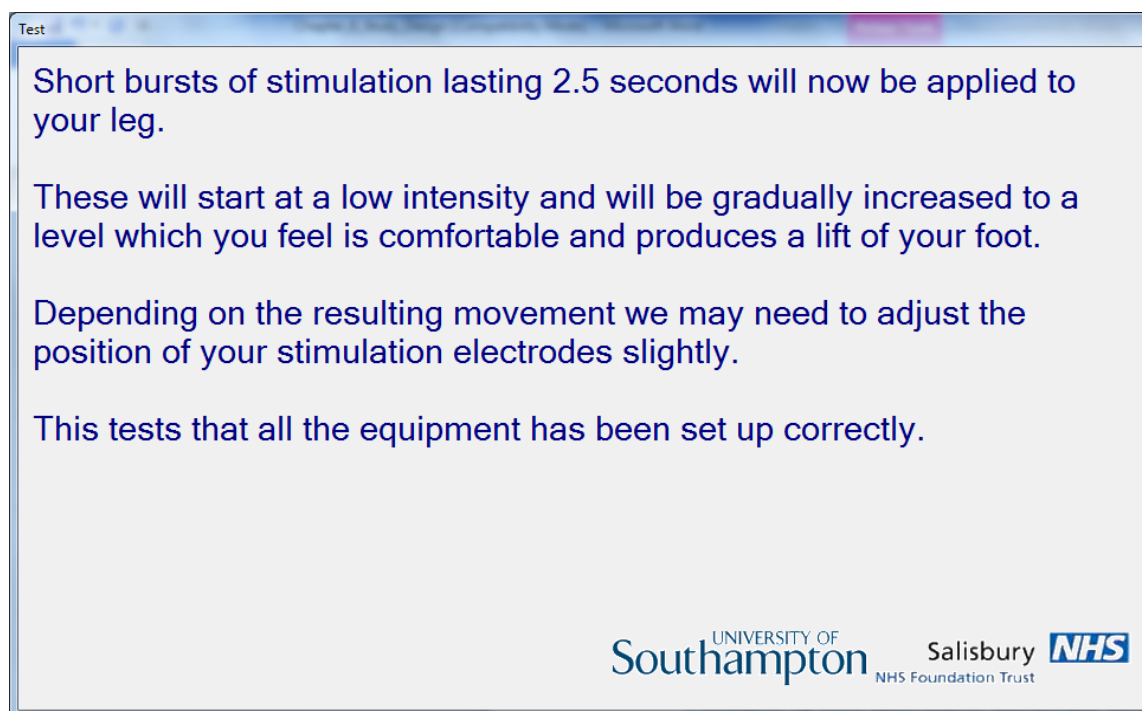
to minimise mains interference. For impaired participants the placement of their FES electrodes generally followed that of their clinic setup and they often attended with them already in place. Unimpaired participants were setup as a new patient would be such that a response of dorsiflexion with moderate eversion was achieved. Bursts of conventional stimulation lasting 2.5 seconds were applied; gradually increasing the current amplitude in 5mA increments until a suitable motor response appropriate for dropped foot correction was attained. This was repeated using catch-like stimulation in order to ensure the participant also tolerated the slightly altered sensation of such stimulation. A depiction of conventional and catch-like stimulation applied as a burst is provided in Figure 8-3 and Figure 8-4 respectively. Further adjustments to electrode positions and stimulation intensity were made as necessary in order to achieve the required ankle movement suitable for dropped foot correction. Stimulation causing moderate to strong contraction of the tibialis anterior generated an M-wave which could be clearly identified on the investigators EMG display of the Stimulation Investigator application. The gain of this EMG channel was increased such that the M-wave exceeded half the maximum range. On the assumption that the soleus EMG signal would not be larger than the tibialis anterior, the gain of this channel was also increased to the same level. If following an increase in tibialis anterior EMG amplifier gain, the M-wave was still absent a number of other factors were assessed. The tibialis anterior was first palpated whilst stimulation applied in order to ensure it was being activated. Should adjustment to stimulation electrodes not be required, reposition and further skin preparation of the skin underneath the stimulation electrodes commonly resolved the problem. Although not found to be required during any of the participant investigation sessions, should artefact have continued to be problematic the EMG amplifier could have been switched to high frequency components only (section 6.3.2).



**Figure 8-3: Depiction of stimuli forming burst of ‘conventional’ stimulation**  
(not to scale)



**Figure 8-4: Depiction of stimuli forming burst of ‘catch-like’ stimulation**  
(not to scale)



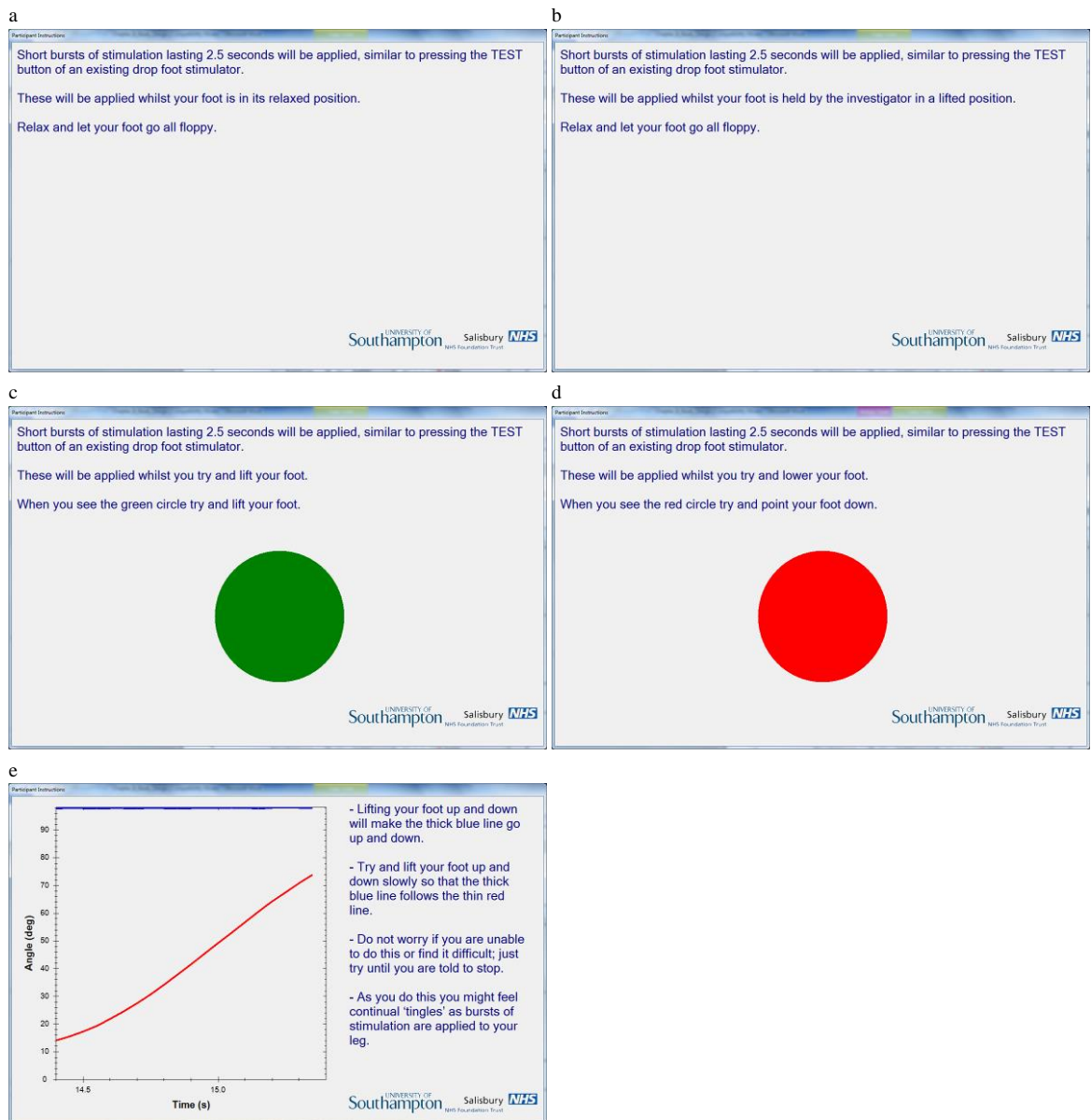
**Figure 8-5: Screenshot of participant display during Phase 1**

### 8.2.2 Phase 2

Phase 2 assessed the effects of bursts of repeated conventional and catch-like stimuli on the excitability and inhibition of spinal reflexes affecting the tibialis anterior and soleus at different muscle lengths and when actively supporting and opposing the movement resulting from stimulation. Having found that the reflex component appeared to be influenced by effort as well as joint position during exploratory data collection, phase 2 sought to control and further investigate these factors.

Figure 8-6 displays screenshot of the participant display which conveyed prompts during each sub-test of phase 2. Bursts of stimulation lasting 2.5 seconds were applied when relaxed with the foot plantarflexed under gravity (Figure 8-6<sup>a</sup>) and when supported in dorsiflexion (Figure 8-6<sup>b</sup>). These two sub-tests investigated the response at different muscle lengths. The same was then repeated when the participant attempted to dorsiflex with (Figure 8-6<sup>c</sup>), and then plantarflex against (Figure 8-6<sup>d</sup>), the movement produced by stimulation. These two sub-tests investigated the response at different muscle length combined with supporting and opposing effort. Each of these scenarios was repeated at 25%, 50%, 75% and 100% (50µs, 100µs, 150µs and 200µs pulse-width respectively) of the identified stimulation intensity. This was completed in order to permit investigation of muscle length and effort effects in addition to possible identification and classification of reflex components depending upon trends with stimulation intensity (i.e. F-wave or H-wave).

Whilst the four sub-tests described so far were in some way representative of a functional task, they were still designed under static conditions i.e. maintained effort either supporting or opposing the movement produced by stimulation. It was wished to repeat this under dynamic conditions therefore sub-test 5 of phase 2 was developed. The participant was asked to dorsiflex and plantarflex their foot in time to a 0.33Hz sinusoid that would vary within 10% of peak plantarflexion and peak dorsiflexion as detected by the ankle goniometer (Figure 8-6<sup>e</sup>). The participant would complete a whole period of this tracking signal (3.0 seconds) before a stimulation burst lasting an additional tracking period was applied.



**Figure 8-6: Screenshot of participant display during Phase 2**

- <sup>a</sup> Relaxed with foot plantarflexed under gravity*
- <sup>b</sup> Relaxed with foot held in dorsiflexion by author*
- <sup>c</sup> Actively dorsiflexing*
- <sup>d</sup> Actively plantarflexing*
- <sup>e</sup> Tracking 0.33Hz sinusoid*

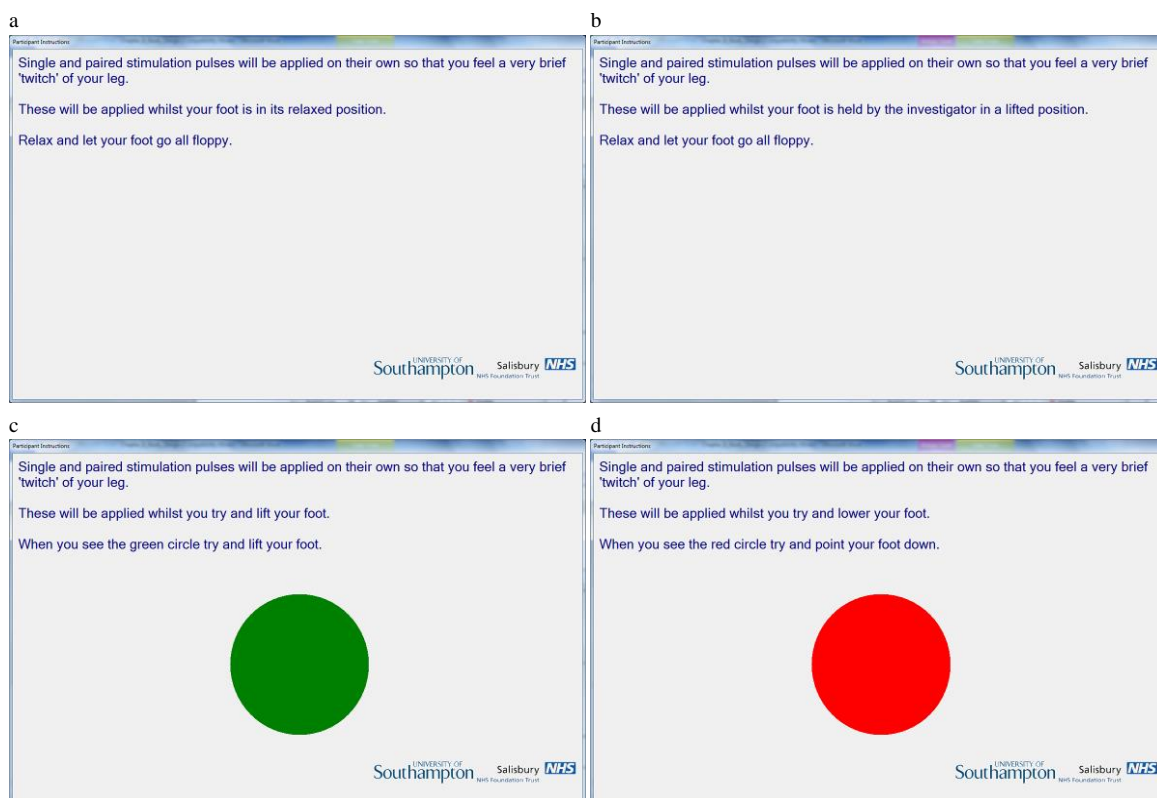
### 8.2.3 Phase 3

Although the bursts of conventional and catch-like stimulation applied in Phase 2 would be akin to that typically applied clinically, interpretation of some measurements would be limited by the properties of applying such a stimulation burst. Other than the final pulse of a burst, EMG features of reflex activity with a latency equal to larger than the



stimulation period of the burst could be occluded by the following artefact or annihilated by subsequent antidromic motor activity. Phase 3 therefore utilised the same protocol as Phase 2 however applied single conventional and catch-like stimulation pulses as opposed to bursts. The presence of longer latency reflexes could be identified prior to the stimulation artefact and activity following subsequent repeated stimuli. The complete physical twitch of a conventional or catch-like twitch rather than just the initial acceleration of the limb could also be assessed.

Figure 8-7 indicates the prompts displayed on the participant display during sub-tests of phase 3. As during phase 2, sub-tests were repeated with the participants' foot plantarflexed under gravity (Figure 8-7<sup>a</sup>), supported in dorsiflexion (Figure 8-7<sup>b</sup>), actively dorsiflexing (Figure 8-7<sup>c</sup>) and actively plantarflexing (Figure 8-7<sup>d</sup>). Twitch stimuli were applied at 25%, 50%, 75% and 100% of the identified stimulation intensity. Measurements made at each stimulation intensity level were automatically repeated five times with a two second pause between each and the mean response computed.



**Figure 8-7: Screenshot of participant display during Phase 3**

<sup>a</sup> Relaxed with foot plantarflexed under gravity

<sup>b</sup> Relaxed with foot held in dorsiflexion by author

<sup>c</sup> Actively dorsiflexing

<sup>d</sup> *Actively plantarflexing*

As concluded during exploratory investigations 2 and 3 (sections 7.2.4 and 7.3.4); it was wished to assess the response of conventional and catch-like twitch stimulation during isotonic and isometric conditions. Through controlling muscle length and hence varying tension, different muscle afferents would be active in conveying information to the CNS (section 2.2.5). Phase 4 and 5 were therefore designed to further investigate these afferent effects on the response to conventional or catch-like stimuli when applied during isometric and isotonic conditions.

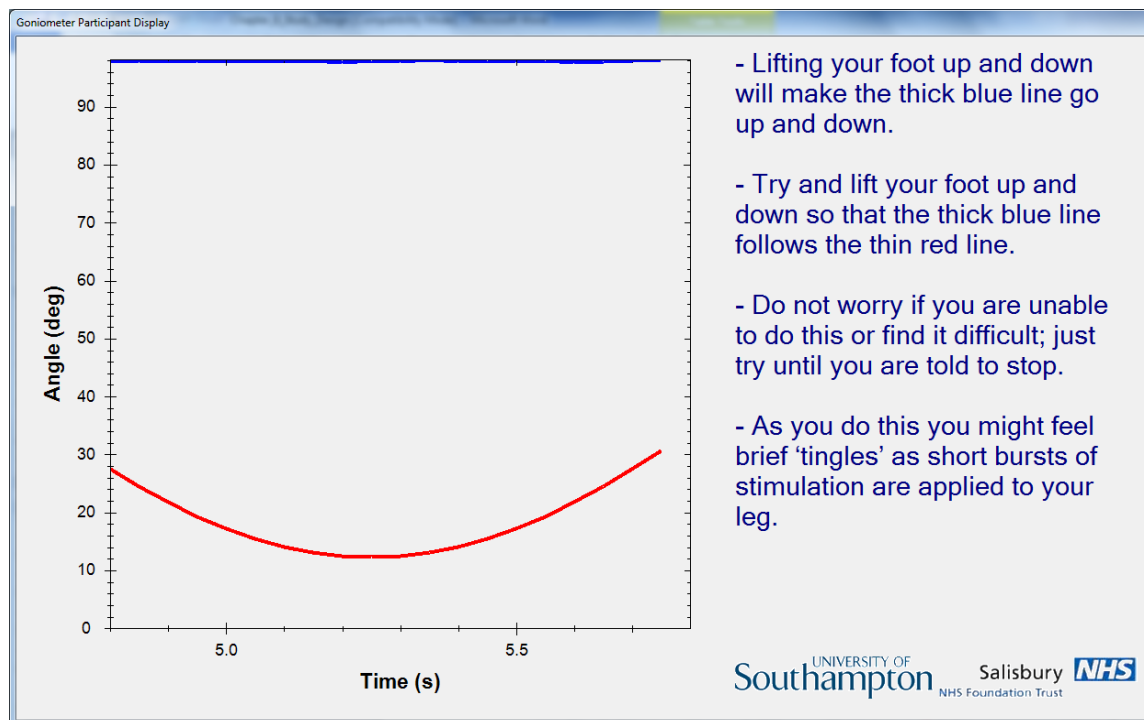
#### 8.2.4 Phase 4

Phase 4 investigated the effect of conventional and catch-like stimuli on the excitability and inhibition of spinal reflexes affecting the tibialis anterior and soleus muscles when triggered from ankle joint angle during isotonic contractions. Single conventional and catch-like stimuli were applied at different joint angles when the foot was free to move suspended over the edge of a clinic plinth and the participant asked to follow a 0.33Hz sinusoidal signal indicating ankle flexion and extension.

As discussed in section 2.2.5, during a muscle contraction different afferent neurons within the muscle will report information to the UMN system. Type Ia afferent neurons report information in response to muscle stretch and rate of muscle stretch. Type II afferent neurons just fire in response to muscle stretch. Type Ib (golgi) afferent neurons fire in response to tension being developed within the muscle. If an isotonic movement is considered the muscle length will vary throughout the contraction and hence neurons reporting stretch and rate of stretch (IA and II) would be expected to fire. During a slow isotonic movement tension in the muscle would be small and hence the type Ib neurons would be expected to fire less. Although this is a crude simplification of a complex system it represents an extreme which will be contrasted to when discussing Phase 5.

At the start of Phase 4 the participant was asked to maximally dorsiflex and plantarflex their foot which would set the maxima and minima of a 0.33Hz sinusoidal angle tracking signal. The participant was then asked to try and dorsiflex and plantarflex their foot in time with this sinusoid whilst the angle of the ankle joint was also displayed on the same plot. Figure 8-8 provides a screenshot of the participant display during this sub-test. Twitch stimulation of 200µs pulse-width was applied as the participant's joint angle passed through neutral from plantarflexion to dorsiflexion. This was repeated

when passing through: 75% maximum dorsiflexion, neutral from dorsiflexion to plantarflexion and 75% maximum plantarflexion. If the participant was unable to follow the tracking signal such that stimulation was not reliably triggered, three attempts were made before this was noted and the next sub-test proceeded to. The above was first completed with single conventional stimuli and then catch-like stimuli. All stimulation was applied at 200 $\mu$ s as repetition at lower intensities was considered to be too demanding on time and physical participant effort.



**Figure 8-8: Screenshot of participant display during Phase 4**

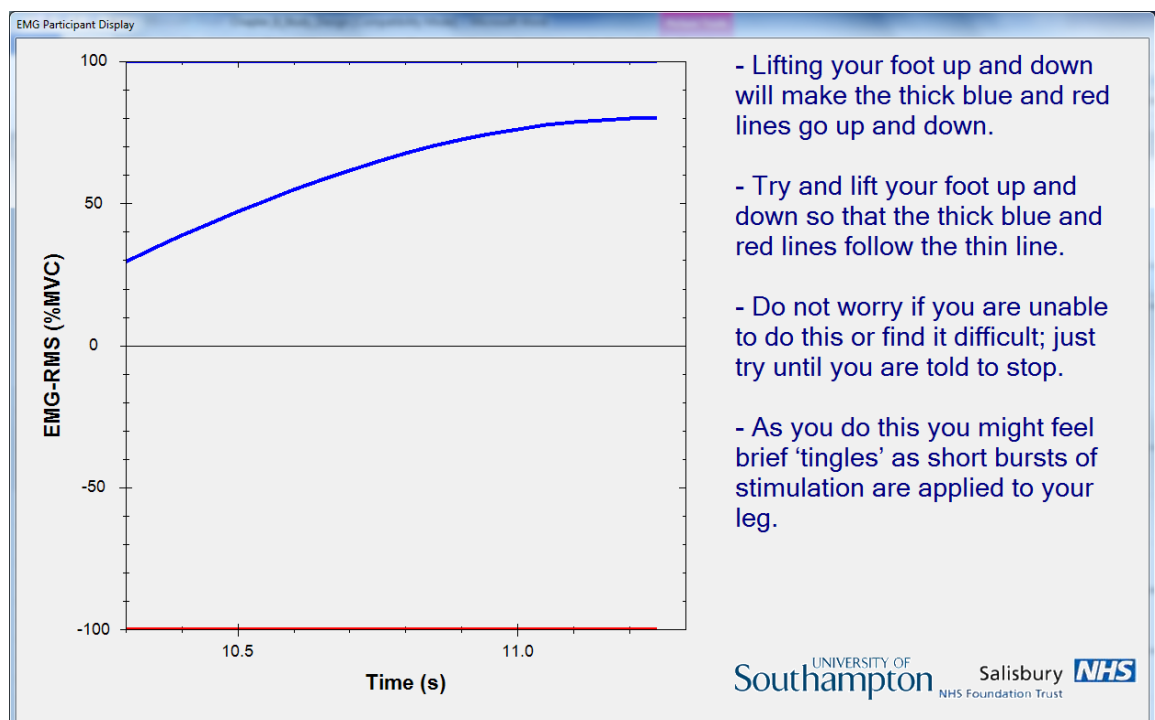
### 8.2.5 Phase 5

Phase 5 investigated the effect of single and catch-like stimuli on the excitability and inhibition of spinal reflexes affecting the tibialis anterior and soleus muscles when triggered from EMG levels during isometric contractions. Stimuli were triggered by the participant as they attempted to follow a 0.33Hz sinusoidal signal indicating percentage of maximum tibialis anterior and soleus smoothed absolute EMG level whilst their the foot was constrained at plantigrade.

The ankle bracket described in section 6.5 constrained the participant's ankle at plantigrade, minimising variations in muscle stretch. With minimal muscle stretch but high levels of muscle tension, considerable activation of Ib (golgi) neurons and little type Ia and II activation was expected. This is opposite to the hypothesised scenario of

afferent neuron activation described in Phase 4 (section 8.2.4). Hence the findings of Phase 5's isometric responses could be compared and contrasted to the isotonic ones of Phase 4.

The participants' foot was held at 90 degrees (or as close to this that can be achieved) by the isometric ankle bracket. They were asked to perform a maximum voluntary dorsiflexion and plantarflexion contraction in order to determine peak tibialis anterior and soleus smoothed absolute EMG levels. A slowly varying sinusoid varied within 80% of these maxima (Figure 8-9) as the participant was asked to dorsiflex and plantarflex their foot against the constraining straps in time with this. The participant's voluntarily achievable smoothed absolute tibialis anterior and soleus EMG activity was also displayed on these plots to act as feedback. If a participant was unable to reliably trigger stimulation via voluntary EMG, three attempts were made before this was noted and the next phase of the study was proceeded to. Single conventional or catch-like stimuli of 200 $\mu$ s pulse-width were applied as the participants muscle activation went from attempting to plantarflex to attempting to dorsiflex, and then attempting to dorsiflex to attempting to plantarflex. All stimulation was applied at 200 $\mu$ s as repetition at lower intensities was considered to be too demanding on time and participant physical effort.



**Figure 8-9: Screenshot of participant display during Phase 5**

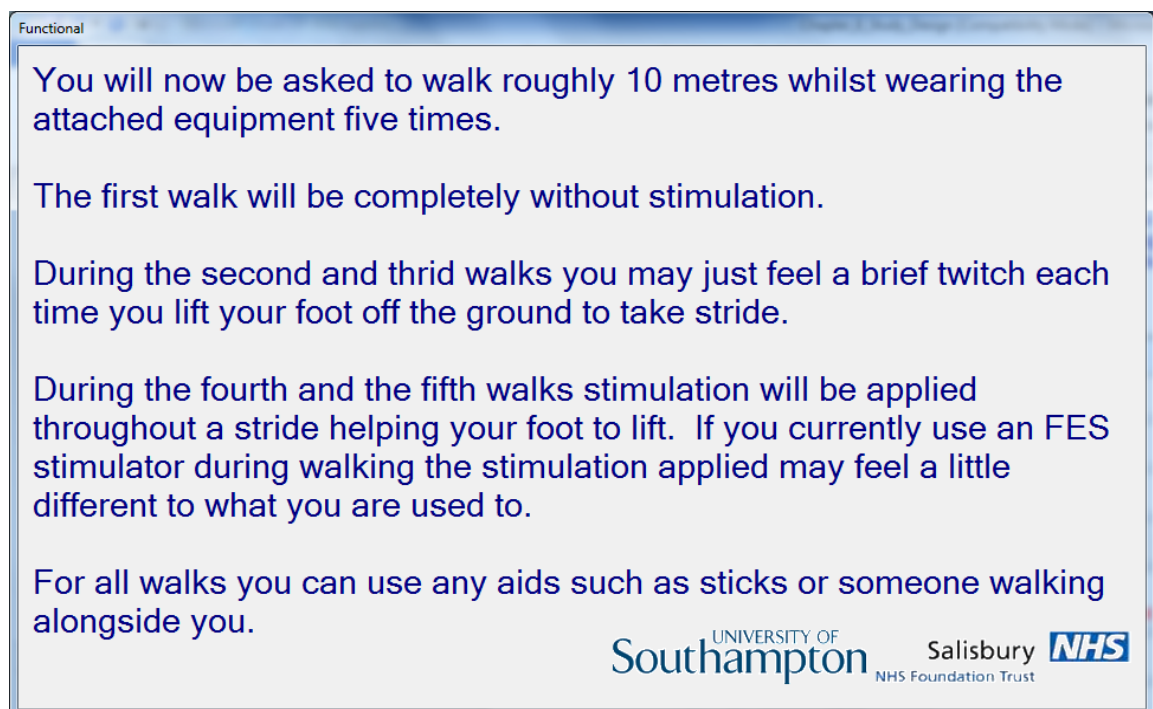
### 8.2.6 *Phase 6*

Phases 2 to 5 took place under controlled conditions where variables such as participant effort, muscle length and muscle tension were controlled in order to improve understanding of using conventional and catch-like stimulation for clinical use. Whilst such controlled conditions enabled individual factors to be assessed, they remained different to the functional scenario of use in a dropped foot stimulation system. In such an instance, factors such as balance, posture and coordinated muscle movements may also influence the response to stimulation. Phase 6 therefore assessed the spinal reflex response to conventional and catch-like stimulation when applied at different instances and durations within the gait cycle. Although there was no attempt to control factors such as muscle length, muscle tension and effort, Phase 6 could be likened to elements of phases 2, 4 and 5 at different points within the gait cycle. The portable nature of the developed instrumentation allowed the function of a dropped foot stimulator incorporating conventional and catch-like stimulation to be realised and investigated during the final two sub-tests of Phase 6.

Throughout sub-tests of Phase 6, stimulation was triggered from a footswitch placed underneath the heel of the leg under investigation. Once participants had replaced their shoe containing a footswitch, the electro-goniometer was reattached in order to record ankle angle during gait. All instrumentation (including the laptop) was powered from batteries and hence was untethered and wheeled on a trolley alongside them during phase 6 sub-tests. The participant was first asked to stand and walk 10 metres without any stimulation. This collected voluntary tibialis and soleus EMG over five unstimulated strides and was intended for comparison purposes with the subsequent four walks. During all 10 metre walks impaired participants could use additional walking aids such as a stick and the author walked alongside them should they require manual handling assistance. The following two walks applied a single conventional and catch-like stimuli respectively following heel rise detected by the footswitch. This investigated tibialis anterior and soleus EMG responses to such stimuli applied in late stance when the swing phase of gait was commencing. It was intended for these findings to be compared and used to evaluate whether there appeared to be a

neurophysiological advantage to commencing an envelope of conventional dropped foot stimulation with a single catch-like stimuli (doublet).

The final two walks applied conventional and catch-like stimulation throughout the swing phase of gait and into the load bearing period of stance. Stimulation was timed using the footswitch and was applied from the detection of heel rise to detection of heel strike with 200ms extension period of stimulation during loading. Such a stimulation envelope was akin to that applied during dropped foot stimulation which was depicted in Figure 4-7.



*Figure 8-10: Screenshot of participant display during Phase 6*

### 8.2.7 Summary

Table 8-2 summarises the described phases and associated sub-tests of the developed investigation protocol. The reader is encouraged to familiarise themselves with this table in order to aid clarity of later chapters when referring to sub-tests. A copy of the approved and utilised study research protocol is included within Appendix E.

<i>Phase</i>	<i>Description</i>	<i>Sub-test name</i>	
		<i>Conven- tional</i>	<i>Catch-like</i>
<b>Phase 1</b>	<b>Confirmation of effective set up and configuration of instrumentation such that M-wave can be identified following an electrical stimulation pulse.</b>	-	-
<b>Phase 2</b>	<b>Stimulation burst applied under static and dynamic conditions.</b> <b>Each test repeated at 25, 50, 75, 100% of normal functional stimulation pulse-width.</b> No effort, foot in plantarflexion at rest under gravity. No effort, foot supported in dorsiflexion by Principal Investigator (PI). Actively dorsiflexing. Actively plantarflexing. Dynamically tracking joint angle sinusoid without support from PI.	211 221 231 241 251	212 222 232 242 252
<b>Phase 3</b>	<b>Stimulation twitch applied under static conditions.</b> <b>Each test repeated at 25, 50, 75, 100% of normal functional stimulation pulse-width.</b> No effort, foot in plantarflexed position under gravity. No effort, foot supported in dorsiflexion by PI. Actively dorsiflexing. Actively plantarflexing.	311 321 331 341	312 322 332 342
<b>Phase 4</b>	<b>Stimulation twitch applied at following phases of goniometer signal when asked to track sinusoid:</b> Plantigrade, progressing into dorsiflexion 75% maximum dorsiflexion, progressing to peak dorsiflexion Plantigrade, progressing into plantarflexion 75% maximum plantarflexion, progressing to peak plantarflexion	411 421 431 441	412 422 432 442
<b>Phase 5</b>	<b>Stimulation twitch applied at following phases of EMG levels when asked to track sinusoid:</b> Tibialis Anterior EMG <sub>ABS</sub> > 50% Max Soleus EMG <sub>ABS</sub> < 50% Max Tibialis Anterior EMG <sub>ABS</sub> < 50% Max Soleus EMG <sub>ABS</sub> > 50% Max	511 521	512 522
<b>Phase 6</b>	<b>During 10m, stimulation synchronised to heel rise by footswitch</b> Unstimulated walking EMG Single stimuli twitch applied at heel rise Doublet stimuli twitch applied at heel rise Conventional stimulation throughout swing Doublet stimulation throughout swing	61 62 64	63 65

Table 8-2: Summary of investigation phases and sub-tests

### 8.3 Research Governance

Within the UK's Department of Health governance role, the National Research Ethics Committee (NRES) requires ethical approval for studies defined as research within the NHS. As a primary aim of this study was to derive generalisable new knowledge it was classed as research and hence required approval.

In order to gain research ethics approval the author submitted an application for the study using the NRES Integrated Research Application System (IRAS). Dr Paul Taylor, Consultant Clinical Engineer, Salisbury NHS Foundation Trust was named as the chief investigator with the author as principal investigator. Local Research and Development Approval within Salisbury NHS Foundation Trust was gained following discussion with the Information Governance Manager, Head of Directorate and research and development support officer of the Research Design Service (RDS).

Following submission of this approval through the IRAS system, the study was reviewed by the Southmead, Bristol Research Ethics Committee. The committee raised concerns regarding the proposed inclusion of female unimpaired participants that may be unknowingly pregnant and their use of electrical stimulation. As the effect of electrical stimulation on the unborn child is not known, the committee requested that female unimpaired participants of child bearing age were asked to complete a pregnancy test. This request generated a number of further ethical issues which could not easily be addressed. Regarding the progression of the study, sufficient unimpaired participant numbers could be gained from solely recruiting males. No gender effects were expected in the study and the population being recruited from was sufficient in size to enable recruitment of 10 unimpaired male participants. An amendment to recruit just male unimpaired participants was therefore re-submitted along with details of how this decision had been reached in light of the committee's request (Appendix F).

In parallel to the IRAS application, documentation was submitted to the School of Electronics and Computer Sciences ethics Committee within the University of Southampton. This was approved subject to a favourable judgement from the NHS ethics committee.

The amendment was submitted to both the NRES and ECS ethics committees and approval was given to begin recruitment.



During unimpaired participant recruitment the 'Participant Information Sheet v1.2u' (Appendix G) was provided to staff and students of the Clinical Science and Engineering Department, Salisbury District Hospital and the Electronic Systems Design Group, School of Electronics and Computer Science (ECS), University of Southampton. Those interested were invited to approach the chief investigator or principal investigator should they wish to participate.

Impaired participants were recruited from patients receiving FES treatment at the National Clinical FES Centre, Salisbury District Hospital with a review appointment scheduled during the research study period. The notes of such patients who had had a stroke were screened by the author at least six weeks in advance of their appointment. The author was an existing member of the clinical care team responsible for seeing such patients. Those thought to meet the research criteria were passed to the chief investigator (Dr Paul Taylor) for review. If in agreement the chief investigator sent a letter inviting them to participate (Appendix H) accompanied by 'Participant Information Sheet v1.1i' (Appendix I). Recipients of the information sheet who expressed an interest in participating in the study were asked to contact the principal investigator. Should they wish to participate in the study an investigation session was scheduled preceding or following their intended outpatient review appointment at the National Clinical FES Centre.

Recruitment of impaired participants was higher than expected with a number expressing a wish to participate on the day of attending their clinic appointment. A substantial amendment to the research protocol in which the sample size of both groups was increased from 10 to 15 was submitted to the NRES and ECS ethics committees. The number of unimpaired participants was also increased so as to improve comparison between the groups and compensate for any incomplete datasets. The amendment was approved such that fourteen impaired participants and twelve unimpaired participants eventually completed the study.

Copies of the consent form, unimpaired and impaired participant information sheets and research protocol that gained approval for use during the study are included in the Appendices of this thesis.

## Chapter 9 Data Analysis

Prior to presenting the results of this study, a brief summary of the data organisation and analysis techniques used will be outlined. Such an overview will convey how trends were identified and analysed whilst keeping analysis of the large dataset manageable.

### 9.1 Motivation

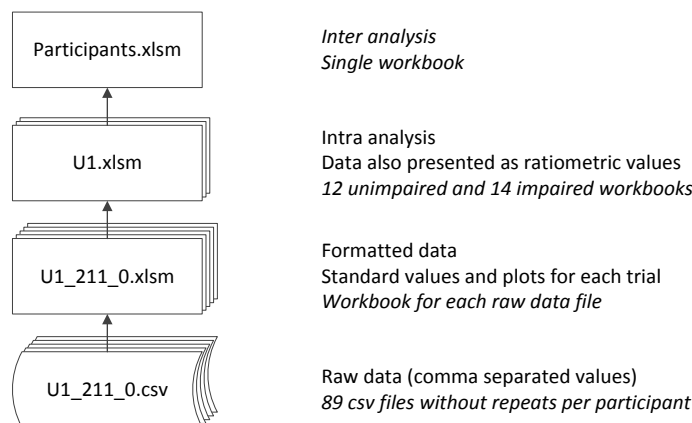
The Stimulation Analyser application of Chapter 6 significantly aided visual comparison and identification of trends across the author's EMG responses during exploratory data collection. However it did not incorporate tools for quantitative measurement and data comparison that would be required when analysing data collected whilst following the research protocol. Following data collection amongst unimpaired and impaired participants, intra and inter-participant analysis required measurement. Over 2400 CSV files with a total file size of over 13 gigabytes were collected during data collection. Due to the size and number of these, a partially automated system which enabled analysis to be applied to one individual participant and effectively stored as a template and applied to others was developed.

### 9.2 Data Analysis: Design and Structure

Microsoft Excel was selected for the purposes of creating a semi-automated data analysis system. In addition to built-in analysis tools, support of the Microsoft Visual Basic programming language to record and create macros to automate analysis was a prime motivation for this choice.

A tree structure of Excel workbooks was used to permit intra and inter-analysis of data (Figure 9-1). The levels of this tree will now be briefly discussed.

At the lowest and most numerous level, were the CSV files automatically generated by the Stimulation Investigator application described in Chapter 6. For each of these files a corresponding 'Formatted Data' workbook was created which automatically imported, formatted and analysed data from each trial. In order to compare trials within a phase and across participant's investigational session, an 'Intra-analysis' workbook the level higher was created. An intra-analysis workbook existed for each participant and contained macros to automatically extract relevant data from each of the formatted data files of the level below. This workbook also had the ability to display data from any trial of that participant through selection from a drop down menu. At the highest level, a workbook entitled 'Participants.xlsm' copied data to and from each of the intra-analysis workbooks below. Data copied from the intra-analysis workbooks was expressed as a percentage of a specific variable such that ratiometric inter-analysis data comparisons could be made. Within 'Participants.xlsm' data was grouped into unimpaired and impaired sets and data comparison completed.



**Figure 9-1: Tree structure of automated data analysis files**

All control of automated analysis was completed from Participants.xlsm with data and function calls sent to the intra-analysis workbooks below it. Formatting, equations and graphical data analysis applied to blank templates of the formatted data workbooks along with an intra-analysis workbook were created and saved within a folder entitled 'master'. A Microsoft C# application was written to search through the folder structure of specified participants searching for comma separated files. Where a CSV file was found an appropriate blank formatted data file was copied and renamed appropriately. Having applied blank templates, automated analysis would be initiated through Participants.xlsm and the computing system left to import and analyse data. On a

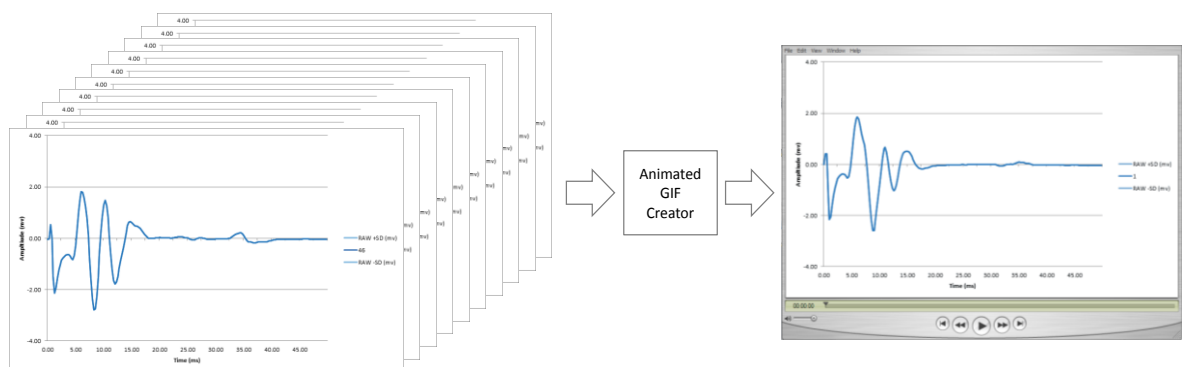
modern computer running the latest operating system and version of Microsoft Excel 2010, formatting and analysis of all participants would be completed within approximately five hours. This system enabled data analysis applied to workbooks within the master folder to be applied to all other participants automatically.

### 9.3 Custom Analysis Tools

Specific features used when identifying data trends and completing analysis will now be discussed.

#### 9.3.1 Burst analysis

Due to the exploratory nature of the data collected not all outcome comparisons were known from the outset of analysis. During analysis of phase 2 trials (utilising a burst of conventional or catch-like stimulation), the response of each individual stimuli plotted against time would be used to identify trends over the burst. Form controls, allowing the response to each stimuli contained within a burst to be scrolled through, aided review and visual identification of data trends. A further refinement of this system included a macro which stepped through each pulse of the burst exporting the EMG - time plot as an image file. A Microsoft Visual C# application was written which combined these graphics files into an animation (animated graphics interchangeable format file -.GIF) that could then be played as a video on loop (Figure 9-2). Animation files were created for all bursts of all participants during early stage data analysis in order to identify trends warranting further investigation.



**Figure 9-2: Animated stimulation GIF creator**

*Custom data analysis/interpretation tool written in Microsoft Visual C#*

During analysis of the bursts of stimulation a small timing inaccuracy was noted between the stimulation output and the DAQ measurements. As an example of this, the 50<sup>th</sup> pulse of a 50ms stimulation period burst may be seen at 2452ms rather than the expected 2450ms. This timing inaccuracy was not consistent across trials or participants and hence needed to be manually corrected for in every data file. The timing inaccuracy was identified for the last pulse of every data file and corrected for. This correction would often be equivalent to adjustment by one sampling period (0.25ms) every 10 stimulation pulses (500ms). Although time consuming, this correction was needed in order to permit analysis of changes in EMG features over the course of a stimulation burst as will be discussed in the following section 9.3.2.

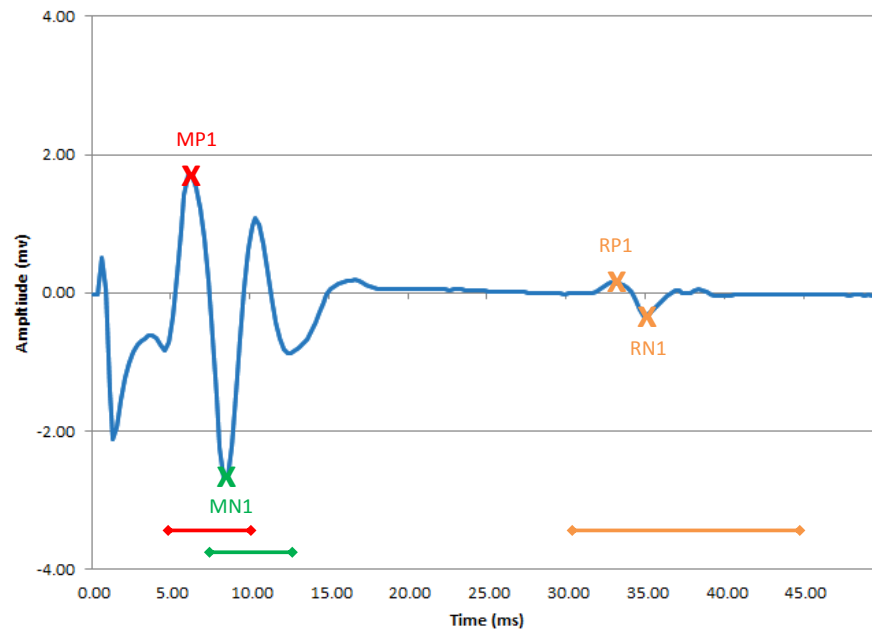
### 9.3.2 *EMG feature analysis*

As discussed in Chapter 5, the principle outcome measurements would be direct and reflex components of tibialis anterior EMG activity. In order to expedite data analysis, an automated method of identifying peak to peak M- and reflex wave amplitude was utilised.

In keeping with literature, each participant's M-wave was consistent in its general shape and latency following a stimulation pulse. Similar to the author's exploratory data collection (section 7.1.3), the minimum and maximum peak latencies of an M-wave following a stimulation pulse were generally identified between 5.0ms and 15.0ms. For all participants, the M-wave was a bi- or tri-phasic waveform in which whether the first peak was positive or negative first was consistent across all following responses of the participant. A separate window for which to identify the maximum positive (maximum) and negative (minimum) of the M-wave was specified for each participant. Separate windows for these peaks were identified as this permitted greater control over avoiding inaccuracies which could potentially be introduced by remaining stimulation artefact.

Whether the first peak of the reflex component was positive or negative was not consistent across responses of a participant. At the latency associated with reflex components (30ms>), the stimulation artefact was no longer present and therefore the minimum and maximum peaks could be identified over a single time window.

Figure 9-3 provides an example of a 50ms tibialis anterior EMG window following a stimulation pulse. The windows in which maximum and minimum values were identified in order to compute peak to peak M-wave and reflex wave amplitudes are indicated.



Measurement Name	Window Start (ms)	Window End (ms)
MP1	5.0	10.0
MN1	7.5	12.5
R1	30.0	45.0

$$M1_{p-p} \text{ (mV)} = MP1 - MN1$$

$$R1_{p-p} \text{ (mV)} = RP1 - RN1$$

*Figure 9-3: Example of peak to peak automated EMG measurement of direct and reflex components*

Having viewed data using the animated GIF format (9.3.1,) the latency of both the M- and reflex waves was seen to vary slightly over bursts as well as different trials. M-wave and reflex window size was identified for tibialis anterior and soleus EMG responses for each participant by reviewing the 200 $\mu$ s pulse-width data files for trials 211, 221, 231 and 241 (Table 8-2).

The results gained when using the data analysis techniques described will be presented in Chapter 10.



## **Chapter 10 Results & Discussion**

### **10.1 Overview**

Results are presented in the order that the investigation phases were completed i.e. 2 to 6. For each phase a summary of its purpose is provided before data from unimpaired and impaired participant groups is presented and discussed. Where trends or features of interest are evident, further discussion and explanation is given. If trends contribute to a theme present across multiple phases, these are reflected upon when encountered. In order to logically introduce and justify analysis of the collected data, examples from individual participants are at times utilised for this purpose. On occasions data has been excluded during analysis and upon such instances the criteria and justification for this is given. Results of individual sub-tests are referred to using the numerical code given in Table 8-2.

### **10.2 Data Collection Process**

Two unimpaired and two impaired participants completed the study before further recruitment took place. Data from these four participants was reviewed and minor amendments made to the formatting of saved data in order to aid analysis of subsequent participants. No significant changes were introduced to the protocol or instrumentation and hence data from these first four participants was included for analysis with subsequent participant data.

During data collection there were no adverse incidents and recruitment and investigation took place within the allocated time periods. Data from one impaired individual was excluded due to incorrectly configured hardware which was identified after data collection and could not easily be corrected for (I3 –Appendix K).



Influenced by the populations from which participants were recruited from, general physical differences existed between the groups. Unimpaired participants were recruited from male staff and students and had a mean age of 33 years. The impaired participant group comprised of five males and nine females and was older with a mean age of 62 years. Appendix K provides the gender and age of each of the unimpaired and impaired participants at time of their assessment.

Whilst other general physical differences were not quantitatively recorded, the impaired participants were typically of larger body-mass-index. This may have been associated with reduced physical ability following motor impairment due to their stroke. With a generally higher body fat composition and weakened paretic muscles under investigation, the magnitude of recorded EMG signal was typically less in the impaired when compared to unimpaired participant group. Slightly poorer skin condition associated with age or impaired circulation, also contributed to this measurement effect and resulted in typically higher EMG amplifier gain settings being required. Use of larger gain settings reduced the signal to noise/artefact ratio, potentially introducing a larger error component to the automated data analysis method of section 9.3.2. Whilst adhesion of EMG recording electrodes could be more challenging with dry or hairy skin (particularly on the soleus where the effect of gravity impeded their adhesion) micropore tape successfully maintained electrode contact.

All impaired participants had been using FES for 6 months or more following a stroke. Within the impaired participant groups a range of impairments were represented e.g. varying voluntary motor activation ability, varying severities of spasticity. Whilst quantitative assessment of such complex characteristics is challenging, attempts at assessment, such as muscle strength testing (e.g. Medical Research Council score) may have aided sub-group analysis and furthered discussion. Where available, Appendix K includes information such as ten metre walking speed at the time of assessment which begins to give an indication of physical ability. Also included are identifiers for unimpaired (U\_) and impaired (I\_) participants when referring to individual datasets.

Neurophysiological responses should be similar across participants irrespective of gender however factors such as obesity, poor skin condition and muscle strength/condition are known to affect measurement of EMG. Due to the exploratory nature of this research it was not possible to recruit a matched control group. Ideally cohorts would be matched for characteristics that may influence their physiological response to electrical stimulation, and the measurement of this, such as body composition, skin/electrode impedance and age.

### 10.3 Phase 2

Phase 2 assessed the effects of bursts of repeated conventional and catch-like stimuli on the excitability and inhibition of spinal reflexes affecting the tibialis anterior and soleus at different muscle lengths and when actively supporting and opposing the movement resulting from stimulation (section 8.2.2). The results from sub-tests 21\_ to 24\_ share a common analysis approach and are presented together to aid comparison between them. As described in section 9.3.2, identification of M1 and M2 and R1 and R2 during sub-tests incorporating catch-like stimulation was complicated due to the apparent delayed and superimposed response of the two stimulation pulses forming the doublet. Therefore only EMG results from sub-tests incorporating conventional stimulation will be presented when exploring Research Question 1 (page 52) through phase 2 analysis.

#### *10.3.1 Phase 2 Analysis: Motor and reflex response to conventional stimulation*

The results from first the unimpaired and then impaired participant groups are presented. For each, the direct motor activation (M-wave) and then reflex components are considered. A summary discusses differences between these groups and summarises the findings from sub-tests 21 to 24.

The peak M-wave and peak reflex component amplitude for each stimulation pulse of the fifty pulse burst was computed using the automated method of section 9.3.2. The mean value over the burst was then calculated for each participant. In order to permit inter-participant analysis, direct and reflex evoked potentials were expressed as a ratio to peak M-wave attained during sub-test 211 at 200 $\mu$ s. Figure 10-1 to Figure 10-4 and Figure 10-5 to Figure 10-8 plot the mean of these values against stimulation pulse-width for unimpaired and impaired participants respectively.

The EMG amplifier of section 6.3 had a maximum gain of 63dB which corresponded with an amplification range of approximately 3.5mV. If expressing EMG features as a ratio to levels less than one tenth of this range (0.35mV), ill-conditioning of these ratiometric outcomes in the presence of measurement noise started to skew data trends. Therefore participants were excluded from analysis if their peak M-wave (peak-to-peak) was less than 0.35mV. Data from one unimpaired participant and one impaired participant were excluded from this specific analysis due to this criterion (U5, I6 - Appendix K).

**Unimpaired participants: Direct motor activation**

Observing Figure 10-1 to Figure 10-4 for all sub-tests, M-wave amplitude increases with pulse-width in a manner similar to that reported in literature. The M-wave amplitude appears to plateau towards a maximum as the pulse-width is increased to a level producing a strong functional movement at a tolerable level of sensation.

Although clear within group variation, there appears elevated M-wave amplitudes at all pulse-width values during sub-test 221 compared to 211. During sub-test 211 (Figure 10-1) the ankle began at rest under gravity and hence the tibialis anterior went from an extended to shortened muscle length over the course of the resulting movement. During sub-test 221 (Figure 10-2) the ankle was supported in full flexion with moderate eversion at the point that stimulation was applied and hence the tibialis anterior began at a shortened muscle length. Comparison of Figure 10-1 to Figure 10-2, suggests that M-wave amplitude increases as the tibialis anterior is shortened.

Sub-tests 231 and 241 incorporated the participant's voluntary effort to dorsiflex (231) and plantarflex (241) whilst conventional stimulation was applied. Comparing the M-wave trace of sub-test 221 (Figure 10-2) to that of 231 (Figure 10-3), they are similar and suggest that the addition of voluntary effort has made little difference to M-wave amplitude.

During sub-test 241 (Figure 10-4) the tibialis anterior remained extended due to the participant's voluntary plantarflexion. The M-wave amplitude during 241 is the lowest across all intensities compared with the other sub-tests of the phase and supports the hypothesis that M-wave amplitude is modulated with muscle length. This characteristic is further discussed during analysis of sub-test 251.

**Unimpaired participants: Reflex mediated activation**

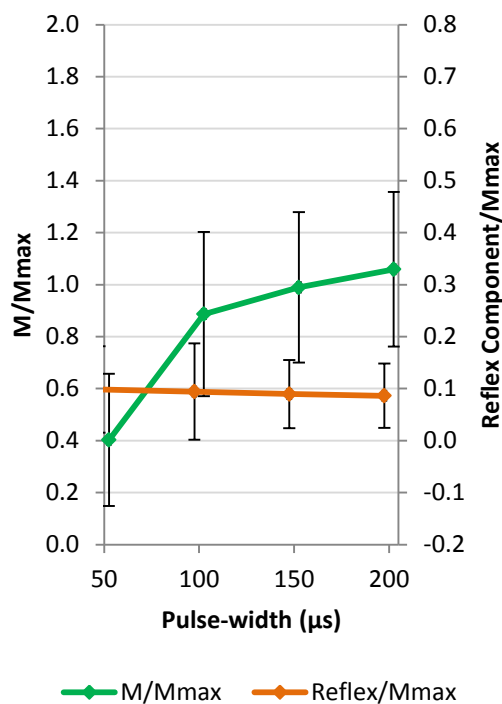
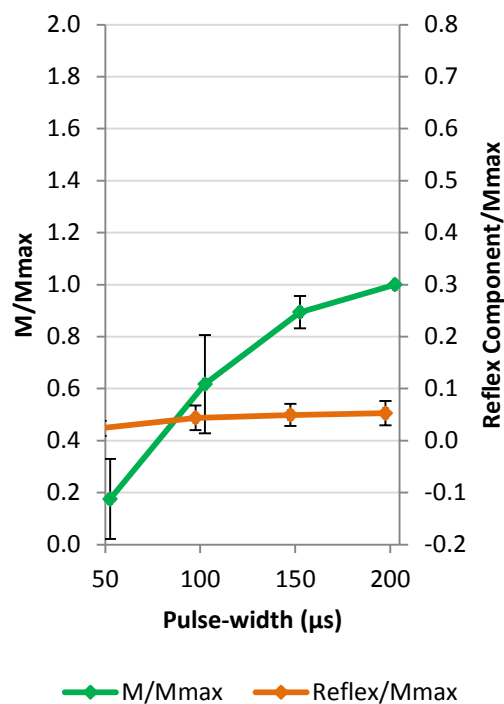
Reviewing a selection of animation sequences using the animated GIF converter of section 9.3.1, when present, reflex wave activity was sporadic with components seen following some rather than all stimulation pulses of a burst.

The trend in reflex component during sub-test 211 (Figure 10-1) appears essentially the same as 241 (Figure 10-4) and reflects that reflex components were minimal and of comparable magnitude to noise. Observing animations of sub-test 221, sporadic reflex activity was more frequent. Assessing this component in relation to pulse-width (Figure 10-2), the amplitude appears reasonably constant. If this reflex component was of H-wave origin, the amplitude would be expected to reduce with increasing stimulation

pulse-width. This however does not appear so, with reflex components appearing approximately constant at the four pulse-width values assessed. The elevated reflex components seen during sub-test 221 compared to sub-tests 211 and 241 suggest that it is partially associated with joint angle.

The reflex component during sub-test 231 (Figure 10-3) is largest but demonstrates substantial variation. Reviewing individual participant trends, the large variation is accountable to what appear two populations: those in which reflex components were present and those where it was essentially absent. In those where reflex component are seen, the magnitude of its presence is influenced by voluntary effort.

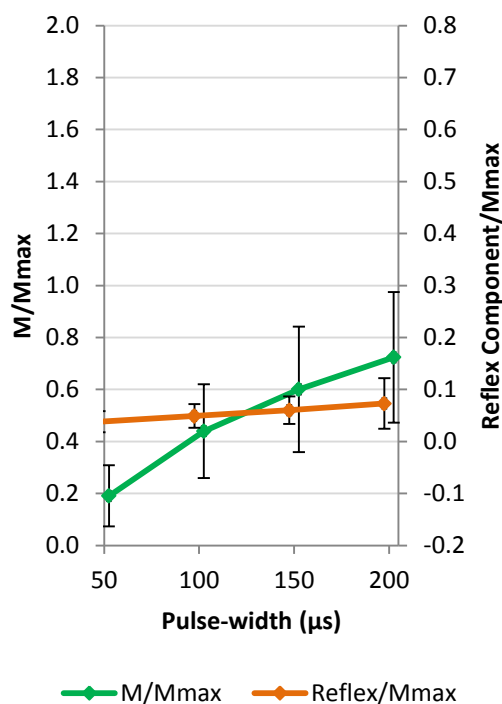
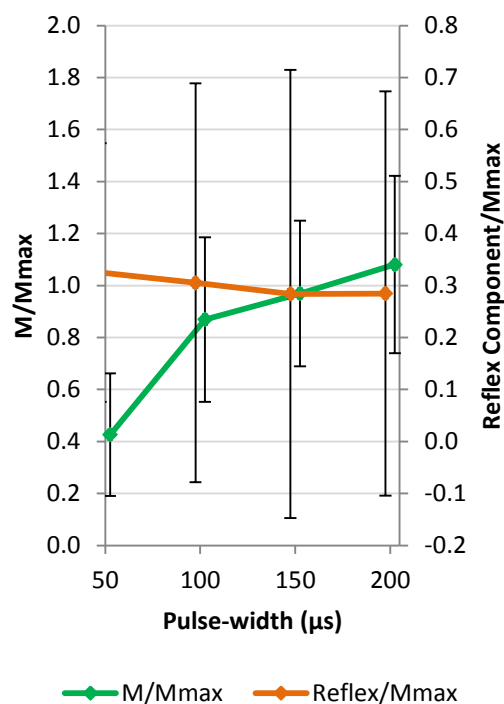
It should be noted that the automated analysis method used to identify reflex components would be susceptible to misinterpretation of voluntary activation and hence the reflex component of Figure 10-3 may be artificially high.



**Figure 10-1: Unimpaired sub-test 211: M-wave and reflex component ratio against pulse-width**

Ankle relaxed and plantarflexed under gravity (n=11)

Ankle relaxed and supported in dorsiflexion (n=11)



**Figure 10-3: Unimpaired sub-test 231: M-wave and reflex component ratio against pulse-width**

Ankle voluntarily dorsiflexed (n=11)

Ankle voluntarily plantarflexed (n=11)

Figures include  $\pm$  one standard deviation error bars

**Impaired participants: Direct motor activation**

In a similar manner to the unimpaired data, M-wave amplitude increases towards a plateau when plotted against pulse-width as shown in Figure 10-5 to Figure 10-8 for all sub-tests.

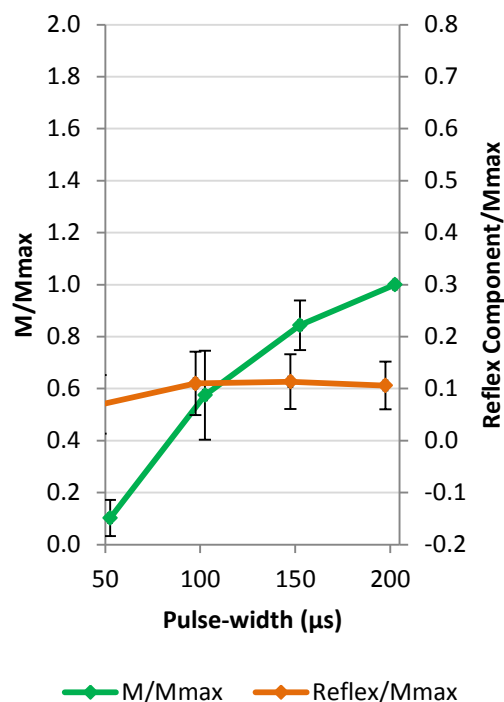
Although clear within group variation, the M-wave amplitude of sub-test 221 (Figure 10-6) appears greater than that of 211 (Figure 10-5) and 241 (Figure 10-8). In some participants, this may suggest that M-wave amplitude appears larger at shortened muscle lengths.

M-wave amplitude appeared slightly smaller during sub-test 231 (Figure 10-7) compared to 221 (Figure 10-6). This may have been due to the impaired participants foot being supported at a greater degree of dorsiflexion in sub-test 221 than what the combination of the electrical stimulation and limited or absent voluntary activity could be achieved in 231. This further supports a trend for the tibialis anterior M-wave amplitude to appear slightly greater when at a shortened muscle length.

M-wave amplitude was lowest at all pulse-width intensities above 50 $\mu$ s during sub-test 241 (Figure 10-8) compared to the other sub-tests. Although not recorded during this investigation, some users of dropped foot stimulation (such as some of the impaired participants) are able to voluntarily plantarflex but not dorsiflex their foot. Therefore for some impaired participants during sub-test 241, their foot will have remained in a plantarflexed position with the tibialis anterior lengthened. This trend suggests that tibialis anterior M-wave amplitude is partially modulated by muscle length.

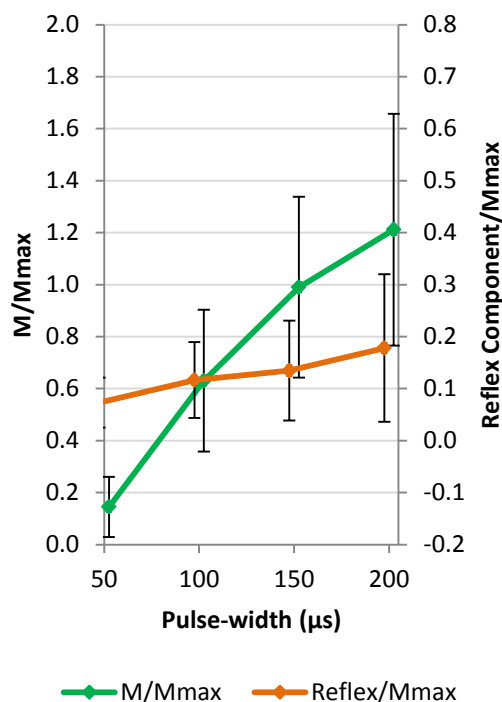
**Impaired participants: Reflex mediated activation**

The magnitude in reflex component seen during sub-tests 211 (Figure 10-5) and 221 (Figure 10-6) was similar. It did not appear to follow a trend with pulse-width and was sporadic in nature i.e. it did not consistently follow all stimulation pulses within the burst. The reflex component seen during sub-test 231 (Figure 10-7) was largest overall. The increased within group variation of sub-test 231 is in keeping with reflex activity being present in some impaired participants and not others. As many of the impaired participants lacked or had reduced voluntary activity, the reflex component was less susceptible to appearing artificially high due to the voluntary activity being potentially misinterpreted as reflex activity.



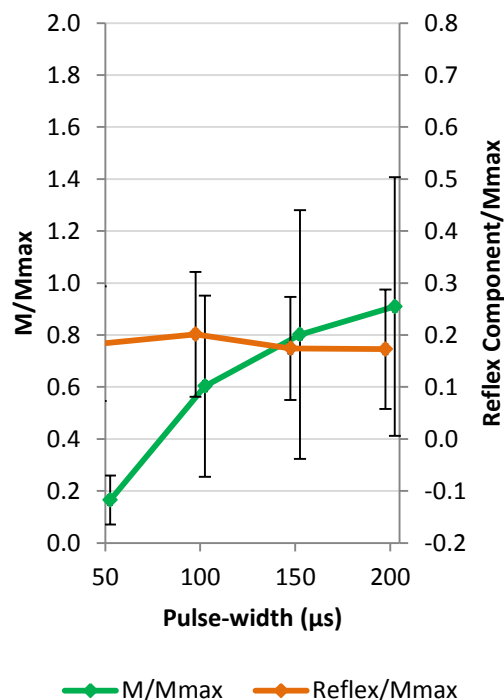
**Figure 10-5: Impaired sub-test 211: M-wave and reflex component ratio against pulse-width**

Ankle relaxed and plantarflexed under gravity  
(n=12)



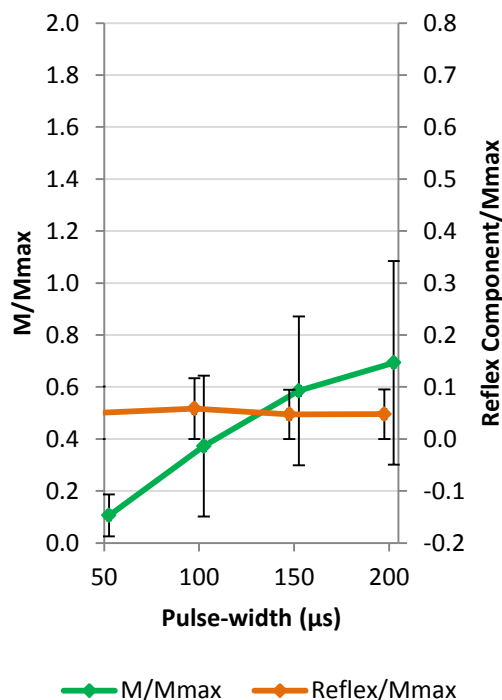
**Figure 10-6: Impaired sub-test 221: M-wave and reflex component ratio against pulse-width**

Ankle relaxed and supported in dorsiflexion (n=12)



**Figure 10-7: Impaired sub-test 231: M-wave and reflex component ratio against pulse-width**

Ankle voluntarily dorsiflexed (n=12)



**Figure 10-8: Impaired sub-test 241: M-wave and reflex component ratio against pulse-width**

Ankle voluntarily plantarflexed (n=12)

Figures include  $\pm$  one standard deviation error bars

### *10.3.2 Phase 2 Summary: Motor and reflex response to conventional stimulation*

For both unimpaired and impaired participants tibialis anterior M-wave amplitude appears to increase slightly at shortened muscle length. Whilst this is not a finding that appears to be reported in literature, it echoes the trend noted during exploratory data collection. Potential mechanisms of the effect were hypothesised in Chapter 7 and will be returned to when further investigating the effect in subsequent phases.

For both unimpaired and impaired participants, tibialis anterior reflex components appear to indicate a small increase with shortened muscle length and a larger one with voluntary effort. The reflex component demonstrated properties characteristic of F-waves (section 4.1.3) rather than H-waves (see Table 4-1 for differences) within both groups. Using the EMG animation software tool described in section 9.3.2, representative traces were shown to a neurophysiologist of Salisbury District Hospital. Due to the sporadic nature, temporal variation and low amplitude they supported the author conclusion that they appeared to be of F-wave origin. An F-wave is produced by the antidromic followed by orthodromic conduction along a motor neuron (Figure 4-5). An H-wave is produced by orthodromic afferent nerve conduction which results in a monosynaptic reflex resulting in orthodromic motor conduction (Figure 4-2). More detailed explanations of H- and F- waves are provided in sections 4.1.2 and 4.1.3 respectively.

F- and H-waves can coexist and it is conceivable that both are present in the observed responses. F-waves amplitude has been shown to increase with voluntary effort [72]. As activation and conduction of the F-wave is along the  $\alpha$ -motor neuron, it is conceivable that their amplitude may vary with muscle length in the manner encountered during phase 2 with M-waves. This may explain the smallest reflex components seen during sub-test 241 when the tibialis anterior is lengthened. When combined with voluntary effort it is expected that both H-waves [61] and F-waves [70, 71] will be facilitated. This may account for the largest reflex components being noted during sub-test 231 when attempting to actively dorsiflex.

Whilst a number of the unimpaired participants were familiar with electrical stimulation; they were not regular users. The impaired participants were current users of FES for dropped foot correction and were hence assumed to be regular users. It is conceivable that the impaired groups' neurophysiological response to FES had become trained in the manner described in section 5.4.1 when describing the study completed by



Crone *et al.* [132]. The same discussion regarding training of reflexes can be made of impaired participants who participated in this study and regularly use dropped foot stimulation.

Notable variation in the ratiometric outcomes of both unimpaired and impaired participant groups was observed. Visual analysis of group data when displayed on common axes suggested further statistical analysis this would not provide meaningful results in light of the variation present.

As discussed in section 10.2, a criticism of this research could be that a wide range of impairment may be represented within the impaired participant group. As an indicator of walking ability, ten metre walking speed with and without FES at the time of participation is included within Appendix K). Other than this data and the inclusion and exclusion criteria of Table 8-1, no further classification or severity of impairment scores were used [158].

#### 10.3.3 Phase 2:

##### *Motor and reflex response to conventional stimulation during movement*

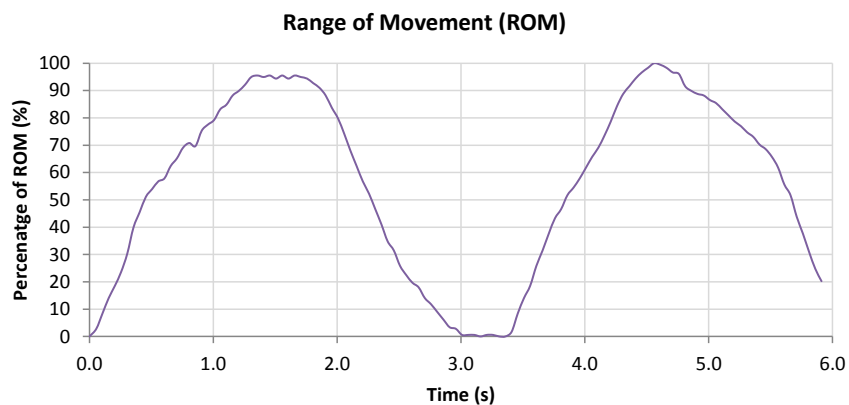
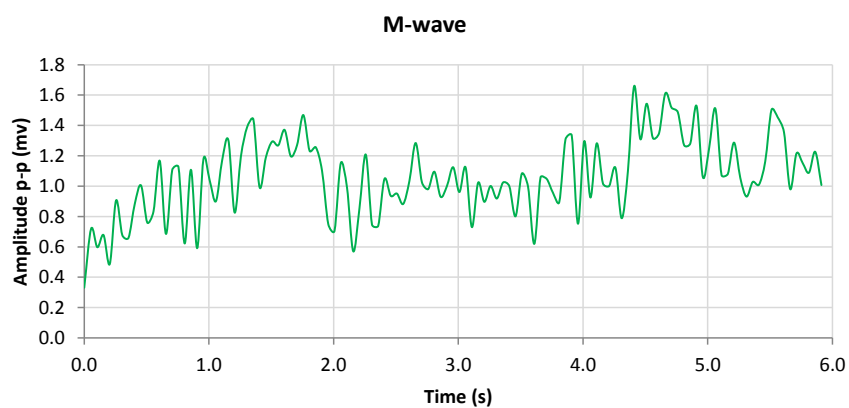
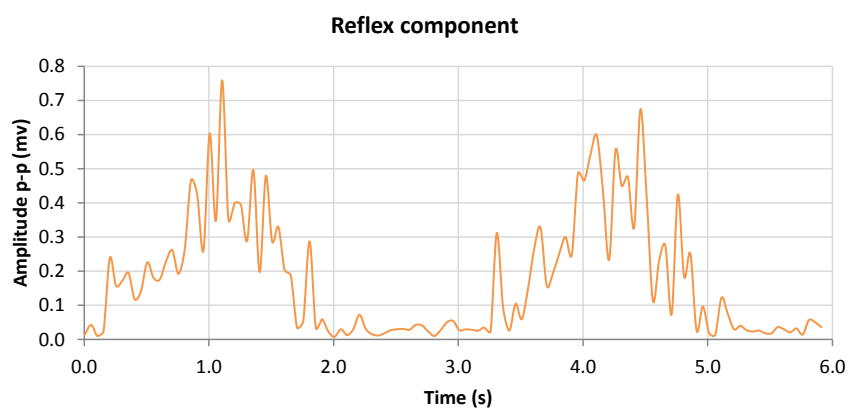
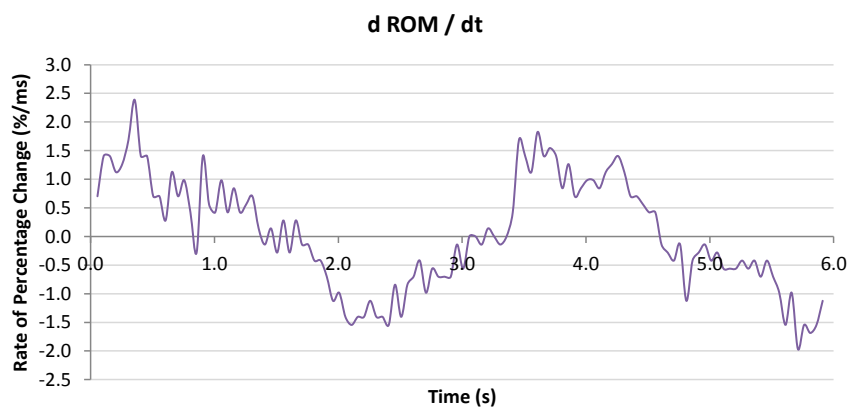
Findings of the previous section suggest motor and reflex responses to conventional electrical stimulation vary with joint angle and effort respectively. Such trends can be further explored utilising the data gained during sub-test 251. During sub-test 251 participants were asked to dorsiflex and plantarflex their foot in time with an animated sinusoidal trace of 0.33Hz that varied between 10% (plantarflexion) and 90% (dorsiflexion) of their ROM.

#### 10.3.4 Phase 2 Analysis:

##### *Motor response to conventional stimulation during movement*

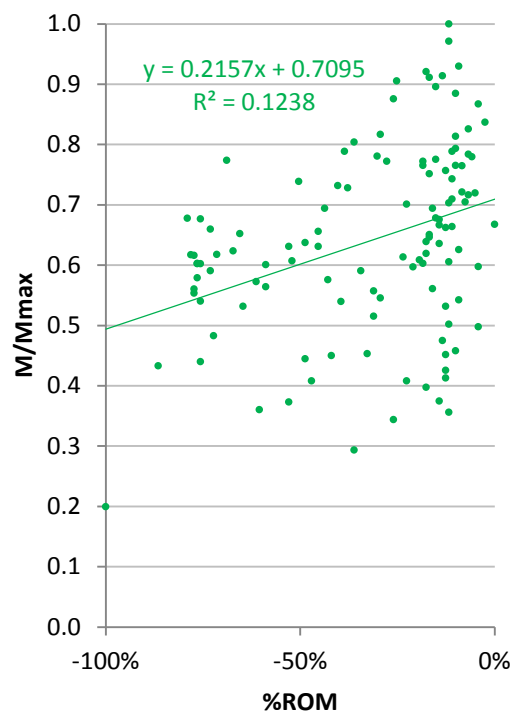
The manner in which the electro-goniometer (section 6.6) was used did not provide accurate measurements of angle suitable for inter-participant comparisons but rather movement expressed as a percentage of ROM specific to each participant.

In order to explain the approach to data analysis during this phase, participant U1 will be presented as an example. Figure 10-9<sup>a</sup> indicates the variation in movement as participant U1 tracked the 0.33Hz sinusoid of sub-test 251.

*a**Movement  
(% of ROM)**b**Tibialis  
Anterior  
M-Wave**c**Tibialis  
Anterior  
Reflex  
Component**d* *$\frac{dROM}{dt}$* 

**Figure 10-9: Tibialis anterior EMG response during movement: U1 example**  
 Data collected during sub-test 251 with 200 $\mu$ s pulse-width stimulation

Observing the M-wave amplitude over this time (Figure 10-9<sup>b</sup>) a weak correlation with the peaks and troughs of percentage of ROM can be identified. This weak correlation can be seen when plotting M-wave amplitude of each pulse divided by the peak M-wave amplitude over the whole burst (Mmax) against percentage of ROM and fitting a linear trend line (Figure 10-10). Whilst in the example given there is not a particularly strong correlation (low  $R^2$  value), the correlation is shown by a small but positive value of linear trend line gradient. With no correlation the linear trend line would be expected to have a gradient of zero with just a constant offset representing the mean value of M-wave ratio (approximately unity) throughout the ROM.



**Figure 10-10: Tibialis anterior M-wave/Mmax vs %ROM linear trend example**

*U1, 200 $\mu$ s pulse-width stimulation.*

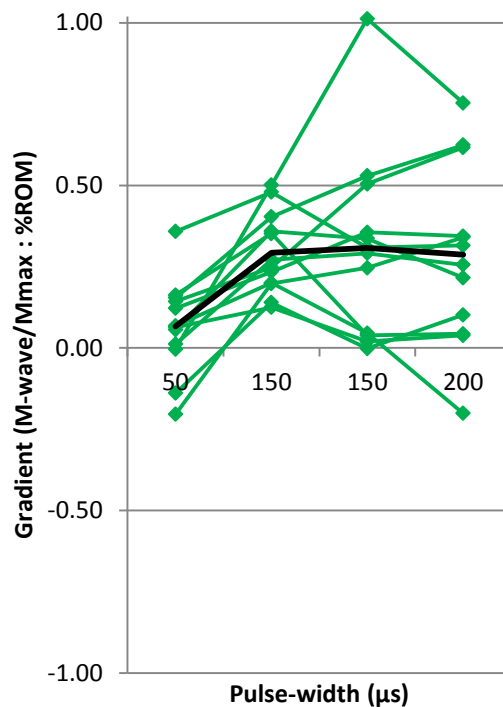
The analysis sequence leading to Figure 10-9 and Figure 10-10 was repeated for all participants of both unimpaired and impaired groups. Figure 10-11 and Figure 10-12 indicate how the value of linear trend line gradient varies for each applied pulse-width intensity for the unimpaired and impaired groups respectively. No participant data was excluded from this analysis.

### Unimpaired participants: Motor response

Observing Figure 10-11, there is a general trend for positive values of gradient at all pulse-width intensities. Gradients appear smallest at the lowest pulse-width of 50 $\mu$ s; this may be due to the stimulation intensity being insufficient to generate either movement or an M-wave. Apart from this there appears no further trend between gradient and pulse-width value.

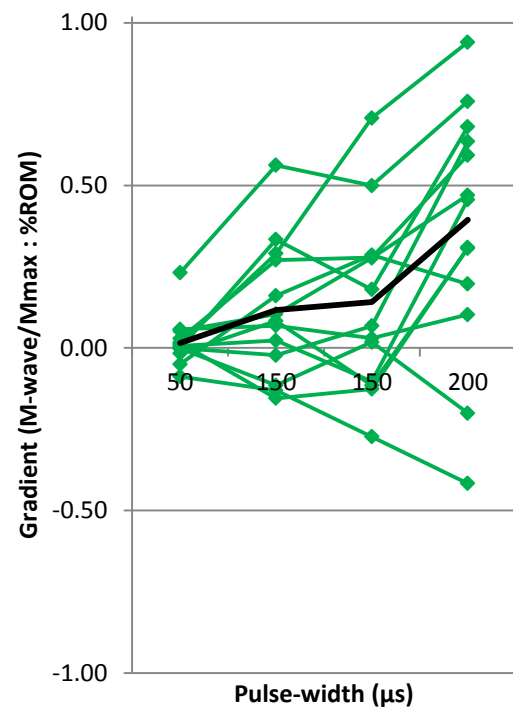
### Impaired participants: Motor response

Observing Figure 10-12, there is also a trend for positive values of gradient at all pulse-width intensities. However this is less prominent than the unimpaired participant group. Again, the mean gradient is smallest at the lowest pulse-width value of 50 $\mu$ s.



**Figure 10-11: Unimpaired participant gradients**  
(Tibialis anterior M-wave/Mmax : %ROM)

Group mean indicated in black (n=12)



**Figure 10-12: Impaired participant gradients**  
(Tibialis anterior M-wave/Mmax : %ROM)

Group mean indicated in black (n=13)

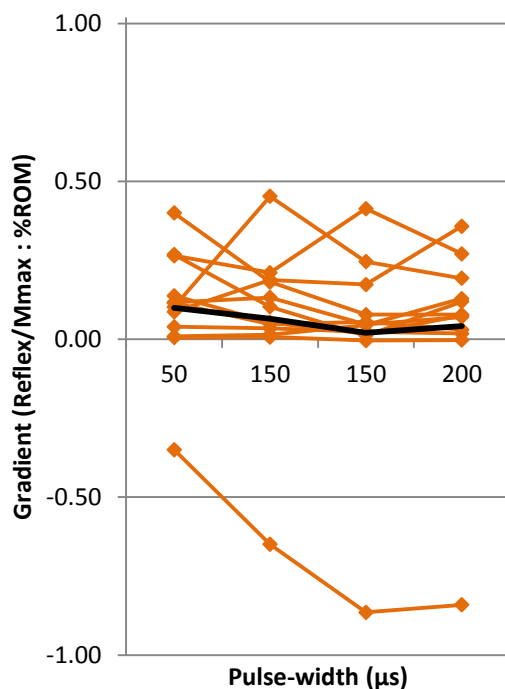
### 10.3.5 Phase 2 Summary: Motor response to conventional stimulation during movement

There appears a general trend for tibialis anterior M-wave amplitude to increase with shortened muscle length for both unimpaired and impaired participants. The effect is most noticeable in the unimpaired group where the magnitude of M-wave and ROM is generally larger than the impaired group.

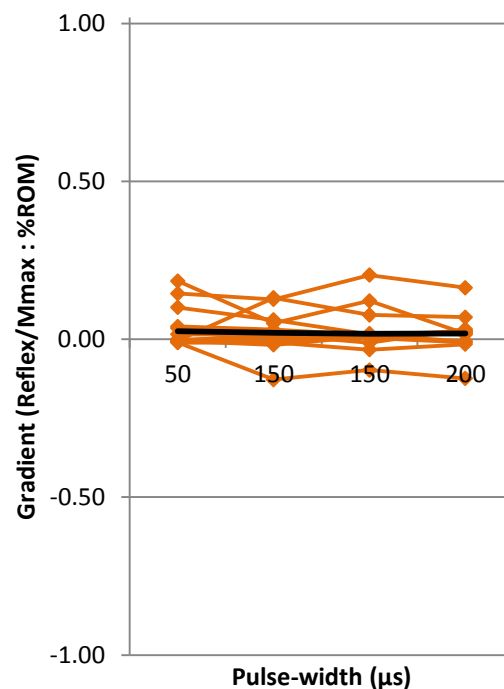
By the nature of the M-wave mechanism its amplitude is not expected to vary with joint angle when stimulation of constant intensity is applied. Therefore, as hypothesised during exploratory data collection, the observed effect may be due to relative movement between stimulation electrodes and the  $\alpha$ -motor neuron bundle or relative movement between the EMG recording electrodes and the tibialis anterior (sections 7.5 and 7.6).

### 10.3.6 Phase 2 Analysis: Reflex response to conventional stimulation during movement

The same analysis techniques as used within the previous section 10.3.4, was applied to the reflex component identified during voluntary movement. Figure 10-13 and Figure 10-14 display the mean linear trend line gradient correlating reflex component against percentage of ROM at the applied pulse-width intensities for unimpaired and impaired participants respectively.



**Figure 10-13: Unimpaired participant gradients (Tibialis anterior Reflex/Mmax : %ROM)**  
Group mean indicated in black (n=12)



**Figure 10-14: Impaired participant gradients (Tibialis anterior Reflex /Mmax : %ROM)**  
Group mean indicated in black (n=13)

### Unimpaired participants Reflex response

Observing Figure 10-13, apart from one unimpaired participant (U10) there is a trend for positive values of gradient at all pulse-width values. There appears no further trend between gradient and pulse-width value.

### Impaired participants Reflex response

Observing Figure 10-14, there is also appears a weak general trend for positive values of gradient at all pulse-width values. This is less prominent than the unimpaired participant group however.

The small positive gradient seen at all pulse-width values for both participant groups indicates a correlation between tibialis anterior reflex activity and muscle length. Upon closer review of participant U1 (Figure 10-9<sup>a+c</sup>) and others, it can be seen that increased reflex activity appears to correspond with voluntary effort (i.e. when passing through neutral into dorsiflexion) rather than the resulting movement i.e. percentage of ROM. A different analysis approach was therefore taken, which is again demonstrated using the example of participant U1 during 200µs pulse-width stimulation (Figure 10-9).

Figure 10-9<sup>a</sup> indicates the goniometer trace, with Figure 10-9<sup>b</sup> and Figure 10-9<sup>c</sup> respectively displaying M-wave and reflex component amplitudes for each of the stimulation pulses over the same time period. In order to quantify this trend across individuals, the rate of change in percentage of ROM was calculated and is plotted in Figure 10-9<sup>d</sup>. Mean M-wave and reflex component amplitude ratios were calculated when  $d(\%ROM)/d(t)$  was positive (tibialis anterior shortening) and negative (tibialis anterior lengthening). If there was no link between the amplitude and muscle shortening/lengthening these values should be equal and the ratio of the two approximately equal to unity (Equation 10-1).

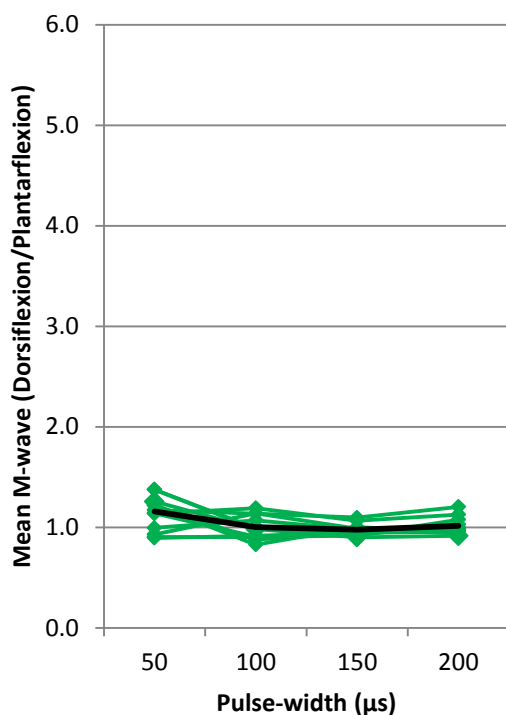
$$Mean\ amplitude\ ratio = \frac{\sum_{\frac{d(\%ROM)}{d(t)} \geq 0} EMG_{P-P}}{\sum_{\frac{d(\%ROM)}{d(t)} < 0} EMG_{P-P}}$$

*Equation 10-1: EMG Amplitude ratio when tibialis anterior is shortening/lengthening*

Whilst this analysis is relevant to the reflex component, the motor component was also assessed for completeness using this analysis method. Resulting plots of mean M-wave amplitude ratio against pulse-width are given in Figure 10-15 and Figure 10-16 for unimpaired and impaired participants respectively. The mean gradient is close to unity at all pulse-widths for both unimpaired and impaired participants. When considered alongside earlier findings, this suggests that M-wave amplitude is modulated by only muscle length and not effort.

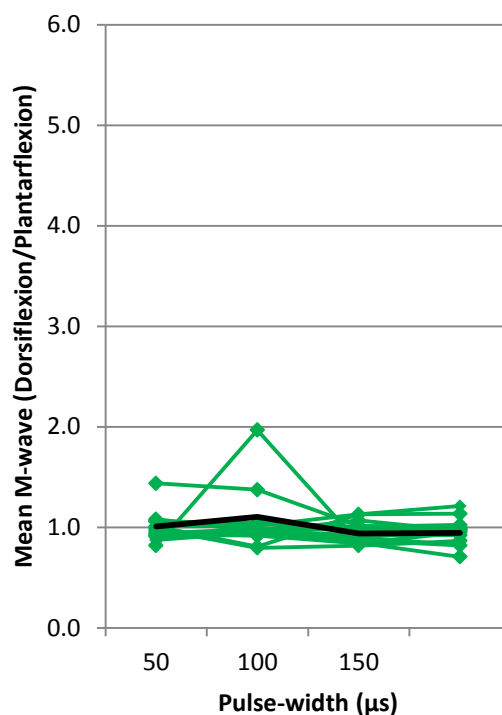
Figure 10-17 and Figure 10-18 show the mean reflex component amplitude ratio against pulse-width for unimpaired and impaired participants respectively. The mean reflex component amplitude ratio is close to unity for all impaired participants (Figure 10-18). This suggests that the reflex components seen are not modulated by voluntary effort in impaired participants. It should be noted that this result is not due to a lack of reflex activation as these were identified and discussed in earlier analysis (Figure 10-7).

In contrast to the impaired participant group, the notably larger than unity mean amplitude ratio of the unimpaired group (Figure 10-17), suggests a modulation of reflex components by voluntary effort in a majority of individuals. There does not appear to be a trend with pulse-width.



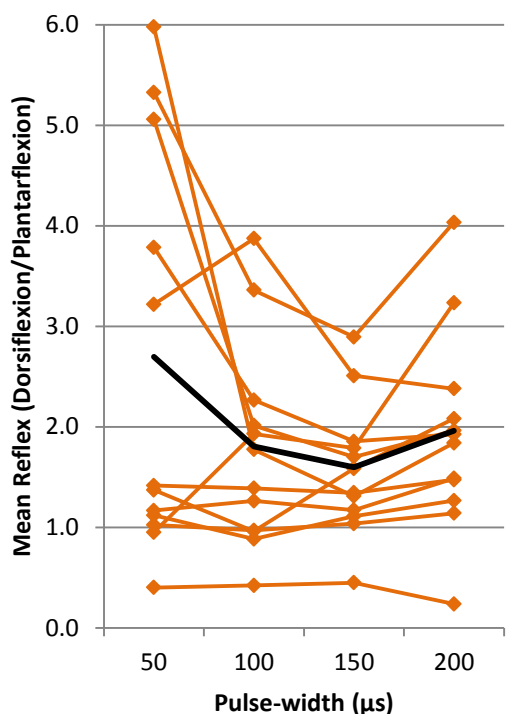
**Figure 10-15: Unimpaired tibialis anterior mean M-wave ratio (dorsiflexion/plantarflexion)**

Group mean indicated in black (n=12)



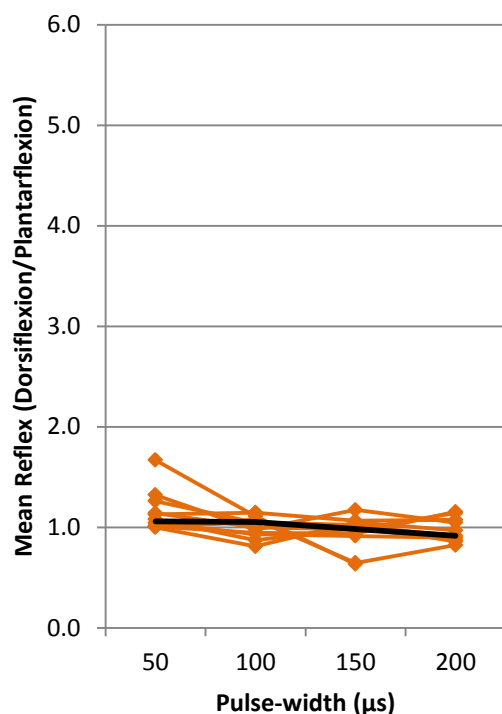
**Figure 10-16: Impaired tibialis anterior mean M-wave ratio (dorsiflexion/plantarflexion)**

Group mean indicated in black (n=13)



**Figure 10-17: Unimpaired mean tibialis anterior reflex ratio (dorsiflexion/plantarflexion)**

Group mean indicated in black (n=12)



**Figure 10-18: Impaired mean tibialis anterior reflex ratio (dorsiflexion/plantarflexion)**

Group mean indicated in black (n=13)



### 10.3.7 Phase 2 Summary:

#### *Reflex response to conventional stimulation during movement*

Assessment of reflex components against percentage of ROM whilst attempting to track a sinusoidal movement suggests a weak correlation with shortened tibialis anterior in both unimpaired and impaired participants. When investigated in relation to the direction of movement i.e. tibialis anterior shortening or lengthening, a marked difference between the unimpaired (Figure 10-17) and impaired (Figure 10-18) groups is identified. The magnitude of reflex component amplitude in the unimpaired participant group shows a correlation with the tibialis anterior length changes towards dorsiflexion. In this scenario, tibialis anterior shortening corresponds with voluntary activation. The impaired group do not demonstrate this apparent modulation of reflex activation with voluntary effort. This may be explained by the limited, or absent ability of voluntary control signal to arrive at the dorsal horn of the spinal cord in impaired participants.

Facilitation of reflex activity with voluntary effort in unimpaired participants is of interest when considering the mechanism of the component (e.g. F- or H-wave). Larger unimpaired mean reflex ratios seen at the lowest pulse-width value suggests reflex components at these intensities may be of H-wave origin. Although facilitated by voluntary effort by a lesser extent than H-waves, F-wave occurrence and amplitude also increases with descending input to the motor neuron pool [70, 71]. In combination with the earlier findings of phase 2 (section 10.3.2), Figure 10-17 suggests a combination of both H- and F-wave mechanisms is present.

The observation of increased F-wave occurrence with voluntary effort may have diagnostic rather than orthotic clinical utility. Rushton [159] has been often cited for a hypothesis published regarding the rehabilitation training effect of FES. As described and also witnessed by the author, some users of FES appear to experience some recovery of voluntary power/movement of their paretic limb linked with stimulation. The mechanism for this 'carry-over' effect is unclear and a presumption has been made that FES somehow promotes adaptive changes in cortical connectivity. As Rushton points out, "*the unique feature of electrical stimulation is that it activates nerve fibres both orthodromically and antidromically*". It is this antidromic motor activity that is integral to Rushton's hypothesis. Donald Hebb proposed that some modifiable synapses would be strengthened if presynaptic firing coincided with or was shortly

followed by postsynaptic discharge, i.e. success breeds success [27]. Conversely if presynaptic and postsynaptic activities are uncorrelated, the connection is weakened. Rushton proposes that such “Hebbian” learning is the reason why dropped foot stimulation can be successful in promoting functional recovery in some patients. In the context of this thesis, it has been shown that F-waves caused by FES correspond with voluntary effort in the unimpaired participant group (Figure 10-17). Following Rushton’s hypothesis, Hebbian learning will occur under the same conditions i.e. if FES coincides with voluntary effort. Where F-waves were noted with voluntary effort (i.e. subset of unimpaired participants) this may represent continued Hebbian learning maintaining the synapse. The lack of correlation of F-wave activity with voluntary effort in the impaired participant group may indicate the absence of pre- and post-synaptic firing and therefore lack of Hebbian learning during the tested conditions.

The identification of F-waves has implications if attempting to use voluntary EMG activation as a control signal. F-wave activity could be interpreted as voluntary EMG despite being the product of the applied electrical stimulation. Due to the known modulation of F-wave amplitude and occurrence with the motor neuron pool, Thorsen *et al.* [160] sought to investigate whether it could be volitionally repressed by visual feedback training given to unimpaired participants. Whilst understandable for the purposes of an EMG controlled FES system, if F-wave activity in combination with voluntary effort is an indicator of the occurrence of neuroplasticity, then this would not wished to be repressed. The authors concluded that there was no indication that participants learnt to volitionally repress the response in the manner described. This finding may suggest that neuroplasticity cannot be voluntarily repressed.

#### *10.3.8 Phase 2: Magnitude and speed of movement*

The magnitude and speed of resulting ankle movement following a stimulation burst will now be assessed and compared between conventional and catch-like stimulation within the unimpaired and impaired participants groups. Data from sub-test 211 and 212 has been used for this purpose as these respectively represent when the foot was relaxed and unsupported whilst a burst of conventional or catch-like stimulation was applied.

Three axis accelerometer data was collected with the purpose of assessing the movement resulting from stimulation. Upon review, this data appeared subject to substantial noise, with notable variation in participant responses. Variation in participant posture and sensor mounting position were thought to account for this. With no reasonable method of comparison between accelerometer traces, angle measurements from the goniometer system were reviewed as an alternative. The goniometer measurement provided meaningful interpretation of the resulting movement that could be compared between participants. For the purposes of assessing the magnitude and speed of movement resulting from stimulation, goniometer data was used in place of accelerometer data.

During Phase 2, all participants were able to gain a functional movement in response to stimulation and therefore data from all unimpaired and impaired groups was eligible for analysis. Catch-like stimulation applied at 150 $\mu$ s and 200 $\mu$ s pulse-width caused a strong withdrawal reflex in one participant. Data from this participant was excluded from analysis as this was not a controlled movement of the manner that FES would be intended to provide (I5 -Appendix K). Data from another impaired participant was excluded due to detachment of the goniometer part way through phase 2 (I1 -Appendix K)

#### *10.3.9 Phase 2: Magnitude of movement: Unimpaired and impaired participants*

When assessing magnitude of resulting movement, goniometer angle was expressed as a percentage of the peak angle range recorded during sub-test 211 at 200 $\mu$ s pulse-width. Expressing the magnitude of movement data in this manner enabled inter-participant analysis whilst aiding comparison between conventional and catch-like stimulation bursts.

During sub-test 211 the participants foot was allowed to rest with gravity, in a plantarflexed position whilst a 2.5 second burst of either conventional or catch-like stimulation was applied.

Figure 10-19 and Figure 10-20 indicate the percentage of peak angle achieved by unimpaired participants during conventional and catch-like burst stimulation respectively. As expected for both, the peak angle increases with increasing pulse-width. Beyond 100 $\mu$ s the increase in peak angle reduces suggesting the participants' foot has reached the end of ROM.

Figure 10-21 and Figure 10-22 indicate the percentage of peak angle achieved by impaired participants during conventional and catch-like burst stimulation respectively. The trend in impaired participant responses is similar to that of the unimpaired participants.

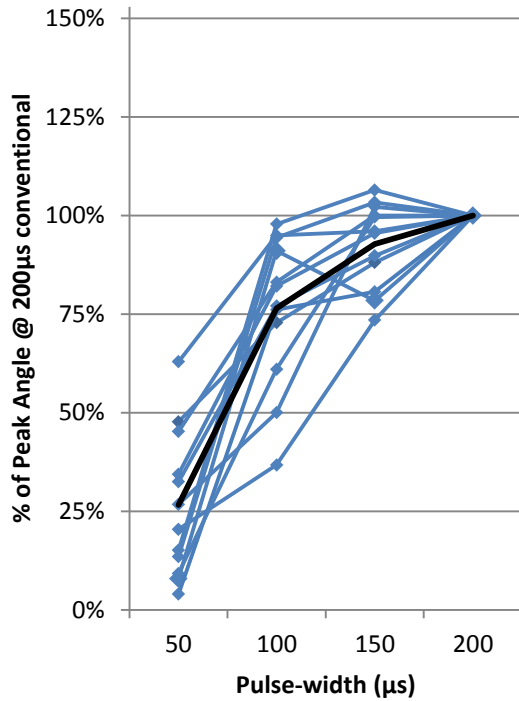
The trend in peak angle with pulse-width appears similar between conventional and catch-like stimulation bursts for both unimpaired and impaired participants groups.

#### *10.3.10 Phase 2: Speed of movement: Unimpaired and impaired participants*

The speed of movement has been assessed by identifying the time at which  $\geq 80\%$  of ROM (dorsiflexion) during sub-test 211 was achieved following the onset of stimulation. Figure 10-25 and Figure 10-26 display the time at which  $\geq 80\%$  of ROM was achieved with a 2.5 second burst of conventional and catch-like stimulation at different pulse-widths for unimpaired and impaired participants respectively. For both groups, the time to  $\geq 80\%$  of ROM appears to reduce with increasing pulse-width.

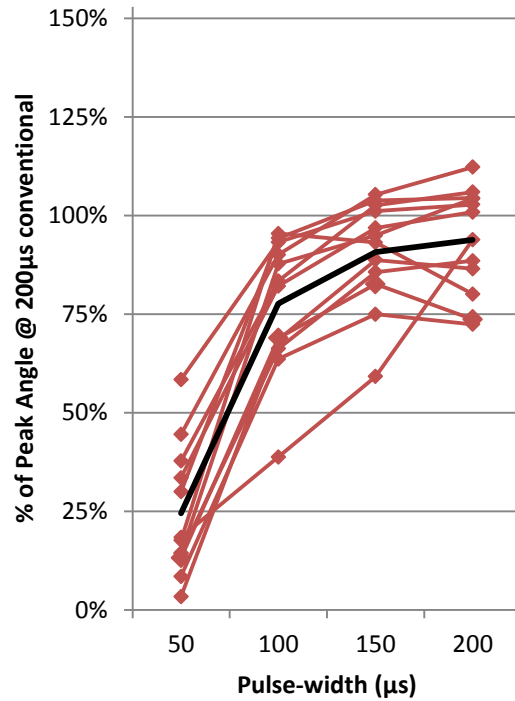
Comparing the unimpaired (Figure 10-23 and Figure 10-24) to impaired (Figure 10-25 and Figure 10-26) participant group plots, less variation and slightly shorter mean times are noted. If not group variation, the slower response of the impaired group may be partly due to muscle atrophy and/or a change of muscle fibre type. Following stroke, muscle deconditioning associated with absence of use results in a propensity towards fast fatigable muscle fibre types (section 3.1.1). The impaired participant group of this study are however established users of FES and hence there may have been a training effect associated with their use of electrical stimulation. In animal studies chronic electrical stimulation has indicated a training effect towards slow-twitch muscle fibres [161]. Spasticity within the impaired participant group may also account for the generally longer time to peak angle due to active antagonist muscles.

Comparing the response to conventional and catch-like stimulation bursts in both unimpaired and impaired participant groups, there does not appear to be notable difference in the time taken to reach  $\geq 80\%$  of ROM in light of inter participant variation.



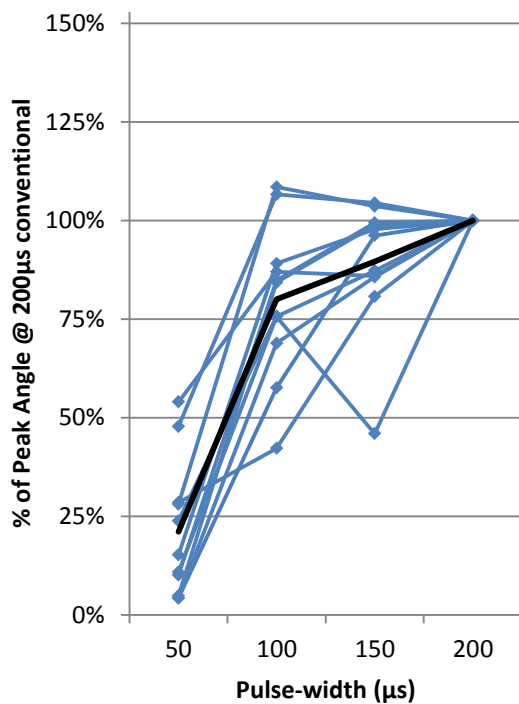
**Figure 10-19: Unimpaired: Peak Angle vs Pulse-width during conventional burst stimulation**

Group mean indicated in black (n=12)



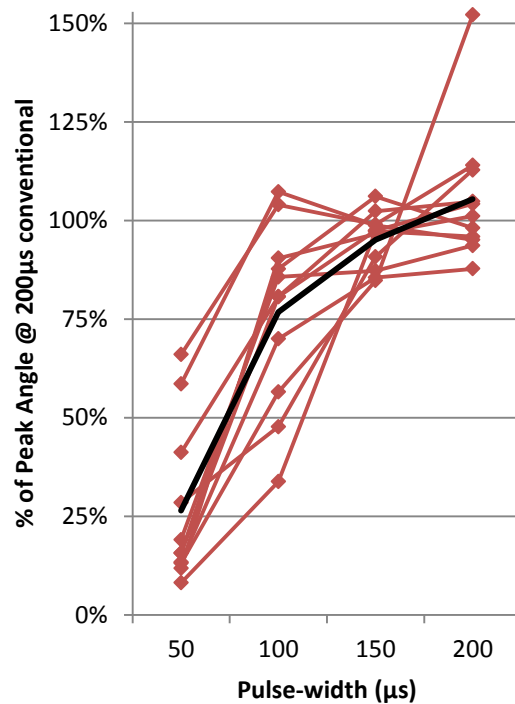
**Figure 10-20: Unimpaired: Peak Angle vs Pulse-width during catch-like burst stimulation**

Group mean indicated in black (n=12)



**Figure 10-21: Impaired: Peak Angle vs Pulse-width during conventional burst stimulation**

Group mean indicated in black (n=12)

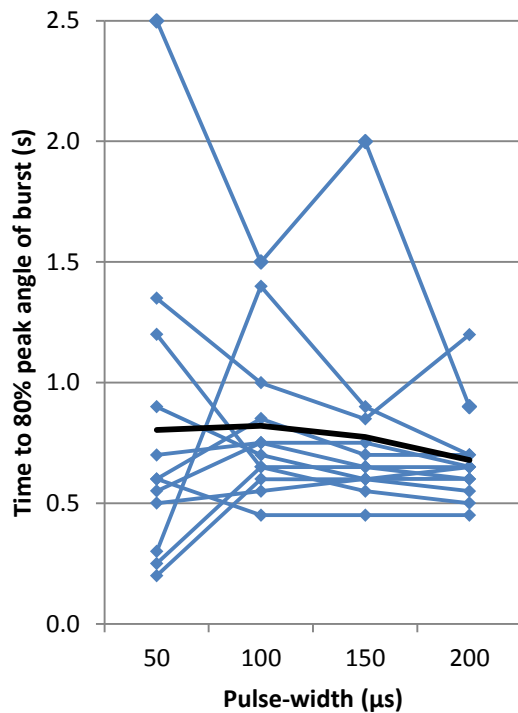


**Figure 10-22: Impaired: Peak Angle vs Pulse-width during catch-like burst stimulation**

Group mean indicated in black (n=12)

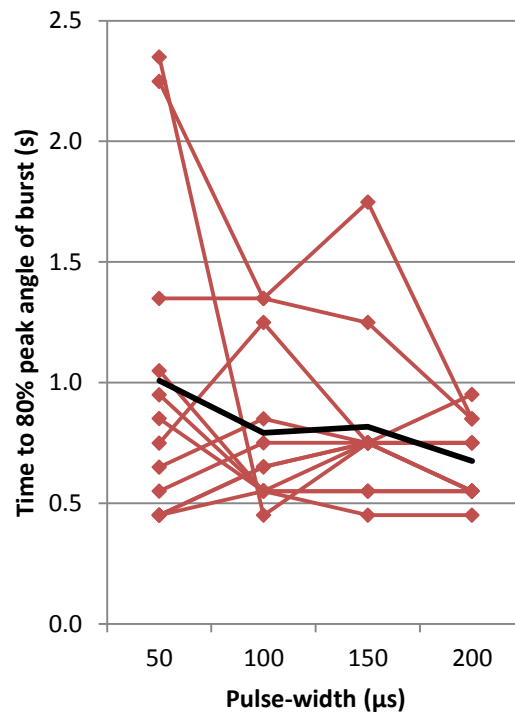
*10.3.11 Phase 2 Summary: Magnitude and speed of movement*

Little difference in magnitude or speed of resulting movement was seen when comparing conventional to catch-like stimulation bursts. A marked difference between the two types of stimulation was not necessarily expected over a burst of 2.5 seconds as this is a reasonable period with which to expect end of ROM to be achieved. In light of literature, a shorter time to 80% of ROM could possibly have been anticipated when utilising catch-like stimulation due to enhanced force development. There was a high degree of variation and the measurement method used may not have been appropriate for this task.



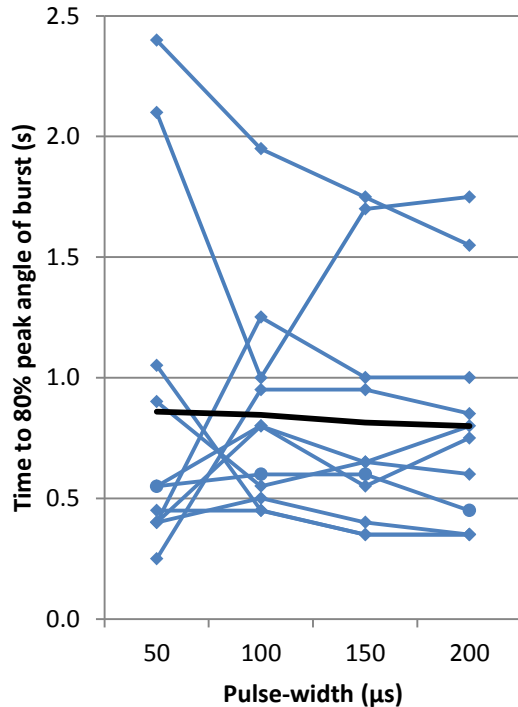
**Figure 10-23: Unimpaired: Time to 80% of Peak Angle vs Pulse-width during conventional burst stimulation**

Group mean indicated in black (n=12)



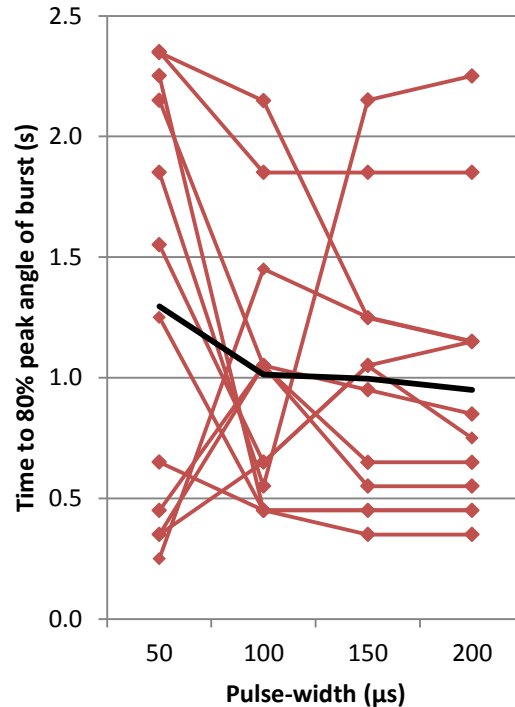
**Figure 10-24: Unimpaired: Time to 80% of Peak Angle vs Pulse-width during catch-like burst stimulation**

Group mean indicated in black (n=12)



**Figure 10-25: Impaired: Time to 80% of Peak Angle vs Pulse-width during conventional burst stimulation**

Group mean indicated in black (n=12)



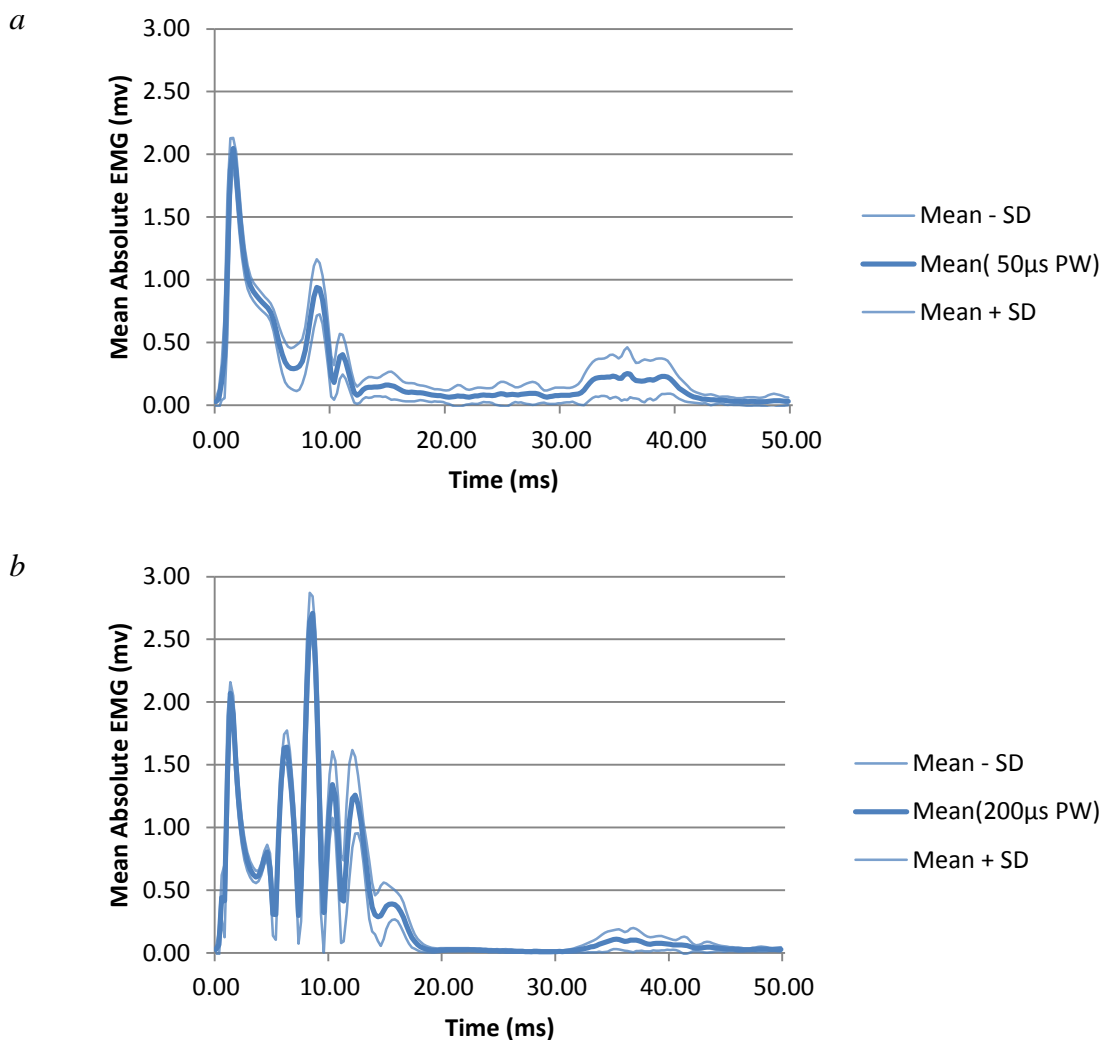
**Figure 10-26: Impaired: Time to 80% of Peak Angle vs Pulse-width during catch-like burst stimulation**

Group mean indicated in black (n=12)

### 10.3.12 Phase 2 Analysis: EMG silent period

When visually analysing unimpaired participant tibialis anterior EMG responses to sub-test 231, it was noted that at higher pulse-width intensities the period between the M-wave and reflex component generally remained absent of activity. This suggested that EMG activity caused by voluntary activation and electrical stimulation were not simply superimposed upon each other but that, at times, the presence of voluntary activation was diminished by the presence of electrical stimulation.

An example of this is given by unimpaired participant U8 in Figure 10-27. Figure 10-27<sup>a</sup> and <sup>b</sup> display mean absolute EMG during the 50ms window that followed each of the 20 pulse burst of stimulation at 50 $\mu$ s and 200 $\mu$ s pulse-width respectively.



**Figure 10-27: Participant U8 -mean absolute tibialis anterior EMG response**

<sup>a</sup> 50 $\mu$ s pulse-width stimulation: voluntary activity seen between 20-30ms following stimulation pulse.

<sup>b</sup> 200 $\mu$ s pulse-width stimulation: absence of voluntary activity between 20-30ms following stimulation pulse. Figures include  $\pm$  one standard deviation error bars



Observing the 50 $\mu$ s response (Figure 10-27<sup>a</sup>) a net level of activity is seen following the M-wave and before the reflex component (15-30ms approximately). This net activity is the mean voluntary EMG. Noting the same window during the 200 $\mu$ s response (Figure 10-27<sup>b</sup>), the trace is essentially zero with the standard deviation also reduced to zero indicating that this is consistent for the majority, if not all, pulses of the burst.

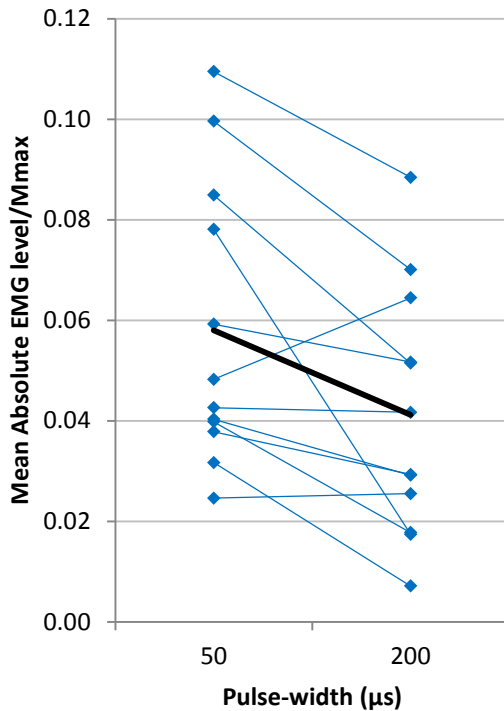
In order to quantify and assess this further for both unimpaired and impaired participants, the time at which peak M-wave and reflex components were identified and reviewed. In combination with viewing EMG responses with the animated GIF converter it was found that M-wave activity had ended by 20ms post stimulation application and the earliest reflex components were seen at approximately 35ms. The mean absolute EMG response at each sample over the 50ms window that followed a stimulation pulse was computed for each burst of stimulation applied during sub-test 231 for each participant. Within this window, the mean absolute EMG level between 20ms and 30ms following the stimulation pulse was then calculated. In order to permit inter-analysis this value was divided by the maximum M-wave amplitude detected during the 200 $\mu$ s pulse-width burst of stimulation during sub-test 231. The results of this when completed at 50 $\mu$ s and 200 $\mu$ s pulse-width is indicated in Figure 10-28 and Figure 10-29 for unimpaired and impaired participants respectively. Data from two impaired participants (I2, I6 -Appendix K) were excluded due to mains interference which artificially elevated mean absolute EMG levels.

### **Unimpaired participants**

There appears a net reduction in mean absolute EMG level (15-30ms) at 200 $\mu$ s compared to 50 $\mu$ s pulse-width. If an assumption is made that the data is normally distributed, a paired two tailed t-test indicates a significant reduction ( $p < 0.05$ ) in mean EMG level normalised to peak M-wave amplitude at 50 $\mu$ s and 200 $\mu$ s pulse-width. A hypothesis for the reduction in EMG level at higher stimulation intensity can be formed from considering the mechanism of activation and will be discussed in the following section (10.3.13).

### **Impaired participants**

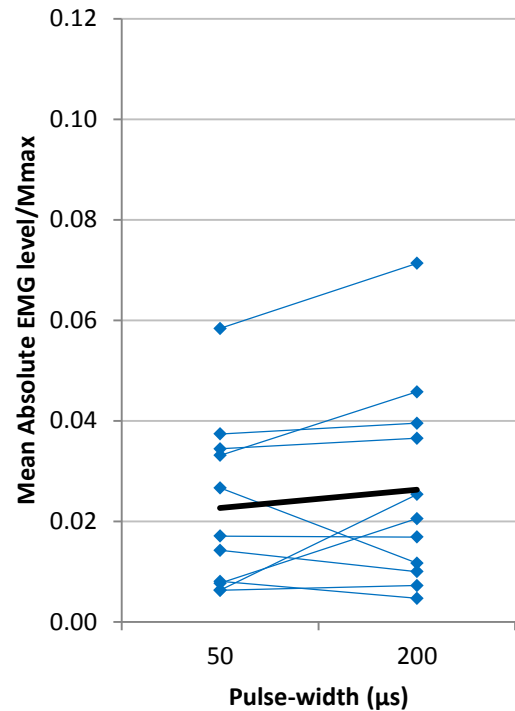
The values of mean absolute EMG level (15-30ms) at both 50 $\mu$ s and 200 $\mu$ s pulse-width appear comparable and suggest minimal activity. Due to the lack of or limited, voluntary activation of impaired participants this is not unexpected.



**Figure 10-28: Unimpaired tibialis anterior silent period**

Black line indicates mean of unimpaired participants ( $n=12$ ).

Significant ( $p=0.013$ ) reduction in activity in window of 20-30ms following stimulation pulse



**Figure 10-29: Impaired tibialis anterior silent period**

Black line indicates mean of impaired participants ( $n=11$ ).

Note reduced levels compared to unimpaired due to lack/limited voluntary activation by impaired participants

### 10.3.13 Phase 2 Summary: EMG silent period

A statistically significant reduction in EMG activity in-between the M-wave and reflex components was observed in the unimpaired group. This was not observed in the impaired group however this can be accounted for by limited, or a lack of, voluntary activation. It is hypothesised that action potentials generated by voluntary activation are being annihilated by antidromic  $\alpha$ -motor neuron action potentials generated by electrical stimulation. At low stimulation intensity this annihilation is partial. As the stimulation intensity is increased however and a greater proportion of the  $\alpha$ -motor neuron bundle is activated, a greater degree is annihilated. The presence of what appears to be F-waves suggests the antidromic  $\alpha$ -motor neuron action potential is of greater intensity than that of the voluntary orthodromic activity, thereby annihilating it and still producing an F-wave. The resulting lack of activation seen in the time period in between the M-wave and reflex response is termed the 'silent period' in the context of this thesis.

It is possible that a recurrent inhibition effect in which Renshaw cells excited by the antidromic action potentials, inhibit the  $\alpha$ -motor neuron at the anterior horn cell. However if this was the primary cause of the silent period any reflex component, be it H- or F-wave, would also be inhibited which does not appear evident.

The identification of the silent period highlights the importance of stimulation frequency in permitting not only volitional control when combined with electrical stimulation, but also reflex mediated activation.

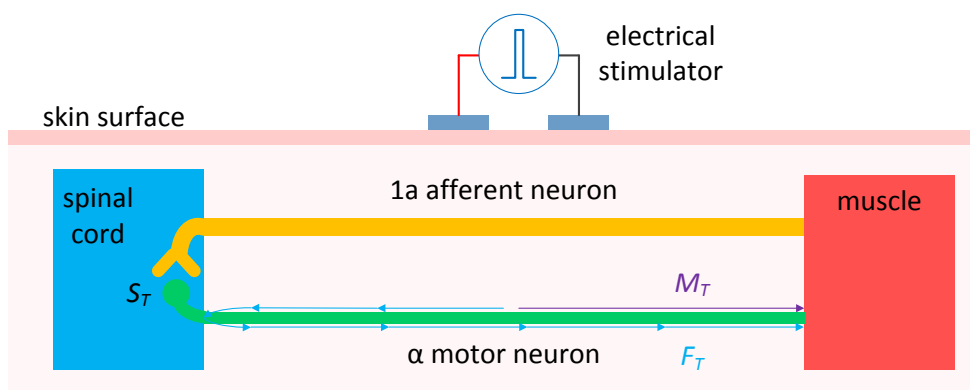
Following the application of a stimulation pulse, any voluntary activity appearing at the anterior horn before the antidromic motor action potential has reached it will be annihilated or reduced by collision. Voluntary activation appearing just after this will then take time to be conducted along the length of the  $\alpha$ -motor neuron to the muscle of primary interest being activated. In theory the minimum time period for this will be that of an F-wave. Provided the action potentials corresponding to volitional activation pass distal of the point at which the action potentials are being generated by electrical stimulation, they should succeed in being conducted to the muscle. Through consideration of this mechanism (Figure 10-30), Equation 10-2 expresses the minimum stimulation time period which is needed to permit F- or H-wave reflex components to be present. Equation 10-2 also represents the theoretical minimum stimulation period needed if volitional activation is to be seen.

$$\text{Stimulation Period} > F_T - M_T$$

**Equation 10-2: Stimulation period required in order to exceed 'silent period'**

$M_T$  = M-wave onset latency

$F_T$  = F-wave onset latency



**Figure 10-30: Orthodromic and antidromic electrical stimulation motor activation**

$M_T$  = M-wave conduction time

$F_T$  = F-wave conduction time

As noted at the beginning of this summary, this finding has potentially important implications when considering the choice of stimulation frequency for clinical FES systems. Typical values for onset latency of M-waves and F-waves amongst the unimpaired and impaired participants groups were 10ms and 40ms respectively. For such values, a stimulation frequency of 33Hz or above would leave the tibialis anterior in a silent period between each successive M-wave of the burst. At supramaximal stimulation intensity any voluntary or reflex mediated contribution to electrically stimulated muscle activation would be antidromically annihilated and only the direct motor effects of stimulation would prevail.

If for example a patient had limited but not absent voluntary control, then there may be a wish for stimulation to augment rather than impede this voluntary control. In this scenario, either a sufficiently low stimulation intensity (in order to avoid complete antidromic annihilation of voluntary activation) or a low stimulation frequency (stimulation period  $> F_T - M_T$ ) would be required. It may be difficult to select an appropriate stimulation intensity without annihilating voluntary activation and therefore it may be more effective to consider choice of stimulation frequency. As noted in section 7.5, it appears conceivable that the relative depth between nerve and stimulation electrodes may vary during a movement and therefore this may further complicate selection of appropriate stimulation intensity.

Considering use of stimulation for exercise and muscle training purposes, Equation 10-2 governs the stimulation time period needed to permit a reflex component (be it F- or H-wave). An H-wave will activate muscle fibres in the natural Henneman size recruitment order. If a stimulation period greater than that of Equation 10-2 is selected during exercise stimulation, then a proportion of muscle fibres may be recruited in this way rather than the reversed or non-selective manner of direct  $\alpha$ -motor neuron activation, and may bring about a different muscle conditioning effect.

## 10.4 Phase 3

Phase 3 assessed the effects of individual conventional and catch-like stimuli on the excitability and inhibition of spinal reflexes affecting the tibialis anterior and soleus at different muscle lengths and when actively supporting and opposing the movement resulting from stimulation (section 8.2.3).

Whilst twitch movements are rarely used for clinically functional purposes, the lack of subsequent stimuli within a burst permit data collected during phase 3 to be used to investigate Research Questions 2 and 3 (pages 56 and 58 respectively).

The automated identification method of section 9.3.2 was used to identify M1 and R1 EMG features of conventional stimuli (sub-tests 311, 321, 331, 341). Data gathered from these sub-tests is first presented when assessing Research Question 1 (page 52). As previously discussed, identification of M2 and R2 using this method during sub-tests incorporating catch-like stimulation was complicated by the apparent super-position of EMG responses and stimulation artefact. A super-positioning method similar to that utilised during section 7.1.4 is therefore used when subsequently comparing conventional to catch-like stimulation in evaluating Research Questions 2 and 3 (pages 56 and 58 respectively).

#### *10.4.1 Phase 3 Analysis: Motor and reflex response to conventional stimulation*

First presented are findings from unimpaired and then impaired participant groups at different muscle lengths and when actively supporting and opposing the movement resulting from stimulation. For each, the direct motor activation (M-wave) and then reflex components are discussed.

The Stimulator Investigator application of section 6.7 was configured to record the mean EMG response over five repetitions of each twitch. The peak M-wave and peak reflex component amplitude for each twitch stimuli was computed using the automated method of section 9.3.2. In order to permit inter-analysis, direct and reflex evoked potentials were expressed as a ratio to peak M-wave attained during sub-test 311 at 200 $\mu$ s. Figure 10-31 to Figure 10-34 and Figure 10-35 to Figure 10-38 plot the mean values of these features at each stimulation pulse-width setting for unimpaired and impaired participants respectively.

As with Phase 2, participants with a peak M-wave of less than 0.35mV were excluded. Data from one unimpaired and one impaired participant were excluded from analysis due to this criterion (U5, I6 -Appendix K).

**Unimpaired participants: Direct motor activation**

Observing Figure 10-31 to Figure 10-34 for all sub-tests, M-wave amplitude increases towards a plateau when plotted against pulse-width in a manner consistent with that reported in literature (Figure 4-4).

M-wave amplitudes are higher at all pulse-width values during sub-test 321 (Figure 10-32) compared to 311 (Figure 10-31). This supports the observation of section 10.3.2 that the M-wave increases as the muscle being stimulated shortens.

Sub-tests 331 and 341 incorporated the participant's voluntary effort to dorsiflex (331) and plantarflex (341) whilst conventional stimulation was applied. The M-wave amplitude trace of sub-test 321 (Figure 10-32) appears comparable to that of 331 (Figure 10-33) in light of the variation present.

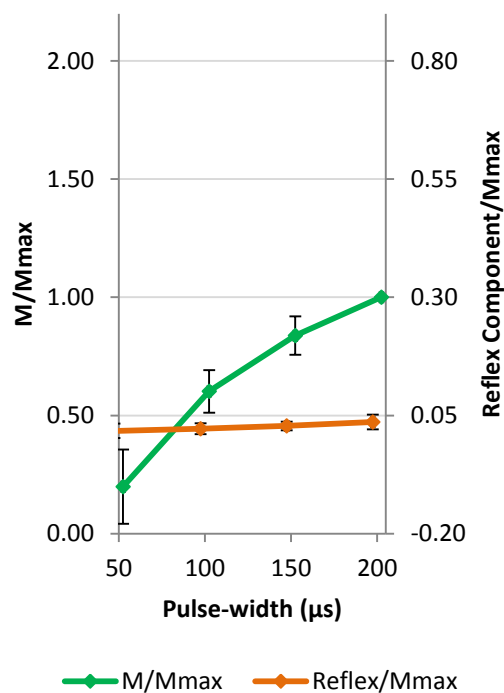
The M-wave amplitude during sub-test 341 (Figure 10-34) appears comparable to 311 (Figure 10-31) and is reduced compared to sub-tests 321 and 331.

**Unimpaired participants: Reflex mediated activation**

Reflex components identified during sub-test 311 (Figure 10-31) and 341 (Figure 10-34) were both essentially absent and of comparable magnitude to noise.

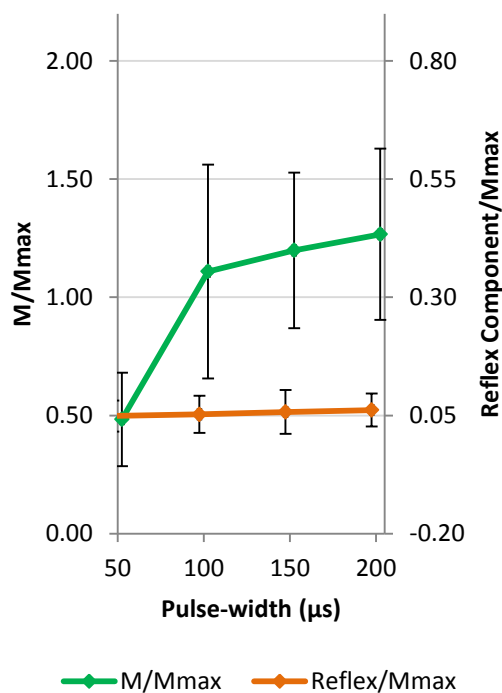
Reflex components identified during sub-test 321 when the tibialis anterior was lengthened are slightly larger than those of 311 and 341 (in which the foot was plantarflexed). This trend supports the observation that tibialis anterior reflex components are greater when the muscle is at a shortened length.

The magnitude of reflex components seen during sub-test 331 (Figure 10-33) are larger than the other sub-tests of this phase. Akin to phase 2, the large variation is accountable to what appear two populations: those in which reflex components were present and those where it was essentially absent. As identified in section 10.3.1, voluntary activation could be misinterpreted as reflex activation and therefore partially account for this elevation. During Phase 3 however, a mean response over five repetitions was recorded. Therefore if an assumption is made that voluntary EMG is stochastic in nature, then this measurement component should decrease proportional to  $1/\sqrt{5}$ . The reflex component does not decrease with increasing pulse-width and therefore does not suggest it is of H-wave origin. Sub-test 331 suggests that in those unimpaired participants in whom an F-wave component is noted, the magnitude of its presence is influenced by effort.



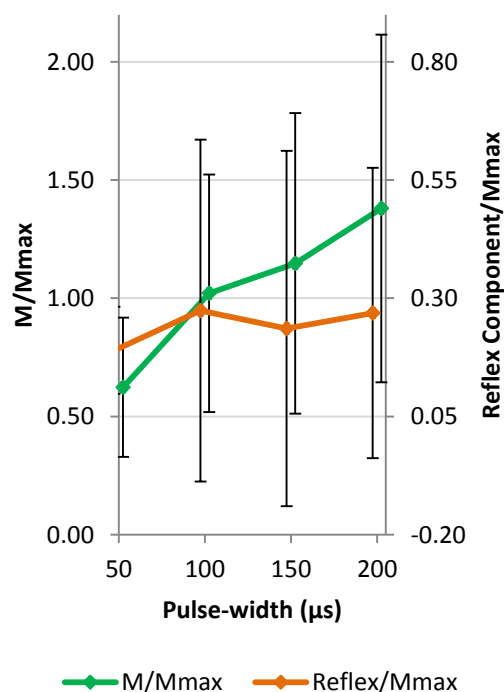
**Figure 10-31: Unimpaired sub-test 311: M-wave and reflex wave component against pulse-width (n=11)**

Ankle relaxed and plantarflexed under gravity



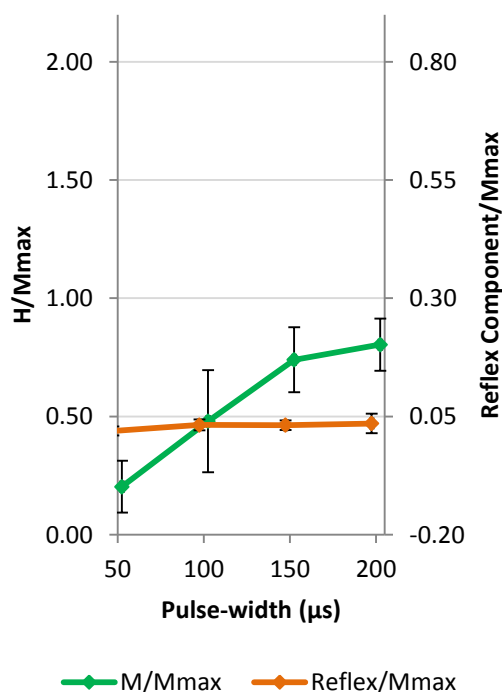
**Figure 10-32: Unimpaired sub-test 321: M-wave and reflex component ratio against pulse-width (n=11)**

Ankle relaxed and supported in dorsiflexion



**Figure 10-33: Unimpaired sub-test 331: M-wave and reflex component ratio against pulse-width (n=11)**

Ankle voluntarily dorsiflexed



**Figure 10-34: Unimpaired sub-test 341: M-wave and reflex component ratio against pulse-width (n=11)**

Ankle voluntarily plantarflexed

Figures include  $\pm$  one standard deviation error bars

**Impaired participants: Direct motor activation**

In a similar manner to the unimpaired data, M-wave amplitude increases towards a plateau when plotted against pulse-width as shown in Figure 10-35 to Figure 10-38 for all sub-tests.

The M-wave amplitude of sub-test 321 (Figure 10-35) is greater than that of 311 (Figure 10-36) and 341 (Figure 10-38). This suggests that M-wave amplitude is slightly greater at shortened muscle lengths.

M-wave amplitude was comparable between sub-tests 331 (Figure 10-37) and 321 (Figure 10-36). This is expected as voluntary effort would not be expected to alter M-wave amplitude.

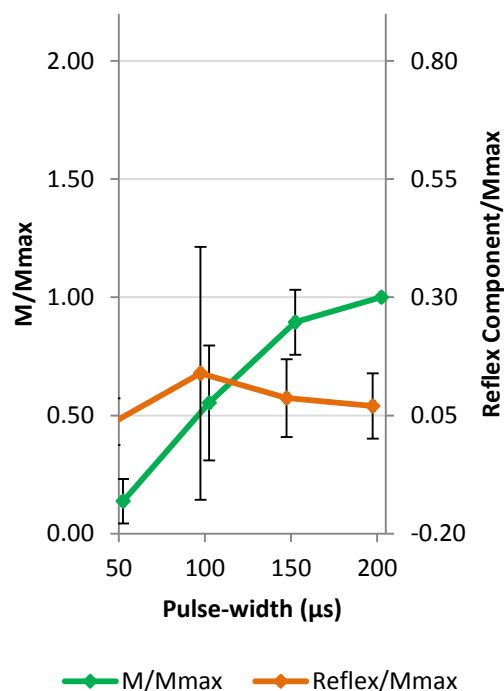
M-wave amplitude was lowest at all pulse-width intensities above 50 $\mu$ s during sub-test 341 (Figure 10-38) compared to the other sub-tests. Although not recorded during this investigation, some impaired participants (such as those seen) are able to actively plantarflex but not dorsiflex their foot. Therefore for some impaired participants during sub-test 341, their foot will have remained in a plantarflexed position with the tibialis lengthened. This trend further supports the observation that tibialis anterior M-wave amplitude appears greatest at shortened muscle length.

**Impaired participants: Reflex mediated activation**

Reflex components identified during sub-test 311 (Figure 10-35) and 341 (Figure 10-38) appear similar and correspond to small sporadic activity identified in some participants.

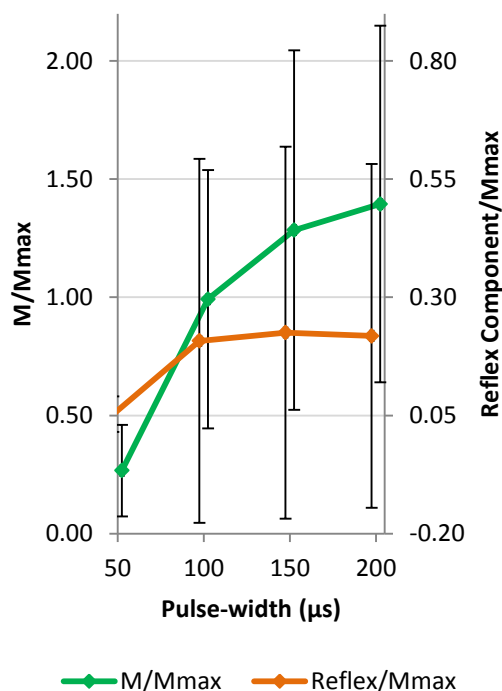
Reflex components identified during sub-tests 321 (Figure 10-36) and 331 (Figure 10-37) appear comparable and are slightly larger than those of 311 and 341. During sub-tests 321 and 331 the foot will have been in a dorsiflexed position. This observation therefore supports the trend that tibialis anterior reflex components are largest when the muscle is at shortened length.





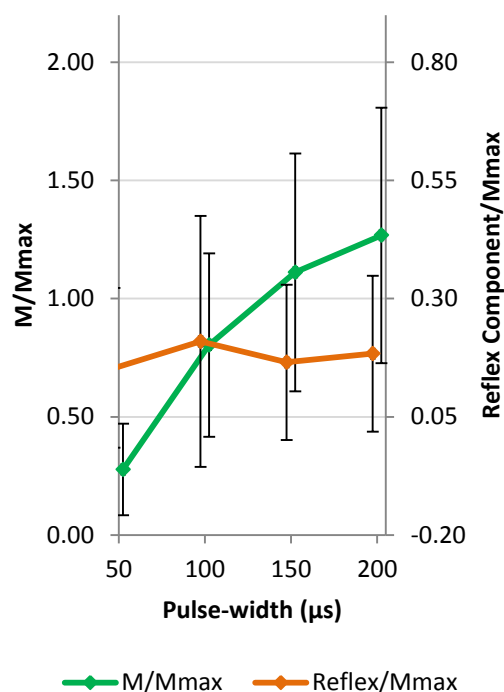
**Figure 10-35: Impaired sub-test 311: M-wave and reflex component ratio against pulse-width**

Ankle relaxed and plantarflexed under gravity  
(n=12)



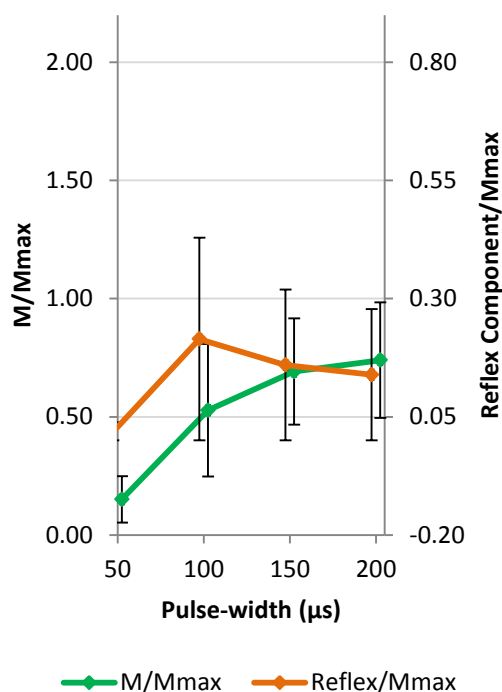
**Figure 10-36: Impaired sub-test 321: M-wave and reflex component ratio against pulse-width**

Ankle relaxed and supported in dorsiflexion (n=12)



**Figure 10-37: Impaired sub-test 331: M-wave and reflex component ratio against pulse-width**

Ankle voluntarily dorsiflexed (n=12)



**Figure 10-38: Impaired sub-test 341: M-wave and reflex component ratio against pulse-width**

Ankle voluntarily plantarflexed (n=12)

Figures include  $\pm$  one standard deviation error bars

#### *10.4.2 Phase 3 Summary: Motor and reflex response to conventional stimulation*

For both unimpaired and impaired participants tibialis anterior M-wave amplitude appears to increase at shortened muscle length during conventional twitch stimuli. This is in-keeping with phase 2 findings and those of the exploratory investigations.

For both unimpaired and impaired participants, tibialis anterior reflex component appears to indicate a small increase with shortened muscle length during conventional twitch stimuli. The reflex component increased further with voluntary effort in the unimpaired group. This property was not seen in the impaired group. As suggested in phase 2 (section 10.3.7), this is thought to be due to the limited or absent voluntary control following the impaired participant's stroke.

Also as noted during phase 2, for both groups, reflex components did not demonstrate characteristic H-wave behaviour. Reflex activity was sporadic in nature with temporal variation suggestive of an F-wave (Figure 4-5).

#### *10.4.3 Phase 3: Magnitude and speed of movement*

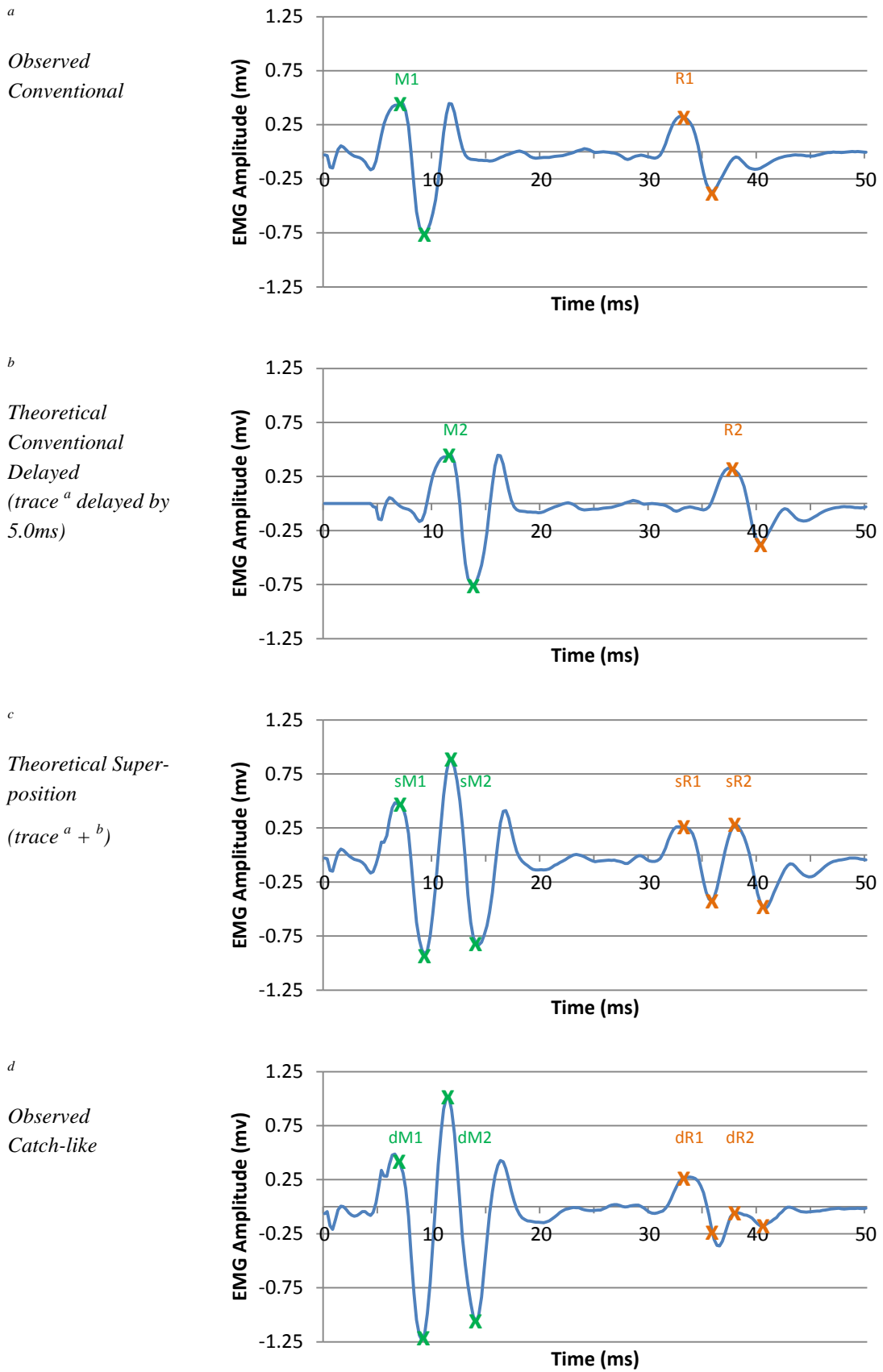
Measurement of the physical movement resulting from twitch stimulation obtained during Phase 3 was intended to be used to compare conventional and catch-like stimulation stimuli. Analysis similar to that of section 10.3.8 was envisaged and would permit assessment of peak angle and time to peak angle.

Upon review it was noted that goniometer data acquisition from some participants was limited to the first 500ms of recording. This discrepancy was traced to a programming error within the Stimulation Investigator application which affected selected participants. Conventional or catch-like stimuli were applied 250ms into the data collection. This provided an adequate data capture window to collect EMG but did not however capture the full dynamic twitch movement. The intended analysis was therefore not possible in the majority of participants. Of the limited remaining data its analysis was complimentary, but not core, to the posed research questions and has therefore has been omitted.

#### *10.4.4 Phase 3 Analysis: Super-position EMG features*

During Phase 3 the EMG response to conventional and catch-like stimulation would be assessed in order to address Research Questions 2 and 3 (pages 56 and 58 respectively). Due principally to stimulation artefact and variation in latency, the method of section 9.3.2 used to automatically measure M-wave and reflex component magnitude was not suitable for catch-like stimulation responses. In light of this, the exploratory data collected during Chapter 7 utilised a delayed super-position technique in order to compare EMG responses gained from individual conventional and catch-like stimuli. This approach made an assumption that in response to stimulation, the nerve, muscle and resulting EMG responded as a linear system. The response of catch-like stimuli could hence be compared to that of single stimuli appropriately delayed and summated with its self. During review of the exploratory data, this assumption and ensuing analysis approach appeared reasonable, producing rational results.

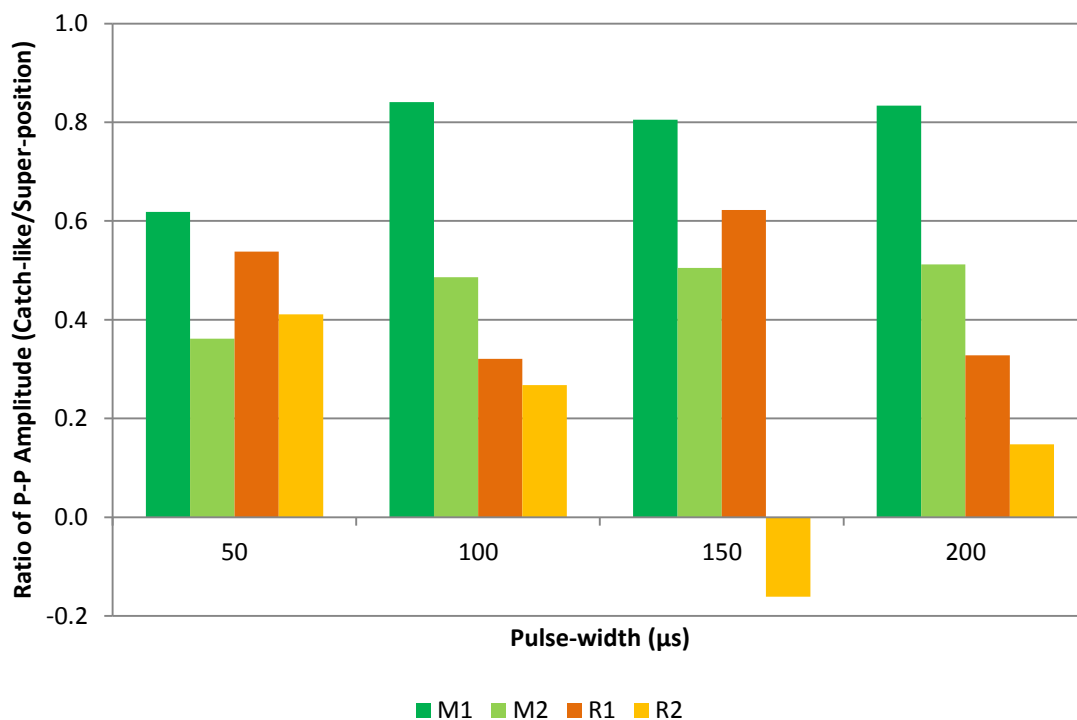
A similar data analysis to that described was utilised with the complete data set in order to answer Research Question 2 (page 56) in the context of unimpaired and impaired participant groups. In order to describe the methods used, data from participant U8 will be presented as an example. As shown in Figure 10-39<sup>a</sup>, M1 and R1 of the conventional stimuli were identified using the automated method of section 9.3.2. A ‘super-position’ response was then gained by delaying this response by 5.0ms and then summing it with itself. This would give theoretical M2 and R2 features as indicated in Figure 10-39<sup>b</sup>. The latencies at which these occurred would be those of M1 and R1 with an additional delay of 5.0ms, equal to the spacing of the applied doublet stimuli. Values at these time points of the catch-like response (Figure 10-39<sup>d</sup>: dM1, dM2, dR1 and dR2) were tabulated for comparison with the theoretical super-positioned values (Figure 10-39<sup>c</sup>: sM1, sM2, sR1 and sR2).



**Figure 10-39: Super-position of tibialis anterior EMG comparison method**

*U8 example*

This analysis was completed for all participants and pulse-width intensities applied during sub-tests 321, 322, 331 and 332. These sub-tests were selected as reflex components measured were greatest when the tibialis anterior was shortened under these conditions (section 10.4.1). In order to permit inter participant comparison, each amplitude was normalised to the value of sM1 at 200 $\mu$ s pulse-width for that sub-test. The ratio of catch-like to super-positioned conventional amplitude for each M1, M2, R1 and R2 are shown for the unimpaired participant group during sub-test 321 and 322 in Figure 10-40.



**Figure 10-40: Unimpaired sub-test 32**

*Note, difficulties with data analysis method limits meaningful interpretation. Included for discussion only.*

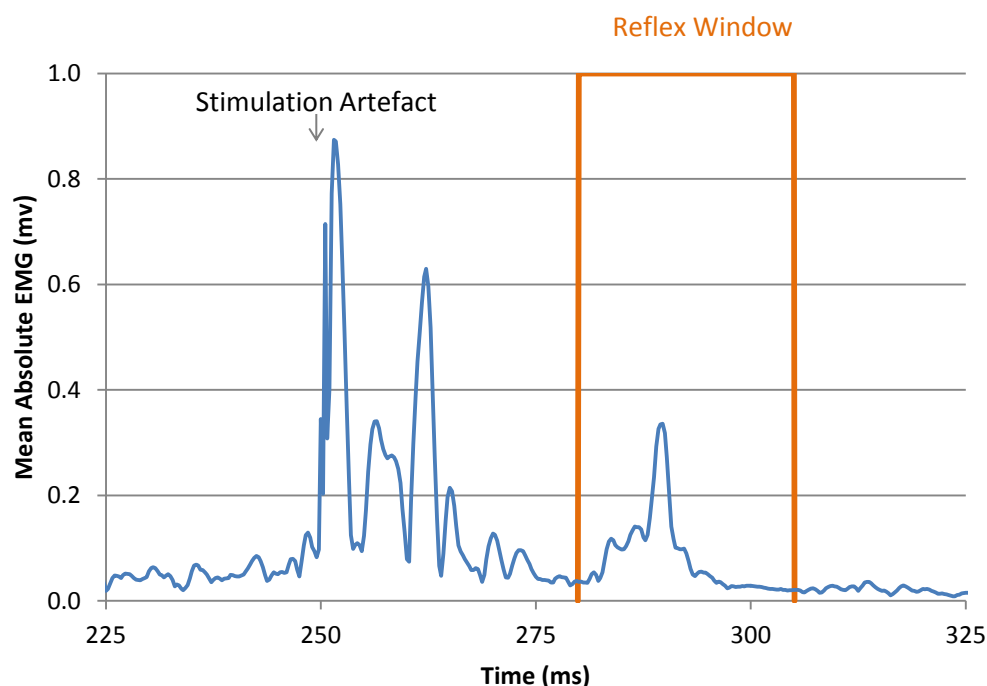
If the theoretical super-positioned conventional response had exactly matched the observed catch-like response, then all ratios of Figure 10-40 would be expected to equal unity. Upon closer inspection it was realised that when the described super-position analysis method was applied to the larger unimpaired and impaired data set, difficulties not observed during the exploratory data analysis were encountered. The stimulation artefact following associated with the second pulse of a doublet appeared to summate with that of the first pulse in a non-linear way. This resulted in the recorded catch-like

responses being more prone to stimulation artefact than the theoretical super-position responses. This was not in keeping with the assumption that a super-position response comparable to the recorded catch-like responses could be formed in the manner described earlier (i.e. Figure 10-39<sup>c</sup> not valid). Difficulties were also encountered when using the super-positioning method to assess differences in reflex components between the super-position and catch-like responses. When developing the analysis method, H-wave rather than F-wave activity had been envisaged based upon the findings of the exploratory data collection. Unlike the M-waves, the apparent F-wave reflex components had an element of temporal variation (often up to 5.0ms). At the time points at which sR1 and sR2 were calculated for, the super-positioned points did not necessarily correspond with these features of the doublet response (dR1, dR2). This explains the falsely negative value of R2 ratio in Figure 10-40.

Although this analysis method did not prove effective in investigating the posed research questions it appeared to provide meaningful comparison for some datasets. This in itself is of interest as it suggests that under certain conditions the EMG system can be assumed to be a linear system. An example of this can be seen if Figure 10-39<sup>c</sup> and Figure 10-39<sup>d</sup> are compared. There generally appears good agreement between the theoretical super-positioned and the observed catch-like responses. As discussed in the preceding paragraph, slight temporal variations in both the M-wave and reflex components can be identified. The most noticeable difference appears to be that the dR2 component is missing in the observed catch-like response compared to the theoretical super-positioned response. Whilst this was noted in the exploratory data and some other participant responses, it was not a consistent characteristic that could be meaningfully quantified during analysis.

#### 10.4.5 Phase 3 Analysis: Super-position EMG reflex component

Due to the limitations of the described analysis approach, an alternative method was utilised in order to assess Research Question 2 (page 56). Rather than comparisons of individual EMG features, mean values of absolute EMG activity during periods where reflex activity occurred were used to compare conventional and catch-like stimulation. Such an analysis method would not be as sensitive to small temporal variations in reflex component features. A ‘reflex window’ was defined between 30ms and 55ms post stimuli and the mean absolute EMG level calculated. Figure 10-41 provides an example for unimpaired participant U8.



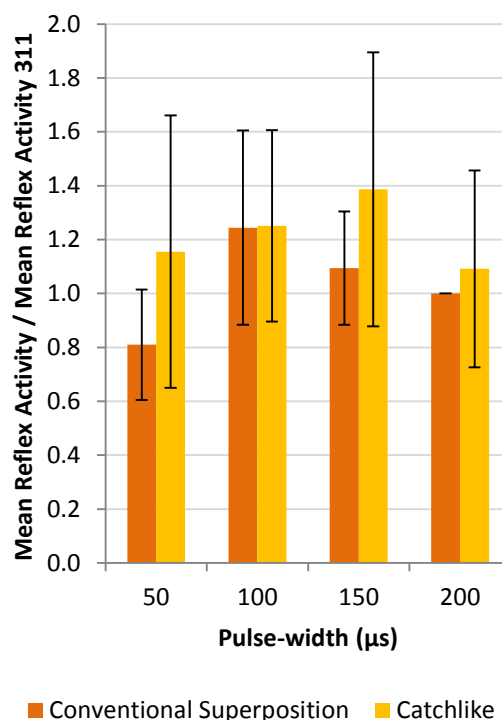
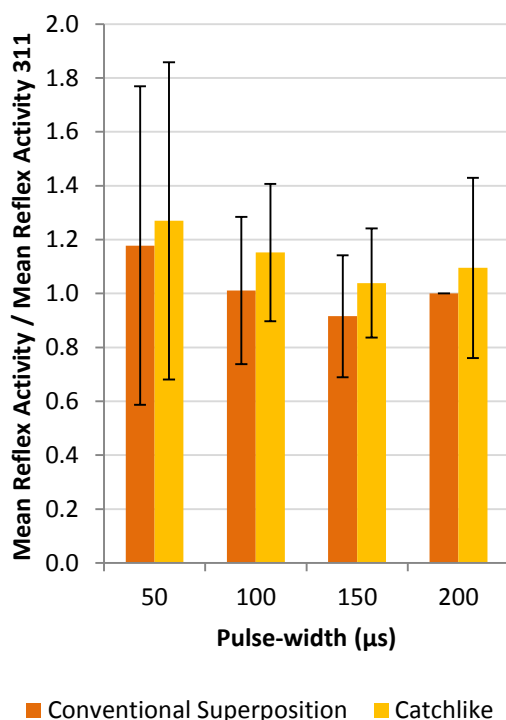
**Figure 10-41: Reflex window technique example: tibialis anterior absolute EMG**

*U10, sub-test 331, 200 $\mu$ s pulse-width.*

*Conventional stimulation pulse applied at 250ms.*

The mean absolute tibialis anterior EMG level was calculated during the reflex window for each pulse-width setting of sub-tests 331 and 332 for both super-positioned conventional and catch-like responses. In order to permit inter-participant comparison, the mean value at each pulse-width intensity was divided by that of the super-positioned conventional stimuli of sub-test 331 at 200 $\mu$ s pulse-width. As described in section 10.4.9, in order to avoid ill-conditioning by participants who with a small or absent a reflex response during phase 3, those with a mean reflex window value of the super-positioned conventional stimuli of sub-test 331 at 200 $\mu$ s pulse-width less than 0.15mV were excluded from analysis (U1, U11, I4, I6, I8, I11, I12, I13, I14 -Appendix K).

Figure 10-42 and Figure 10-43 display the normalised mean reflex window values for unimpaired and impaired participant groups respectively. Whilst there appears a trend for the mean values to be marginally higher for catch-like stimulation, this is present amongst a large amount of variation. Comparing the trends of individuals, no consistent trend amongst this variation appeared present and therefore further statistical analysis was not warranted. For both groups all ratios are within one standard deviation of unity.



**Figure 10-42: Unimpaired tibialis anterior reflex window ratio against pulse-width**

Ratio of mean absolute tibialis anterior EMG during reflex window (catch-like/conventional super-positioned response) (n=10)

**Figure 10-43: Impaired tibialis anterior reflex window ratio against pulse-width**

Ratio of mean absolute tibialis anterior EMG during reflex window (catch-like/conventional super-positioned response) (n=5)

**Figures include  $\pm$  one standard deviation error bars**

#### 10.4.6 Phase 3 Summary: Super-position EMG reflex component

The lack of elevation in catch-like mean amplitude during the reflex window with respect to conventional super-positioned response for both unimpaired and impaired participant groups suggests that catch-like stimulation does not provide marked increase or decreased reflex activity compared to that of a super-position of two conventional stimuli. The presented analysis method therefore suggests a negative outcome to Research Question 2 (page 56).



#### *10.4.7 Phase 3 Introduction: Inhibition effects*

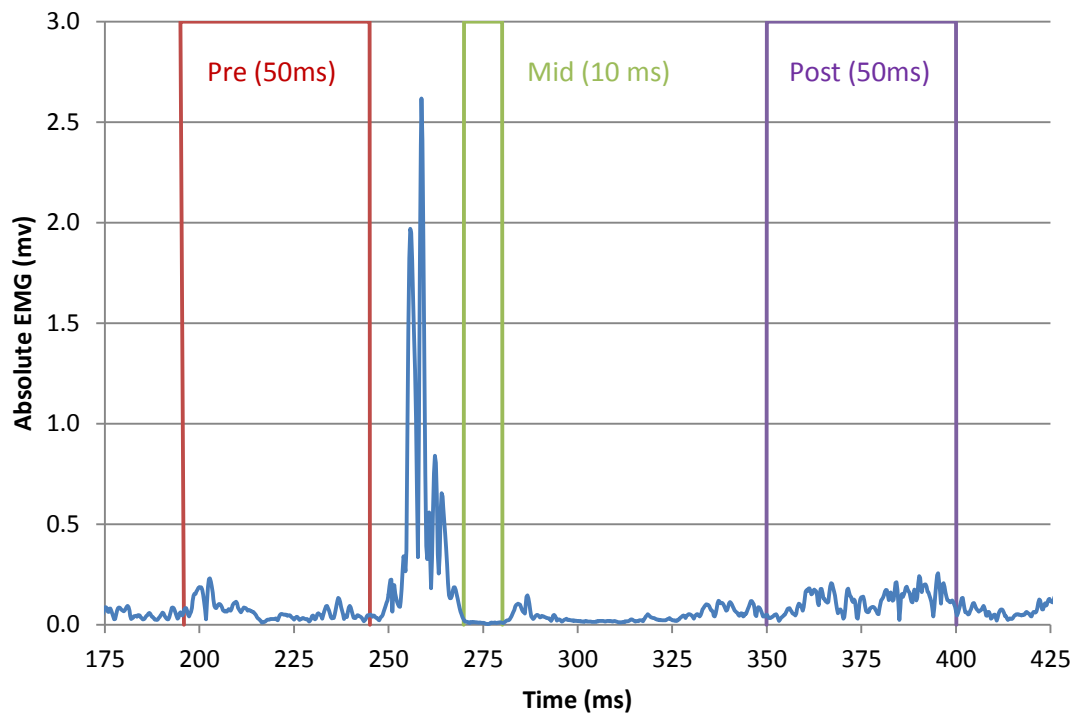
The super-position analysis of section 10.4.4 suggested that catch-like stimulation did not have an enhanced reflex component (negative outcome to Research Question 2, page 56). The increased magnitude and rate of developed force could however be due to increased activity of supporting muscles or reduced resistance from muscles acting in an opposing function (Research Question 3, page 58). This mechanism is known as reciprocal inhibition and was discussed in section 2.2.6. Phase 3 was designed to enable investigation of reciprocal inhibition through analysis of sub-tests 341 and 342 in which the participant applied effort to oppose the physical twitch movement produced by stimulation. Phase 3 also incorporated sub-tests 331 and 332 in order to enable the inhibition effects of conventional and catch-like stimuli applied to the already active tibialis anterior to be assessed.

As such, analysis was reliant upon a participant's ability to voluntarily activate their lower leg muscles in order to support or oppose movement. Only data from unimpaired participants was hence used during this analysis.

The effect of conventional and catch-like stimulation applied to an already active tibialis anterior and soleus was assessed in sub-tests 331, 332 and 341, 342 respectively.

#### *10.4.8 Phase 3 Analysis: Inhibition effects*

In order to demonstrate the analysis procedure used to assess inhibition, an example of absolute EMG waveform from participant U8 is presented. Absolute EMG averaged over five repetitions of each sub-test was calculated during data collection in order to assess mean activation levels. For each sub-test, three analysis windows were defined: pre, mid and post as indicated in Figure 10-44. The pre window consisted of the mean absolute EMG level attained over the 50ms which preceded the application of the stimuli. The mid window was defined as the 10ms prior to the window used to detect reflex components. For the majority of unimpaired participants, the mid window was the window of activity between 20ms and 30ms following the stimuli. This window allowed sufficient time for the M-wave and any stimulation artefact to pass but ended before reflex components would be recorded. The post window was 50ms in duration and delayed by 100ms after the application of stimulation. This delay allowed for any late reflex responses to be avoided.



**Figure 10-44: Pre, mid and post window technique example: tibialis anterior absolute EMG**

*U8, sub-test 331, 200 $\mu$ s pulse-width*

*(window duration included in brackets)*

The mean absolute EMG activity levels of the pre, mid and post windows were compared for each sub-test of phase 3. With consideration of the muscle from which the EMG was recorded from and the movement being completed, the presence of inhibition effects could be identified and contrasted between conventional and catch-like twitch stimuli.

#### *10.4.9 Phase 3 Tibialis Anterior: Recurrent inhibition*

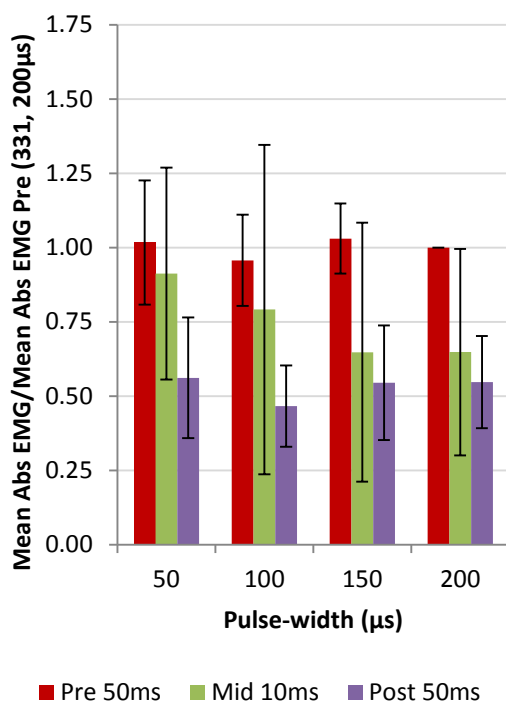
Findings from the tibialis anterior will first be discussed. In order to permit inter-participant comparison data was divided by the pre window level identified during sub-test 331 at 200 $\mu$ s pulse-width. To avoid skewing data trends with ill-conditioned data, an unimpaired participant's data was excluded if this pre window level was less than 0.15mV. This mean absolute EMG threshold is approximately the prior 0.35mV threshold multiplied by the reduction in noise factor ( $1/\sqrt{5}$ ) due to calculating a mean over five repetitions. This criterion was applicable to two unimpaired participants and hence these were excluded from tibialis anterior EMG analysis (U5, U6 -Appendix K).

Tibialis anterior mean absolute EMG data is plotted from sub-tests 331, 332, 341 and 342 in Figure 10-45 to Figure 10-48 respectively.

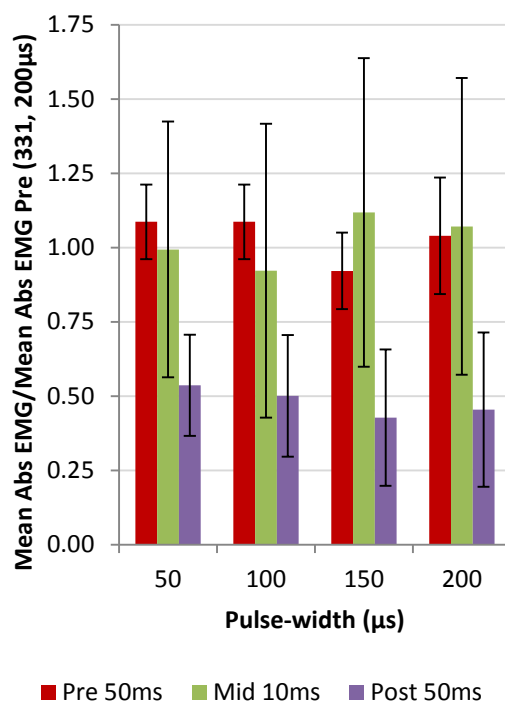
Regarding sub-tests 331 (Figure 10-45) and 332 (Figure 10-46) the mean absolute EMG ratio of the pre window is within one standard deviation of unity for all pulse-width values. This suggests that participants were successful in applying similar levels of voluntary activation when instructed to maximally dorsiflex their foot during sub-tests 331 and 332. The mean absolute EMG activation ratio drops to an average of approximately 0.3 during sub-tests 341 and 342 and suggests some remaining tibialis anterior activity. Upon closer inspection of absolute EMG waveforms using the animated GIF tool of section 9.3.1, it appeared that some co-activation between the tibialis anterior and soleus was present in unimpaired participants when plantarflexing during these sub-tests.

During sub-test 331 which applied a single conventional stimuli, there appears a trend for the mean absolute EMG ratio during the mid window to decrease with increasing pulse-width. Due to the relatively large variation as noted by the error bars of Figure 10-45, confidence in identifying this trend is limited. This appears to support the presence of the 'silent period' as defined in section 10.3.12. There appears a trend for the value of the mid window to increase in sub-tests 332 and 342; this is an artefact. As discussed earlier, the stimulation artefact caused by a catch-like stimuli lasted longer than that of a conventional pulse and hence for some participants the EMG amplifier was still recovering by 30ms when the mid window began.

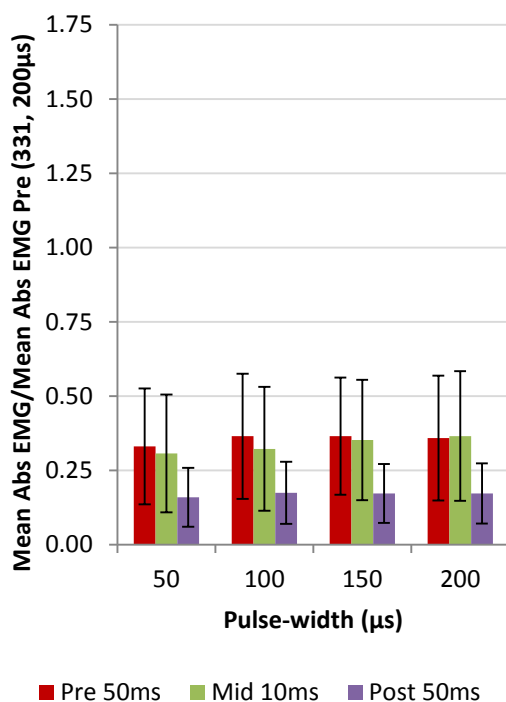
For both the conventional (331) and catch-like (332) sub-tests the post windows appears significantly reduced with respect to the pre window. The reduction occurs within an approximately 130ms window and is shorter than what would be expected if this was subject to higher level control e.g. by the brain. It therefore appears reasonable that a faster mechanism is responsible for this post window reduction. It is conceivable that the recurrent inhibition is due to Renshaw cell excitation by the antidromic  $\alpha$ -motor neuron action potential caused by stimulation [162].



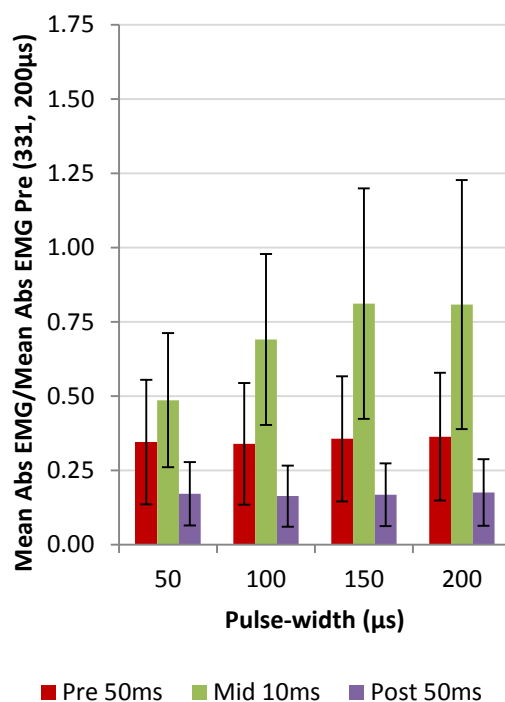
**Figure 10-45: 331 Conventional unimpaired twitch, mean absolute tibialis anterior, pre, mid and post windows**  
(n=10)



**Figure 10-46: 332 Catch-like unimpaired twitch, mean absolute tibialis anterior, pre, mid\* and post windows**  
\* appears void due to stimulation artefact (n=10)



**Figure 10-47: 341 Conventional unimpaired twitch, mean absolute tibialis anterior, pre, mid and post windows**  
(n=10)



**Figure 10-48: 342 Catch-like unimpaired twitch, mean absolute tibialis anterior, pre, mid\* and post windows**  
\* appears void due to stimulation artefact (n=10)

Figures include  $\pm$  one standard deviation error bars

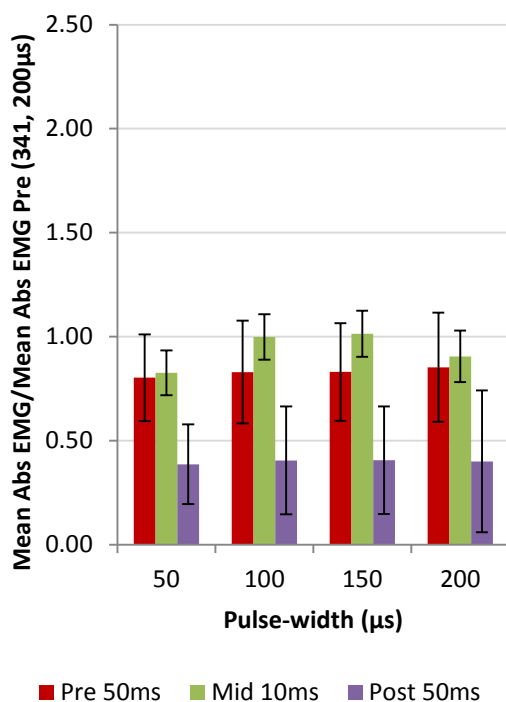
#### *10.4.10 Phase 3 Soleus: Reciprocal inhibition*

In order to address Research Question 3 (page 58), reciprocal inhibition of soleus EMG activity was assessed in response to conventional and catch-like stimulation. This was completed whilst actively plantarflexing and either a conventional or catch-like twitch stimuli applied to the common peroneal nerve in order to produce dorsiflexion.

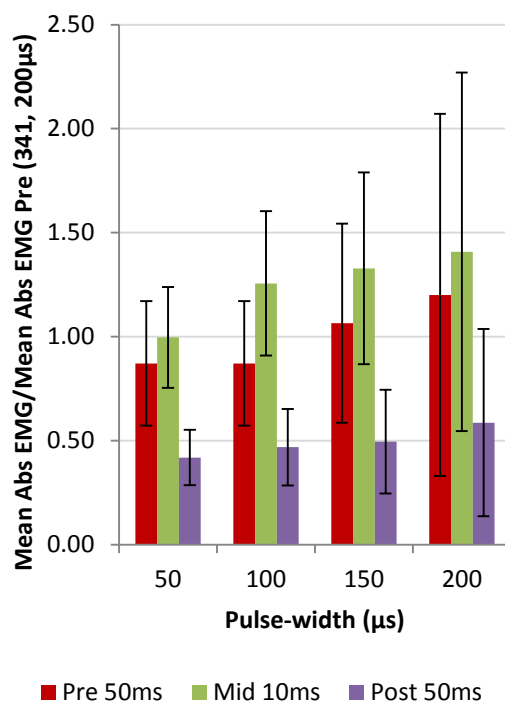
EMG activity measured from the soleus was generally smaller in amplitude compared to the tibialis anterior. This was expected due to the profile, size and location of the muscle with respect to the recording electrodes. Applying the same criterion of at least 0.15mV mean amplitude during the pre window of sub-test 341, six of the twelve unimpaired participants were excluded from analysis (U1, U4, U9, U10, U11, U12 - Appendix K). The lower sample numbers and generally smaller EMG levels, reduces confidence gained from these findings. Mean absolute soleus EMG data from sub-tests 331, 332, 341 and 342 is plotted in Figure 10-49 to Figure 10-52 respectively.

Regarding the pre window of sub-test 341 (Figure 10-51) and 342 (Figure 10-52), what appears a consistent level of voluntary activation was achieved when unimpaired participants were asked to plantarflex their foot. The pre window of sub-test 331 (Figure 10-49) and 332 (Figure 10-50) does not appear to be notably less in comparison. This higher than expected pre window activity may indicate co-activation with the tibialis anterior when participants maximally dorsiflexed their foot.

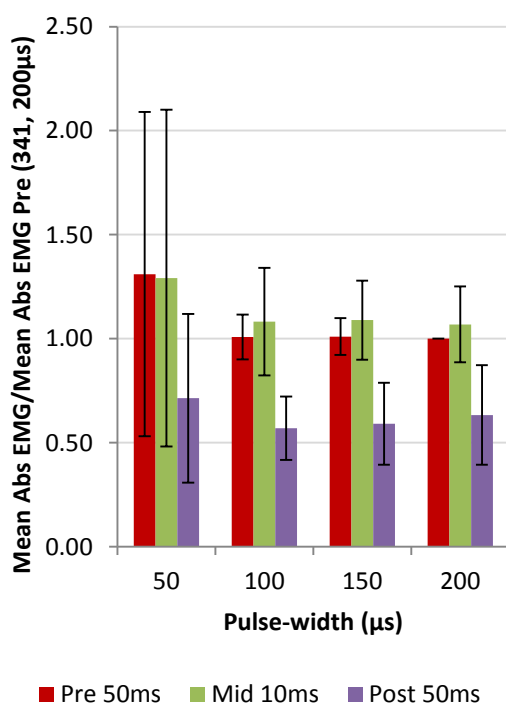
For both sub-test 331 (Figure 10-49) and 341 (Figure 10-51), the mid window activity appears comparable to that of the pre window. This is expected as the tibial nerve was not directly activated by stimulation and hence voluntary activation will not have been antidromic annihilated in the manner seen in the tibialis anterior. As there was generally less stimulation artefact present on the soleus than the tibialis anterior EMG responses, the mid windows of these conventional stimulation twitch responses are not adversely affected by stimulation artefact. Similar to tibialis anterior responses, additional stimulation artefact associated with catch-like stimuli bias assessment of mid window activity levels however. This is noted by the mid window trend to increase with pulse-width during catch-like sub-tests 332 (Figure 10-50) and 342 (Figure 10-52). During sub-test 341 and 342 the post window appears to have reduced by a similar amount to that seen in the tibialis anterior. This is thought to be due to reciprocal inhibition rather than recurrent inhibition however. There appears no noticeable difference between conventional (sub-test 341: Figure 10-51) and catch-like (sub-test 342: Figure 10-52) stimulation and therefore this suggests a negative outcome to Research Question 3 (page 58).



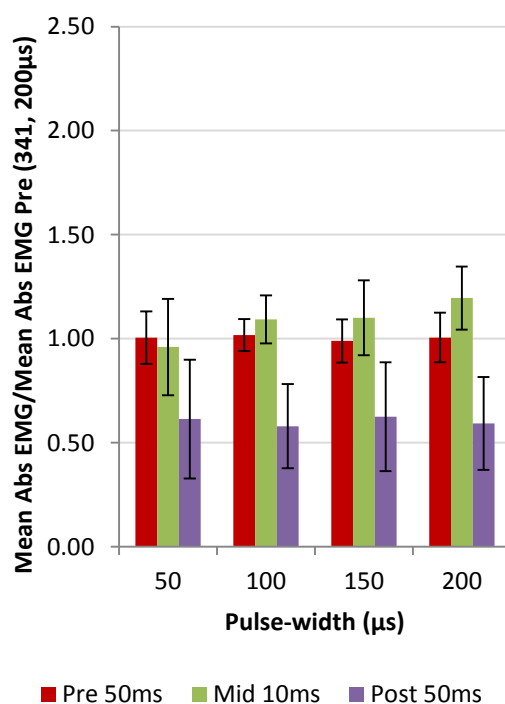
**Figure 10-49: 331 Conventional unimpaired twitch, mean absolute soleus, pre, mid and post windows**  
(n=6)



**Figure 10-50: 332 Catch-like unimpaired twitch, mean absolute soleus, pre, mid and post windows**  
(n=6)



**Figure 10-51: 341 Conventional unimpaired twitch, mean absolute soleus, pre, mid and post windows**  
(n=6)



**Figure 10-52: 342 Catch-like unimpaired twitch, mean absolute soleus, pre, mid and post windows**  
(n=6)

Figures include  $\pm$  one standard deviation error bars

#### 10.4.11 Phase 3 Summary: Inhibition effects

The adopted analysis approach appeared largely successful. The generally small magnitude of soleus EMG required the EMG amplifier to be used at its maximum gain setting. Ultimately data from some participants had to be excluded from analysis due to measurement precision limitations (e.g. mean absolute EMG amplitude  $<0.15\text{mV}$ ).

Assessment of reciprocal inhibition during phase 3 was primarily included in order to address Research Question 3 (page 58). Whilst reciprocal inhibition was observed, no noticeable difference in the magnitude of this was seen between the tibialis anterior and soleus when utilising conventional and catch-like twitches. Therefore these findings do not suggest that the catch-like effect is due to an increased inhibition effect and a negative answer to Research Question 3 is supported.

Subsequent to addressing this research question, other characteristics of interest were noted. Whilst this investigation was initiated with a view to identifying reciprocal inhibition in the soleus, what appeared to be recurrent inhibition of the tibialis anterior was also observed. This is an interesting finding as it has implications if attempting to combine FES with voluntary contractions. If, such as Yeom *et al.* [163], a closed loop FES control system using voluntary EMG acquired in-between stimulation pulses to control stimulation is implemented, then the recurrent inhibition effects of stimulation (i.e. the control signal) should be accounted for. Shalaby *et al.* [164] have demonstrated such an FES control system in which gain applied to EMG is varied by the intensity of preceding stimulation. If using FES to encourage and strengthen voluntary movements as part of a therapy programme then recurrent inhibition may be undesired. Alternatively if a twitch stimuli applied to an overactive antagonist muscle prior to movement had a recurrent inhibition effect, then a weak voluntary agonist movement may not be dominated by spasticity. For the above scenarios the duration and properties of the recurrent inhibition effect would require further investigation. It is also conceivable that conventional and catch-like stimulation may have different excitatory effects upon Renshaw cells and further investigation of this may be warranted.

Whilst in the presence of variation, the tibialis anterior data supports the presence of the 'silent period' identified during Phase 2 (section 10.3.12). The lack of notable reduction in soleus mid window to pre-window further supports the proposed mechanism of the effect.

## 10.5 Phase 4

Phase 4 investigated the effect of conventional and catch-like stimuli on the excitability and inhibition of spinal reflexes affecting the tibialis anterior and soleus muscles when triggered from ankle joint angle during isotonic contractions (section 8.2.4). Conventional or catch-like twitch stimuli were triggered when ankle angle passed through 50% ROM into dorsiflexion, 80% ROM into peak dorsiflexion, 50% ROM into plantarflexion and 20% ROM into peak plantarflexion when following a sinusoidal trace representing percentage of ROM. During presentation and discussion of these results, these trigger points will be referred to by the phase of the sinusoidal tracking signal e.g. 0, 90, 180 and 270 degrees respectively (Figure 7-12). The Stimulator Investigator application of section 6.7 was configured to record the mean EMG response over five twitch responses at each of these tracking angle trigger points. Despite often limited or absent voluntary dorsiflexion, the majority of impaired participants were still able to consistently trigger the application of stimulation. This was due to the triggering method being reliant upon a consistent, even if small, ROM. Phase 4 analysis is therefore reported for both unimpaired and impaired participant groups.

### 10.5.1 Phase 4 Analysis:

#### *Motor and reflex response to conventional stimulation during isotonic movement*

As in previous phases, the trends of conventional stimulation will first be assessed in order to address Research Question 1 (page 52). The peak to peak mean M-wave and reflex component amplitudes gained at each trigger angle were computed using the automated method of section 9.3.2. In order to enable inter participant comparison these values were divided by the mean M-wave amplitude recorded at the 90 degree tracking angle (sub-test 42\_). Participants with a mean M-wave amplitude of less than 0.35mV at this tracking angle were excluded from analysis in order to avoid ill-conditioning. Two unimpaired and three impaired participants were excluded due to this criterion (U4, U5, I1, I2, I6 -Appendix K).



**Unimpaired participants**

The mean unimpaired M-wave amplitude ratio at each tracking angle is indicated in Figure 10-53. A few outliers either side of the mean increase the variance of the group, however the mean appears largely constant around unity. There may be a slight trend for larger M-wave amplitudes when attempting to dorsiflex (0 and 90 degree tracking angle).

The mean unimpaired reflex component ratio at each tracking angle is shown in Figure 10-54. Although accentuated by an outlier, there appears a trend for the reflex component to be larger at 0 and 90 degrees tracking angle when the participant was actively dorsiflexing their foot.

**Impaired participants**

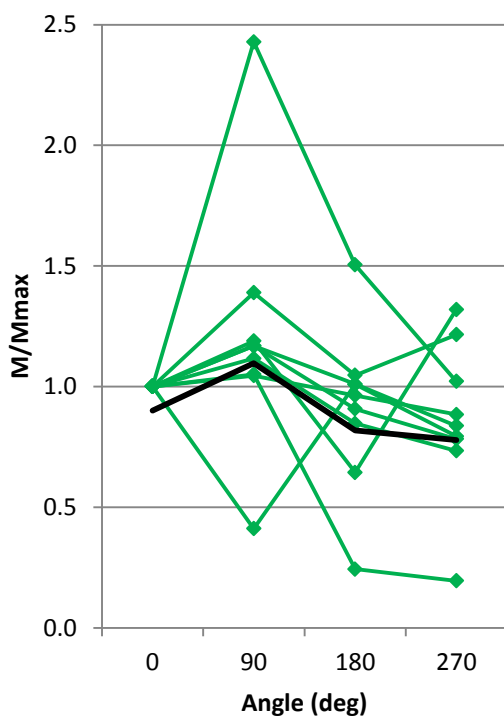
The mean impaired M-wave amplitude ratio at each tracking angle is given in Figure 10-55. The mean amplitude ratio appears largely constant around unity. This suggests that no change in M-wave amplitude is seen with changing joint angle or effort.

The mean impaired reflex component ratio at each tracking angle is shown in Figure 10-56. It would appear that the reflex component is lacking or very small in most impaired participants. A trend for the reflex component to be larger at 0 and 90 degrees tracking angle appears evident in some participants however this is not representative of the group as a whole.

*10.5.2 Phase 4 Summary:**Motor and reflex response to conventional stimulation during isotonic movement*

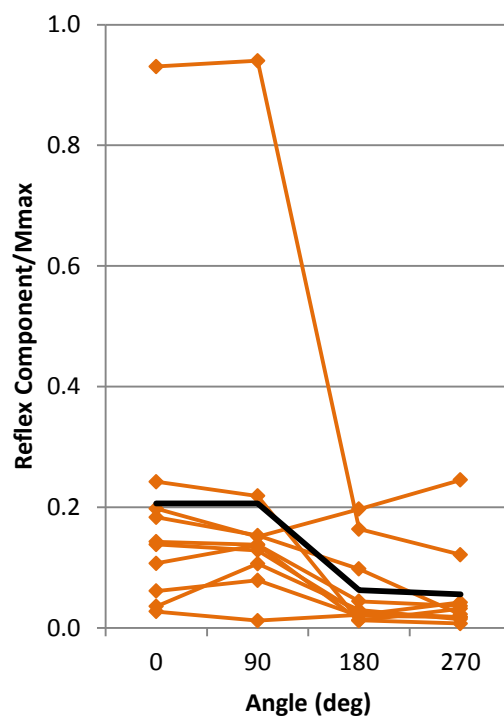
Neither group demonstrated notable modulation of M-wave amplitude with joint angle as seen in preceding phases. The effect may have been present amongst the unimpaired group however it was masked by within group variation. Its absence in the impaired group may have been due to the small ROM when reliant upon voluntary control only.

In keeping with phases 2 and 3, there was less noticeable modulation of reflex component magnitude with effort in the impaired compared to unimpaired group.



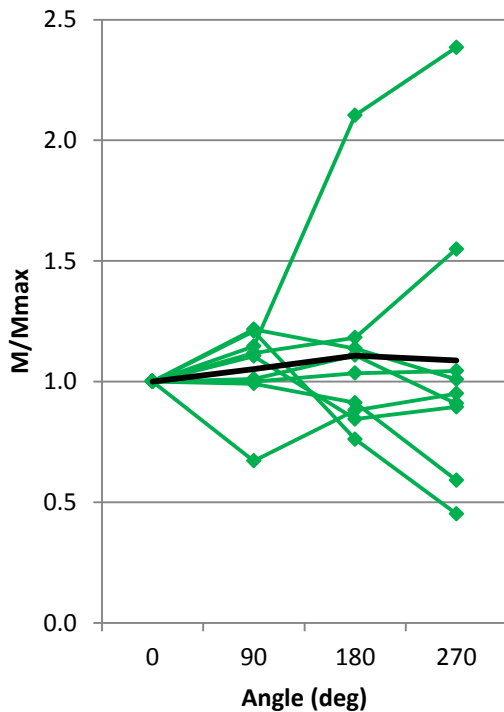
**Figure 10-53: Unimpaired tibialis anterior M-wave ratio against sinusoidal tracking angle**

Group mean indicated in black (n=10)



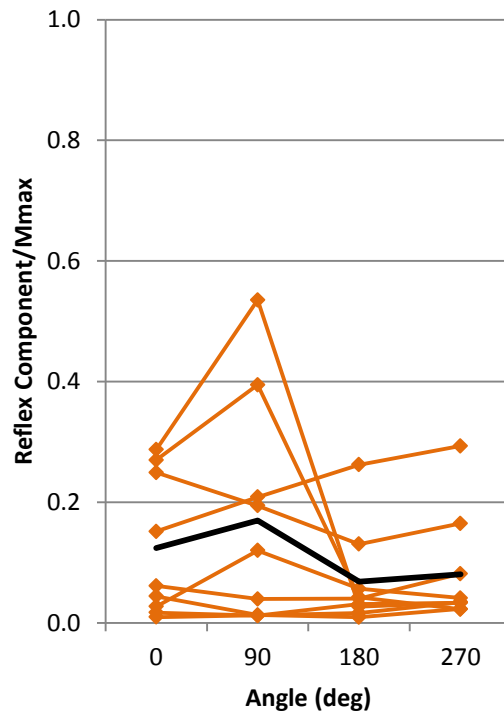
**Figure 10-54: Unimpaired tibialis anterior reflex component ratio against sinusoidal tracking angle**

Group mean indicated in black (n=10)



**Figure 10-55: Impaired tibialis anterior M-wave ratio against sinusoidal tracking angle**

Group mean indicated in black (n=9)



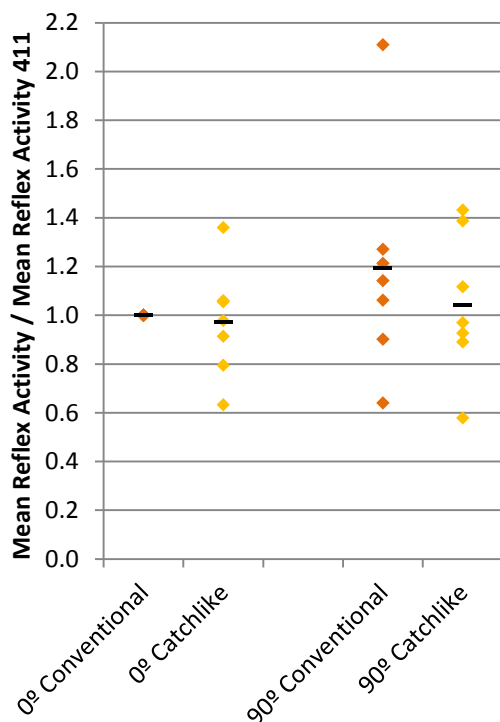
**Figure 10-56: Impaired tibialis anterior reflex component ratio against sinusoidal tracking angle**

Group mean indicated in black mean (n=9)

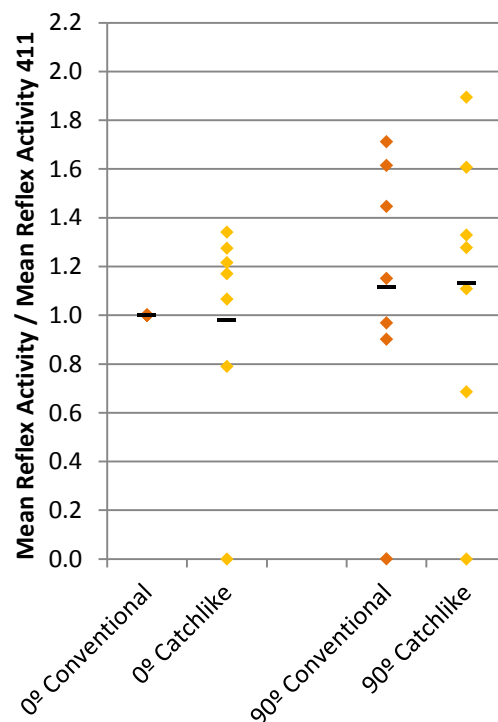
### 10.5.3 Phase 4: EMG super-position

In order to address Research Question 2 (page 56) during the isotonic movement of phase 4 the super-positioning method of section 9.3.2 was utilised. The mean absolute EMG level during 30-55ms post stimulation (akin to Figure 10-41 but for Phase 4 data) was calculated and compared between catch-like twitch responses and the super-positioned conventional twitch responses at 0 and 90 degree tracking angles. Following findings of the earlier section, reflex components were largest at these tracking angles when voluntary effort was present and therefore only these were assessed. As when assessing recurrent and reciprocal inhibition, only participants with a pre window of greater than 0.15mV were included during analysis. Five unimpaired and six impaired participants were excluded due to this criterion (U5, U6, U9, U11, U12, I4, I6, I7, I11, I12, I14 -Appendix K).

For each tracking angle the value for each catch-like sub-test (412 and 422) was divided by the super-positioned conventional 411 sub-test (90 degrees tracking angle) value, thus giving a ratio with which to compare the two. Figure 10-57 and Figure 10-58 provide plots of these ratios at 0 and 90 degree tracking angles for unimpaired and impaired groups respectively.



**Figure 10-57: Unimpaired tibialis anterior reflex component ratio against sinusoidal tracking angle**  
Group mean indicated in black (n=7)



**Figure 10-58: Impaired tibialis anterior reflex component ratio against sinusoidal tracking angle**  
Group mean indicated in black (n=7)

In light of the within group variation, there appears no substantial difference between the mean absolute reflex activity of catch-like stimulation to that of a super-position of two conventional stimuli shown when actively dorsiflexing the foot under isotonic conditions. This is applicable to both the unimpaired and impaired participant groups.

A negative outcome to Research Question 2 (page 56) is therefore suggested by Phase 4. Whilst not expected to conflict with that of Phase 3, Phase 4 demonstrates this during isotonic conditions when triggered from a percentage of ROM.

## 10.6 Phase 5

Phase 5 investigated the effect of conventional and catch-like stimuli on the excitability and inhibition of spinal reflexes affecting the tibialis anterior and soleus muscles when triggered from EMG during isometric conditions (section 8.2.5).

Conventional or catch-like twitch stimuli were triggered when either tibialis anterior or soleus smoothed absolute EMG levels exceeded 50% of that attained during a maximal voluntary contraction against the ankle bracket of section 6.5 when dorsiflexing or plantarflexing respectively. The Stimulator Investigator application of section 6.7 was configured to record the mean EMG response over five twitch responses at each of these EMG level trigger points.

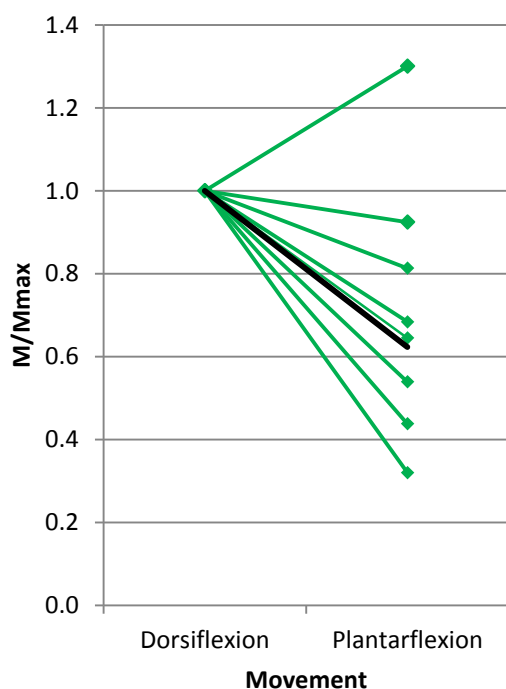
Phase 5 of the investigational session was completed with both unimpaired and impaired participant groups. Due to limited or absent voluntary EMG activity, all but one impaired participant was unable to consistently trigger the application of stimulation. Phase 5 analysis is therefore only presented for unimpaired participants.

### *10.6.1 Phase 5 Analysis: Conventional stimulation during isometric movement*

Research Question 1 (page 52) will first be considered through assessment of responses gained from conventional stimulation twitches. The peak to peak M-wave and reflex component amplitudes of responses gained when attempting to dorsiflex and plantarflex were computed using the automated method of section 9.3.2. In order to enable inter-participant comparison these values were divided by the mean M-wave amplitude recorded when attempting to dorsiflex (sub-test 51\_). Participants with a mean M-wave amplitude of less than 0.35mV when attempting to dorsiflex were excluded from analysis in order to avoid ill-conditioning. Four unimpaired participants were excluded due to this criterion (U2, U3, U5, U10 -Appendix K).

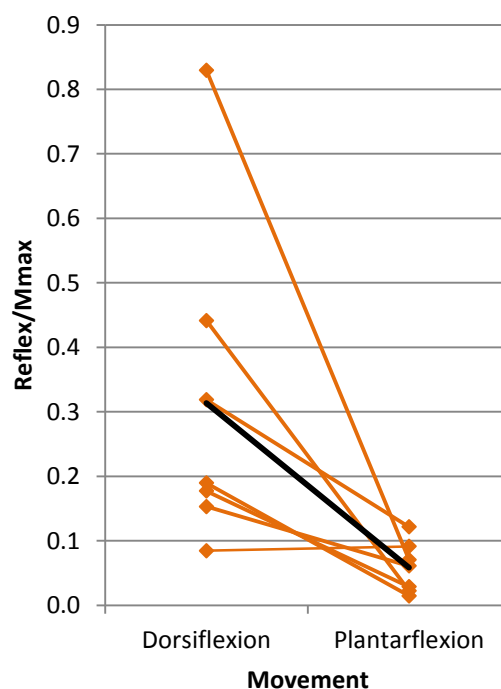
The mean unimpaired M-wave amplitude ratio when attempting to dorsiflex or plantarflex is shown in Figure 10-59. There appears a trend for reduced M-wave when plantarflexing compared to dorsiflexing. Six out of seven of the unimpaired participant datasets included within the analysis demonstrated this characteristic.

The mean unimpaired reflex component ratio when attempting to dorsiflex or plantarflex is shown in Figure 10-60. Reflex activity was essentially absent in the majority of unimpaired participants when plantarflexing the foot. Six of seven of the unimpaired participants demonstrated larger reflex activity when attempting to dorsiflex rather than plantarflex. The tibialis anterior would be under tension when attempting to dorsiflex against the isometric ankle bracket. The observation of reflex components during these conditions suggests muscle tension does not have an inhibitory effect on their mechanism. This supports the conclusion that F-wave activity was modulated by voluntary effort, rather than reduced muscle tension, when isotonicly progressing into dorsiflexion during sub-test 251 (section 10.3.7).



**Figure 10-59 Unimpaired: tibialis anterior M-wave ratio during isometric dorsiflexion, plantarflexion attempts**

Triggered as smoothed absolute EMG exceeded 50% of that attained during maximal voluntary contraction and opposing muscle less than 25%. Group mean indicated in black (n=7)



**Figure 10-60 Unimpaired: tibialis anterior reflex component ratio during isometric dorsiflexion, plantarflexion attempts**

Triggered as smoothed absolute EMG exceeded 50% of that attained during maximal voluntary contraction and opposing muscle less than 25%. Group mean indicated in black (n=7)

As discussed in earlier phases, a trend for increased reflex components when attempting to dorsiflex may be artificially strengthened by voluntary activation being misinterpreted as reflex activity by the peak to peak amplitude measurement algorithm described in section 9.3.2. Use of mean responses over five repetitions sought to minimise this through attenuation of temporally asynchronous voluntary EMG by a factor of  $1/\sqrt{5}$ .

#### *10.6.2 Phase 5 Summary: Conventional stimulation during isometric movement*

In order to consistently trigger the application of stimulation, unimpaired participants were required to exert large voluntary forces against the ankle bracket. The high levels of voluntary effort and force that were developed may account for differences in trends noted between the isotonic conditions of phase 4 and the isometric conditions of Phase 5.

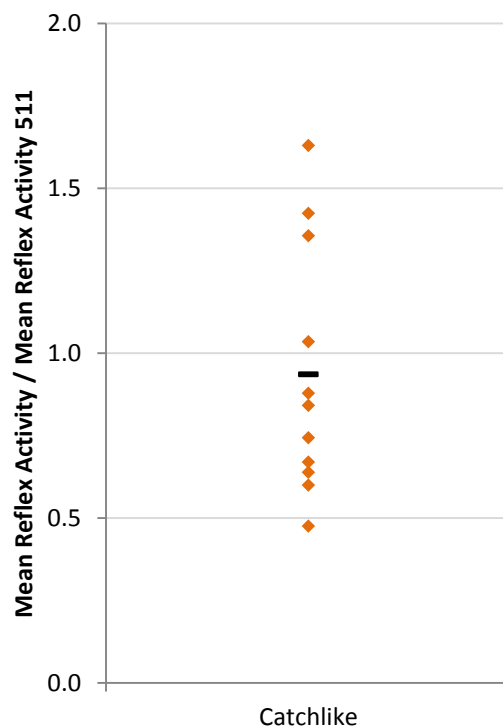
M-wave amplitude varied between attempting to dorsiflex and attempting to plantarflex despite the muscle length being restricted by the isometric conditions. Although muscle length was constrained, the cross-sectional area of the tibialis anterior still varied with muscle tension. In keeping with the hypothesis and experimentation of section 7.7, this may account for the large M-wave amplitudes noted when participants were attempting to dorsiflex the foot. Amongst the supervision team and author it was also noted that contraction of the tibialis anterior can be felt at the skin surface above the fibula head. Relative movement between this skin surface and the common peroneal nerve caused by contraction of the tibialis anterior may also affect the extent to which the nerve is depolarised by stimulation (section 7.5).

The magnitude of which reflex components were affected by voluntary effort in Phase 5 was greater than that of Phase 4. Having stimulated at only 200 $\mu$ s pulse-width and with a single stimulation twitch, an indication of whether the reflex components appeared of H- or F-waves mechanism could not be gained. The greater facilitation effect of effort on the reflex component of Phase 5 may have been due to afferent input caused by the isometric conditions (i.e. muscle tension, Ib golgi firing, section 2.2.5) or the high levels of voluntary effort having a facilitatory effect at the dorsal horn of the spinal cord.

### 10.6.3 Phase 5 Analysis: EMG super-position

In order to address Research Question 2 (page 56) during the isometric movement of Phase 5, the super-positioning method of section 9.3.2 was utilised. The mean absolute EMG level during 30-55ms post stimulation (akin to Figure 10-41 but for Phase 5 data) was calculated and compared between the catch-like twitch response and the super-positioned conventional twitch response for unimpaired participants when attempting to dorsiflex their foot during sub-test 51\_. As when assessing recurrent and reciprocal inhibition, only participants with a pre window of greater than 0.15mV were included during analysis. One unimpaired participant was excluded due to this criterion (U3 - Appendix K).

The absolute EMG value for catch-like sub-test (512) was divided by the super-positioned conventional sub-test (511) value, thus giving a ratio with which to compare the two. Figure 10-61 plots this ratio for the unimpaired group when attempting to dorsiflex the foot during sub-test 51\_.



**Figure 10-61: Unimpaired tibialis anterior reflex component ratio when attempting to dorsiflex**  
Group mean indicated in black (n=11)

There appears a large amount of variation and a clear trend cannot be identified between the mean absolute reflex activity of catch-like stimulation to that of a super-position of two conventional stimuli. The group mean appears close to unity.

When considering the group response, phase 5 suggests a negative outcome to Research Question 2 (page 56) during isometric conditions. Whilst this is stated with limited certainty due to the large variation shown, it is in keeping with earlier findings from phase 3 and 4.

### 10.7 Phase 6

Phase 6 was designed to investigate the motor and reflex effects of conventional and catch-like stimulation when applied during the swing phase of gait whilst walking 10 metres indoors. Stimulation was triggered using a footswitch and applied from heel rise through to heel strike with a short extension period during initial stance. Where previous investigation phases had sort to evaluate individual aspects such as effort or movement in a controlled manner, Phase 6 would assess motor and reflexes responses in the presence of many of these factors changing throughout gait (section 8.2.6).

Whilst a mean EMG response over five strides was initially computed, variations in swing period complicated subsequent analysis and ultimately limited interpretation of data. For example if stimulation was miss-triggered or a short (e.g. shuffling) stride taken, data from the complete walk was compromised. This issue was identified following the first two impaired participants to complete the investigation protocol. The Stimulation Investigator application was modified such that data from the third stride following commencement of the sub-test was recorded. This permitted time for acceleration and avoided miss-triggering sometimes associated with initiation of gait. Data from the third stride of walking is therefore presented during Phase 6 analysis.

A participant's swing period was not necessarily the same between conventional and catch-like stimulation tests for a participant. Due to the varying duration of applied stimulation, comparisons between conventional and catch-like responses throughout swing were hence not straight forward and potentially of limited interpretation.

During phases 3, 4 and 5, a negative outcome to both Research Questions 2 and 3 (pages 56 and 58 respectively) under passive, isometric and isotonic conditions had been concluded. These findings were not expected to differ during gait and hence phase 6 analysis was restricted to further exploring Research Question 1 (page 52) with

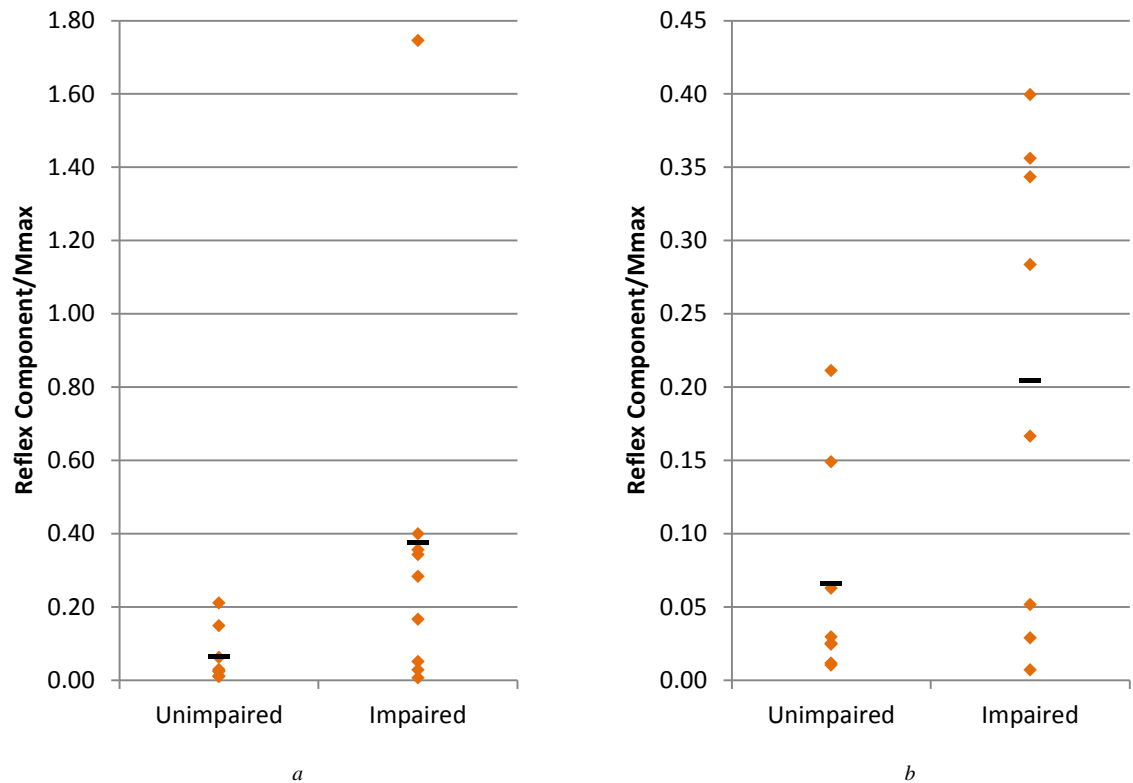


conventional stimulation only. Therefore only sub-tests 62 and 64 are utilised by this analysis. Sub-test 64 may have notable interest to some, as the manner in which electrical stimulation was applied mimicked that of the clinical application of dropped foot correction commonly used at the National Clinical FES Centre.

The response to an individual conventional stimuli applied at heel rise will first be contrasted between unimpaired and impaired participant groups (sub-test 62). Whilst a single twitch at heel rise would not be used functionally in this manner, it is of interest when comparing to the findings of phases 3, 4 and 5. Following this the response to a burst of conventional stimulation triggered at heel rise and applied throughout swing into initial stance is presented and discussed (sub-test 64).

#### *10.7.1 Phase 6: Conventional stimulation twitch triggered at heel rise*

Sub-test 62 applied a single 200 $\mu$ s pulse-width stimuli triggered at heel rise. As previous, the automated method of section 9.3.2 was used to identify the amplitude of the resulting M-wave and any reflex components. In order to permit inter participant comparison the reflex component amplitude was represented as a ratio to M-wave amplitude for the twitch. Participants with a mean M-wave amplitude of less than 0.35mV at heel rise were excluded from analysis in order to avoid ill-conditioning. Four unimpaired participants and four impaired participants were excluded due to this criterion (U2, U3, U5, U10, I1, I2, I4, I6 -Appendix K). Figure 10-62 displays these ratios for unimpaired and impaired participants during sub-test 62.



**Figure 10-62: Unimpaired and impaired tibialis anterior reflex component at heel rise**

Expressed as a ratio to maximum M-wave amplitude for each participant

Group mean indicated in black

<sup>a</sup> Unimpaired  $n=8$ , Impaired  $n=9$

<sup>b</sup> Unimpaired  $n=8$ , Impaired  $n=8$  (impaired participant outlier of <sup>a</sup> removed from analysis)

Comparing the reflex component of unimpaired and impaired participants in Figure 10-62<sup>a</sup> there clearly appears an outlier amongst the impaired participant group. There however appears a trend for a larger reflex component at heel rise in the impaired than unimpaired group. For five out of nine impaired participants the reflex component was greater than 20% of the M-wave amplitude. This is of comparable magnitude to the maximum component seen during phase 3 and 4 when attempting to dorsiflex the foot.

#### 10.7.2 Phase 6: Conventional stimulation burst triggered at heel rise

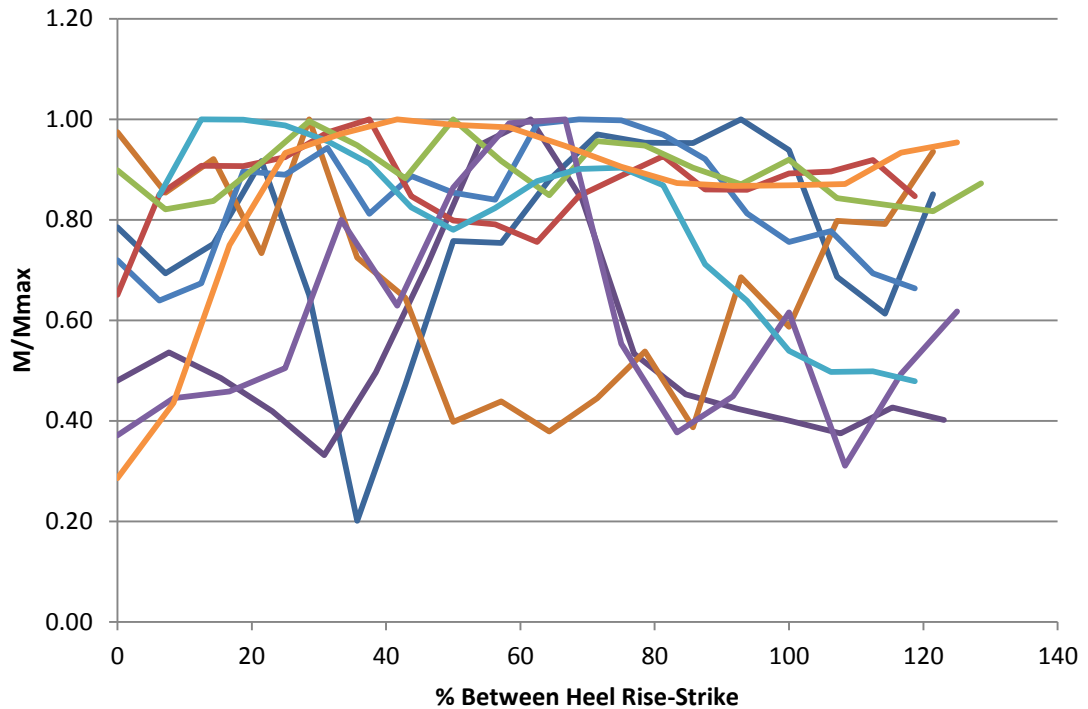
During sub-test 64 a 200 $\mu$ s pulse-width conventional stimulation burst was applied at detection of heel rise during walking. Upon either detection of heel strike or after one second of stimulation (20 pulses) a 200ms fixed period of extension was added (4 pulses). The time at which a stimulation pulse was applied was expressed as a percentage between when heel rise (0%) and heel strike (100%) was detected by the footswitch.

During analysis, the M-wave amplitude following each stimuli of the burst was expressed as a ratio to the peak M-wave recorded during the burst and plotted against the percentage between heel rise and heel strike. This is shown for unimpaired and impaired participants in Figure 10-63 and Figure 10-64 respectively. Participants with a peak M-wave of less than 0.35mV were excluded from analysis in order to avoid ill-conditioning. Three unimpaired participants and four impaired participants were excluded due to this criterion (U2, U3, U5, I1, I2, I4, I6 -Appendix K).

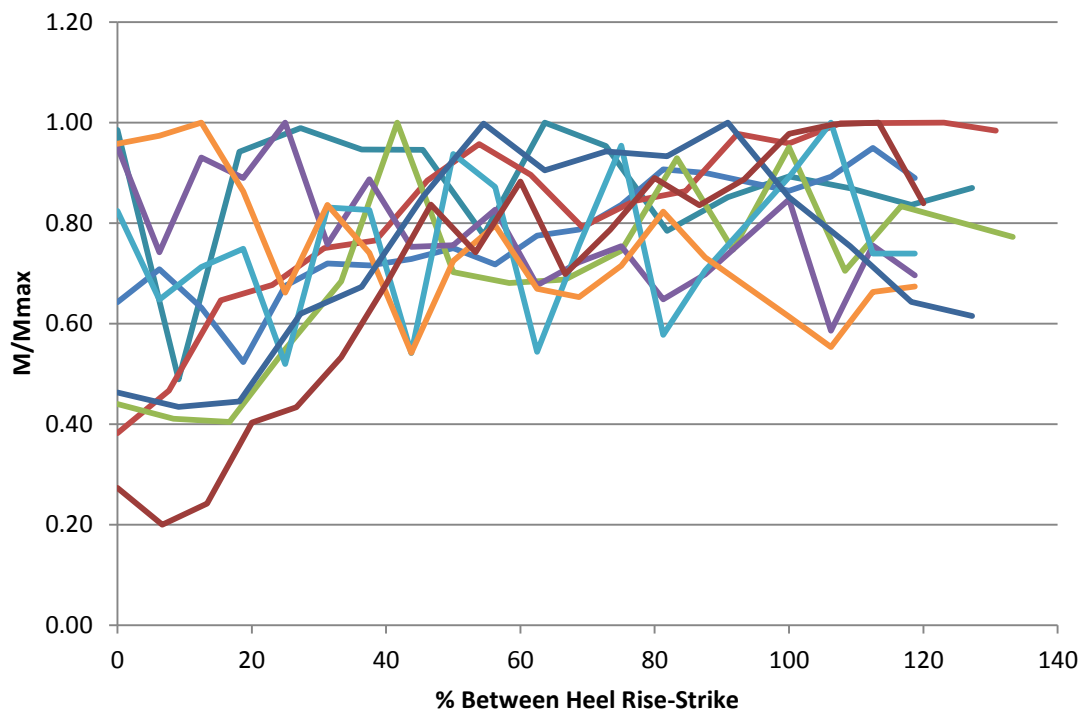
For both unimpaired and impaired groups there appears a large amount of variation in M-wave amplitude during the burst of conventional stimulation. M-wave amplitude often reduces to below 75% of peak value recorded during the burst.

In case this was an artefact caused by the basic peak amplitude measurement method of section 9.3.2, animations of all participant bursts were reviewed and the time periods in which to identify peaks and troughs checked. Whilst this led to minor adjustment of values for some participants the net overall response was unchanged.

As noted previously, M-wave amplitude appears to vary with muscle length and tension. Potential mechanisms for this effect were discussed in Chapter 7 and initial exploratory investigations completed by the author. If the effect is not that of a measurement artefact but one that indicates that activation of the  $\alpha$ -motor neuron bundle and hence muscle varies during gait, then this effect warrants further investigation and characterisation. Although there appeared large inter participant variation, intra-variation may be less. If this was consistent across a dropped foot stimulation users swing period, then M-wave variation may be able to be characterised over a number of strides and compensated for by the intensity or frequency of applied stimulation. This would have pertinence if attempting to modulate stimulation intensity during swing in order to mimic natural firing patterns of unimpaired individuals. When attempting this, O'Keefe and Lyon [165] have used a scaled linear envelope of voluntary tibialis anterior EMG acquired from unimpaired individuals during gait as a waveform to control FES amplitude intensity. The tibialis anterior EMG data used was acquired over the ankle range of interest (occurring during active dorsiflexion and loading response) and took into account the type of muscle contraction (concentric, eccentric, and isometric) and the speed of hemiplegic ankle joint rotation. This research study supports the need to assess the EMG response at different muscle lengths such that the effects can be accounted for. In doing this, the assumption that the pre-set EMG envelope likens volitional intent is strengthened as the influence of muscle length can be accounted for.



**Figure 10-63: Unimpaired: tibialis anterior M-wave ratio against percentage of swing**  
 Heel rise = 0%, heel strike = 100% (n=9).



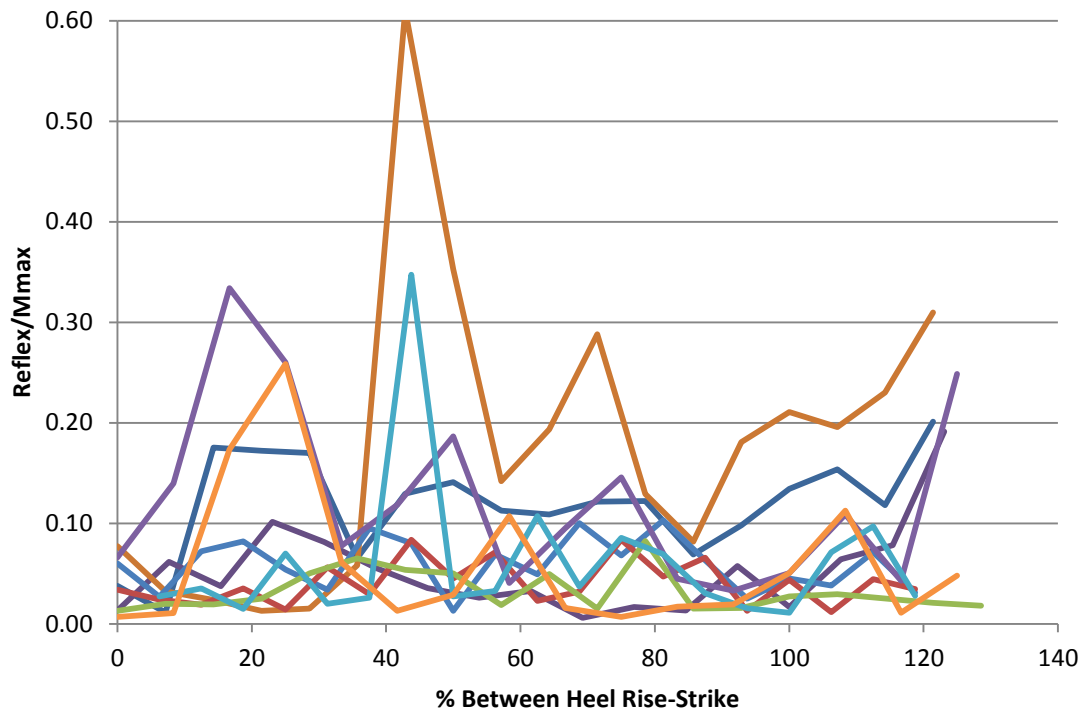
**Figure 10-64: Impaired: tibialis anterior M-wave ratio against percentage of swing**  
 Heel rise = 0%, heel strike = 100% (n=9).

In a similar manner to the motor response, the reflex component amplitude following each stimuli of the burst was expressed as a ratio to the peak M-wave amplitude recorded during the burst and plotted against the percentage between heel rise and heel strike. This is shown for unimpaired and impaired participants in Figure 10-65 and Figure 10-66 respectively.

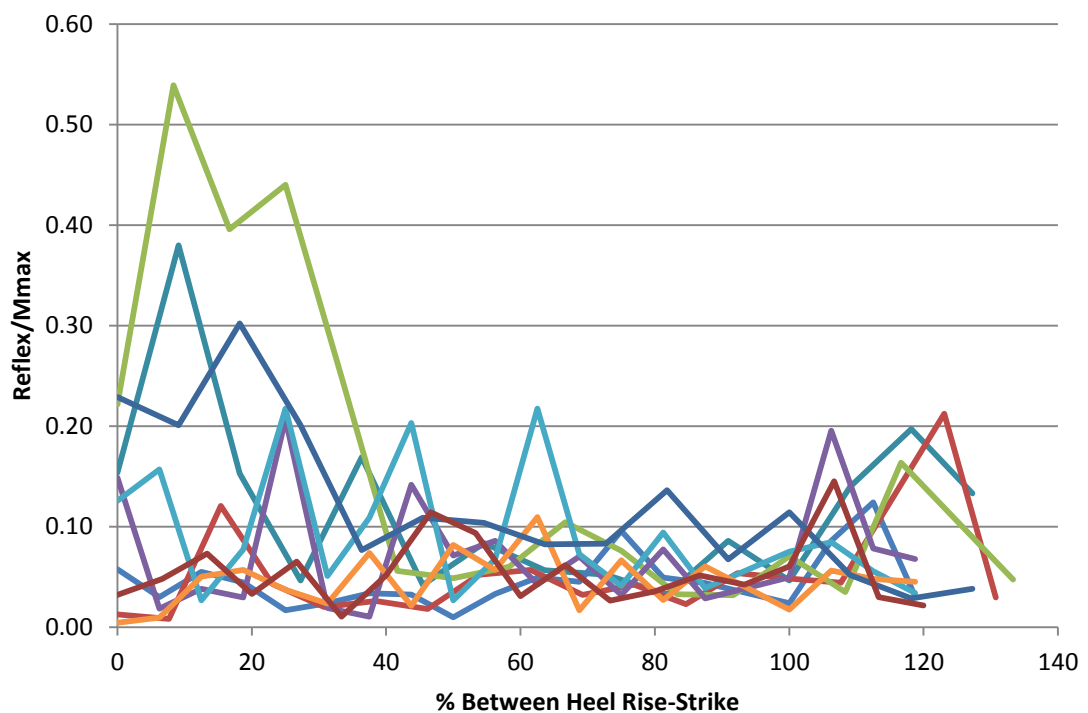
For some participants a substantial reflex component ( $>10\%$  of Mmax) is seen. In the impaired group there possibly appears a trend for larger reflex components during initial swing in the impaired group. This is in-keeping with the trend identified in Figure 10-62 and is not apparent in the unimpaired group.

If the identified reflex activity is of F-wave origin it would be expected to vary in a similar manner to the M-waves. The initial peak in reflex activity at heel rise in the impaired participations is not accompanied by a peak in M-wave. This suggests that at least this component is spinally mediated reflex activity (e.g. H-wave) rather than of F-wave mechanism.

Whilst EMG activity and muscle activation are not directly proportional, it suggests that a proportion of muscle activation observed when using 20Hz conventional stimulation for dropped foot correction is a reflex component rather than purely direct motor activation.



**Figure 10-65: Unimpaired: tibialis anterior reflex component ratio against percentage of swing**  
 Heel rise = 0%, heel strike = 100% (n=9).



**Figure 10-66: Impaired: tibialis anterior reflex component ratio against percentage of swing**  
 Heel rise = 0%, heel strike = 100% (n=9).

### *10.7.3 Phase 6: Conventional stimulation triggered during gait*

The observed variation in both M-wave and reflex component amplitude appeared to be in-keeping with the multitude of potentially influential factors present when walking (e.g. proprioceptive input). Despite large variation there appeared a trend for a number of the impaired participants to have large reflex components at, and shortly after, heel rise. This trend was observed during single twitch (sub-test 61) and burst stimulation (sub-test 64) applied at heel rise which was not reproduced in the unimpaired participant group.

The large variation noted may be due to the data being presented in an inter-, rather than intra-, participant manner. This would however require further assessment and may be dependent upon the mechanism responsible for the effect, which is still unclear. Should intra variation be assessed and found to have repeatability, these variations could be characterised for an individual.

Assessment of reflex component during the use of FES for dropped foot correction is not an aspect which appears to have been previously assessed, be it due to scientific motivation or the challenges of measurement. The unimpaired and impaired investigations completed during this study have begun to explore this and identified a number of characteristics that warrant further research.

## 10.8 Summary

The results and findings of Phases 2 to 6 have been presented and discussed in sections 10.3 to 10.7 respectively. Where appropriate, discussions have referenced the research question(s) informed by the investigational phase being considered. During analysis, trends and features that were not envisaged when designing the study were noted and have also been explored. Table 10-1 provides a summary of how each phase informed the research questions of Chapter 5 and also notes trends and features of interest.

<i>Original Research Question</i>			
	<i>1) How significant are reflexes to conventional and catch-like stimulation?</i>	<i>2) Is increased torque commonly observed when utilising catch-like stimulation caused, in part, by enhanced excitatory spinal reflex components?</i>	<i>3) Is increased torque commonly observed when utilising catch-like stimulation caused, in part, by enhanced reciprocal inhibition reflex effects?</i>
Phase 2	Tibialis anterior M-wave amplitude increases with shortened muscle length. Reflex components exhibit properties of F- and H-waves. Modulation with voluntary effort seen in unimpaired participants. Silent period noted, Equation 10-2 formed to define stimulation period required to permit activation by reflex components.	Not assessed.	Not assessed.
Phase 3	Findings of Phase 2 supported. Recurrent inhibition of tibialis anterior observed –relevance when combining voluntary effort and FES.	Hypothesis not supported.	Hypothesis not supported. Reciprocal inhibition observed however not noticeably different between conventional and catch-like stimulation.
Phase 4	Small modulation of tibialis anterior M-wave and reflex components under isotonic conditions.	Hypothesis not supported during isotonic conditions within both unimpaired and impaired participant groups.	Not assessed.
Phase 5	Isometric conditions corresponded with what appeared near maximal levels of voluntary effort. Noticeable modulation of m-wave and reflex component amplitude with effort.	Hypothesis not supported during isometric conditions within the unimpaired participant group.	Not assessed.
Phase 6	M-wave amplitude varies during gait cycle. Reflex component possibly appeared greatest at heel rise of impaired participants.	Not assessed.	Not assessed.

Table 10-1: Summary of findings from research phases 2 - 6





## Chapter 11 Conclusions

In addition to investigating the posed research questions, exploratory aspects of this research study have provided information relevant to the use and development of clinical FES systems. Broader conclusions of this research, related to the field of neurophysiological investigations, will first be outlined followed by principal conclusions specific to the research questions.

### **Contribution of this research to neurophysiological investigation techniques**

Identification of EMG features such as M-, H- and F-waves, form the primary outcome measures of this research. They are most commonly measured within clinical neurophysiology investigations where they are routinely assessed during non-functional tasks to evaluate specific properties of the nervous system. The instrumentation developed as part of this research extends the measurement capabilities of such investigational setups to include assessment of these EMG features during functional activities. It has been possible to investigate the neurophysiological response to electrical stimulation when used as an orthotic or rehabilitative tool as opposed to a stimulus purely as part of a diagnostic assessment. Being able to assess and quantify a muscle's activation in response to FES and correlating this with biomechanical measures may improve efficacy of clinical FES systems. This is an important outcome from this research as it enables the EMG response to FES to be assessed during its actual clinical application, opening up new opportunities for future research which are discussed in Chapter 12.

Tibialis anterior M-wave amplitude appeared largest when actively dorsiflexing the foot and at shortened muscle length in both unimpaired and impaired participant groups (section 10.3.5). Possible hypotheses for the variation in M-wave amplitude were developed and explored within Chapter 7 and are discussed in respect to future further

work described in Chapter 12. This may be a characteristic inherent to surface stimulation and/or surface EMG measurement that needs to be considered when utilising these during functional activities. If using surface stimulation and EMG in this manner when utilising M-wave amplitude as a control signal within a closed loop FES system, the effect of muscle length and type of contraction (i.e. concentric, eccentric, isometric, isotonic) needs to be accounted for.

Of the realised hardware and software, innovative development of the fast recovery EMG amplifier in unison with the computer controlled stimulation output was integral to enabling this research to be completed. Feedback loops within the EMG amplifier design concept described by Thorsen [137] were reconfigured in order to tailor function to the properties of a transformer based stimulation output stage used clinically. Extensive re-design, circuit simulation and practical testing demonstrated the measurement of EMG within 10ms of applying a stimulation pulse of an order  $>10^4$  larger in magnitude. Realisation of this portable dual channel fast recovery EMG amplifier tailored to the properties of the computer controlled stimulation output marked successful accomplishment of a significant physiological measurement and electronic engineering design challenge.

To the best of the author's knowledge, this is the first time that animations of tibialis anterior EMG activity in between the pulses of a stimulation burst have been created. When presented to the clinical FES research community at conferences, visualisation of EMG in this manner generated interest and discussion. Such animations, created using the developed animated stimulation GIF converter, may also function as useful teaching aids.

In addition to the findings of this study, a significant achievement has been the development of a flexible research system which can be used when undertaking similar research in the future. Both the computer controlled stimulation output and dual channel fast recovery amplifier can be operated via computers supporting a USB interface. High level control of the computer controlled stimulation output by the Stimulation Investigator software application enables parameters of individual pulses to be specified such that individual or multiple pulse sequences of customised stimulation can be realised. This permits modulation of both amplitude and timing parameters over a burst of stimulation. With only modest refinement, this could be incorporated within future clinical or research devices.

## 11.1 Research Question 1 Conclusions

### *1) How significant are reflexes to conventional and catch-like stimulation?*

Excitation of peripheral nerves midway along their length by electrical stimulation causes antidromic  $\alpha$ -motor neuron activation as well as orthodromic sensory nerve activation. Excitatory and inhibitory motor effects resulting from these components of activation have been observed and characterised during this research. At typical stimulation intensities and frequencies (40Hz) used during dropped foot correction, direct (orthodromic) motor activation appears to dominate voluntary or reflex mediated activation of the tibialis anterior through antidromic  $\alpha$ -motor neuron annihilation effects.

Whilst reaching this broad conclusion to Research Question 1, observed variations in M-wave and reflex components have raised questions regarding the neurophysiological mechanism of FES and subsequently how it may be utilised to greatest clinical effect. This has important implications for combining FES with voluntary activation and can be summarised as:

*The antidromic motor effect of electrical stimulation should be considered when using FES in the presence of voluntary activation.*

This principal conclusion to this research question encompasses a number of aspects relating to the antidromic motor effect of electrical stimulation and reflects the many complex interactions present when FES is applied to the impaired nervous system. Aspects of this conclusion will now be outlined in greater detail.

### **Identifying voluntary activation during the application of electrical stimulation**

The antidromic  $\alpha$ -motor neuron action potential which results from a stimulation pulse will collide with and attenuate or annihilate orthodromic reflex mediated or voluntary motor activity. This has been demonstrated during this research by observation of a 'silent period' in tibialis anterior activity when stimulating the common peroneal nerve in the presence of voluntary activation in unimpaired participants (section 10.3.13). Despite being previously reported in literature, the 'silent period' appears, at times, to be overlooked when seeking to develop control systems to assist impaired voluntary movement with the application of FES. Its observation during this research highlights the challenge of developing such a system in which the sensing signal (voluntary EMG)

is impeded by application of the control signal (stimulation). Measures to compensate for this, such as the adaptive gain system proposed by Shalaby *et al.* [164], are supported if attempting to use voluntary EMG as a feedback signal to control FES assisted movements.

### **Choice of stimulation frequency**

The silent period has implications regarding the mechanism of muscle activation by electrical stimulation. Equation 10-2 defines the minimum theoretical stimulation period (and hence maximum stimulation frequency) needed to permit such reflex mediated or voluntary activation to contribute to muscle activation. If the example of common peroneal nerve stimulation at the fibula head for dropped foot correction is considered, for people of typical height and nerve conduction speed, the difference between 20Hz and 40Hz stimulation would govern different potential activation mechanisms. Stimulation applied at a frequency of 40Hz would permit primarily just orthodromic motor activation resulting in a non-selective [43] or reversed [82] muscle fibre recruitment order with respect to that of the natural Henneman recruitment order. Stimulation applied at 20Hz stimulation would also permit voluntary or spinal reflex mediated activity which would follow the more efficient Henneman size principle (Figure 2-12). Muscle fibres repeatedly activated by either activation mechanism would be expected to increase in size and strength. Therefore the mechanism of muscle activation governed by stimulation frequency may influence muscle conditioning.

### **Reflex response to electrical stimulation**

This research has demonstrated that excitatory reflex components are present in response to typically applied FES bursts and can be influenced by effort and muscle length. The properties of the identified reflex components are predominantly consistent with those of F-waves and are caused by antidromic  $\alpha$ -motor neuron action potentials being effectively reflected at the cell body of the anterior horn motor cell. With respect to the preceding M-wave, F-waves are small and activate a subset of the same motor units. Occasional larger reflex waves consistent with the properties of being of H-wave origin were identified. These are caused by a monosynaptic reflex activated by Ia afferent excitation and are believed to result in the activation of a different subset of muscle fibres to those of the M-wave resulting from each stimulation pulse.

**Rehabilitation potential**

An increase in F-wave incidence and magnitude with voluntary activation was demonstrated in unimpaired participants and contrasted to the impaired group where voluntary activation was reduced or absent. This suggests the excitability of the motor neuron pool to antidromic stimulation is influenced by voluntary input. From a clinical perspective, the identification of, rather than activation by, F-waves coinciding with voluntary effort may be of diagnostic indication rather than orthotic function. Rushton hypothesised that antidromic  $\alpha$ -motor neuron action potentials in co-incidence with voluntary effort increase the likelihood of synaptic connections being formed [159]. Since this research has demonstrated F-wave production is dependent upon voluntary input, if Rushton's theory is correct then a measure of F-wave activity would be an indicator of neuroplasticity taking place and hence possible rehabilitation potential. This also supports the review completed by Kroon *et al.* [166], which indicated in the upper limb, those with some voluntary ability such that they are able to trigger the application of stimulation had improved motor recovery following stroke.

The observation of F-wave facilitation in unimpaired participants suggests that for UMN injury patients of lesser impairment, F-wave may be proportional to voluntary effort and therefore could be used as a proxy measure of this. If sufficiently consistent, F-waves could be used as a control signal when assisting a weak voluntary movement with FES.

**Awareness of inhibition effects**

The antidromic  $\alpha$ -motor neuron action potential following a stimulation pulse will excite Renshaw cells causing a recurrent inhibition effect [167]. Such recurrent inhibition was observed during this research and may be undesired if attempting to support and combine weak voluntary activation with FES. The identification of recurrent and reciprocal inhibition highlights the need to consider and further the understanding of such inhibition effects when developing clinical FES systems.

## 11.2 Research Question 2 and 3 Conclusions

*2) Is increased torque commonly observed when utilising catch-like stimulation caused, in part, by enhanced excitatory spinal reflex components?*

*3) Is increased torque commonly observed when utilising catch-like stimulation caused, in part, by enhanced reciprocal inhibition reflex effects?*

Following identification of difficulties when applying the super-positioning method used during exploratory data collection (section 10.4.4), a revised method with reduced sensitivity to temporal variation in reflex components was utilised when assessing research questions 2 and 3 with the gathered unimpaired and impaired data (section 10.4.5). The lack of elevation in catch-like mean amplitude during the reflex window with respect to conventional super-positioned response for both unimpaired and impaired participant groups discussed in section 10.4.6, suggested a negative outcome to Research Question 2. Whilst reciprocal inhibition was observed when assessing Research Question 3 in section 10.4.11, no noticeable difference in the magnitude of this was seen between the tibialis anterior and soleus when utilising conventional and catch-like twitches. This suggested a negative outcome to research question 3.

The principal conclusion of Research Questions 2 and 3 can therefore be summarised as follows:

*Enhanced contractile force previously reported when utilising catch-like stimulation is solely an effect inherent to the muscle and no excitatory or inhibitory spinal reflex contribution is supported.*

Having established the above, investigation of responsible mechanisms inherent to the muscle can be focused upon for understanding and characterisation of the effect. In light of current literature, calcium release [107] or changes in series elastic stiffness of muscle filaments [110] appear regarded as the most likely explanation of the effect.

Whilst this outcome of Research Questions 2 and 3 concerns the mechanism of the effect, catch-like stimulation was used successfully for dropped foot correction during this study. The speed and magnitude of the resulting movements acquired during burst stimulation when supine or during walking appeared comparable to that of conventional stimulation. Users tolerated it and anecdotal reports from study participants suggest catch-like stimulation may be an accepted and effective alternative to conventional stimulation that should be further investigated.

### 11.3 Conclusion Summary

Instrumentation developed as part of this research permits the EMG response in-between pulses of FES to be assessed and may be of use within research or clinical rehabilitation devices. This instrumentation has allowed variation in M-wave to be noted with muscle length and type of contraction. In addressing Research Question 1, both excitatory and inhibitory reflex effects were shown to be present during FES contractions. During typical FES dropped foot correction, antidromic  $\alpha$ -motor neuron conduction will annihilate voluntary or reflex mediated activation such that the direct orthodromic motor effects of stimulation appear to dominate activation of the tibialis anterior. The principal conclusion following investigation of Research Question 1 is the need to consider the antidromic motor effects of electrical stimulation when combining FES with voluntary activation. Implications of this extend to recording voluntary EMG alongside electrical stimulation and potential muscle fibre type activation influenced by choice of stimulation frequency. If the hypothesis put forward by Rushton is true [159], the identification F-waves in coincidence with voluntary effort may be an indication of on-going neuroplasticity at the spinal cord. Assessment of Research Questions 2 and 3 has concluded that force enhancement previously reported when using catch-like stimulation with participants with intact lower motor neurons is inherent to the muscle and not a spinal reflex effect. Other findings and observations suggest catch-like stimulation should be further investigated with a view to assessing if it provides clinical benefits to that of conventional stimulation.





## Chapter 12 Further Work

During investigation of the posed research questions, areas of future research relevant to the clinical use of FES have been identified. A number of these research opportunities are ready for exploration using the developed hardware and software tools. Those considered most important to developing the outcomes of this study are now described.

In common with many other studies, surface EMG was the primary outcome measure used during this research. Whilst relatively easy to measure in isolation, it represents a complex series of neurophysiological processes resulting in current flow within a volume conductor. Consideration of these processes was highlighted by the unexpected but observed variations in M-wave amplitude during isotonic and isometric investigations despite constant stimulation intensity. Although studies such as the SENIAM project [134] have sought to model and characterise properties of surface EMG, there appears a void between this founding, scientific knowledge of the signal and its practical use during clinical measurement.

Further investigation should identify the cause of M-wave amplitude variation with movement and determine whether a similar modulation effect on voluntary EMG is present. Hypotheses that may account for this effect were proposed and investigated within Chapter 7. Two hypotheses were supported by both the initial exploratory data and the main study and are suggested for further investigation:

1. Relative movement between surface stimulation electrodes and the common peroneal nerve, causes changes in electric field strength at the nerve and hence motor unit activation during a contraction.
2. Changes in cross-sectional area of the muscle or reduction in muscle surface to EMG electrodes distance, increases the magnitude of surface EMG signal during contraction of the muscle.

In order to investigate the first hypothesis, a comparison of tibialis anterior surface EMG in response to stimulation applied by an implanted or surface dropped foot stimulator is suggested. The developed EMG amplifier could be used when recording the EMG response to either system. An implanted system such as the STIMuSTEP (section 7.5.1) uses electrodes tethered to the deep and superficial branches of the common peroneal nerve. Relative movement between electrodes and common peroneal nerve would therefore be markedly reduced, if not eliminated, using such an implanted stimulator. If the first hypothesis is positive, the effect would be expected to be observed during burst stimulation delivered by a surface but not implanted stimulator. Whilst these systems are described as having comparable orthotic effect [4, 158], to date, a comparison of the neurophysiological differences between surface and implanted systems does not appear to have been completed.

Further refinement of the ultrasound method utilised during exploratory data collection (section 7.7) would enable investigation of the second described hypothesis. Attachment of a portable ultrasound probe to the skin surface could be used to assess relative changes in surface EMG electrode position to muscle surface displacement and the cross sectional area of the muscle during movement. If the second hypothesis is supported, then use of such spatial variables may enable variations observed in M-wave amplitude to be corrected for when assessing the effect of electrical stimulation applied during the gait cycle.

As outlined in Chapter 11, the findings of this research have relevance if attempting to combine voluntary effort and FES. Further investigation of the ‘silent period’ is suggested in order to identify how FES and voluntary control can be most effectively combined. If attempting to develop a control system to apply FES to support voluntary movement then the silent period as well as the effects of recurrent inhibition should be assessed and characterised. It would be possible to complete this using the developed instrumentation to assess EMG within the silent period over successive stimulation pulses of a burst. Characterisation of how voluntary activation recovers from the silent period and the effects of recurrent inhibition following stimulation would aid the effectiveness with which FES could be combined with voluntary activation.

For a FES user with impaired but not absent voluntary muscle control, choice of stimulation frequency (Equation 10-2) can determine whether muscle is activated by primarily direct motor activation alone or whether augmentation by voluntary activation

is possible. In such a scenario, the author is aware of clinicians who perceive low frequency stimulation to improve fatigue resistance of muscles through preferential conditioning of slow twitch muscle fibres. Scientific investigation to support or refute this viewpoint does not appear to be reported in literature. The Microstim 2V2 neuromuscular stimulator<sup>21</sup> [159] used by clinicians of the National Clinical FES centre has pre-configured programmes incorporating conventional stimulation applied at either 20Hz or 40Hz. As discussed in Chapter 11, for typical dropped foot application, choice between these two stimulation frequencies would be expected to affect the mechanisms by which the muscle could be potentially activated. Low frequency stimulation may allow different muscle fibre types to just those of surface stimulation to be activated; either through voluntary or spinal reflex (e.g. H-wave) activation. This prompts the hypothesis that stimulation of the common peroneal nerve at 20Hz is more effective in conditioning fatigue resistant muscles fibres of the tibialis anterior than stimulation applied at 40Hz. A randomised controlled trial in which the total amount of received stimulation is matched between groups and either 20Hz or 40Hz stimulation is used could assess this over an exercise programme in-which voluntary effort was combined. A pilot investigation would be needed in order to inform subsequent power calculations, assessing muscle fatigue resistance and maximum force development between groups. An invasive but more definitive method of assessing muscle fibre type changes may be to use a muscle biopsy at the beginning and end of the intervention period.

Some users of dropped foot stimulation appear to experience a training effect on their walking ability when not using stimulation in addition to the immediate orthotic benefit. Improvements in a user's unaided walking ability (10 metre walking speed and physiological cost index) have been identified following 18 weeks regular use of dropped foot stimulation in patients who have had a stroke [160, 161]. If the occurrence of F-waves with voluntary effort does predict rehabilitation potential then this would be expected to be observed in patients who demonstrate the training effect following commencement of dropped foot stimulation. Assessment of F-wave occurrence with voluntary effort at 0, 6, 12 and 24 weeks following commencement of dropped foot stimulation could be correlated with other indicators of walking ability (e.g. 10 metre walking speed, physiological cost index) in order to test this hypothesis. If a correlation

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<sup>21</sup> Odstock Medical Limited, Salisbury, England. [www.odstockmedical.com](http://www.odstockmedical.com)

was identified then this could be a useful secondary measure in future controlled clinical studies to predict those with best potential for training by FES.

Although not completed as part of this thesis, impaired participant sub-group analysis in which identified trends are correlated with other measures or indicators relating to condition or rehabilitation may further inform the findings of this study. Appendix K includes basic clinical data such as time since stroke and walking speed at initial setup and walking speed at time of study participation. The orthotic gain at each of these appointments and the total orthotic and training effect is reported [161]. Those which have demonstrated greatest training effect may be those that exhibit F-wave modulation with voluntary effort.

As described in section 4.2.2, stimulation of the common peroneal nerve above the popliteal fossa is commonly used by clinicians of the National Clinical FES Centre when using FES for the correction of dropped foot during gait. Clinical experience is that more proximal stimulation of the common peroneal nerve in this manner results in greater afferent activation, producing hip and knee flexion during the swing phase of gait through activation of the withdrawal reflex. Whilst this is clinically successful [131], the extent of its activation does not appear to have been quantified. In order to investigate the mechanism of this well established clinical technique, kinematic gait analysis synchronised with multiple muscle group EMG measurement should be conducted. Such research could further optimise stimulation to maximise this effect and also identify those in which the technique may be most successful. Whilst measurement of hip flexor EMG would require fine wire intramuscular EMG recordings, surface EMG measurement from hamstring muscles could be gained using the developed system.

A number of the impaired participants of this study commented that catch-like stimulation applied during the swing phase of gait was of comparable, if not preferred, sensation and functional benefit to their existing ODFS dropped foot stimulator (40Hz conventional stimulation). Although this was not explicitly asked and those who expressed this perception may not have been representative of a wider population, this appears to support further clinical investigation of catch-like stimulation for dropped foot correction.

Investigation of the perceived sensation of stimulation may enable identification of stimulation timing patterns generally regarded more comfortable by FES users. This

would have relevance to those who are unable, or find it unpleasant, to tolerate the sensation of surface stimulation [143]. An assessment in which impaired participants are blinded to intensity matched conventional or catch-like stimulation applied to the common peroneal nerve when seated with leg extended, would assess whether a difference in sensation between these could be reliably identified. Stimulation could be applied in a randomised order and users asked to express a preference of comfort. How the user assesses the strength or ‘quality’ of the resulting movement could also be investigated. For those with impaired sensation, a stimulation pattern which provides strong proprioceptive input without discomfort may give increased confidence of the orthotic effect of dropped foot stimulation during use.

If seeking to address whether catch-like stimulation used during dropped foot correction provides functional benefits over conventional stimulation, objective assessments of gait could be used. Outcome measures such as ten metre walking speed or 6 minute walking distance [162], that are reliable and sensitive to change and can easily be completed within most clinical environments may be appropriate. It should be noted that slight changes in stimulation parameters can have a marked effect on gait and therefore precise control of these using a digitally configured stimulator would be required. Existing users of conventional stimulation may have become accustomed to its effect on their gait and therefore such initial investigations should be completed with impaired participants who have not previously used FES for dropped foot correction.

The proliferation of low cost, power efficient digital electronics, has led to their common adoption within modern FES control systems. Such systems could be used to deliver catch-like stimulation patterns with comparable ease to that of implementing conventional stimulation. In order to facilitate further research into whether the use of catch-like stimulation is clinically advantageous, such hardware systems should support the use of stimulation timing patterns which incorporate catch-like stimulation. This could be through the use of stimulation doublets throughout (as utilised within this research) or the inclusion of stimulation doublets at events within the gait cycle when additional activation of the muscle may be beneficial. This may for example be at heel rise or strike to mimic increased motor activation during normal gait [115].

The negative answers to Research Questions 2 and 3 suggest the observed force enhancement associated with catch-like stimulation is linked to an effect inherent to the muscle. With this knowledge, focus can be returned to existing theories such as an increase in sarcoplasmic reticulum calcium [107] and/or an increase in series elastic

stiffness [110] to account for the effect. A non-lasting method of controlling these factors in humans may not be possible and therefore ethical investigation using other animal models may be required. Improved understanding of mechanisms responsible for the catch-like effect and how they are influenced by the effects of UMN injury may enable the effect to be utilised for maximal clinical benefit.

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## Appendix A: Electrical Safety Certificate of Investigational Setup

Metron - PRO-Soft QA-90 Ver. 3.1.2		Salisbury District Hospital	
<b>METRON QA-90 Safety Test Report</b>			
<b>Operator</b> : MEDELEC			
<b>Establishment</b> : Salisbury District Hospital			
<b>QA-90 serial #</b> : 11987	<b>Date:</b> 11/06/2010		
<b>Firmware</b> : 03.44	<b>Time:</b> 14:30		
<b>Appliance Code</b> : 2345	<b>Serial Number</b> :		
<b>Manufacturer</b> :	<b>Group</b> :		
<b>Type</b> :	<b>Status</b> :		
<b>Model</b> :	<b>Location</b> :		
<b>Address 1</b> :	<b>Address 2</b> :		
<b>Equipment classification</b> : CL1		<b>Limits according to</b> : IEC 60601.1	

## TEST RESULTS

-- MODULE INFORMATION --

<b>Module Code</b>	<b>Module Type</b>	<b>No of leads</b>
ECG10	CF	10

-- SETUP DATA --

Power Up Delay Time	: 2	Stop after new power config	: No
Stop at new module	: No	Stop before new power config	: No
Multiple Protective Earth Tests	: Yes	Multiple Enclosure Tests	: No
Protective Earth test current	: 25 A	External Isolating Transformer	: No

Test	Limit	Result	Warning
<b>Supply Voltage</b>			
L-N	50.0 V	229.2 V	
L-G		230.1 V	
N-G		0.6 V	
<b>Current Consumption</b>		156 mA	
<b>Protective Earth</b>	200 mΩ	XX mΩ	X
<b>Insulating Resistance</b>			
Mains-Case		>200 MΩ	
Applied Part-Case, Module : ECG10, Lead : ALL		>200 MΩ	
<b>Earth Leakage Current</b>			
OS	1000 μA	136 μA	
NC	500 μA	71 μA	
OS-RM	1000 μA	132 μA	
NC-RM	500 μA	69 μA	
<b>Enclosure Leakage Current</b>			
OS	500 μA	4 μA	
NC	100 μA	0 μA	
OE	500 μA	2 μA	
OS-RM	500 μA	4 μA	
NC-RM	100 μA	0 μA	
OE-RM	500 μA	3 μA	
<b>Mains on Applied Parts</b>			
SFC, Module : ECG10, Lead : ALL	50 μA	18 μA	

Page 1

Metron - PRO-Soft QA-90 Ver. 3.1.2 Salisbury District Hospital

Mains on Applied Parts (continued)		
SFC-RM, Module : ECG10, Lead : ALL	50 $\mu$ A	18 $\mu$ A
<b>Patient Leakage Current AC</b>		
OS, Module : ECG10, Lead : ALL	50 $\mu$ A	0 $\mu$ A
NC, Module : ECG10, Lead : ALL	10 $\mu$ A	0 $\mu$ A
OE, Module : ECG10, Lead : ALL	50 $\mu$ A	4 $\mu$ A
OS-RM, Module : ECG10, Lead : ALL	50 $\mu$ A	0 $\mu$ A
NC-RM, Module : ECG10, Lead : ALL	10 $\mu$ A	0 $\mu$ A
OE-RM, Module : ECG10, Lead : ALL	50 $\mu$ A	4 $\mu$ A
<b>Patient Auxiliary Current AC</b>		
OS, Module : ECG10, Lead : ALL	50 $\mu$ A	0 $\mu$ A
NC, Module : ECG10, Lead : ALL	10 $\mu$ A	0 $\mu$ A
OE, Module : ECG10, Lead : ALL	50 $\mu$ A	4 $\mu$ A
OS-RM, Module : ECG10, Lead : ALL	50 $\mu$ A	0 $\mu$ A
NC-RM, Module : ECG10, Lead : ALL	10 $\mu$ A	0 $\mu$ A
OE-RM, Module : ECG10, Lead : ALL	50 $\mu$ A	4 $\mu$ A
<b>Patient Leakage Current DC</b>		
OS, Module : ECG10, Lead : ALL	50 $\mu$ A	0 $\mu$ A
NC, Module : ECG10, Lead : ALL	10 $\mu$ A	0 $\mu$ A
OE, Module : ECG10, Lead : ALL	50 $\mu$ A	0 $\mu$ A
OS-RM, Module : ECG10, Lead : ALL	50 $\mu$ A	0 $\mu$ A
NC-RM, Module : ECG10, Lead : ALL	10 $\mu$ A	0 $\mu$ A
OE-RM, Module : ECG10, Lead : ALL	50 $\mu$ A	0 $\mu$ A
<b>Patient Auxiliary Current DC</b>		
OS, Module : ECG10, Lead : ALL	50 $\mu$ A	0 $\mu$ A
NC, Module : ECG10, Lead : ALL	10 $\mu$ A	0 $\mu$ A
OE, Module : ECG10, Lead : ALL	50 $\mu$ A	0 $\mu$ A
OS-RM, Module : ECG10, Lead : ALL	50 $\mu$ A	0 $\mu$ A
NC-RM, Module : ECG10, Lead : ALL	10 $\mu$ A	0 $\mu$ A
OE-RM, Module : ECG10, Lead : ALL	50 $\mu$ A	0 $\mu$ A

\*\*\*\*\* UNIT FAILED TEST! \*\*\*\*\*

Signature : \_\_\_\_\_

Equipment tested using Class I sequence, only failed Protective Earth, all other tests passed. Equipment is Class II

Page 2

A class II electrical system does not require a protective earth connection.

The unit would therefore pass a class II sequence.

## Appendix B: Investigational Session Risk Assessment

RISK ASSESSMENT				Assessor: Darren Hart	Date Assessed: 30 <sup>th</sup> March 2010
Sequential list of Activity Steps	Risk Ref.	Identified Hazards	People at Risk	Measures in Place	Brief description of Control Measure
Patient welcomed into clinic room and asked to roll up trousers or change into shorts/loose fitting trousers.	1	Privacy and dignity	Participant	Yes	Changing facilities will be provided. Participants may be accompanied by friends/family/carers during investigational session. If wished, a chaperone can be provided.
	2	Lone working	Participant & Researcher	Yes	Salisbury NHS Trust's lone working policy will be followed at all times. Other staff also trained in manual handling and first aid will be on hand. Remote panic alarms are also provided in clinical areas in case of assistance/crash calls.
Participant asked to lie on clinic plinth with foot suspended over end.	3	Manual handling	Participant	Yes	Clinic plinth used will be placed against wall. It can be adjusted in height to aid transfer on to and off of. The principal investigator has completed Salisbury NHS Trust's manual handling training.
Sensors and electrodes placed on subject's lower leg.	4	Infection control	Participant & Researcher	Yes	Stimulation and recording electrodes are single use only. All other equipment will be thoroughly cleaned with detergents wipes before and after tests. Salisbury NHS Trust's infection control policy will be followed at all times.
Stimulation applied, data collected.	5	Electrical safety	Participant	Yes	Developed medical electronic instrumentation has been designed to the essential requirements of medical device directive. Applied parts are optically isolated from mains power. A chartered engineer external to the project has reviewed the design files.
	6	Unnecessary discomfort	Participant	Yes	Stimulation will be applied at intensities no higher than that used by their existing stimulator or that the participant expresses as being the maximum comfortably tolerated.
Patient asked to walk 5 x 10 metres with and without stimulation in the clinic room. Assistant pushes trolley. Researcher walks alongside patient participants.	7	Skin irritation	Participant	No	In light of intensity and duration that stimulation will be applied for this will be a very small risk. Skin will be checked following the investigation and if an irritation is evident, or later appears, the participant will be encouraged to contact the researcher who will then discuss the National Clinical FES centre's skin care guidance in the presence of a skin irritation.
		Manual handling	Participant & Researcher	Yes	Participants who already receive FES treatment for drop foot correction will be able to safely mobilise with and without stimulation over 10 metres. Participant can use any existing walking aids and the researcher will walk with them for assistance.
	8	Wire trip hazard	Participant & Researcher	Yes	An assistant will push the trolley with equipment required for the investigation such that there is adequate length and that the wires remain out of the way of the participant and researcher in order to minimise the risk of trip over these.
	9	Transportation of trolley and equipment causing damage or injury	Participant & Researcher	Yes	The investigation will take place over smooth and level ground. There will be at least 3 metres wire between the participant and trolley. The patient monitor will be laid flat on the trolley during phase 5 of testing in order to minimise risk of it falling over.

RISK REGISTER		Assessor: Darren Hart			Date Assessed: 30 <sup>th</sup> March 2010		
Risk Ref.	Description of Risk	Adequacy of existing controls			Risk Assessment		Risk Treatment Option
		A	I	U	Consequences	Likelihood	
					Catastrophic 5 Major 4 Moderate 3 Minor 2 Negligible 1	Certain 5 Likely 4 Possible 3 Unlikely 2 Rare 1	Risk Ranking Low 1-3 Moderate 4-6 High 8-12 Extreme 15-25
1	Privacy and dignity	✓			2	2	4
2	Lone working	✓			4	1	4
3	Manual handling	✓			3	2	6
4	Infection control	✓			2	2	4
5	Electrical safety	✓			4	1	4
6	Unnecessary discomfort	✓			2	2	4
7	Skin irritation	✓			2	2	4
8	Wire trip hazard	✓			3	2	6
9	Transportation of trolley	✓			2	2	4
							Accept risk and review

## Appendix C: Study Consent Form

26<sup>th</sup> April 2010

Participant code:

Salisbury   
NHS Foundation Trust

### CONSENT FORM

Optimally spaced stimulation for clinical use with electrical stimulation

*– Its affect on spinal reflexes and muscle activation*

Centre Number:

Study Number:

Chief Investigator: Dr Paul Taylor, Consultant Clinical Scientist

Principal Investigator: Darren Hart, Clinical Scientist

*Please initial box*

- 1 I confirm that I have read and understand the participant information sheet entitled 'The effect of electrical stimulation patterns on muscles & reflexes' dated 26<sup>th</sup> April 2010 (version 1.0). I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.
- 2 I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.
- 3 I understand that relevant sections of my medical notes and data collected during the study, may be looked at by individuals from the National Clinical FES centre, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.
- 4 I agree to take part in the above study.





\_\_\_\_\_  
Name of Patient

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Person taking consent

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature

*When completed, 1 for patient; 1 for researcher site file; 1 (original) to be kept in medical notes*

Consent Form V1.0

Page 1 of 1



**Appendix D: Participant Study Form**

Participant code:

Salisbury  
NHS Foundation Trust**PARTICIPANT STUDY FORM**

Optimally spaced stimulation for clinical use with electrical  
stimulation

*– Its effect on spinal reflexes and muscle activation*

Medication:

Leg under investigation

LEFT / RIGHT

Notes:

\_\_\_\_\_  
Name\_\_\_\_\_  
Date\_\_\_\_\_  
Signature





## Appendix E: Research Protocol

### Research Protocol University of Southampton

#### Optimally spaced stimulation for clinical use with functional electrical stimulation

---

*– Its affect on spinal reflexes and muscle activation*

Version 1.1

7<sup>th</sup> July 2010

7<sup>th</sup> July 2010

## Summary

Functional Electrical Stimulation (FES) can provide the useful contraction of muscles which have been paralysed by upper motor neuron injury (e.g. stroke, multiple sclerosis, spinal cord injury) through the artificial electrical activation of nerves supplying them. During FES contractions both motor and sensory nerves are activated. The electrically excited sensory nerves produce spinal reflex responses which can excite or relax different muscles and hence affect movements resulting from FES. The effects of these spinal reflexes on muscles during FES contractions are not well understood. The speed and strength of FES contractions can be influenced by the spacing of the stimulation pulses applied. Conventional electrical stimulation applies very brief stimulation pulses which are applied at a constant spacing (typically 40 pulses per second). It has been shown that stimulation envelopes beginning with or completely comprising of doublets of stimulation, rather than single stimulation pulses, can produce larger, more sudden forces. This effect is known as the catch-like effect and the mechanisms behind it are not fully understood.

This research will investigate how much of the muscle activation is due to purely motor nerve excitement and how much is due to spinal reflexes during both conventional stimulation and catch-like stimulation. If a greater spinal reflex component is activated by the catch-like stimulation this may partially explain positive findings of the effect whilst also helping to inform whether it could be utilised in future clinical FES systems. A test protocol comprising a series of specified tests will control factors known to influence spinal reflexes whilst conventional and catch-like stimulation is applied to participants. Measurements of electrical muscle activity (using an electromyographic amplifier), joint angle (using goniometers) and limb movement (using accelerometers) will enable the posed research questions to be investigated.

7<sup>th</sup> July 2010

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2<sup>nd</sup> September 2010**List of Symbols**

ATP	Adenosine Triphosphate
CMAP	Compound Muscle Action Potential
CSE	Clinical Science and Engineering
EMG	Electromyography
EMG <sub>ABS</sub>	Electromyography (absolute value)
FES	Functional Electrical Stimulation
MS	Multiple Sclerosis
SCI	Spinal Cord Injury
UMN	Upper Motor Neuron

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## Background and Introduction

### What is Electrical Stimulation and How is it Used Clinically?

Functional Electrical Stimulation (FES) is the use of electrical stimulation in order to produce and control functional movements in muscles paralysed by Upper Motor Neuron (UMN) injury by artificially activating nerves which supply them [1].

FES has a number of applications such as FES rowing, FES cycling, upper limb neuroprosthesis and gait assistance systems. In the example of drop foot (Figure 1), FES applied to the common peroneal nerve can provide dorsiflexion with moderate eversion during the swing phase of gait hence significantly increasing walking speed and reducing energy expenditure [2]. It is typically timed using a footswitch placed underneath the heel of the effected side. So as not to provoke a stretch reflex of the calf muscles (see: *The Reflex Effects of Electrical Stimulation*), stimulation is ramped on following heel rise. At heel strike an extension period of stimulation is applied to mimic eccentric activity of the dorsiflexors thus preventing foot slap due to the natural moment formed about the ankle. Following the extension period stimulation is ramped off (Figure 2).

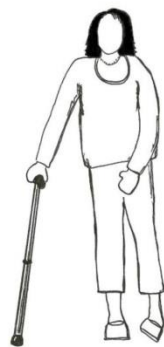


Figure 1: Depiction of dropped foot following stroke

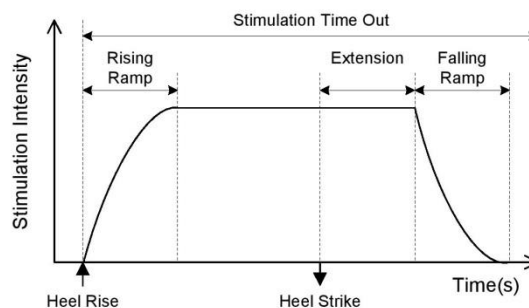


Figure 2: Trapezoidal stimulation envelope of ODFSIII dropped foot stimulator

Stimulation can be transcutaneously applied using skin surface electrodes or directly applied using implanted electrodes. The proportion of neurons within a nerve bundle depolarised by a stimulation pulse depends upon the amplitude and duration of the applied pulse. Each stimulation pulse of sufficient intensity generates action potentials in motor and sensory neuron axons which are in close proximity to the electrodes. These action potentials conduct away in both directions along the neuron i.e. the normal direction of travel (known as orthodromic conduction) and the opposite direction of normal travel (known as antidromic conduction). In motor neurons the arrival of the orthodromic action potential (i.e. normal direction of travel towards muscle) at the neuromuscular junction is shortly followed by a momentary synchronous contraction of



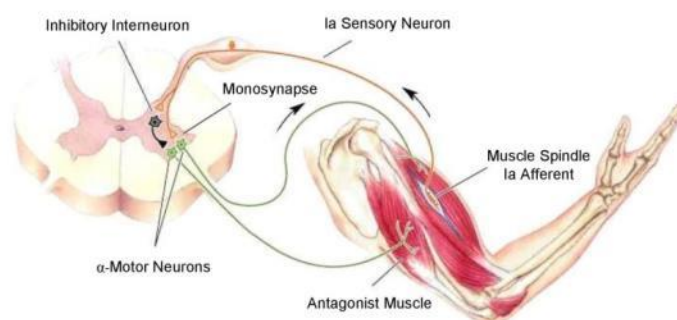
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activation, the stimulation frequency must be selected so as to produce a smooth tetanic response whilst not causing rapid muscle fatigue. Practical FES systems typically apply stimulation between 20 and 60Hz.

### The Reflex Effects of Electrical Stimulation

As discussed, electrical stimulation causes the propagation of orthodromic and antidromic action potentials in *both* efferent (motor) and afferent (sensory) neurons. Orthodromic afferent stimulation (sensory stimulation travelling towards spinal cord) can cause a spinal reflex response. Reflexes are fast, involuntary coordinated patterns of muscle activation and relaxation that are elicited by peripheral stimuli and are utilised throughout movement. Some reflexes are inborn, others are learned or acquired.

The most commonly described monosynaptic spinal reflex is the stretch reflex. If a muscle is suddenly lengthened, its Ia afferents signal this muscle stretch through orthodromic conduction of action potentials to the spinal cord. At the spinal cord the Ia afferents form excitatory monosynapses with motor neurons of the same muscle (Figure 3). Hence this reflex attempts to maintain muscle length by counteracting a sudden muscle stretch by contracting the stretched muscle.



**Figure 3: Stretch and reciprocal inhibition reflexes**

*Modified from Bear, Connors, Paradiso 2001 [3]*

The Ia afferent neuron which activates the monosynaptic stretch reflex also activates an inhibitory reflex known as reciprocal inhibition. The Ia afferent branches in the spinal cord and synapses with an inhibitory interneuron which inhibits an  $\alpha$ -motor neuron that innervates the antagonist muscle (Figure 3). This has the effect of inhibiting the antagonistic muscle that opposes the stretch reflex muscle contraction. Reciprocal inhibition prevents conflict between opposing muscles and is utilised when coordinating movement.

During the clinical use of FES, electrically activated reflexes can have a substantial excitatory and inhibitory affect upon the response gained. For example, during use for

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drop foot correction, stimulation needs to be set up to avoid provoking a stretch reflex in the antagonist calf muscles. In parallel, the reciprocal inhibition may be utilised to inhibit overactive calf muscles. Often an exercise stimulator may be used to condition a patient to the use of FES prior to using a walking stimulator. Such an exercise stimulator would typically apply a gradual ramp (1-2 seconds) in order to avoid and desensitise the stretch reflex whilst enabling the calf muscle to become accustomed to being stretched and inhibited by the reciprocal inhibition reflex.

During correction of dropped foot using FES, stimulation applied to the common peroneal nerve can evoke and utilise a withdrawal reflex during the swing phase of gait [4]. The flexor withdrawal reflex is an inter-segmental reflex which activates interneurons at different spinal cord segments so as to provide hip, knee and ankle flexion. An example of its function would be when inadvertently stepping on a sharp object to quickly withdraw weight from the painful stimulus. It also provokes a crossed extensor reflex which again operates at inter-segmental levels so as to activate extensor muscles in the contra-lateral lower limb to shift weight on to this side whilst maintaining balance.

Although the stretch (analogous to H-reflex in neurophysiology) and reciprocal inhibition reflexes are well characterised in the field of neurophysiology, in many published FES studies there appears a tendency for only the direct motor effects to be considered. There appears a disparity between clinical usage and research literature. Although this will often not be relevant to in-vitro animal studies in which nervous connection to the spinal cord has been severed, when applying FES for clinical benefit with UMN injury patients these reflex effects should be considered. Few studies appear to consider the orthodromic afferent or antidromic motor effects of FES and the effects of these may be particularly relevant in the presence of spasticity.

Mela et al appear to be amongst the few authors to have investigated the contribution of secondary reflex activity to the force elicited by a muscle stimulated by a single pulse during a functional movement [5]. Reflex mediated activity was found to be accountable for torque moments in the order of 10-15% during twitch stimulation of a group of six unimpaired participants. Although a small unimpaired participant group, this study indicated the need to consider such components when ascertaining the effects of FES.

Collins et al have reported torques larger than expected from direct motor axon activation alone, when applying wide-pulse width, high frequency stimulation either continuously or in two seconds bursts to muscles of the lower limb. Such increased torques were present when applied to complete SCI participants [6, 7] or healthy sleeping participants but not when a nerve block was applied proximal to the stimulation site [6, 8]. The additional torque has been attributed to being of central nervous system origin, being initiated by evoked sensory volleys that provide excitatory input to neurons in the spinal cord. The authors propose that the sensory volley generates persistent inward currents, referred to as plateau potentials which produce self sustained  $\alpha$ -motor neuron discharge [6].

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As Collins et al have shown how to turn these central components of force on [9], they have also investigated how to turn them off [10]. This is needed if such techniques are to be used to control functional movements. It is also of particular interest when considering its use with UMN injury patients with over-active spastic muscles. If stimulation can be tailored to have an increased inhibitory effect on these spastic muscles then the functional response to stimulation may be improved.

### **Muscle Fibre Types and Activation**

Muscle activated through reflex pathways is thought to be recruited in a different manner to that during FES contractions. The following section will introduce the different muscle types before then explaining these differences in recruitment.

#### **Skeletal Muscle Fibre Types**

Muscle fibres are not all alike in composition and function and differ in the rate at which they can split ATP molecules (affecting speed and strength of contraction) and the type of enzymatic process they use to synthesize ATP (affecting fatigue resistance). Based upon these structural and functional differences, three principal types of fibre have been classified:

- Slow (type S or I) fibres are smallest in diameter and produce only small amounts of force. They have large amounts of myoglobin and mitochondria enabling them to generate ATP quickly. ATP is hydrolysed slowly by myosin heads and hence they have a slow speed of contraction. They are fatigue resistant and are capable of prolonged, sustained contraction such as those involved maintaining posture and for aerobic, endurance activities.
- Fast fatigue Resistant (type FR or IIa) fibres also contain large amounts of myoglobin and have good fatigue resistance. Their myosin heads hydrolyse ATP 3-5 times faster than type I fibres and hence have a faster contraction time.
- Fast fatiguable (type FF or IIb) fibres are largest in diameter and contain the most myofibrils. They generate very powerful contractions quickly but hydrolyse ATP rapidly. Hence they are adapted for intense anaerobic movements of short duration.

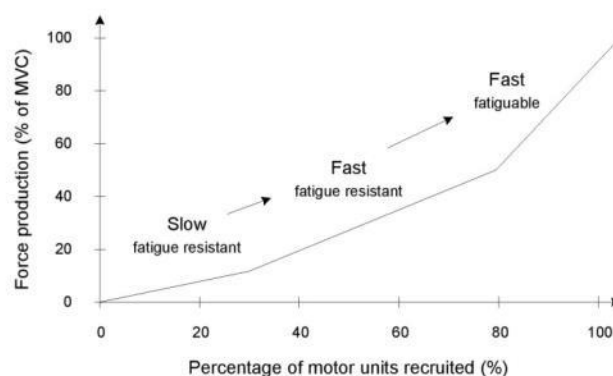
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Some muscles are of predominantly one type of muscle fibre, most contain a mixture however. In this way the total range of operation of a muscle is extended beyond that of any single unit type. For example, the soleus which is used throughout standing is typically composed of slow twitch fibres. The gastrocnemius however, which is used for sudden but brief contractions such as running or jumping, is predominantly composed of fast fibre types. Although the total number of muscle fibres is established at birth, the type of each fibre can change throughout life in response to factors such as exercise or inactivity as well as electrical stimulation [11].

Each muscle fibre has a single neuromuscular junction and those innervated within a common motor unit are of the same fibre type. The size, metabolism and functional properties of muscle fibres are matched to the  $\alpha$ -motor neuron that innervates them. That is, small diameter  $\alpha$ -motor neurons innervate slow twitch muscle fibres, and large diameter  $\alpha$ -motor neurons innervate fast twitch muscle fibres

### Recruitment Order

In order to make best use of the properties of these different muscle fibre types during voluntary contractions, motor units are recruited in a specific order depending on the requirements of the task being performed. If a weak contraction is required, slow twitch fibres are recruited, if a greater force is required fast fatigue resistant followed by fast fatiguable fibres are recruited (Figure 4). This is known as the Henneman recruitment order and is based upon the assumption that in all types of contraction the order in which a motor unit is recruited in depends solely on the size of its motor neuron axon [12].



**Figure 4: Motor unit recruitment order trend during voluntary skeletal muscle activation**

As described by Henneman et al [12], based upon graphical depiction by Gregory & Bickel 2005 [13]  
(MVC = maximal voluntary contraction)



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Due to the different method of activation electrical stimulation contractions do not obey this orderly recruitment order. Neurophysiology studies have indicated that large diameter neuron axons are more easily excited than smaller diameter ones by an extracellular electrical stimulation pulse [14, 15]. In order to bring a point along a nerve axon to threshold during transcutaneous stimulation, sufficient extracellular current must pass across the cell membrane into the axon and then out again. For any given axon, the majority of stimulation current bypasses it, moving instead through other axons or the low resistant pathway provided by extracellular fluid. It follows that axons into which current can most easily enter are depolarised most and have the lowest threshold for extracellular current activation. Since a greater fraction of total extracellular current will flow through axons with a large cross sectional area those that innervate fast twitch fibres will be activated at a lower extracellular current intensity than smaller axons innervating slow twitch muscle fibres. This preferentially recruitment of larger motor units prior to smaller ones amounts to a reversal of the efficient Hennemann's size principle [12, 16]. Coupled with the synchronous, spatially fixed activation of motor neurons during electrical stimulation this recruitment order reversal is thought significant to the rapid rate of fatigue experienced with respect to voluntary activation by the CNS.

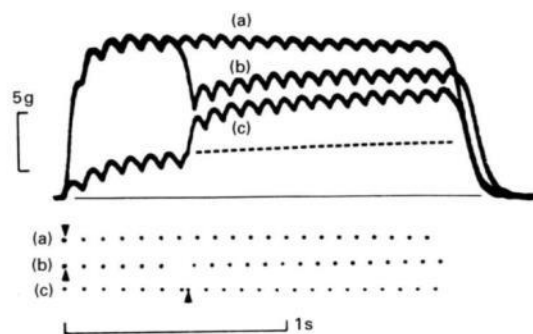
A number of recent research and reviewed studies suggest motor unit recruitment order during transcutaneous electrical stimulation is not as consistent as this and may be non-selective [13, 17]. Gregory and Bickel [13] outline such a conjecture however do not discuss the afferent affect of stimulation and resulting activation of motor neurons via spinal reflexes. Due to the increased size of the Ia afferent neurons it is reasonable, and widely acknowledged through H-reflex studies, that these afferents will be stimulated at a lower threshold than  $\alpha$ -motor neurons. If the afferent stimuli of electrical stimulation cause reflex responses then these will follow the efficient Henneman size principle [18]. If direct motor activation by electrical stimulation marks a complete reversal of this, then it is this author's view that in combination with reflex responses, the net summated effect would appear that of a non-selective recruitment order.

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## The Catch-like Effect

### Overview of the Catch-like Effect

In 1970 Burke and colleagues reported a 'catch-like' property of muscle in which force augmentation was produced by the inclusion of an initial, high-frequency burst of two or more pulses at the start of a sub-tetanic low-frequency train of stimulation [19]. A 10ms initial doublet electrical stimulus was shown to provide sudden non-linear summation of force that was accompanied by an enhanced level of force that could be maintained by low frequency stimulation (Figure 5). Similar discharge patterns have been reported in motor units during voluntary contractions and may be a strategy employed to develop sudden torques when muscles are fatigued [20-23].



**Figure 5: Tension responses of cat medial gastrocnemius, slow motor unit [19]**

Upper three traces (a, b & c): isometric force measured in grams, plotted against time.  
Lower three corresponding traces: stimulation timing -  $\blacktriangle$  = 10ms doublet,  $\bullet$  = 82ms spaced single pulse.  
Each train contains 22 stimuli and depicts effects of timing changes in doublet application.

Trace (a): sudden increase in torque due to initial 10ms doublet ( $\blacktriangle$ ) at start of train.

Elevated tension maintained by constant 12.2Hz (82ms period) stimulation.

Trace (b): as (a) until drop in tension when interval after 7<sup>th</sup> stimuli is lengthened to 117ms.

Trace (c): gradual increase in tension with 12.2Hz stimulation until moderate increase in tension seen when 26ms doublet applied at 7<sup>th</sup> & 8<sup>th</sup> pulse.

This catch-like effect has drawn interest when assessing its use for FES applications. Neuromuscular factors such as level of fatigue [24, 25], prior muscle activation [26, 27], fibre-type composition [28-30], contraction type [31] and muscle length [32, 33] have been shown to affect the extent of force augmentation due to the effect. Additionally timing [34, 35] and intensity [36] characteristics of the stimulation applied have been shown to influence the effect. With this said however, such catch-like inducing stimulation trains have been consistently shown to enhance both isometric and non-isometric muscle force, especially when muscles are fatigued when compared to constant frequency stimulation of comparable frequency [37].

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### Mechanisms of the Catch-like Effect

The catch-like property was originally demonstrated in single mammalian motor units over which nervous control had been acutely severed [19]. This complete transection of the motor unit from the spinal cord undoubtedly removes spinal reflex components. Hence as defined the catch-like effect is an inherent property of skeletal muscle. The mechanism of the effect remains unclear but the two primary mechanisms that have been proposed are increased  $\text{Ca}^{2+}$  concentration within the sarcoplasmic reticulum of muscle fibres or increased stiffness of the series elastic elements [38-41]. Studies which have sought to confirm these hypotheses have not been conclusive and suggest other mechanisms in addition to these should also be considered [42-44].

### Use of Catch-like Stimulation with Human Participants

For FES to be successful an intact lower motor neuron system is required. Such suitable patients with an intact lower motor neuron system will also have intact spinal reflex pathways. If catch-like stimulation is ever to be utilised clinically it's affect on spinal reflexes in both unimpaired participants and patients with a UMN injury should be assessed.

With the many complex neurophysiological systems associated with movement, coupled with an UMN injury affecting one or many of these, numerous speculations regarding these mixed findings could be made. Existing explanations of the catch-like effect such as increased  $\text{Ca}^{2+}$  and increased series elastic stiffness may be affected by UMN injury. The effect of spinal reflexes on both conventional stimulation and catch-like stimulation are also likely to be affected by UMN injury. As patients who have sustained an UMN injury are the intended recipients of such a clinical intervention it is necessary to identify any differences in response caused by this condition.

The catch-like effect appears a largely experimental finding which is yet to be knowingly utilised within a clinical application [45]. Few studies have investigated its use with UMN injury patients and those which have often report mixed results [46-52]. Some of this variation may be explained by protocol and patient choice however there is a consensus amongst authors that the pathological effect of UMN injury appears to affect mechanisms responsible for the catch-like effect.



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### Summary

Whilst the afferent effects of electrical stimulation inform the clinical use of FES, these effects do not appear to be fully understood or characterised in a quantitative manner. For example, the withdrawal reflex is commonly utilised by clinical FES systems to good clinical benefit however knowledge of exactly how substantial this spinal reflex mediated activation of muscle is or why this works better for some than others is not known. The work of Mela et al [5] raises the question *-do spinal reflexes play a greater role in resulting muscle activation during FES contractions than previously thought?* If so, this finding would have relevance to the ongoing debate of what is the muscle fibre recruitment order during transcutaneous electrical stimulation? A combination of the Henneman recruitment order due to reflex activation and a reversal of this due to direct motor activation by FES would support the net non-selective recruitment order that Gregory and Scott Bickel outline in their recent perspective [13].

Although the catch-like effect is an inherent property of skeletal muscle [19] whether there are any further spinal reflexes effects resulting from stimulation incorporating doublets does not appear to have been pursued. The work of Collin's et al focuses attention towards the spinal reflex response during FES following bursts of high frequency stimulation akin to the instantaneous high frequency of a doublet [53, 54]. Although investigations using catch-like trains typically assess dynamic torque responses over hundreds of milli-seconds, and the results of Collins et al [53] are of an elevation in torque over a number of seconds, it raises the question *-is torque enhancements seen in previous human catch-like stimulation studies are partly due to spinal reflex components?* If this conjecture were to prove well founded then the changes in recruitment order during reflex mediated responses could also contribute to the positive effects seen on fatigue as well as force enhancement.

If catch-like stimulation is to be utilised clinically it will be with human subjects with an intact lower motor neuron system and hence intact spinal reflex pathway. When applied to a UMN injury patient group the effects of spasticity would be expected to alter the function and sensitivity of these spinal reflex pathways. It is hence wished to investigate the study research questions in both unimpaired and impaired participants who have an UMN injury.

### Hypothesis

- Reflex mediated muscle activity (excitatory and inhibitory) plays a more substantial role during FES contractions than currently reported.
- Muscle activated through reflex pathways partly explains the widely thought non-selective recruitment order of muscle during FES contractions.
- Reflex effects partly account for mixed findings utilising catch-like stimulation.
- Reflex effects to FES differ due to UMN injury.



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### Research Objective

This study seeks to provide exploratory data with which to investigate the effect of FES on centrally generated spinal reflex components which contribute to functional muscle effects. Specifically it will investigate whether the use of doublets (catch-like stimulation) rather than single electrical stimulation pulses cause greater activation of spinal reflexes resulting in:

- Greater excitatory input to the muscles being stimulated, hence increasing contribution to the produced muscle contraction.
- Greater inhibitory input to the muscles which oppose the muscles being stimulated, hence reducing opposition to the produced muscle contraction.

Stimulation intensity, muscle length, muscle tension, effort and completion of functional tasks are expected to affect the spinal reflex response to FES [55]. The designed study procedure hence comprises of a number of phased tests which assess factors such as stimulation intensity (phases 2 & 3), supporting and opposing effort (phase 2 & 3), muscle length (phase 2, 3 & 4), muscle tension (phase 5) and the effect of completing this during walking (phase 6).

The effects of single and doublet stimulation will be contrasted when applying burst stimulation (phases 2 & 6) and twitch stimulation (phases 3, 4, 5 & 6). Tests completed during phase 2 and 3 will investigate the direct and reflex evoked response to burst and twitch stimulation respectively at different stimulation intensities, different joint angles (measured using a goniometer) and when actively supporting or opposing the effects of stimulation.

Burst stimulation in this study refers to either repeated single or doublet stimulation pulses repeated by a constant period (50ms single, 95ms doublet). Burst stimulation mimics that typically applied functionally to produce a sustained contraction. Phase 2 will also assess the dynamic effects when combining a voluntary movement with burst stimulation as may again be typically completed clinically.

Twitch stimulation in this study refers to either a single or doublet stimulation pulses applied on their own which produce a 'twitch' of muscle contraction. Applying twitch stimulation in this manner aids identification and analysis of reflex components as it is not occluded by preceding or following stimulation artefact or activity. Phase 3 will also assess the effects of reciprocal inhibition and whether there appears differences in the physical twitch of the foot which correlates to whether the corresponding muscle is activated directly or by reflexes. Measuring the physical twitch of the foot (using accelerometers) due to twitch stimulation may enable inferences of what type of muscle fibre types are being activated at different stimulation intensities.

Through completion of the test protocol with unimpaired participants and participants with an UMN injury, differences in the above effects within these groups can be investigated. This will also assess and demonstrate the feasibility of the research protocol within these two participant groups.

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## Study Design

### Study Type and Population

This study will collect exploratory data in order to investigate the posed research objectives. This will be completed through a case study series comparing data obtained from the following two groups:

- Participants with no known UMN injury
- Participants who have had a stroke (more than 6 months post stroke)

Unimpaired male participants will be recruited from male staff and students at the School of Electronics and Computer Science at the University of Southampton and the National Clinical Functional Electrical Stimulation Centre, Salisbury District Hospital. Recruiting only male unimpaired participants eliminates any possible risk of unimpaired females participating whilst being unknowingly pregnant. Although the National Clinical FES centre has not experienced, or is aware of any adverse incidents regarding the use of FES when pregnant, without confirmation that no risk is posed to the unborn child, pregnancy is deemed a contraindication to FES. No gender effects are expected in this study and the population being recruited from is sufficient in size to enable recruitment of 10 unimpaired male subjects.

Impaired participants will be recruited from patients seen for FES treatment at the National Clinical Functional Electrical Stimulation Centre, Salisbury District Hospital. The research hypothesis is applicable across all UMN injury groups which benefit from FES i.e. stroke, incomplete spinal cord injury, multiple sclerosis. Due to the small recruitment numbers of this exploratory study, only participants who have had a stroke will be considered in order to avoid subgroup effects due to different conditions. As seen at the National Clinical FES Centre, this chronic patient group is typically stable in condition and less prone to rapid fatigue compared to some other patient groups e.g. multiple sclerosis.

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### Study Duration

Participation in this study will require participants to attend a single investigation session which will last no longer than 90 minutes. This will take place at the National Clinical Functional Electrical Stimulation Centre, Salisbury District Hospital. For impaired participants this will be arranged for the same day shortly after their next planned review appointment.

The duration of the study will be 6 months. Should all participants be recruited before this end date then the study will be concluded.

### Inclusions and Exclusion Criteria

#### Inclusion Criteria

1. For impaired participants: chronic (more than 6 months) UMN injury patients who have a dropped foot due to stroke and are currently using a single channel FES device.
2. For unimpaired participants: male participants with no history of UMN injury/condition.
3. Able to tolerate the sensation FES transcutaneously applied to the common peroneal nerve at the popliteal fossa.
4. No known neurophysiologic conditions affecting the lower motor neuron system.
5. Medically stable.
6. Able to understand and follow simple instructions.
7. Able to walk at least 10 metres with and without the stimulator.
8. Able to independently transfer to and from clinic plinth.
9. Intact skin condition of lower limb such that necessary electrodes and sensors can be placed using adhesive tape.
10. Over the age of 18.
11. Does not rely on use of any other orthotic device in conjunction with FES for drop foot correction (innersoles not included).

#### Exclusion Criteria

1. Allergic to plastic material or micropore tape.
2. Contra-indications to FES (already applied for participants using FES).
3. Poor skin condition.
4. Pregnancy (the affects of FES on the unborn child is unknown).
5. Pacemaker users.
6. Poorly controlled epilepsy.
7. Fixed ankle contracture on side to be tested.
8. Type I diabetes.



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### Outcome Measures

The following outcome measures will be collected before, during and after the application of different electrical stimulation patterns:

#### Primary Outcome Measures

- Electromyographic recordings (electrical muscle activity) from the tibialis anterior and soleus muscles of the lower limb.

#### Secondary Outcome Measures

- Goniometer (ankle joint angle).
- Accelerometer (physical twitch of lower limb).

### Developed Investigational Instrumentation

Custom made medical instrumentation has been designed and developed exclusively for clinical investigation or the research hypothesis. As such CE marking of such instrumentation is not required and will not be pursued.

All instrumentation has been designed by the Principal Investigator (PI) to the essential requirements of the Medical Devices Directive (93/42/EEC) [56]. Chartered engineers within and external to the supervision team have reviewed design documentation and confirmed safe and effective operation. The developed instrumentation has also passed electrical safety tests relevant to a class IIa, type BF medical device completed by the Medical Electronics department at Salisbury District Hospital.

The developed instrumentation is only intended for use by the PI and is clearly labelled "exclusively for clinical investigation". A risk assessment of the system during its intended use is included in Appendix E.

### Recruitment Size and Data Analysis

In order to provide exploratory data to assess whether further investigation of the research hypothesis is warranted, the following sample groups have been selected.

- 10 unimpaired male participants
- 10 participants who have had a stroke.

Two participants from each of these groups will be recruited and complete the study first in order to permit the feasibility of the research protocol to be assessed. Although not purposefully envisaged, should this identify necessary amendments to the research protocol these will be communicated to the ethics committee and sponsor before data from the remaining 16 participants is collected.

The sample size has is based upon recruiting sufficient numbers for group effects to be identified whilst providing a reasonably small standard deviation. Once data is collected, descriptive statistics (i.e. mean, standard deviation) will be used for analysis. Group comparisons will use non-parametric analysis techniques.

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### **Recruitment and Obtaining Informed Consent**

During unimpaired participant recruitment the 'Participant Information Sheet V1.2U' - Appendix A, will be provided to staff and students of the National Clinical Functional Electrical Stimulation Centre by the PI. Those interested will be invited to approach the CI or PI should they wish to participate.

Participants who have had a stroke will be identified from those receiving FES treatment at the National Clinical FES centre, Salisbury District Hospital and who have a review appointment scheduled during the research study period. The PI will screen the notes of patient participants due to attend the National Clinical FES centre for follow up review appointments 6 weeks in advance. The PI (Darren Hart, Clinical Scientist) is an existing member of the clinical care team responsible for seeing such patients. Those thought to meet the research criteria will be passed to the chief investigator (Dr Paul Taylor, Consultant Clinical Scientist) for review. If in agreement the Chief Investigator (CI) will send a letter inviting them to receive further information ('Participant Information Sheet V1.1I' -Appendix B) regarding the study. Recipients of the information sheet who express an interest in participating in the study will be asked to contact the PI. Should recipients of the participant information sheet wish to volunteer for the research an appointment will be made on the same day following their next intended outpatient appointment at the National Clinical FES centre.

All participants will be asked to reply at least two weeks prior to their intended review appointment. All participants will hence have at least two weeks in which to decide if they wish to participate. Informed written consent will be gained by the PI using the 'Informed Consent Form' of Appendix C. The PI has received training in gaining informed consent from the CI and will be supervised for when gaining consent from initial participants. The PI has also completed the trusts 'Consent computer based training' course of the Managed Learning Environment system.

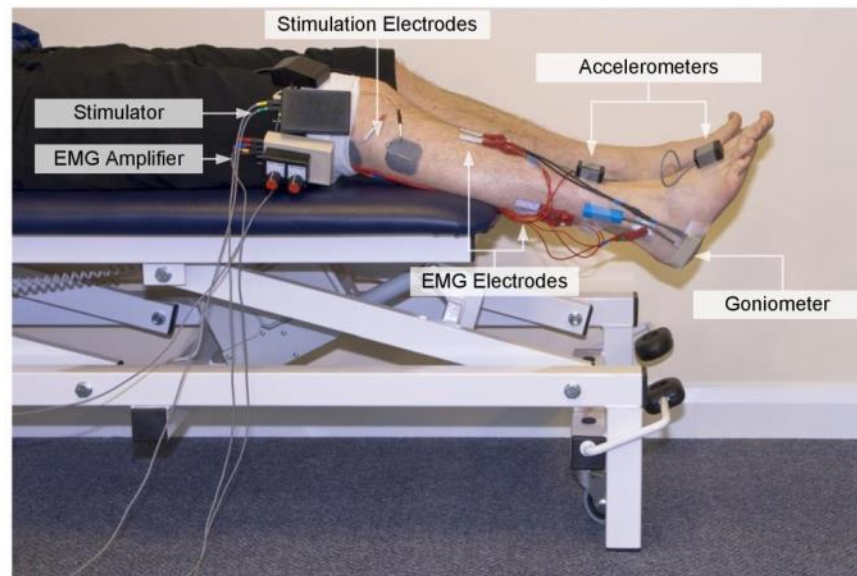
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Figure 6: Labeled photograph of developed instrumentation set up on participant's lower limb

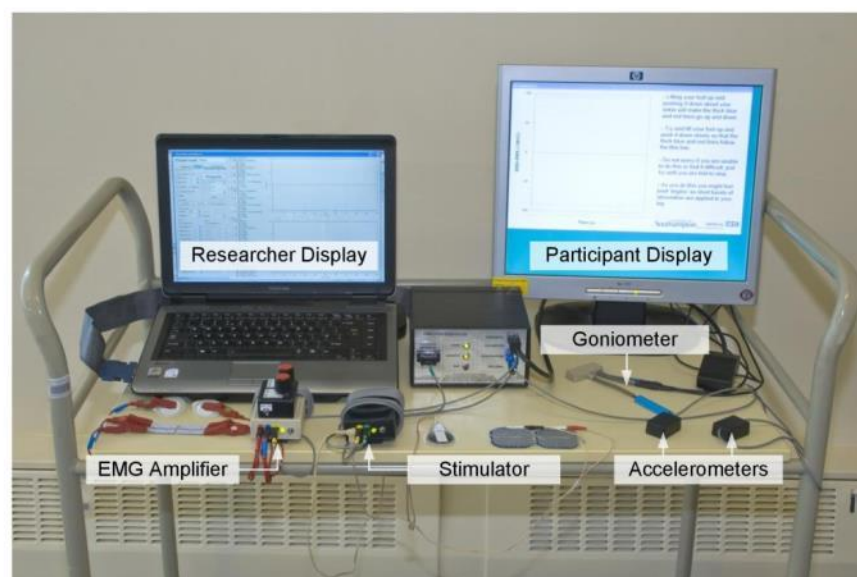


Figure 7: Labeled photograph of investigation system on wheeled trolley



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### Study Procedure

All participants will be given adequate time prior to the investigational session in order to have a drink, use bathroom facilities etc. The study will take place within clinical treatment area of the National Clinical FES centre. There will be room for carers or relatives who may have accompanied the participant to wait. Should the participant prefer, they may also be joined by such individuals during the investigation study in the clinic room or a chaperone may be provided.

### Procedure Prior to Participant Arrival

Prior to an investigation session the following checks will be completed:

- The inventory of equipment on the wheel trolley (Figure 7) will be checked.
- New or fully recharged batteries will be used in order to avoid possible disruption caused by replacement part way through the investigation session.
- Necessary measurement equipment and software programs will be readied.
- All equipment which is not single use and comes into contact with participants will be cleaned using detergent wipes i.e. clinic plinth, instrumentation.

### Procedure Following Participant Arrival

Participants will be invited into a consultation room where any questions or concerns they have regarding participation which they need to clarify in order to be able make an informed decision of whether to participate can be addressed. Informed written consent will be taken and the participant given a unique anonymous code (Appendix C).

Participants will be asked to move to the clinical area where the study will take place. The PI will begin to complete the 'Participant Study Form' -Appendix D. The medication list of impaired participants as shown in the clinical notes will be checked and recorded on the participant study form. Whether the participants left or right leg will be under investigation will be recorded. Unimpaired participants will use their dominant leg. Impaired participants will use their effected side.

Participants will be asked to transfer on to or sit on the clinic plinth. The height of the plinth can be varied appropriately. Participant will be asked to remove their socks and shoes and either change into shorts or roll their trousers up to approximately 10 cm above their knee. Participants may make use of a changing area adjacent to the clinic area or curtains can be drawn around the clinic plinth for privacy.

Skin condition around the stimulation electrode and EMG recording sites will be checked in order to ensure the integrity of skin condition. If required, excessive hair at these electrode sites will be trimmed with an electric trimmer. Skin underneath the recording electrodes sites will be cleaned using alcohol wipes in order to ensure good electrode contact through lightly abrading the top layer of dermis skin. This may cause minor

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temporary discomfort to the participant. Should the participant find it painful it will be stopped. The PI will manual identify correct EMG electrode placements using a measuring tape and palpation of the lower limb in line with the SENIAM guidelines [57]. With stimulation and recording electrodes attached the stimulation controller and EMG amplifier will be connected to these by wired leads.

The participant will be asked to lay supine such that they are comfortable with their lower leg, midway down their calf, suspended over the end of the clinic plinth (Figure 6). The clinic plinth will be arranged with one side against a wall such that the risk of falling is minimised. A goniometer will be affixed using micropore tape to the dorsal aspect of the participant's ankle (Figure 6). Two accelerometers blocks will be affixed to the participant's leg using micropore tape. One will be mounted on the dorsal aspect of the foot, the second to the mid-point of the anterior aspect of the tibia. A Urisleeve elasticated bandage (single use) will be used to contain and support all the wires and sensors around the participants lower leg (not shown). Once all instrumentation has been attached the PI will verbally check that the participant remains comfortable and the attached instrumentation are not applying excessive pressure to points along lower leg.

Throughout phases 1 – 5 of the study the participant will ask to remain relaxed and observe a 'participant display' monitor positioned on the wheeled trolley such that they can comfortably and clearly view it (Figure 7). Instructions displayed on the participant display (large size 20 point+ font) will also be repeated verbally by the PI.

#### Phase 1:

*Confirms effective set up of electrodes and instrumentation prior to data collection informing the research hypothesis. The primary function of this test is to successfully demonstrate detection of the compound muscle action potential which follows a stimulation pulse of sufficient intensity to cause a muscle contraction. This test also permits suitable selection of stimulation intensity and EMG amplifier gain.*

- 1.1. The stimulation current used by participants who are existing drop foot stimulator users will be recorded by the PI. For unimpaired participants an ODFS Pace will be used in test mode to ascertain what current to the nearest 5mA is needed to gain a functional contraction.
- 1.2. The current intensity of the research stimulation controller will be set to this amount and a 2.5 second burst of 100µs pulsewidth (50% intended stimulation intensity) will be applied. The pulsewidth will be gradually increased to 200µs (full stimulation intensity) where small adjustments to electrode positions may be required in order to produce the correct balance of dorsiflexion with moderate eversion as utilised clinically during drop foot stimulation.
- 1.3. If required, adjustments to recording electrode positions will be made such that the Compound Muscle Action Potential (CMAP) can be identified. If following skin preparation, electrode replacement there remains substantial stimulation artefact preventing identification of the compound muscle action potential the



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EMG amplifier will be set to record only high frequency components. Once the CMAP is identified the EMG gain will be set appropriately such that its magnitude fulfils at least 25% of the available measurement range.

- 1.4. Verbally instruct participant to relax and allow foot under test to rest under gravity. Goniometer will be zeroed by the PI in software.

#### Phase 2:

*The effect of bursts of repeated single and doublet stimuli on the excitability and inhibition of spinal reflexes affecting the tibialis anterior and soleus muscles will be assessed at different muscle lengths and when actively supporting and opposing the movement that the stimulation produces.*

- 2.1. Verbally instruct participant to relax and allow foot under test to rest under gravity. Warn participant that they will feel a buzzing sensation as a 2.5 second burst of stimulation is applied. They should remain relaxed and not consciously support or oppose the resulting muscle contraction.
- 2.2. Apply stimulation at 50, 100, 150 and 200µs pulsewidth (25, 50, 75 and 100% normal intensity). Measurements made at each stimulation intensity level will be automatically repeated and averaged 5 times with a 2 second pause between each.
- 2.3. The PI will support the foot at its end of range of dorsiflexion and eversion. The participant will again be asked to relax and not consciously support or oppose the muscle twitch.
- 2.4. Repeat step 2.2.
- 2.5. Verbally instruct participant that when the green indicator on the screen shows, the participant should oppose the movement i.e. push foot down (green indicator lit for 6.5 seconds with a 2.5 second burst of stimulation applied 2 seconds after indicator lit). These instructions will also be displayed on the participant display.
- 2.6. Repeat step 2.2.
- 2.7. Verbally instruct participant that when the green indicator on the screen shows, the participant should support the movement i.e. lift foot up (green indicator lit for 6.5 seconds with a 2.5 second burst of stimulation applied 2 seconds after indicator lit). These instructions will also be displayed on the participant display.
- 2.8. Repeat step 2.2.
- 2.9. Participant display (Figure 7) will show joint angle as measured by the goniometer affixed about the participant's ankle. Verbally instruct participant to attempt to track a 3 second period sinusoid with this angle trace whilst a 6.0 second burst of stimulation is applied. Complete this using stimulation at 50µs

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pulsewidth (25% normal intensity). If no compound muscle action potential is recorded, repeat as necessary using 100, 150 and then 200 $\mu$ s until observed whilst remaining comfortable for the participant to oppose the resulting movement.

- 2.10. Steps 2.1 - 2.9 will be repeated for doublet stimuli bursts applied at the same intensity level as for the single stimuli bursts.

### Phase 3:

*The effect of single repetitions (twitches) of single and doublet stimulation pulses on the excitability and inhibition of spinal reflexes affecting the tibialis anterior and soleus muscles will be assessed at different muscle lengths and when actively supporting and opposing the movement that the stimulation is attempting to produce.*

- 3.1. Verbally instruct participant to relax and allow foot under test to rest under gravity. Warn participant that they will feel a brief twitch when stimulation is applied. They should remain relaxed and not consciously support or oppose the resulting muscle twitch.
- 3.2. Apply twitch stimulation at 50, 100, 150 and 200 $\mu$ s (25, 50, 75 and 100% normal intensity). Measurements made at each stimulation intensity level will be automatically repeated and averaged 5 times with a 2 second pause between each stimuli.
- 3.3. The PI will support the foot at its end of range of dorsiflexion and eversion. The participant will again be asked to relax and not consciously support or oppose the muscle twitch.
- 3.4. Repeat step 3.2.
- 3.5. Verbally instruct that when the green indicator on the screen shows, the participant should oppose the twitch movement i.e. push foot down (2 seconds before and after stimulation applied). These instructions will also be displayed on the participant display.
- 3.6. Repeat step 3.2.
- 3.7. Verbally instruct that when the green indicator on the screen shows, the participant should support the twitch movement i.e. lift foot up (2 seconds before and after stimulation applied). These instructions will also be displayed on the participant display.
- 3.8. Repeat step 3.2.
- 3.9. Steps 3.1 - 3.8 will be repeated for doublet stimuli applied at the same intensity level as for the single stimuli.

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*The effect of single and doublet stimuli on the excitability and inhibition of spinal reflexes affecting the tibialis anterior and soleus muscles will be assessed when triggered from joint angle measured whilst the foot is free to move suspended over the edge of the clinic plinth.*

- 4.1. The participants' foot will be allowed to move freely whilst suspended over the end of the clinic plinth.
- 4.2. Participant asked to maximally dorsiflex and plantarflex their foot.
- 4.3. Participant asked to try and raise and lower their foot in time with a slowly varying sinusoid shown on the participant display which relates to their voluntarily achievable range of movement about the ankle. Should they be unable to do this on 3 repeated attempts this result will be recorded and the next phase of the study will be moved on to.
- 4.4. Twitch stimulation of 200 $\mu$ s pulsewidth will be applied as participant's joint angle passes through neutral from plantarflexion to dorsiflexion.
- 4.5. Step 4.4 will be repeated when passing through:
  - a. 75% maximum dorsiflexion
  - b. neutral from dorsiflexion to plantarflexion.
  - c. 75% maximum plantarflexion
- 4.6. Steps 4.3 - 4.5 will be repeated for doublet stimuli applied at the same intensity level as the single stimuli.

**Phase 5:**

*The effect of single and doublet stimuli on the excitability and inhibition of spinal reflexes affecting the tibialis anterior and soleus muscles will be assessed when triggered from EMG levels during an isometric (foot constrained at neutral) contraction.*

- 5.1. The participants' foot will be strapped to a support which holds their ankle at 90 degrees (or as close to this that can be achieved).
- 5.2. Participant asked to maximally dorsiflex and plantarflex their foot.
- 5.3. Participant asked to try and raise and lower their foot against constraining straps in time with a slowly varying sinusoid shown on the participant display which relates to their voluntarily achievable absolute EMG activity of the tibialis anterior and soleus muscles. Should they be unable to do this on 3 repeated attempts this result will be recorded and the next phase of the study will be moved on to.
- 5.4. Twitch stimulation of 200 $\mu$ s pulsewidth will be applied as participant muscle activation goes from opposing to supporting.



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- 5.5. Step 5.4 will be repeated when going from supporting to opposing.
- 5.6. Steps 5.3 - 5.5 will be repeated for doublet stimuli applied at the same intensity level as the single stimuli.

#### Phase 6:

*Phase 6 will assess the effects of conscious effort during a functional task when analysing results with respect to that gathered during phases 2-5.*

- 6.1. Accelerometers and goniometers will be removed
- 6.2. If not already present, a footswitch will be placed within the participant's shoe.
- 6.3. The participant will be asked to sit up on plinth and put their shoe on.
- 6.4. The goniometer will be reattached about the lateral side of the ankle joint.
- 6.5. An assistant will be asked to push the wheeled trolley (Figure 7) a few meters alongside patient.
- 6.6. Participant asked to stand whilst the goniometer will be zeroed in software.
- 6.7. Participant asked to walk 10 metres (this should be sufficient distance to record EMG over 5 paces. Participants can use any normal walking aids i.e. crutches, walking stick etc. The PI will walk alongside the participant in case assistance is required.
- 6.8. Step 6.7 will be repeated whilst applying the following stimulation:
  - a. None -this will enable the participants un-stimulated voluntary EMG to be recorded for comparison to the other four walks incorporating stimulation.
  - b. Single twitch stimuli following heel rise detected by footswitch
  - c. Double twitch stimuli pulse following heel rise detected by footswitch
  - d. Conventional single stimuli burst (repeated single pulses) from heel rise to heel strike with additional 300ms extension period of stimulation following heels strike. Such a stimulation envelope is akin to that applied during drop foot stimulation.
  - e. Doublet stimuli burst (repeated doublet pulses) from heel rise to heel strike with additional 300ms extension period of stimulation following heels strike. The same intensity and net amount of stimulation per unit time will be applied as in 6.8d.

#### End of Investigation Session

Participants will ask to be seated on the clinic plinth whilst all electrodes, sensors etc are removed. Minor discomfort experienced when micropore tape or electrodes are removed will be mild and acute. Should they require, the participant will be offered an area to redress before being thanked and accompanied out to the waiting room.

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Table 1 details each of the individual phased tests that the stimulation controller software automatically configures such that each individual test can be efficiently completed. Completing these tests into a passive load takes less than 60 minutes.

Phase	Description	Stim. Order	
		Single	Doublet
Phase 1	Confirmation of effective set up and configuration of instrumentation such that compound muscle action potential can be identified following an electrical stimulation pulse.	1-4	
Phase 2	Stimulation burst applied under static & dynamic conditions. Each test repeated at 25, 50, 75, 100% of normal functional stimulation pulse width.		
	No effort, foot in plantarflexion at rest under gravity.	5-8	22-25
	No effort, foot supported in dorsiflexion by PI.	9-12	26-29
	Actively plantarflexing, foot in plantarflexion at rest under gravity.	13-16	30-33
	Actively dorsiflexing, foot supported in dorsiflexion by PI.	17-20	34-37
	Dynamically tracking joint angle sinusoid without support from PI.	21	38
Phase 3	Stimulation twitch applied under static conditions. Each test repeated at 25, 50, 75, 100% of normal functional stimulation pulse width.		
	No effort, foot in plantarflexed position under gravity.	39-42	55-58
	No effort, foot supported in dorsiflexion by PI.	43-46	59-62
	Actively plantarflexing, foot in plantarflexed position under gravity.	47-50	63-66
	Actively dorsiflexing, foot supported in dorsiflexion by PI.	51-54	67-70
Phase 4	Stimulation twitch applied at following phases of goniometer signal when asked to track sinusoid: Goniometer crossing point - 0° Goniometer at 75% maximum dorsiflexion Goniometer crossing point - 180° Goniometer at 75% maximum plantarflexion	71 72 73 74	75 76 77 78
Phase 5	Stimulation twitch applied at following phases of EMG levels when asked to track sinusoid: Tibialis Anterior EMG <sub>ABS</sub> > 50% Max Soleus EMG <sub>ABS</sub> < 50% Max Tibialis Anterior EMG <sub>ABS</sub> < 50% Max Soleus EMG <sub>ABS</sub> > 50% Max	79 80	81 82
Phase 6	In walking over 10m synchronised to heel rise by footswitch		
	Unstimulated walking EMG		
	Single stimuli twitch applied at heel rise	83	
	Doublet stimuli twitch applied at heel rise		84
	Conventional stimulation throughout swing	85	
	Doublet stimulation throughout swing		86

Table 1: Study procedure test summary

2<sup>nd</sup> September 2010**Assessment of Safety**

A risk assessment sequentially assessing the activities of the investigational session has been completed and is included in Appendix E.

**Participant Withdrawal**

Participants can withdraw from the study at any time. Data already collected will be kept and utilised unless otherwise specified by the participant.

**Confidentiality and Anonymity**

Patient confidentiality will be maintained at all times throughout the study. Research volunteers will be allotted an anonymous code at the time of providing written informed consent. All data collected from an individual will be referenced to their anonymous participant code. Only the chief investigator (Dr Paul Taylor, Consultant Clinical Scientist) and the PI (Darren Hart, Clinical Scientist) will have access the written informed consent sheets which will be stored securely in a locked filing cabinet within the CSE department. Analysis will take place at the CSE department, Salisbury District Hospital by the PI. The academic supervision team of the PI will also have access to this anonymous data.

**Data Storage**

No person identifiable information will be stored electronically. Paper documentation linking participant names to participant codes will be the only identifiable piece of stored information. This will be stored in a locked cabinet within the Clinical Science and Engineering department. All anonymous data collected during the investigation session will be stored on a password protected laptop. The use of any participant identifiable information collected during the study will comply with the data protection act 1998.

**Ethical Considerations**

Informed consent will be gained from participants prior to participation with the study. Participants are free to withdraw from the study at any time. Efforts will be made to prevent any adverse reactions by taking action to reduce the risks identified in the following paragraphs.

Data from unimpaired participants' selected from the PI's supervision team will first test the feasibility of the research protocol. Following unimpaired participant recruitment, participants with an UMN injury that are already being treated as an outpatient of the National Clinical FES centre will be recruited. Patient's clinical notes will only be accessed by NHS staff when identifying individuals who may wish to participate in the study. Once recruited all data will be made anonymous through use of codes.

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Information linking codes to patient details will be kept secure within the CSE department as described in *Confidentiality and Anonymity*.

Participants will be required to attend a single investigation session which will last no more than 90 minutes. This will be scheduled following their review appointment at the National Clinical FES Centre in order to minimise travel and time disruption. Should the participant feel fatigued or wish to stop the session they may do this at anytime. The participant will lay down for the majority of the session before completing five 10 metre walks during the final test. Participants will be offered water refreshments. Seating for family/friends/carers will also be provided should they wish to observe or wait.

The PI will place sensors and electrodes on the participant's lower leg and conduct all experiments. The PI is a Health Professions Council registered Clinical Scientist who runs a regular FES clinic at the National Clinical FES Centre. Salisbury NHS Trusts lone working and manual handling policies will be followed at all times during data collection.

The sensation of stimulation is often described as being moderately uncomfortable. Existing FES users will be accustomed to this and the stimulation intensity used during the study will not exceed that which they currently use. Due to the differences in stimulation timing there may be some difference in perceived sensation however this is thought to not be significant. If a participant finds the sensation of stimulation intolerable then the stimulation intensity will be reduced appropriately. Unimpaired participants not familiar with the sensation of electrical stimulation may require some time during Phase 1 to become accustomed to the sensation. Stimulation intensity will not be increased beyond that which is needed to provide a functional contraction or that they can tolerate. Should this level be too low the research session will be prematurely concluded.

Participants may experience very mild acute discomfort as sensors are attached and removed from the lower leg using micropore tape. Participants will be warned of this potential discomfort before attaching or removing sensors.

The CSE departments' infection control policy will be followed at all times throughout the study. Stimulation and recording electrodes will be single use only. Bandaging used to keep wires and electrodes in place will also be single use only. All sensors which come in to contact with participants will be thoroughly cleaned using detergent wipes.

Skin irritations can follow prolonged use of electrical stimulation. This risk will be no greater than normally present and would not be expected over the relatively short duration and amount of stimulation that will be applied as part of the study. Hypoallergenic, single-patient use electrodes will be used for each research participant. The stimulation intensity will not exceed that found comfortable or typically used by a users existing FES drop foot stimulator. Should a participant's skin react adversely to the electrical stimulation, the investigation session will be discontinued.

There is a very small risk that electrical stimulation of a slightly different sensation to that accustomed to could adversely affect some participants balance during the 10 metre



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walks of phase 6 tests (Table 1). Participants will therefore be accompanied by the PI who is trained in manual handling. A manual handling belt will also be tightened around impaired participants' waists in order to aid the principal investigator in steadying them should it be judged to be required

There is a small risk of patients tripping over wires; the researchers will minimise this risk by careful supervision and ensuring that the environment remains safe at all times.

There is a small manual handling risk. The PI has completed departmental and trust manual handling training. Other clinical staff trained in manual handling will also be working in adjacent clinic areas. The department's lone working policy will also be followed such that access to an alarm system or other work colleagues will always be in place.

### **Management Audit and Peer Review**

The scientific basis of this research has been critically reviewed by University of Southampton examiners external to the immediate supervision team. This has been completed during progress review vivas and when transferring from study towards a Masters of Philosophy to a Doctoral of Research qualification.

Supervision team and student will meet monthly to ensure that the study is progressing satisfactorily. Should an adverse event occur as deemed by the chief investigator the study will be immediately stopped.

The protocol and supporting documentation has been reviewed by the academic supervision team. Ethical approval is also being sought from the school of Electronics and Computer Science who will act as legal sponsor.

### **Potential Difficulties in Completing Research**

Although the recruitment size is thought reasonable in light of the study duration, it may not be possible to recruit sufficient participants. The study is not based on power calculations and hence does not rely on a specific number of recruits. If less than the intended participant groups are recruited the data obtained can still be used to evaluate the research hypothesis.

As stated under details of the phase 1, due to the geometry and skin condition of different participants some may have a large stimulation artefact still present which will impede measurement of primary outcomes. Measures have been taken to overcome this by providing different EMG amplifier gain settings as well as an option to only measure high frequency components of the response, hence removing the low frequency stimulation artefact.

Some patient may not have sufficient voluntary movement/muscle activation to complete phases 4 and 5; in this case these phases will be omitted. Should participants not have sufficient fatigue resistance the tests have been ordered such that phases 4 onwards



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could be omitted whilst still providing useful data which can be used to investigate the research objectives.

### **Publication Policy**

Participants will be sent a paper copy explaining the findings of the research. The results of the study will be submitted for publication in an appropriate scientific journal and will also be presented at appropriate conferences.

### **Travel Costs**

As participants will be attending the National Clinical FES Centre as part of their employment or routine clinical treatment they will not be reimbursed for travel costs.

### **Indemnity**

For negligent harm NHS indemnity applies for NHS employees through the clinical Negligence Scheme for Trusts and Risk Pooling Scheme for Trusts in the event of a claim by or on behalf of participants. There is no indemnity for non negligent harm in the event of any claim made by or on behalf of participants.

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## **Appendix F: Response to Research Ethics Committee**



Clinical Science and Engineering Department  
Salisbury District Hospital  
Salisbury  
Wiltshire  
SP2 8BJ  
Email: darren@salisburyfes.com  
Telephone: 01722 439567

15<sup>th</sup> June 2010

**Re: REC Reference: 10/H0102/44**

**Project title: The effect of electrical stimulation patterns on muscles & reflexes**

Dear Chair of Ethics

Thank you for your email dated 14<sup>th</sup> June 2010 providing details of the ethics committee meeting at which the above study will be reviewed. I look forward to attending this meeting and gaining the committees feedback on the proposed study. Attached are my initial responses to the issues raised for discussion and clarification within your earlier email. I hope these may aid the committee in their task and welcome any further input from the committee as they see fit in resolving these issues. I shall formally follow up these points by sending a dated letter with accompanying documentation after the meeting.

Yours sincerely

Darren Hart  
Clinical Scientist

## **10/H0102/44 – Optimally spaced stimulation for clinical use with FES**

### **Ethical Issues to be discussed in Committee**

*Will there be easy/fairly immediate access to medically qualified support if required during the testing of subjects?*

*Please clarify on the comment of 'lone working procedure being followed' (A22). Suggest that on no account is a researcher on their own with a subject in case there is need to raise an alarm for help and in order to be able to steady subjects on either side when walking during the test.*

All testing will take place within the clinical treatment area of the National Clinical FES Centre. This is onsite to Salisbury District Hospital and hence there will be access to the hospital's crash call response team, A & E department and the stroke unit should participants suddenly require medical intervention. FES treatment carried out at the National FES Centre is under the medical supervision of Dr Walters, Consultant Stroke Physician.

The principal investigator has completed standard and advanced resuscitation training and a crash trolley is positioned in the corridor adjacent to the clinical treatment area. At all times during the investigation session there will be other clinical and non-clinical staff within earshot, working in adjacent clinic rooms. All staff are trained in resuscitation and are aware of the hospitals crash call system.

During the last phase of the investigation session (phase 6) an assistant will be present to push the wheeled trolley of instrumentation as the participant completes five 10 metre walks. The department has a wireless panic alarms system which the principal investigator will wear an alarm trigger for. Should additional assistance (such as in the event of a crash call) be required this alarm will be activated in order to request immediate assistance from all those in the building and it's adjacent building.

### **Issues that need clarification by correspondence**

*How are the non-impaired controls to be recruited? How are they to be approached?*

Copies of the participant information sheet will be distributed to potential participants within the department by the principal investigator. Those participants will then be invited to contact the chief or principal investigator should they have any further queries or wish to participate in the study.

*Stats input – few subjects and possibility of some subjects not being able to complete all phases of the study. Can the primary objective be met?*

The phases of the proposed test are partially ordered in importance of investigating the fundamental research hypothesis. Phases 1-3 are expected to be completed by all participants and primarily investigate the posed research objectives. Phases 4-6

further investigate the effects of muscle length, muscle tension and effort on these. The study in effect is a feasibility study to assess whether an effect is present. Should the initial two unimpaired and two impaired subjects be unable to complete all phases of the test, consideration will be given to whether the tests completed need to be reassessed.

*Please confirm that no person-identifiable information will be stored on the laptop.*

No person identifiable information will be stored on the laptop. Only a paper copy of a sheet linking patient names to participant codes will be stored in a locked cabinet within the Clinical Science and Engineering department. The research protocol will be amended and a revised version sent to the research ethics committee in order to clarify this point.

*Please confirm satisfactory indemnity arrangements (at present pending consideration by University ethics committee)*

See letter sent 13<sup>th</sup> of May 2010 confirming indemnity subject to approval for the study by the NHS research ethics committee.

*Need to exclude pregnant subjects – consider urine pregnancy tests for all pre- and peri-menopausal females.*

The National Clinical FES Centre has not experienced, or is aware, of any adverse events to pregnancy when using FES. Without confirmation that no risk is posed however, pregnancy is deemed a contraindication to FES.

Impaired subjects recruited to the study will be current users of FES. When initially set up and at subsequent review appointments they will have been alerted to pregnancy being a contraindication to FES.

At present, unimpaired female subjects of child bearing age could be recruited to the study. In such a case, the contraindication of pregnancy will be explained to them such that they can make an informed decision as to whether this may apply and hence whether or not they wish to participate. Page 3, section 'What are the side effects of any treatment received when taking part?' of the participant information sheet will be updated accordingly in light of this. A copy of the updated participant information sheet will be sent to the ethics committee.

*Is the duration of the test longer for the stroke group's usual FES treatment session? If so, would it be possible to consider the possibility of veering additional parking costs for subjects if applicable?*

Participants with disability badges are able to park for free at the National Clinical FES Centre. There are also a number of free parking spaces which the principal investigator can reserve for participants. The participant information sheet will be appropriately amended to clarify this issue and a revised version sent to the committee.



*The information sheet does not detail the fact that two unimpaired participants and two UMN injury participants will complete the study first. Suggest that this is added.*

Appropriate amendments will be made to the participant information sheet and a revised version sent to the ethics committee.

*Perhaps consider expanding a little the section on side effects with the treatment including the discomfort possibly experienced when attaching sensors and removed from lower leg, and the possibility of a differing sensation to that accustomed that may affect the patient's balance in the last section of the test – provide reassurance that there will be staff support to ensure that subjects do not fall etc...*

A section will be added to Part 1, page 4 of the 'What are the possible disadvantages and risks of taking part?' section of the participant information sheet, warning participants of 'mild and very brief discomfort' as sensors are attached and removed. Part 1, page 1 already warns participants that the sensation of stimulation may be different to that which they are used to however a manual handling belt will also be tightened around their waste in order to aid the principal investigator in steadying them if required. The research protocol and participant information sheets will be suitably amended.

*For those subjects with no experience with a UMN and FES they may have difficulty generally with the information sheet, and this may also be true of the other group of subjects with possibly some experience of FES. It's difficult to know quite how to pitch the explanation – might be worth testing the ICF on a few people to make sure that its explanation is clear.*

Participants will have as much opportunity as wished to discuss the study with the chief or principal investigator. The revised participant information sheet plus any further amendments will be given to a few existing patients for their comment on the clarity and readability. It will then be amended suitably before resubmitting. The revised participant information sheet will be trialled with the initial two unimpaired and two impaired subject recruited to the study.

*"Centre Number" on consent form not applicable, as single centre. Suggest just having "Salisbury DGH National Clinical Functional Electrical Stimulation Centre".*

The participant consent form will be amended appropriately and a revised version sent to the ethics committee.

## Appendix G: Unimpaired Participant Information Sheet

2<sup>nd</sup> September 2010

Salisbury   
NHS Foundation Trust

### PARTICIPANT INFORMATION SHEET – PART 1

#### The effect of electrical stimulation patterns on muscles & reflexes

*You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being completed and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.*

*Part 1 tells you the purpose of this study and what will happen to you if you take part. Part 2 gives you more detailed information about the conduct of the study.*

***Thank you for reading this.***

#### What is the purpose of the study?

We are trying to understand more about the effects of electrical stimulation on muscles and reflexes. In doing this we want to compare two types of stimulation.

Conventional Functional Electrical Stimulation (FES) stimulators apply very brief electrical stimulation pulses about 40 times a second. If we recorded the current which flows into a users leg and zoomed in it would look similar to below:



The alternative pattern of stimulation we want investigate looks like this:



Rather than equally spaced stimulation pulses they are applied half as frequently in pairs. The same total amount of stimulation is applied so although the sensation may feel a little different the 'intensity' of stimulation should feel similar.

When we apply stimulation to someone's leg some of it goes up their nerves to their spinal cord. This can cause reflex signals to be sent back down their leg which help the foot to lift. We want to investigate how significant these reflex signals are and whether they are different between the two types of stimulation shown above.

2<sup>nd</sup> September 2010

**Why have I been chosen?**

You have been asked if you would like to participate as you are a male member of the National Clinical Functional Electrical Stimulation Centre who has not had a stroke

We intend to recruit 10 people who have had a stroke and currently use FES and 10 people who do not normally use FES and have not had a stroke. We will then compare the results from the two groups. To start with, 2 people from each group will be recruited so that we can be make sure the tests completed are effective before recruiting the remaining 8 people to each group.

**Do I have to take part?**

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form which you will also keep a copy of. If you decide to take part you are still free to withdraw at any time and without giving a reason.

**What will happen to me if I take part?**

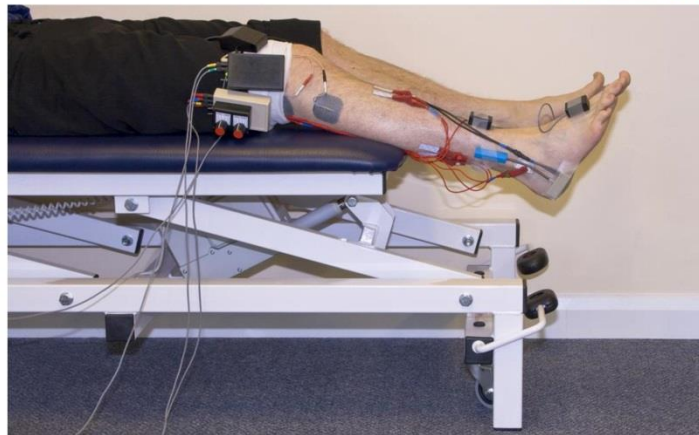
If you choose to take part you will need to attend the National Clinical Functional Electrical Stimulation Centre on one occasion for a series of tests which should not last longer than 1 hour 30 minutes. The tests will involve stimulation with different timing patterns being applied to your leg whilst a number of measurements are taken.

**Expenses and Payments**

We are unable to offer travel expenses or payment for taking part in this study.

**What do I have to do?**

We will need to place electrodes just above and beyond your knee so will ask you to either roll your clothing up to approximately 10 cm above your knee or bring shorts or loose fitting trousers to change in to. Changing facilities will be available to ensure privacy. You will also need to remove your sock and shoe so that we can attach various sensors to your leg. These sensors will measure the electrical activity of your muscles as well as the movements of your leg. A photograph of someone's leg set up with these sensors is shown at the top of the next page.

2<sup>nd</sup> September 2010Salisbury   
NHS Foundation Trust

During most of the test session you will be asked to lie on your back on a clinic bed with your foot hanging over the end. Once all the equipment has been set up a few short bursts of stimulation will be applied to check correct set up. The intensity of stimulation will be gradually increased to a level which you feel is comfortable and produces a lift of your foot. After this the five tests explained below will be completed. Each test comprises of a number of individual applications of stimulation which investigate factors that may affect your response to stimulation.

*Test**Description*

- 1 Bursts of stimulation lasting two and a half seconds, similar to pressing the TEST button of an existing drop foot stimulator, will be applied. This will be repeated a number of times whilst you are asked to relax, point your foot up, point your foot down, try and lift your foot up and down in time with an indicator on a computer screen and whilst the investigator supports your foot in an upwards position.
- 2 Single and paired stimulation pulses will be applied on their own so that you feel a very brief 'twitch' of your leg. This will happen in the same manner as test 1.
- 3 Your foot will be free to move up and down as it hangs over the end of the clinic bed. You will be asked to try and lift your foot up and down in time with an indicator on a computer screen. Whilst you do this you will feel brief twitches of stimulation as single and paired stimulation pulses are applied.
- 4 Your foot will be strapped to a support so that it is held still at a right angle. Test 3 will then be repeated but now your foot will be held in place by straps.
- 5 We shall ask you to get up and walk 10 metres (the length of the clinic room) five times. The first will be completely without stimulation. The second and third you will feel just a brief twitch each time you lift your foot off the ground to take a stride. During the fourth and fifth walks stimulation will be applied to help lift your foot on each stride (similar to a drop foot stimulator).

If you feel too tired or are unable to complete a particular test it will be missed.

2<sup>nd</sup> September 2010

**What are the side effects of any treatment received when taking part?**

There are no known side effects from using FES, but there are some minor risks.

The following are contraindications to the use of FES:

- Pregnancy (the effects of FES on the unborn child is not known, only male subjects who have not had a stroke are being recruited).
- Pacemaker user.
- Allergic to plastic material or micropore tape.
- Poor skin condition.
- Poorly controlled epilepsy.
- Fixed ankle contracture on side to be tested.
- Type I diabetes.

FES can feel like pins and needles. Most people quickly become used to it, if during the test session you find the sensation too uncomfortable the study will be stopped.

Some people can develop skin irritations underneath the stimulation electrodes. As the amount of stimulation that will be applied is very short compared to normal use, this is very unlikely.

**What are the possible disadvantages and risks of taking part?**

During the test session you may feel mild and very brief discomfort as the sensors are attached and removed from your leg.

You should not feel any different after the session. Your leg may feel a little tired if the muscles of it have been activated more than what they are used to. If this is so this feeling should quickly go away with rest.

**What are the possible benefits of taking part?**

There is no intended clinical benefit from taking part in this study.

The results gained will hopefully help improve understanding and use of FES with people in the future.

**What happens when the research study stops?**

You should not experience any lasting effects from taking part in this study. All participants will be sent a brief summary of the outcomes of the study when it is written up.

**What if there is a problem?**

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. Detailed information on this is given on page 6 of Part 2 of this information sheet.



2<sup>nd</sup> September 2010



**Will my taking part in this study be kept confidential?**

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are included on page 6 of Part 2.

**If the information in Part 1 has interested you and you are considering participating, please read the additional information in Part 2 before making any decision.**

***Thank you.***

2<sup>nd</sup> September 2010



## **PARTICIPANT INFORMATION SHEET – PART 2**

### **The effect of electrical stimulation patterns on muscles & reflexes**

#### **What if relevant new information becomes available?**

Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, the chief investigator of this study will tell you about it and discuss with you whether you want to continue. If you decide to continue in the study you will be asked to sign an updated consent form.

If the study is stopped for any reason before you are due to attend, we will tell you.

#### **What happens if I don't want to carry on with the study?**

You can withdraw from the study any time before or during the test session without giving a reason.

#### **What if there is a problem?**

If you have concerns about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions (see contact details on page 7). If you remain unhappy and wish to complain formally, you can do this through the NHS complaints procedure. Details can be obtained from the patient advice and liaison service known as PALS. They can be contacted on 0800 374 208 and act on the patient's behalf.

In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against Salisbury District Hospital but you may have to pay your legal costs. Then normal National Health Service complaints mechanisms will still be available to you.

#### **Will my taking part in this study be kept confidential?**

All information which is collected about you during this research will be kept strictly confidential and will comply with the data protection act 1998. Any information about you which leaves the National Clinical FES Centre will have your name and address removed so that you cannot be recognised.

#### **What will happen to the results of the research study?**

If you participate in the study you will be allocated an anonymous participant code. All data will then be stored using this code. The only means of identifying you to a code will be with the consent form you are asked to fill out. This form will be kept securely in a locked filing cabinet within the Clinical Science and Engineering department, Salisbury District Hospital and will only be accessed by the researchers.

2<sup>nd</sup> September 2010



The anonymous data obtained from tests done on your leg will be stored on a password protected computer. This data will be written up and submitted as part of a doctorate of philosophy (PhD) by the principal researcher. If data from the study is published or presented, in journals or at conferences, your data will not be identifiable.

**Who is organising and funding the research?**

This research is being supported by the University of Southampton. The National Clinical FES Centre is not being paid for you to be involved in this research.

**Who has reviewed the study?**

All research in the National Health Service is looked at by an independent group of people called a Research Ethics Committee to protect your safety, rights, wellbeing and dignity. This study has been reviewed and given favourable opinion by the South West Research Ethics Committee.

The Ethics Committee of the school of Electronics and Computer Science at the University of Southampton has also reviewed the study and given it its approval.

**What do I do now?**

If you do not want to participate in this study you do not need to do anything.

If you think you would like to participate or have any further questions please contact one of the researchers below.

**Further Information and Contact Details**

The main researchers on this project are:

Darren Hart (Principal Researcher)  
Clinical Scientist  
Salisbury District Hospital  
Telephone: 01722 439567  
Email: darren@salisburyfes.com

Dr Paul Taylor  
Consultant Clinical Scientist  
Salisbury District Hospital  
Telephone: 01722 439542  
Email: p.taylor@salisburyfes.com

***Thank you for your time reading this information sheet.***





## Appendix H: Patient Letter of Invite

26<sup>th</sup> April 2010



Department of Clinical Science and Engineering  
Salisbury District Hospital  
Salisbury  
Wiltshire  
SP2 8BJ

Tel 01722 429119  
Fax 01722 425263  
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Web [www.salisburyfes.com](http://www.salisburyfes.com)

**# Date #**

Dear \_\_\_\_\_

I am writing to you to invite you to take part in a research project. The aim of the project is to investigate a new way of controlling FES devices for improving walking.

The project is being carried out by Darren Hart, a Clinical Scientist at the National Clinical FES Centre who is also completing a PhD with the University of Southampton. His academic supervisor is Dr Paul Chappell and his clinical research at Salisbury is supervised by Dr Duncan Wood and myself.

Please read the enclosed information sheet. If you would like to take part in the project please complete the return form. If you have any questions please do not hesitate to contact me.

I see from our clinic list that you are attending the Salisbury FES Clinic on

**# Patients Appointment Details #**

If you are willing to take part in the study, the measurement session can take place immediately after your clinic appointment. The measurement session will take about 1 hour 30 minutes.

Yours sincerely

Dr Paul Taylor  
Clinical Engineer  
The National Clinical FES Centre



## Appendix I: Impaired Participant Information Sheet

7<sup>th</sup> July 2010

Salisbury **NHS**  
NHS Foundation Trust

### PARTICIPANT INFORMATION SHEET – PART 1

#### The effect of electrical stimulation patterns on muscles & reflexes

*You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being completed and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.*

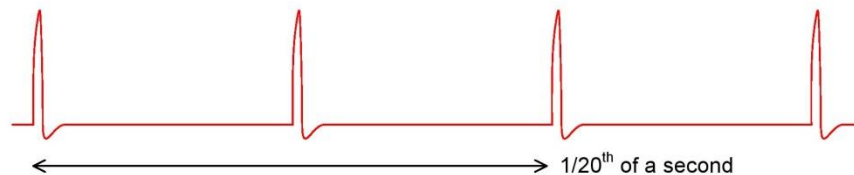
*Part 1 tells you the purpose of this study and what will happen to you if you take part. Part 2 gives you more detailed information about the conduct of the study.*

***Thank you for reading this.***

#### What is the purpose of the study?

We are trying to understand more about the effects of electrical stimulation on muscles and reflexes. In doing this we want to compare two types of stimulation.

Conventional Functional Electrical Stimulation (FES) stimulators apply very brief electrical stimulation pulses about 40 times a second. If we recorded the current which flows into your leg and zoomed in it would look similar to below:



The alternative pattern of stimulation we want to investigate looks like this:



Rather than equally spaced stimulation pulses they are applied half as frequently in pairs. The same total amount of stimulation is applied so although the sensation may feel a little different the 'intensity' of stimulation should feel similar.

When we apply stimulation to your leg some of it goes up your nerves to your spinal cord. This can cause reflex signals to be sent back down your leg which help your foot to lift. We want to investigate how significant these reflex signals are and whether they are different between the two types of stimulation shown above.

7<sup>th</sup> July 2010



### **Why have I been chosen?**

You have been asked if you would like to participate as you are an existing user of drop foot stimulation and are due for a review appointment in the next 6 weeks at the National Clinical FES Centre, Salisbury.

We intend to recruit 10 people who have had a stroke and currently use FES and 10 people who do not normally use FES and have not had a stroke. We will then compare the results from the two groups. To start with, 2 people from each group will be recruited so that we can be make sure the tests completed are effective before recruiting the remaining 8 people to each group.

### **Do I have to take part?**

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form which you will also keep a copy of. If you decide to take part you are still free to withdraw at any time and without giving a reason. If you decide not to take part, or wish to withdraw at any time, this will not affect the standard of care you receive during your normal FES review appointments at the National Clinical FES Centre.

### **What will happen to me if I take part?**

If you choose to take part you will need to attend the department on one occasion for a series of tests which should not last longer than 1 hour 30 minutes. This will be arranged around your existing review appointment so that you will not have to make an additional journey. The tests will involve stimulation with different timing patterns being applied to your leg whilst a number of measurements are taken.

### **Expenses and Payments**

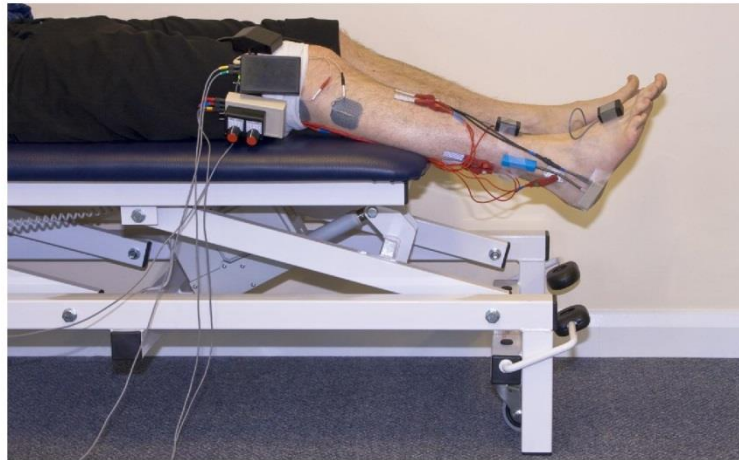
We are unable to offer travel expenses or payment for taking part in this study. Blue badge holders can park for free in allocated parking spaces adjacent to the National Clinical FES Centre. There are also a number of allocated car parking spaces which can be reserved for those who do not hold a blue badge.

### **What do I have to do?**

If you decide to participate and the test session will be arranged on the same day as your next review appointment with a brief gap in between to enable you to have a drink, visit the bathroom etc. You may be accompanied by relatives/carers during the test session or if you wish a chaperone can be provided.

We will need to place electrodes just above and beyond your knee so will ask you to either roll your clothing up to approximately 10 cm above your knee or bring shorts or loose fitting trousers to change in to. Changing facilities will be available to ensure privacy. You will also need to remove your sock and shoe so that we can attach various sensors to your leg. These sensors will measure the electrical activity of your muscles as well as the movements of your leg. A photograph of someone's leg set up with these sensors is shown on the top of the next page.



7<sup>th</sup> July 2010Salisbury **NHS**  
NHS Foundation Trust

During most of the test session you will be asked to lie on your back on a clinic bed with your foot hanging over the end. Once all the equipment has been set up a few short bursts of stimulation will be applied to check correct set up. The intensity of stimulation will be gradually increased to either the same as your existing stimulator or to a level which you feel is comfortable and produces a lift of your foot. After this the five tests explained below will be completed. Each test comprises of a number of individual applications of stimulation which investigate factors that may affect your response to stimulation.

<i>Test</i>	<i>Description</i>
1	Bursts of stimulation lasting two and a half seconds, similar to pressing the TEST button of an existing drop foot stimulator, will be applied. This will be repeated a number of times whilst you are asked to relax, point your foot up, point your foot down, try and lift your foot up and down in time with an indicator on a computer screen and whilst the investigator supports your foot in an upwards position.
2	Single and paired stimulation pulses will be applied on their own so that you feel a very brief 'twitch' of your leg. This will happen in the same manner as test 1.
3	Your foot will be free to move up and down as it hangs over the end of the clinic bed. You will be asked to try and lift your foot up and down in time with an indicator on a computer screen. Whilst you do this you will feel brief twitches of stimulation as single and paired stimulation pulses are applied.
4	Your foot will be strapped to a support so that it is held still at a right angle. Test 3 will then be repeated but now your foot will be held in place by straps.
5	We shall ask you to get up and walk 10 metres (the length of the clinic room) five times. The first will be completely without stimulation. The second and third you will feel just a brief twitch each time you lift your foot off the ground to take a stride. During the fourth and fifth walks stimulation will be applied to help lift your foot on each stride (similar to a drop foot stimulator). Although the stimulation applied will

7<sup>th</sup> July 2010



be at a very similar intensity level to your normal stimulator, it may feel a little different to what you are used to due to the different timing of stimulation. For all walks you can use any aids such as sticks and someone will also walk alongside you in case you need support. If you often feel unsteady whilst walking we may ask that you wear a padded 'handling belt' around your waist so that we can easily provide additional support should you need it.

If you feel too tired or are unable to complete a particular test it will be missed.

### **What are the side effects of any treatment received when taking part?**

There are no known side effects from using FES, but there are some minor risks.

FES can feel like pins and needles. Most people quickly become used to it, if during the test session you find the sensation too uncomfortable the study will be stopped.

Some people can develop skin irritations underneath the stimulation electrodes. As the amount of stimulation that will be applied is very short compared to normal use, this is very unlikely. Such risks will have been explained during your normal FES treatment.

### **What are the possible disadvantages and risks of taking part?**

No changes will be made to your existing stimulator and hence the benefit you receive from this will not be influenced by participating in this study.

During the test session you may feel mild and very brief discomfort as the sensors are attached and removed from your leg.

You should not feel any different after the session. Your leg may feel a little tired if the muscles of it have been activated more than what they are used to. If this is so this feeling should quickly go away with rest.

### **What are the possible benefits of taking part?**

There is no intended clinical benefit from taking part in this study.

The results gained will hopefully help improve understanding and use of FES with people in the future.

### **What happens when the research study stops?**

As already stated, there will not be any changes to any continuing FES treatment you receive after participating in the study. Your next FES review appointment will have been booked as usual and your normal treatment will continue. All participants will be sent a brief summary of the outcomes of the study when it is written up.

### **What if there is a problem?**

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. Detailed information on this is given on page 6 of Part 2 of this information sheet.

7<sup>th</sup> July 2010



**Will my taking part in this study be kept confidential?**

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are included on page 6 of Part 2.

**If the information in Part 1 has interested you and you are considering participating, please read the additional information in Part 2 before making any decision.**

***Thank you.***



7<sup>th</sup> July 2010



## **PARTICIPANT INFORMATION SHEET – PART 2**

### **The effect of electrical stimulation patterns on muscles & reflexes**

#### **What if relevant new information becomes available?**

Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, the chief investigator of this study will tell you about it and discuss with you whether you want to continue. If you decide to continue in the study you will be asked to sign an updated consent form.

If the study is stopped for any reason before you are due to attend, we will tell you.

#### **What happens if I don't want to carry on with the study?**

You can withdraw from the study any time before or during the test session without giving a reason. If you decide to withdraw the standard of care you receive during your normal FES review appointments at the National Clinical FES Centre will be in no way effected.

#### **What if there is a problem?**

If you have concerns about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions (see contact details on page 7). If you remain unhappy and wish to complain formally, you can do this through the NHS complaints procedure. Details can be obtained from the patient advice and liaison service known as PALS. They can be contacted on 0800 374 208 and act on the patient's behalf.

In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against Salisbury District Hospital but you may have to pay your legal costs. Then normal National Health Service complaints mechanisms will still be available to you.

#### **Will my taking part in this study be kept confidential?**

All information which is collected about you during this research will be kept strictly confidential and will comply with the data protection act 1998. Any information about you which leaves the National Clinical FES Centre will have your name and address removed so that you cannot be recognised.

#### **What will happen to the results of the research study?**

If you participate in the study you will be allocated an anonymous participant code. All data will then be stored using this code. The only means of identifying you to a code will be with the consent form you are asked to fill out. This form will be kept securely in a locked filing cabinet within the Clinical Science and Engineering department, Salisbury District Hospital and will only be accessed by the researchers.

7<sup>th</sup> July 2010



The anonymous data obtained from tests completed on your leg will be stored on a password protected computer. This data will be written up and submitted as part of a doctorate of philosophy (PhD) by the principal researcher. If data from the study is published or presented, in journals or at conferences, your data will not be identifiable.

**Who is organising and funding the research?**

This research is being supported by the University of Southampton. The National Clinical FES Centre is not being paid for you to be involved in this research.

**Who has reviewed the study?**

All research in the National Health Service is looked at by an independent group of people called a Research Ethics Committee to protect your safety, rights, wellbeing and dignity. This study has been reviewed and given favourable opinion by the South West Research Ethics Committee.

The Ethics Committee of the school of Electronics and Computer Science at the University of Southampton has also reviewed the study and given it its approval.

**What do I do now?**

If you do not want to participate in this study you do not need to do anything.

If you think you would like to participate or have any further questions please contact one of the researchers below.

**Further Information and Contact Details**

The main researchers on this project are:

Darren Hart (Principal Researcher)  
Clinical Scientist  
Salisbury District Hospital  
Telephone: 01722 439567  
Email: darren@salisburyfes.com

Dr Paul Taylor  
Consultant Clinical Scientist  
Salisbury District Hospital  
Telephone: 01722 439542  
Email: p.taylor@salisburyfes.com

***Thank you for your time reading this information sheet.***



## Appendix J: Participant Consent Form

Participant code:

Salisbury  
NHS Foundation Trust



### CONSENT FORM

Optimally spaced stimulation for clinical use with electrical  
stimulation

– *Its effect on spinal reflexes and muscle activation*

Chief Investigator: Dr Paul Taylor, Consultant Clinical Scientist

Principal Investigator: Darren Hart, Clinical Scientist

The National Functional Electrical Stimulation Centre, Salisbury District Hospital

*Please initial box*

- 1 I confirm that I have read and understand the participant information sheet entitled 'The effect of electrical stimulation patterns on muscles & reflexes' (version 1.2U 2<sup>nd</sup> September 2010 or version 1.1I 7<sup>th</sup> July 2010). I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.
- 2 I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.
- 3 I understand that relevant sections of my medical notes and data collected during the study, may be looked at by individuals from the National Clinical FES centre, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.
- 4 I have read and understood the contra-indications to the use of FES and do not know of any which apply to me.
- 5 I agree to take part in the above study.







---

Name of Patient

---

Date

---

Signature

---

Person taking consent

---

Date

---

Signature

*When completed, 1 for patient; 1 for researcher site file; 1 (original) to be kept in medical notes*



## Appendix K: Participant Details Summary

Code	Age	M/F	IMPAIRED										UNIMPAIRED	
			Duration at Assessment		FES Setup Walking Speeds			Assessment Walking Speeds			Total Effect		Code	Age
			Since CVA (years, month)	Since FES Setup (years, month)	No FES walking speed (m/s)	With FES walking speed (m/s)	Orthotic Effect (%)	No FES walking speed (m/s)	With FES walking speed (m/s)	Orthotic Effect (%)	Total Training Effect (%)	Total Orthotic Effect (%)		
I1	61	F	16 yr, 8 m	2 yr, 0 m	0.23	0.52	126.1	0.39	0.48	23.1	69.6	108.7	U1	47
I2	68	M	8 yr, 8 m	2 yr, 0 m	0.66	0.66	0.0	0.65	0.82	26.2	-1.5	24.2	U2	31
I3	42	M	3 yr, 0 m	2 yr, 2 m	0.47	0.55	17.0	0.57	0.53	-7.0	21.3	12.8	U3	27
I4	50	M											U4	35
I5	54	F	21 yr, 9 m	8 yr, 6 m				0.71	0.86	21.1			U5	24
I6	65	F	9 yr, 2 m	4 yr, 4 m	0.29	0.33	13.8	0.89	1.03	15.7	206.9	255.2	U6	35
I7	52	F	3 yr, 3 m	2 yr, 0	0.81	0.74	-8.6	0.67	0.85	26.9	-17.3	4.9	U7	20
I8	76	F		0 yr, 6 m				0.76	0.83	9.2			U8	28
I9	54	M	3 yr, 9 m	2 yr, 1 m	0.54	0.56	3.7	0.75	0.68	-9.3	38.9	25.9	U9	42
I10	75	F						0.47	0.61	29.8			U10	27
I11	70	F		1 yr, 10 m				0.35	0.37	5.7			U11	26
I12	59	F	2 yr, 4 m	1 yr, 4 m	0.62	0.51	-17.7	0.92	0.95	3.3	48.4	53.2	U12	59
I13	71	F	5 yr, 4 m	3 yr, 5 m	0.49	0.45	-8.2	0.65	0.71	9.2	32.7	44.9		
I14	75	M												

All males



## Glossary of Terms

Afferent nerves	Nerves that carry sensory information from the peripheral nervous system towards the central nervous system.
Agonist	A muscle primarily responsible for generating a specific movement.
Antagonist	A muscle that acts in opposition to the specific movement generated by the agonist and responsible for returning a limb to its initial position.
Anterior	Orientated towards the front of the body.
Antidromic	Opposite direction to normal physiological conduction.
Biphasic stimulation	Current flows in one direction then the other between electrodes.
Catch-like effect	Force augmentation occurring when an initial brief, high frequency burst is included at the onset of a subtetanic low-frequency train of electrical stimulation.
Distal	Orientated further from the point of attachment to the body.
Dorsal	Orientated towards the back of the body.
Efferent nerves	Nerves that carry motor information from the central nervous system towards the peripheral nervous system.
Faradic stimulation	Stimulation of innervated muscle by depolarisation of motor neurons.



F-wave	Electromyographic activity seen due orthodromic $\alpha$ -motor neuron activation following repolarisation of anterior horn cell after antidromic $\alpha$ -motor neuron activation by electrical stimulation.
Henneman size principle	The orderly recruitment order of small followed by large motor neurons during voluntary contracts of increasing force.
H-reflex test	A common neurophysiology test assessing reflex response of muscles following electrical stimulation of peripheral nerves.
H-wave	Electromyographic activity seen due to spinal reflex response to orthodromic activation of Ia sensory neurons by electrical stimulation.
Innervated muscle	Muscle supplied by an intact lower motor neuron connecting it to the central nervous system.
Isometric	Contraction in which the muscle length remains constant.
Isotonic	Contraction in which muscle tension remains constant.
Lateral	Away from the midline of the body.
Medial	Towards the midline of the body.
Monophasic stimulation	Current flows in one direction between electrodes.
Motor unit	Comprising a single motor neuron and all the muscle fibres of common type innervated by it.
Muscle Action Potential	The multi-peaked summated electromyographic response recorded due to simultaneous excitation of one or more motor units.
M-wave	Electromyographic activity seen due to orthodromic activation of $\alpha$ -motor neuron to electrical stimulation. ( <i>aka compound muscle action potential</i> )
Orthodromic	Direction of normal physiological conduction.

Percutaneous	Passing through a disruption in skin.
Plantigrade	Position of foot when full sole of foot is on the ground during walking.
Posterior	Orientated towards the back of the body.
Porcine	Pertaining to a pig model.
Proximal	Orientated closer to the point of attachment to the body.
Reciprocal inhibition	A reflex process of agonist muscle contraction whilst antagonists relax thus allowing movement to occur without co-contraction.
Recurrent inhibition	A reflex process inhibiting $\alpha$ -motor neurons providing negative feedback to an active muscle.
Spinal reflex	Involuntary coordinated patterns of muscle activation and relaxation which are integrated within the spinal cords grey matter and are elicited by peripheral stimuli.
Stretch reflex	A monosynaptic reflex which provides automatic regulation of skeletal muscle length.
<i>Sub-</i>	Below
<i>Supra-</i>	Above
Supramaximal	In the context of electrical stimulation intensity: above the level required to produce maximum response from targeted motor units.
Tetanic contraction	Motor nerve action potentials are incident at sufficient frequency to cause smooth, steady contractions.
Transcutaneous	Passing through intact skin.



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