Structural mechanics of skeletal muscle contractions:
Mechanistic findings using a finite element model

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Abstract

This thesis examines relations between skeletal muscle structure, function and mechanical output. Specifically, this thesis considers the effect of regionalization of muscle activity, changes in connective tissue properties and the inclusion of intramuscular fat on the mechanical output from the muscle. These phenomena are typically hard to measure experimentally, and so in order to study these effects a modelling framework was developed to allow manipulations of the structural and functional parameters of the in silico muscles and observe the predicted outcome of the simulations. The tissues within the muscle-tendon unit were modelled as transversely isotropic and nearly incompressible biomaterials. The material properties of the tissues were based on those of previously measured for the human gastrocnemius muscle. The model was tested mathematically and physiologically. Muscle fibre curvatures, along – and cross-fibre strains and muscle belly force-length predictions were validated against published experimental values.

The validated model of human gastrocnemius was used to predict muscle forces for different muscle properties, architectures and contraction conditions. A change in the activity levels between different regions of the muscle resulted in substantial differences in the magnitude and direction of the force vector from the muscle. The stiffness of the aponeuroses highly influenced the magnitude of the force transferred to the tendon at the muscle-tendon junction. The higher the stiffness, the greater the force. This indicates the importance of understanding the differences in the structure and material properties between aponeurosis and tendon with regard to their functions. The increase in adipose tissue (fat) in the skeletal muscles (characteristic of elderly and obese muscle) was simulated by describing the fat distribution in six different ways. The results showed that fatty muscles generate lower force and stress, and the distribution of the fat also impacts the muscle force.
To my parents,
for all their love and support.
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Chapter 1

Introduction

Skeletal muscles provide the force needed for everyday activity such as locomotion [1] and maintaining balance (e.g. [2]). The body is also provided with heat through contractions of the muscles [3]. Along with subcutaneous tissue, skeletal muscles work as a protective layer against mechanical impacts the body endures. The versatile roles of skeletal muscle are co-dependent on muscle structure and functional properties, that change with age [4], injury [5], disease [6] and physical activity [7]. The complexity of muscle function has made skeletal muscle the focus of many scientific studies for centuries. In this chapter we will review some of the factors that are known to contribute to muscle performance and some of the challenges that still remain to better understand their role. We will also review modelling approaches that have helped people to study skeletal muscles and are sometimes the only tool to look into aforementioned challenges.

1.1 Muscle structure

The way a muscle functions is highly dependent on its anatomical position in an animal body (e.g. its position relative to a joint) as well as its architecture and geometrical shape. Muscle architectural design can be characterized by muscle volume, physiological cross-sectional area (PCSA), muscle pennation angle, muscle fibre planes and tissue distribution (i.e. with respect to physiological properties of the tissue). Tissue distribution can be described in terms of the relative spatial location of tendons, aponeurosis and muscle tissue. At the level of the muscle belly, specifically, it can also be described by the distribution of different fibre types.
PCSA, pennation angle and fibre length are the three main parameters that can be used to describe a muscle's mechanical structure [7, 8]. Changes in these three variables may alter muscle mechanics (i.e. force, power output and deformation) substantially. PCSA is defined as the total cross-sectional area of the fibres in a muscle acting in parallel. It is a measure of muscle force generation capacity (strength). In other words, muscles with larger PCSAs can produce larger forces. This is mainly because the maximum force over cross-sectional area of fibres (stress) is almost constant (approximately 200 KPa). Therefore, the force output of a muscle is scaled by its PCSA.

The second structural parameter of skeletal muscles is the fibre pennation angle. It is calculated as the angle between the muscle fibre and the line of action of a muscle. In resting human muscles, pennation angles have been measured to have a range between 0° to 30° [7, 9], but it can change dramatically to approximately 45° or greater during muscle contraction [10, 11]. Fibre rotation (change in pennation angle), may contribute to changes in the thickness and width (Figure 1.1) of a muscle which may change the structure of a muscle. Many researchers have measured fibre rotation for active muscles [12, 13, 14, 15]. Fibre rotation deviates fibre force trajectory from the line of action of a muscle. However, it is believed that rotating fibres of pennate muscles contract with a lower velocity than the muscle belly and are able to produce higher levels of force [16].

Despite the evidence that some fibres run through the whole length of human muscles [17], the majority of fibres hardly get longer than 60% of the muscle length [7] and terminate intrafascicularly. Conceptually, it is usually assumed that fibres run from one aponeurosis to another and the multiplication of fibre length and PCSA gives the muscle volume.

The length of fibre at different passive and active states of a muscle modulates the force a fibre can produce [18]. This relation between the force and the length of a fibre is called the force-length property of a fibre. While the active forces length curve (Figure 1.2) depends on the average overlap of actin and myosin filaments of fibre sarcomeres (Figure 1.1; [18]), the passive force-length curve (Figure 1.2) is mostly related to elastic elements in the myofilaments within sarcomeres [19]. Additionally, fibre force depends on the rate of change in fibre length or fibre contraction velocity. This relation is named the force velocity property of a fibre (Figure 1.3; [20, 21]).

From an engineering perspective, in addition to PCSA, fibre pennation and fibre length, the distribution of different tissues (i.e. muscle and tendon) as well as similar tissues with
Figure 1.1: Muscle anatomy: from the whole MTU structure of calf muscles to molecular details of a sarcomere. Reconstructed from several sources with permission.
Figure 1.2: A typical force-length curve for active isometric contractions and passive extension of a sarcomere. The ascending limb is the result of sarcomeres contracting at lengths shorter than the optimal (with maximum force in isometric contractions). The descending limb is the result of sarcomeres contracting at lengths longer than the optimal length.

different properties (i.e. fast and slow twitch fibres) are also part of the structural design of a muscle. The distribution of tissues in a muscle-tendon unit is dependent on its mechanical usage. For example, aponeurosis thickness changes along the length of the muscle [22]. The thickness increases where the forces are transmitted to the tendon to reduce stress concentration. Another example is the distribution of different fibre types with different contractile properties in the muscle belly.

Different muscle fibres, have been classified as fast or slow twitch fibres based on their response time to stimulation [23]. Burke et al. [23] categorized different fibre types in a muscle based on their histochemical properties and twitch response time. They suggested that fibres are either fast fatigable (FF), fast fatigue resistant (FR) or slow muscle fibres (S). The difference in response time of a muscle fibre is due to the rate of \( \text{Ca}^{2+} \) movement in and out of the muscle cell [24]. Fast fibres are usually larger in cross-section, have a higher density of myofibrils and are able to produce higher levels of force. Slow fibres conversely have smaller cross-sections and develop lower forces than fast fibres [23]. The maximum intrinsic speed \( (V_0; \text{Figure 1.3}) \) of a fast fibre contraction is up to 2.5 times greater than
Figure 1.3: A typical force-velocity curve for concentric contractions of a muscle. Note that $V_0$ is the maximum intrinsic speed or maximum unloaded shortening velocity.

a slow fibre. Since Burke et al [23], fibres with a range of different twitch response times have been identified (e.g. [25]). These differences in fibre-types allows for a fine control over muscle contraction.

The structural parameters of skeletal muscle-tendon units within and between individuals are extremely divergent (e.g. [9]). One of the goals of this thesis is to examine the effect of some of these structural differences on human muscle mechanics. While observing different structures and their outputs allows experimental scientists to find relations between muscle structure and function, the approach chosen in this work (explained in more depth later in this Chapter and Chapter 2) allows direct manipulation of muscle structure to directly test the effects of a specific parameter on the muscle output. Chapter 5 in particular, studies the effects of different pennation, connective tissue and intramuscular fat distribution on muscle force.

1.2 Functional characteristics of skeletal muscles

Anatomical distributions of structural parameters within a single skeletal muscle have been linked to differences in muscle function. For example, Chanaud et al. [26] reported three regions in the biceps femoris of cats with distinct fibre pennation and fibre length with isolated nerve branches activating each region. Such observations are part of a large body of literature that has tried to explain how the complex structure of a muscle is used for different tasks.
The control over muscle function starts from a fibre level. Each muscle fibre is individually innervated by an axon branch of an alpha motor neuron. The smallest independently activated sub-unit of a muscle, is called a motor unit [27]. A motor unit is a group of muscle fibres innervated by axons of a single motor neuron. Fibres of each motor unit are distributed across the muscle, but there is evidence that different regions of muscles contain a higher density of similar motor units (e.g. [28]). Therefore a muscle can be activated in a regionalized fashion.

The firing rate of an alpha motor neuron is modulated via feedback from muscle spindles, Golgi tendon organs, pressure and joint proprioceptive receptors, as well as supraspinal commands [29]. The excitation in alpha motor neurons leads to excitation of muscle fibres. This excitation is usually measured using electromyography (EMG). The signal intensity of the collected EMG is used to estimate muscle activity [30] that is the concentration of calcium ions in the sarcoplasm [31, 32].

In many daily activities muscles are not maximally activated and therefore, besides the fact that a muscle can be activated at different regions, it can also be activated in different levels. Each possible combination of activation regions and levels can be called an activation pattern. Such activation patterns have been reported for a variety of activities in humans and animals (e.g. [33, 34, 35]). Different muscle activation patterns may lead to changes in the tension of different regions of the muscle-tendon unit (MTU) and the muscle belly structure. These may change the line of action of a muscle [36]. The change in the line of action of the muscle is important in animal locomotion as it changes moment arms about a joint.

The importance of the existence of different types of fibre in the muscle is shown in animals, where different activation or recruitment patterns are chosen for a specific movement (e.g. [37, 38]). In 1957, Henneman [39] observed that motoneuron recruitment follows an orderly pattern with change in stimulation level. He reported that motoneurons are recruited in order of their size. Small motoneurons were recruited first, and larger motoneurons are recruited upon an increase in stimulation. This order of motoneuron recruitment was named "the size principal" [40, 41]. Therefore, smaller motor units, which mostly have slow fibres [42] and a lower nerve action potential conduction velocity, are recruited before and derecruited after faster (larger) motor units. This allows faster (higher force level) units to be used when the task is more demanding [43]. Many studies (e.g.
[44, 45]) provided data that support the size principal (orderly recruitment); however, other studies (e.g. [46, 47]) have suggested that, depending on task or environmental variables, alternate (task-dependent) patterns may be used. Thus, different task-dependent recruitment would conceptually change mechanical behaviour of the muscle. The complexity of the functional characteristics of skeletal muscles has inspired many for a lifetime of research and will continue to do so. This thesis focuses on quantifying the effect of activity in different regions of a muscle on the force output of that muscle. Chapter 4 brings evidence of substantial differences in force and line of action of a muscle with changes in activation pattern.

1.3 Connective tissues and skeletal muscles

The force developed by a muscle has to be transmitted to the skeleton to initiate movement or to control posture. Connective tissues are used for this purpose. The force is transferred to the aponeuroses and then to the tendons and eventually to the bones. Just as the structural and functional characteristics of the muscle tissue have been frequently investigated so has the role of connective tissues on the mechanical performance of the muscle-tendon unit (e.g. [48, 49, 50]).

Besides the force transference properties, tendons may also act as an energy storage unit to help with the energy demands of highly dynamic activities [50]. The mechanical properties of tendons can be described by a stress-strain (or force-length) relation (e.g. [51, 52]). The stress-strain curve for tendon has a nonlinear toe region following a linear section as the strain increases. The toe region of a tendon stress-strain curve is extended up to a 2% strain. Though, this also depends on the anatomical and functional role of the tendon. The linear part of the stress-strain curve introduces a constant modulus of elasticity (or stiffness) which will hold until failure of the tissue [53]. This relationship is both history and strain-rate (viscoelastic behavior) dependent [53].

Similar to tendons, aponeuroses are used to transfer muscle force. However the stress in the aponeuroses is more likely to have a nonlinear distribution (e.g. [54]). This can partly be due to differences in aponeurosis thickness along its length and also different activation patterns of the muscle tissue that may create different force distributions on the aponeuroses.
The experimental data describing the mechanical properties of connective tissues will be reviewed in more detail in chapter 2. In this thesis we have investigated the effect of differences in mechanical properties of tendon and aponeurosis (Chapter 3) as well as the effect of aponeurosis stiffness on muscle force output when activity is regionalized (Chapter 4), or the tissue properties are altered within the muscle belly (Chapter 5).

1.4 Biomechanical modelling of skeletal muscles

Modelling or simulation of physiological phenomena is commonly carried out to allow physiologists to explore ideas that are hard to test in experiments. Limitations in experiments include ethical restrictions for in-vivo testing on human and animal tissue, hard or expensive processes of using a human cadaver or an animal corpse and lack of technology and equipment to measure desired data. Another reason for developing models to study muscle biology is that some physiological conditions are difficult to produce in experiments. An example of this is to recreate a predefined activation (or recruitment) pattern using a model.

Three different types of models have been used in biomechanics; conceptual, physical and mathematical [55]. Conceptual models are useful for understanding a phenomenon without any experiment and computation. An example would be modelling of the changes in the potential energy of the centre of gravity of humans during walking, by comparing them to a rolling egg [56]. Physical models are used for different purposes. They may be used to show that a proposed idea actually works (e.g. [57]), or to look at biological facts that are difficult to study in animals (e.g. [58]). For instance, Haas and Wootton [57] developed paper models of insect wings to explain folding mechanisms in beetles and some other insects. Mathematical modelling is the most often used method in computational biomechanics. Simple models are used to illustrate principals (e.g. [20]). Whereas more sophisticated (realistic) models are usually developed to predict a greater variety of results accounting for structural and functional complexities of the biomechanical systems such as skeletal muscles (e.g. [59]).

Predicting force production in the muscle fibres is key to the development of a mathematical model of muscle contraction. There are two important experimental theories that are usually utilized and are named after their developers: Hill [20] and
Huxley [60] models. While Hill’s model is an empirical model and Huxley’s sliding filament model is mechanistic, an important additional difference between them is the scale level at which they predict the force production. Huxley [60] used the probability of actin and myosin cross-bridge formation as the force generation mechanism. On the other hand, Hill [20] measured the contraction velocity of an isolated sartorius muscle of frog when pulled it at different loads. Despite the differences in these two models of muscle force development the Hill and Huxley models have been frequently used in mathematical modelling. However, we will focus more on describing Hill-type models since provides a mathematically simple representation of contractile properties of the muscle tissue.

Early Hill-type models included a (non-)linear actuators connected in series and (or) parallel with passive elastic elements. Such models were usually point to point (one-dimensional; 1D) muscle models. Many (e.g. [61, 62, 53, 63]) have used this type of modelling to investigate contraction force and (or) energy output of the muscle in different loading conditions. The benefit of these models can be seen in musculoskeletal simulations of human movement where the function of multiple muscles can simultaneously be studied. However, these models cannot explain the internal mechanisms that develop mechanical output of skeletal muscles.

In the late 1980s and through the 1990s, a number of research groups built two-dimensional (2D; panel) models of muscle (e.g. [64, 65, 66, 67, 19]). Van Leeuwen, in 1992 [65], introduced a dynamic bipennate model of the muscle-tendon unit (MTU). The model had a single, large and incompressible (constant area in 2D) fibre in each pennate region. The model was used to compare twitch, tetanus and dynamic (sinusoidal length change) responses (force and power output) between single fibre and muscle with different compliances (no tendon, stiff/compliant tendon/aponeurosis). He concluded that selecting the proper stiffness for tendon and aponeurosis would considerably increase the mean MTU power output. The benefit of using such a model was that it included the basic architecture of the muscle by including parameters such as fibre pennation.

Van Leeuwen and Spoor in 1993 [66] developed a mechanically stable model of skeletal muscles. Their model had curved fibres and considered the internal pressure in each panel to balance forces in the aponeurosis and fibres. They calculated changes in internal pressure, the pennation angle of fibres and fibre length and curvature along the muscle belly length for isometric contractions of seven stable configurations of a
bi-pennate muscle. Epstein and Herzog [19] published another model with a similar architecture later in 1998. They used the principal of virtual work to deal with the instability of their panel model. Their model predicted the total length change in a muscle under different static and dynamic loads.

Despite a large leap towards connecting the muscle structure and function, in 2D panel models (e.g [65, 66, 67]), fibres are considered a 1D contractile element separating 2D incompressible mediums. This assumption is not realistic enough and ignores the transverse properties of the muscle tissue. In addition, changes in depth due to bulging are usually not investigated by these models. However, even when depth change is allowed, the fact that bulging is a three-dimensional (3D) phenomenon and depends on 3D architecture of the skeletal muscle, illustrates that 2D muscles are unable to predict structural changes and therefore mechanical functions accurately.

As the level of detail (dimension and architecture) in modelling increases, modelling becomes so complex that in most cases an explicit analytical solution cannot be found and numerical techniques have to be used. The finite element method (FEM), an effective, powerful and complementary tool, is one of these numerical methods. It has been used to develop muscle models subjected to various internal and external loadings (e.g. [59, 68, 69, 70]). Depending on their complexity, (including geometry, mathematical formulation, architecture, activation pattern) models need different numbers of input parameters as well as different mechanical modelling approaches. Here, we focus on the models which used FEM as their analytical approach to address the nonlinear nature of muscle structure and function by reviewing simpler one or two-dimensional and up to complex three-dimensional structures.

One of the earliest FEM spring-damper models was introduced by Chen and Zeltzer in 1992 [71]. They considered each node to be connected to a spring like element, which defined the stiffness of that element at the node with respect to adjacent node(s). These elements considered passive, active and dynamic properties of the connected tissue. They used their model to check tension-length properties of the whole muscle-tendon unit by contracting the muscle isometrically in different lengths. A quick release experiment from an isometric active condition was also carried out to show muscle response to sudden unloading conditions. They also used their model to simulate isometric contractions in the human gastrocnemius and biceps brachii. However, this model didn’t
include the nearly incompressible behaviour of the muscle. Otten and Hulliger [68] also modelled skeletal muscles using finite elements in 1995. Their elements were incompressible planar rectangles having 1D contractile elements on the edges that were considered to be in the fibre direction. They included both the tendonious sheet and fibre properties in the model. Different physiological states of the muscle were simulated. This included partial activation of muscle fibres by either fully activating half of the muscle or by fully activating every other fibre in the muscle. They found that output force was about 57% to 59% of a fully activated muscle. This was above the predicted 50% because (as they argued) sarcomeres in a submaximally contracted muscle have longer lengths and are on the ascending limb of the force length curve (Figure 1.2), muscle produces higher forces. They also modelled a bipennate muscle with twice the area of a unipennate muscle. The output force for an isometric contraction of a bipennate muscle was 3.2 times that of the force of the unipennate geometry. The difference in the developed force when compared to the predictable amount of twice the unipennate muscle force, was explained by arguing that in the bipennate muscles the length of an average sarcomere is 1.57 times the length of the sarcomere in the unipennate muscle. They also measured changes in the muscle pressure and external curvature when the muscle geometry was supported by an external tissue. This model was one of the most advanced muscle models at the time, but it still had many of the described limitations of 2D muscle models.

In order to produce more realistic models of muscles, continuum mechanics models were introduced. In this approach mechanics of the muscle tissue is modelled as a whole compared to previous approaches with individual contractile elements, series and parallel elastic elements, as well as separate incompressible medium. This is usually done by using finite elasticity theory (e.g. [72]) where the change in tissue shape (strains) is associated with an energy function. This function is usually called the strain-energy function of a tissue. All active, passive and incompressibility behaviours of a biological soft tissue are described using this function and tissue properties are passed to the mathematical formulation and numerically solved to compute the strains and stresses in the tissue.

Many have used this approach to describe elastic behaviour of the muscle (e.g. [73, 74, 69, 59, 75, 70]). The differences in these models were mostly in how they predicted fibre force. Some, like Oomens [69], used the Huxley model for predicting the number of
attached cross-bridges and therefore the output force in fibre level. Others ([74, 59, 70]), used a Hill-based model for forces in the contractile fibres. Although these models are the most realistic models for replicating the muscle tissue behaviour so far, the developers usually have not investigated detailed muscle physiology such as the effects of differential muscle activation on its performance. Bol and Reese [70] used a unique definition of strain-energy. Their model was somewhat similar in the form of the element type to Otten and Hulliger’s [68] work, as their tetrahedral elements with elastic beam elements on the edges and an isotropic incompressible volume in the middle, just defined a particular form of a 3D panel model. The edge elements, which were aligned with fibre directions, had fibre contraction properties. Other edge elements had connective tissue (collagen) properties. Their method developed a simpler mathematical system and allowed them to simulate muscle with different fibre types and at different activation rates.

Another continuum-mechanics model of skeletal muscles was developed by Blemker et al. in 2005 [59]. A composite design for the material was considered by developing an elasticity formulation for a transversely isotropic material. Muscle properties along and transverse to the fibre direction were put into the model and tissue strains were compared to those of experimentally measured [76] for validation. The same model was used to investigate the effects of aponeurosis geometry (structure) on injuries of the biceps femoris long-head in athletes [77]. This clinical study found that muscles with a thicker (higher stiffness) aponeurosis are less likely to be injured.

A large number of continuum models have been developed over the last fifteen years (e.g. [73, 74, 69, 59, 75]) but none of them have precisely investigated the architectural design and the effect of recruitment physiology in depth. We believe that these parameters play a significant role in muscle performance and need further investigation.

The purpose of this thesis is to develop a modelling framework to be used in applied and conceptual studies of human muscle function and to use this framework to investigate the effect of change in some of the architectural and functional parameters of skeletal muscles (e.g. activity distribution) on the mechanical performance of human muscles. In other words, the goal of this thesis is to find mechanistic links between changes in mechanics at the tissue level and the overall output of a skeletal muscle.
1.5 Outline of this thesis

The modelling approach, including mathematical formulation, analytical method and choice of material properties for the purpose of this thesis is brought in Chapter 2. The implementation, validation and basic physiological simulations using the developed framework are brought in chapter 3. Chapter 4, studies the concept of regionalized activity in the muscle and how this factor changes muscle output in presence of different aponeuroses stiffness. Chapter 5 studies the effect of fat accumulation in the skeletal muscle tissue. This chapter investigates the effects of different fat distributions, the percentage of fat content, different geometries and connective tissue properties on the force output of the elderly and the obese gastrocnemius muscles. Finally, Chapter 6 has been devoted to review the current work and explain the limitations and possible extensions in the future.

A concise version of Chapter 2 is being prepared to be submitted for publication. The contents of Chapter 3 have been submitted as a research article and is currently under review. Chapter 4 is based on a research article published by Rahemi et al. (2014; [78]). Chapter 5 is based on another research article currently under review for a journal publication.
Chapter 2

Mathematical model: Development and implementation

2.1 Introduction

The deformation of the muscle-tendon unit (MTU) in response to loading depends on many parameters including architectural design, mechanical properties of tissues and activation patterns. In order to properly simulate the nearly incompressible, highly nonlinear and anisotropic behaviour of the MTU, these parameters need to be carefully specified. The over-arching goal of this thesis is to create a mathematical model capable of reproducing some of the mechanical properties of an MTU, and which is able to predict muscle behaviour based on its functional properties (i.e. activation level). Achieving this goal needs a good choice of modelling approach as well as quantified data on muscle architecture and its functional properties. Since the resultant mathematical model is complex and nonlinear, exact analytical solutions are not available except in the simplest situations. It is for this reason that careful numerical simulations are vital in the study of MTU.

The novel contributions of this thesis are:

- the design of a mathematical model of the full MTU unit;
- the fitting of parameters from experimental data;
- the development of a C++ 3-D finite element software architecture capable of
simulating MTU behaviour, and

- the use of these mathematical and computational tools to answer basic scientific questions about muscle.

In this chapter we shall focus on the development of the mathematical model of MTU behaviour, based on a three-field formulation. We recall the foundations of such a theory in 2.2. The specific form of the model in turn relies on modelling the strain energy associated with the muscle, tendon and aponeurosis, the effect of muscle and collagen fibres, passive and active behaviour and muscle geometry. The strain-energy functions are discussed 2.3, and we discuss the choices of parameters in the model based on available experimental data. The resultant mathematical model is discretized using a Discontinuous Galerkin finite element method (DG-FEM) and solved using a nonlinear algorithm in a manner described in section 2.8.

Some mathematical models (e.g. [53, 62]) consider MTU as a scaled up fibre or contractile element (CE) in combination with parallel (PEE) and series (SEE) elastic elements. The benefit in such simplified models is their ability to predict rough muscle force and length with a low computational cost. These models usually assume that the muscle has a constant depth that provides a direct relationship between pennation angle and muscle fibre length, and allows for a straightforward calculation of muscle length and pennation angle change. The constant depth assumption for a model with a certain muscle fibre length, besides ignoring the physiological phenomenon of bulging, also results in a single and fixed initial pennation. Therefore, another technique was introduced in muscle modelling where individual 1D contractile elements were located inside a 2D (e.g. [65, 68, 19]) or a 3D (e.g. [70]) isometric incompressible medium. This approach created a class of muscle models often called panel models. The assumption of fibre distribution in these panel models, regardless of the computational technique applied to solve for the outputs, does not quite represent the muscle tissue composition and ignores connection of fascicles by connective tissue and eventually the mechanical properties of muscle tissue in its continuum form. On the other hand, panel models are more detailed in terms of architectural (e.g. [66]) and functional properties (e.g. [68]).

A more complete representation of muscle architecture needs a 3D continuum based model of the soft tissues of the MTU. This method can provide the tools for describing
mechanical properties MTU tissue with its 3D structure, and a larger capacity to create physiologically relevant functionality inside the muscle. Also, it does not have some of major issues of the other methods. The problem with this technique is usually the computational cost. Continuum modelling is based on the finite elasticity theory and provides tools to simulate more realistic structure and function of the MTU. To simulate the muscle response under different loading we need to solve for the elasticity equation (see the next section). In continuum mechanics, soft tissues are often modelled as hyperelastic materials with transversely isotropic mechanical properties. The behaviour of a hyperelastic material is described using strain-energy functions. Different strain-energy functions (which can be interpreted as constitutive equations) were used in previous continuum models (e.g. [59, 79, 73, 74, 69, 75]). The main difference was due to force and deformation predicting factors. For example, Oomens et al. [69] used the sliding filament theory of Huxley (1954; [60]) for predicting the number of attached cross-bridges and therefore the output force in fibre level, but Blemker et al [59], used a Hill (1938; [20]) theory based model for estimating forces in fibre level. While Huxley based models have many disadvantage in estimating force in high-speed contractions ([80]), Hill type models can be used in both slow and fast contractions. The benefit of Huxley models is mostly in sub-macroscopic studies of muscle contraction.

Despite the availability of different commercial and free platforms such as FEBio, Ansys and Artisynth that allow for modelling of soft-tissue including the muscle tissue, the questions of this work and the approach towards implementing the details of architecture and function of skeletal muscles in the mathematical formulation was not always possible to achieve when working within the framework of such platforms. As mathematical education was part of the program that was needed to develop the necessary mathematical framework, the only way to use very established aforementioned modelling platforms was to work with closely with developers so that we could access and change the mathematical system their software use. These reasons led us to use a very well-documented freeware named deal.II [111] were a mathematical formulation can be built up from the basic mathematical operators such as gradient, divergence and entities such as vectors and tensors.

In this thesis we will try to harvest continuum mechanics capabilities in order to simulate the function of muscles while acting in different loading and constraints
conditions. This chapter is a review of fundamentals of the mathematics and continuum mechanics modelling as well as computational techniques that were used or developed to build the model. For a more complete description of these fundamentals most of the continuum mechanics books (e.g. [81, 82]) are good resources.

2.2 Mechanics and Hyperelastic Materials: background

The soft tissues in this project can be mathematically described as a fibre-reinforced composite biomaterial [83]. Specifically, they are described as nearly incompressible (e.g., for muscle Baskin and Paolini, 1967; [84]), transversely isotropic hyperelastic materials. In order to fix notation and define frequently-used terms, we will now recall well-established fundamental concepts in continuum-mechanics that are used to describe the mechanics (kinematics and kinetics) of an elastic object when loaded.

The constitutive properties of a material can be described in a variety of ways. For example, in linear elasticity the stress and strains are linearly related; specification of the constitutive properties can be done by using Lamé constants. In this thesis, we choose a description of the constitutive properties of hyper elastic materials by linking the response to physical loading to the strain energy.

2.2.1 Kinematics of an elastic object

In the kinematics, we wish to track the position vector of an object (particle’s) position. Let us denote the current state position vector \((x)\); this can usually be found as a function of the original state position vector \((X)\) and time \((T)\),

\[
x = x(X, T).
\]

The displacement vector \(u\) that will be used very often in this text is calculated by:

\[
x = X + u.
\]

The deformation gradient \(F\) is a second order tensor defined as:

\[
F = \left[ \frac{\partial x_i}{\partial X_j} \right] = I + \nabla u.
\]

where \(I\) is the second-order identity tensor, operator \(\nabla\) is the (vectorial) gradient and \(i\) and \(j\) indexes represent the component of vector. The determinant of \(F\) is called the dilation \(J\)
and represents the connection between the object volume in its current \((dv)\) and original state \((dV)\),
\[
dv = J \, dV, \quad J := \text{det}(F).
\]
The deformation gradient is used to calculate the right \((C)\) and left \((B)\) Cauchy-Green tensors as:
\[
C := F^T F = [F_{ki} F_{kj}] = \left[ \frac{\partial x_k}{\partial X_i} \frac{\partial x_k}{\partial X_j} \right], \quad (2.1)
\]
\[
B := FF^T = [F_{ik} F_{jk}] = \left[ \frac{\partial x_i}{\partial X_k} \frac{\partial x_j}{\partial X_k} \right]. \quad (2.2)
\]
The strain tensor \((E)\) becomes
\[
E := \frac{1}{2} (C - I). \quad (2.3)
\]
Here again indexes \(i, j,\) and \(k\) are used to identify the components of the vectors and tensors.

### 2.2.2 Kinetics of an elastic object

As described above, the constitutive properties of a material can be characterized by its strain energy. The strain-energy functional \(W\) will play an important role in the modelling process, and we will need to specify the strain energies for different types of tissue in the MTU. We remark that if the material under consideration were behaving in a linear, isotropic and homogenously elastic manner, then the strain energy can be written as
\[
W = \frac{1}{2} \lambda [\text{tr}(E)]^2 + \mu \text{tr}(E^2) \quad (2.4)
\]
where \(\lambda\) and \(\mu\) are Lame constants.

The Cauchy stress \((\sigma)\) developed inside a continuum material is calculated by differentiating the strain-energy function \(W\) with respect to the strain tensor components,
\[
\sigma := \left[ \frac{\delta W}{\delta E_{ij}} \right] = \frac{1}{\text{det}(F)} F^T \tau F. \quad (2.5)
\]
where \(\tau\) is the Kirchoff stress and can be calculated as:
\[
\tau = 2 \left[ \frac{\delta W(C)}{\delta C_{ij}} \right] = 2 \left[ B_{ij} \frac{\delta W(B)}{\delta B_{ij}} \right] = J \sigma F^{-T}. \quad (2.6)
\]
The second Piola-Kirchoff stress is defined as:
\[
S := F^{-1} \tau F^{-T}. \quad (2.7)
\]
Frequently, knowledge of the externally-applied Cauchy stress is useful for calculating tractions. These are the natural boundary conditions for the elasticity equations, analogous to the Neumann conditions for the Laplacian. Tractions are applied to the boundary sections with a Neumann boundary and are given by
\[ t = \sigma n. \]
Here \( n \) is the normal vector to the surface where the traction is being applied.

### 2.2.3 Hyperelastic material continuum response

The assumption of a nearly incompressible fibre-reinforced composite biomaterial creates two distinct parts in the strain-energy formulation; a volume changing (volumetric) part that represents the incompressibility characteristics of material and a volume-preserving (isochoric) part representing the composite response. In order to mathematically account for both volume changing and volume-preserving responses in stretch or shear loadings we multiplicatively decompose the deformation gradient and left Cauchy-Green tensors,
\[ F = (J^{\frac{1}{3}} I) \bar{F}, \quad B = (J^{\frac{2}{3}} I) \bar{F} \bar{F}^T = (J^{\frac{2}{3}} I) \bar{B}. \]
Here \( \bar{F} \) and \( \bar{B} \) are the isochoric parts of the deformation gradient and left Cauchy-green tensor respectively. The strain energy function can be similarly decomposed into volumetric (subscripts ‘vol’) and isochoric (subscripts ‘iso’) parts as:
\[ W(B) = W_{vol}(J) + W_{iso}(\bar{B}). \tag{2.8} \]
Likewise, the Kirchhoff stress \( \tau \) from equation (2.6) can also be decomposed,
\[ \tau = 2B \frac{\delta W(B)}{\delta B} = \tau_{vol} + \tau_{iso} \]
where
\[ \tau_{vol} = 2B \frac{\delta W_{dev}(B)}{\delta B} = pJI, \]
and
\[ \tau_{iso} = 2B \frac{\delta W_{iso}(B)}{\delta B} = (I - \frac{1}{3} I \otimes I) : \bar{\tau}. \]
Here \( \otimes \) is tensor inner product operator, \( \mathcal{I} \) is the fourth-order identity tensor. The variable \( p \) is the hydrostatic pressure, and \( \bar{\tau} \) is the fictitious Kirchoff stress and is defined by

\[
\bar{\tau} := 2B \frac{\delta W_{iso}(\bar{B})}{\delta \bar{B}}.
\]

The elasticity tensor \( \mathcal{C} \) is a rank four tensor which is defined in the material description as:

\[
\mathcal{C} := 2 \frac{\delta \tau(C)}{\delta C} = 4 \frac{\delta^2 W(C)}{\delta C^2}
\]

and in spatial coordinates as:

\[
c := 4J^{-1}B \frac{\delta^2 W(B)}{\delta B^2} B
\]

(2.9)

The elasticity tensor can also be decomposed into deviatory and isochoric components the same way as the spatial Kirchoff stress.

### 2.2.4 Potential energy minimization and the three-field formulation

The total potential energy of a physical system \( U \) can be defined as the sum of internal \( U_{int} \) and external \( U_{ext} \) potential energies. The actual state of the physical system is obtained by minimizing the potential energy. The potential energy of the described system can be written as:

\[
U(u, \tilde{J}, \bar{p}) = U_{int} + U_{ext} = \int_\Omega W_{vol} + \bar{p}(J(u) - \tilde{J}) \, dv + \int_\Omega W_{iso}(\bar{B}(u)) \, dv - \int_{\Omega} f_b \cdot u \, dv - \int_{\partial\Omega} f_t \cdot u \, da
\]

(2.10)

where \( \tilde{J} \) is the dilation constraint enforced by a Lagrange multiplier to the system \( \bar{p} \) that represents systems internal pressure (i.e. intramuscular pressure), and \( \Omega, \partial\Omega, v \) and \( a \) are the system’s domain, boundary, volume and boundary area respectively. Finally \( f_b \) and \( f_t \) are body and traction forces acting on the domain and boundary of the system respectively.

Using a variational argument, the Euler-Lagrange equations for the stationarity of the potential can be written in terms of the deformation \( u \), dilation \( \tilde{J} \) and pressure \( \bar{p} \)

\[
div(\sigma(\tau(C(u)))) + f_b = \rho \frac{\partial^2 u}{\partial t^2}
\]

\[
J(u) = \tilde{J}
\]

\[
\bar{p} = \frac{\delta W_{vol}(\tilde{J})}{\delta \tilde{J}}
\]

(2.11a, 2.11b, 2.11c)
In our computational process we try to find the equilibrium of the system described by a three-field formulation (equations 2.11 a to c) by minimizing its potential energy. Details on the computational strategy will be provided in section 2.8.

2.3 Strain-energy function

The use of strain-energy functions $W$ to describe the constitutive behaviour of soft tissues (including muscle) is well-established. There are broadly two different ways in which the strain-energy is described.

In the first approach (e.g. [85]), the strain-energy is based on physically-based invariants of the stress tensor. This allows a faster and more direct way to extract material constants from experimentally measured material properties. Unfortunately, if we use such invariants the underlying mathematical formulation becomes highly nonlinear, leading to computational challenges. Another, deeper issue is that there are few experimental studies that provide the necessary measurements for estimating the material constants. Even in presence of enough data for a specific tissue, variations in the literature are high and in some cases contradictory. (e.g. for the muscle tissue see [86] vs. [87]).

In the second, more classical approach (e.g. [88]), the strain energy is based on the invariants of the Cauchy-Green deformation tensor. Compared to the first approach, the use of the Cauchy-Green invariants leads to a mathematically simpler formulation. In this thesis we use this classical approach that allows for a full flexibility in all input parameters, i.e. the fibre orientation, the activation level and the material parameters can vary throughout the tissue geometry both spatially and in time.

We recall the description of the classical strain energy for a hyperelastic material that will be subsequently modified to represent the mechanical response of a muscle-tendon unit. As mentioned, the (classical strain) energy function is defined in terms of the invariants of the Cauchy-Green deformation tensors (Equation 2.1, Equation 2.2) (e.g. see Spencer 1984; [83]) and has a general form of:

$$ W = W(X, B, a_0) = W(I_1, I_2, I_3, I_4, I_5) $$

(2.12)

where $a_0$ is the direction of fibres in the undeformed state of the material. The invariants
of $B$, $I_1$ to $I_5$, are calculated as:

$$I_1 = tr(B), I_2 = \frac{1}{2} [(tr(B))^2 - tr(B^2)] , I_3 = det(B) = J^2, \quad \text{(2.13a)}$$

$$I_4 = a_0 \cdot B \cdot a_0, I_5 = a_0 \cdot B^2 \cdot a_0. \quad \text{(2.13b)}$$

As a result the elasticity tensor in the spatial description Equation 2.9 can be written in terms of derivatives of the strain-energy function with respect to the invariants, for example (Weiss et al 1996):

$$c = 4 \left\{ \left( W_{11} + 2W_{12}I_1 + W_2 + \frac{W_{22}}{I_1^2} \right) B \otimes B - (W_{12} + W_{22}I_1)(B \otimes B^2 + B \otimes B) + W_{22}(B^2 \otimes B^2) - W_2I_1(W_{14} + W_{24}I_1)I_4(a_0 \otimes a_0 \otimes B + B \otimes a_0 \otimes a_0) + W_5 \phi_5 \frac{\delta^2 I_5}{\delta C^2}
+ (W_{15} + W_{25}I_1) \left( B \otimes [\phi_5 \frac{\delta I_5}{\delta C}] + [\phi_5 \frac{\delta I_5}{\delta C}] \otimes a_0 \otimes a_0 \right) - W_4I_4 \left( a_0 \otimes a_0 \otimes B^2 + B \otimes a_0 \otimes a_0 \right)
- W_{25} \left( B^2 \otimes [\phi_5 \frac{\delta I_5}{\delta C}] + [\phi_5 \frac{\delta I_5}{\delta C}] \otimes B^2 \right) + W_{44}I_4^2 \left( a_0 \otimes a_0 \otimes a_0 \otimes a_0 \right)
+ W_{45}I_4 \left( a_0 \otimes a_0 \otimes [\phi_5 \frac{\delta I_5}{\delta C}] + [\phi_5 \frac{\delta I_5}{\delta C}] \otimes a_0 \otimes a_0 \right) + W_{55} \left( \otimes [\phi_5 \frac{\delta I_5}{\delta C}] + [\phi_5 \frac{\delta I_5}{\delta C}] \right) \right\} \quad \text{(2.14)}$$

where $[\phi_5 \frac{\delta I_5}{\delta C}] := I_4(a_0 \otimes B \cdot a_0 + a_0 \cdot B \otimes a_0)$ and $W_{ij} = \frac{\partial^2 W}{\partial I_i \partial I_j}$. To account for incompressibility, an additional Lagrange multiplier term ($pl$) could be added to the elasticity tensor.

We work with a modification of this classical strain energy function that is based on the decomposable into volumetric and isochoric parts Equation 2.8. Following (see Holzapfel 2000; [89]), we can write

$$W_{vol}(J) := \frac{\kappa}{4} (J^2 - 1 - 2 \log(J)), \quad \text{(2.15)}$$

and from the above definition of the invariants $J = \sqrt[3]{3}$. Using these invariants we can also describe the along-fibre isochoric strain energy ($W_{tissue}$) and the base material isochoric energy ($W_{base}$):

$$W_{iso} = W_{tissue} + W_{base}. \quad \text{(2.16)}$$

The contribution of the base material to the strain energy, $W_{base}$, encapsulates the elastic properties of the connective tissue within muscle, tendon and the aponeurosis (i.e. the extracellular connective tissue in the muscle belly). Many different models of $W_{base}$ can be considered for modelling a soft tissue. These range in complexity from assuming the tissue is simply a Neo-Hookean material model to more sophisticated,
physically-measurable model based on physical invariants, Criscione et al. (2001; [85]). In this thesis, such contributions are mathematically modelled by fitting material models based on only the first invariant ($I_1$) of the Cauchy-Green tensor to experimental data. The details of how we model the base muscle, tendon and aponeurosis tissues in this thesis will be discussed in section 2.4.

The isochoric strain energy contributions $W_{\text{tissue}}$ arise from the stretching of fibres along their length. If we denote the Cauchy stress in the fibre caused by a stretch of $\lambda$ as $\sigma_{\text{tissue}}(\lambda)$, then the isochoric strain energy for the tissues modelled in this work becomes

$$\lambda \frac{\partial W_{\text{tissue}}(\lambda)}{\partial \lambda} = \sigma_{\text{tissue}}(\lambda).$$

(2.17)

The along-fibre stretch $\lambda$ for any of the four tissues and is described by ([83]):

$$\lambda = \sqrt{I_4}$$

(2.18)

where $I_4$ is the fourth invariant of the isochoric part of the left Cauchy tensor.

Soft tissues are distinguished by the specific form of their Cauchy stress-stretch functions, $\sigma_{\text{tissue}}(\lambda)$ used in (equation 2.17). For this thesis, we constructed stress-stretch relationships from experimental data (see section 2.4), using the curve-fitting functions in MATLAB (2014; [90]).

Any material in this thesis will be described in terms of two components for the isochoric part $W_{\text{iso}}$ of the strain-energy functions (equation 2.16). The first component, $W_{\text{tissue}}$ describes how fibres affect the mechanical response of the tissue along their length. The second, $W_{\text{base}}$ represents the base isotropic properties. In most of the following sections, modelling decisions had to be made to balance the accuracy of the model, and its simplicity. Often, the experimental data could be fitted by curves with different characteristics; we describe how we pick a fitted curve among available options. These choices were made based on many factors including: the data source, goodness of fit, the shape of the fitted curve, values and slopes at the extreme stretches, and computational cost. The source data was important in terms of whether the data were from animal or human experiments and which muscle, tendon and aponeurosis material properties were measured.
2.4 Choice of materials, constants estimation, strain energies

In what follows, we describe the development of mathematical models for the strain energy in tendon, aponeurosis and muscle tissue. We present our modelling ideas within the context of the human triceps-surae, and take care to discuss how the availability of specific experimental data affects various modelling choices. In principle, a similar methodology can be used with other muscles, leading to other constitutive laws.

2.5 Tendon

There are numerous studies (e.g. [91], [92], [93], [94],[52] and [51]) on the measurement of tendon material properties along their line of action (a good assumption for along-fibre tensile response). Many of these studies have been done in vitro (e.g. [91] and [51]) and some have measured these mechanical properties in vivo (e.g. [95] and [54]).

Since the focus in this thesis was on the muscles from human triceps-surae, the measured data from human triceps-surae tendon (Achilles) were of higher interest. Among the studies which were found in the literature, only Magnusson et al. [54] has data on both the Achilles tendon and triceps-surae aponeurosis, which made it a more complete set of information for our modelling goals. In this thesis, therefore, the modelling of the material properties of both the tendon and aponeurosis tissues was based on the results of Magnusson et al. [54].

2.5.1 Tendon: Along-fibre properties

The along-fibre stress-stretch curve of human free Achilles tendon is shown in Figure 2.1. The curve is calculated from the force-stretch curve and cross sectional area data from Magnusson et al [54].

In most of the studies on longitudinal tensile response of tendons, whether modelling (e.g. [59] and [88]) or experimental (e.g. [92] and [91]), the stress-stretch curve is divided into a non-linear toe region and a linear region. The tendon material properties defined for this work also had a toe region which was represented using a power function and a linear section continuously extending the toe region. However, the toe region is extended
to higher stretch values compared to experimental data. This choice was solely made to use a single well-fitted function for the most of the range of action of the tendon. The fitting of functions was done in the MATLAB Curve Fitting Toolbox. It is possible to fit many kinds of functions- polynomial, exponential, and others - and we use fitted curves based on a higher coefficient of determination (R-Squared) value of the fit, as well as the simplicity of the final expression. These functions are described below,

$$\sigma_{tendon}(\lambda) = \begin{cases} 0.3504 \times 10^6 (\lambda^{68.8} - 1) & 1 \leq \lambda \leq 1.07, \\ 0.3504 \times 10^6 (68.8 \times 1.07^{768.8} (\lambda - 1.07) + (1.07^{68.8} - 1)) & 1.07 < \lambda. \end{cases} \quad (2.19)$$

Here, as before, $\sigma$ is the Cauchy stress and $\lambda$ is the along-fibre stretch. Using equation 2.17 the strain energy function for along-fibre tensile properties of tendon is represented by,

$$\lambda \frac{\partial W_{tendon}}{\partial \lambda} = \sigma_{tendon}(\lambda). \quad (2.20)$$
2.5.2 Tendon: Base isotropic properties

Since soft tissues were modelled as transversely isotropic materials, the transverse uniaxial tensile properties were assumed to be represented by the uniaxial tensile properties (i.e. modulus of elasticity) of the base isotropic part of the tissue. In tendon and tendon-like materials (mostly ligaments) the longitudinal stiffness (and/or modulus of elasticity) of the tissue has been reported [92] to be about two orders of magnitude larger than the transverse stiffness (and/or transverse modulus of elasticity). As a result, in this thesis we assume that the uniaxial tensile modulus of base tendon material is approximately one-hundredth of that of along-fibre tensile response.

Among many material models (e.g. Neo-Hookean, or those due to Mooney-Rivlin, Yeoh, or Ogden) we seek the simplest model which is capable of accurately and comprehensively representing the behaviour of the material. It is worth mentioning that Neo-hookean material model is mechanistic model and is based on the real physical properties of a material but the models such as those presented by Yoeh, Moony-Rivlin, Humphery are phenomenological. As a result of the two orders of magnitude (one hundred times) difference between along- and cross-fibre stiffness, the cross fibre mechanical properties play a very minor role in the mechanical response of the whole tendon. In this case, we tested two of the simplest material models – the Neo-Hookean [96] and a model due to Yeoh [97] – to fit the base material properties. In these two material models, only the first invariant $I_1$ of Cauchy-Green deformation tensor is used. Also, the strain energy is a first or third order polynomial. These models can significantly reduce the overall computation time. The general form of strain energy function for these two basic models are,

$$W_{\text{Neo-Hookean}} = c_1(I_1 - 3)$$  \hspace{1cm} (2.21a)

and

$$W_{\text{Yeoh}} = \sum_{i=1}^{3} c_i(I_1 - 3)^i$$  \hspace{1cm} (2.21b)

Here, $c_i$s are material constants. In order to find the parameters $c_i$ in any of the two models Equation 2.21a or Equation 2.21b, we need to solve a simple extension problem as follows (methodology is adopted from Martins et al. 2006 [98]).

Recall the deformation gradient $F$ of an incompressible rectangular cube elongated along the first axis of a Cartesian coordinate system under uniaxial stretch ($\lambda$) is shown by:
\[ F = \begin{bmatrix} \lambda & 0 & 0 \\ 0 & \frac{1}{\sqrt{\lambda}} & 0 \\ 0 & 0 & \frac{1}{\sqrt{\lambda}} \end{bmatrix} \]  

(2.22)

where the stretches in the direction of the other two axes of the coordinate system are \( \lambda_2 = \lambda_3 = \frac{1}{\sqrt{\lambda}} \). These are derived based on considerations of symmetry and the incompressibility of the continuum with \( J = det F = 1 \). Then the right Cauchy-Green tensor \((C)\) is calculated as,

\[ C = \begin{bmatrix} \lambda^2 & 0 & 0 \\ 0 & \lambda^{-1} & 0 \\ 0 & 0 & \lambda^{-1} \end{bmatrix} \]  

(2.23)

The next step is to calculate the invariants of \( C \) (similar to Equation 2.13) under the further assumption of isotropy:

\[
  I_1 = tr \ C = \lambda^2 + \frac{2}{\lambda}, \quad I_2 = \frac{1}{2}((tr(C))^2 - tr(C^2)) = 2\lambda + \frac{1}{\lambda^2}, \\
  I_3 = det \ C = 1
\]  

(2.24a, 2.24b)

To calculate the stress-stretch function for any material model under such a loading and boundary condition (no second and third principal stresses, \( \sigma_2 = \sigma_3 = 0 \)), we start with the general form for principal Cauchy stresses,

\[
  \sigma_i = J^{-1} \lambda_i \frac{\partial W}{\partial \lambda_i}, \quad i = 1, 2, 3.
\]  

(2.25)

Applying boundary conditions to equation 2.25, the first principal stresses will look like:

\[
  \sigma_1 = \lambda_1 \frac{\partial W}{\partial \lambda_1} - \lambda_2 \frac{\partial W}{\partial \lambda_2} \quad \text{or} \quad \sigma_1 = \lambda_1 \frac{\partial W}{\partial \lambda_1} - \lambda_3 \frac{\partial W}{\partial \lambda_3}.
\]  

(2.26)

Holzapfel [89] describes the Cauchy stress during uniaxial stretch \((\sigma_1)\) in such a material in terms of the invariants of \( C \) as:

\[
  \sigma_1 = 2(\lambda^2 - \frac{1}{\lambda})(\frac{\partial W}{\partial I_1} + \frac{1}{\lambda} \frac{\partial W}{\partial I_2})
\]  

(2.27)

Using equations 2.21a and 2.21b, we obtain that the stress-stretch functions for the two discussed material models are:

\[
  \sigma_{Neo-Hookean} = 2c_1(\lambda^2 - \frac{1}{\lambda})
\]  

(2.28)
and

\[ \sigma_{Yeoh} = 2(\lambda^2 - \frac{1}{\lambda})(c_1 + 2c_2(I_1 - 3) + 3c_3(I_1 - 3)^2) = 2(\lambda^2 - \frac{1}{\lambda})(c_1 + 2c_2(\frac{2}{\lambda} - 3) + 3c_3(\frac{2}{\lambda} - 3)^2). \]  

(2.29)

Assuming that uniaxial modulus of base materials are approximately one-hundredth of its along-fibre modulus (slope of the curve in Figure 2.1) and using equations 2.28 and 2.29, material constants for the Neo-Hookean and Yeoh’s models were estimated. This was done using the MATLAB Curve Fitting Toolbox. The results are shown in the Table 2.1,

<table>
<thead>
<tr>
<th>Constants (Pa)</th>
<th>Neo-Hookean</th>
<th>Yeoh</th>
</tr>
</thead>
<tbody>
<tr>
<td>( c_1 )</td>
<td>0.5256 \times 10^6</td>
<td>0.2083 \times 10^6</td>
</tr>
<tr>
<td>( c_2 )</td>
<td>-</td>
<td>-4.63 \times 10^6</td>
</tr>
<tr>
<td>( c_3 )</td>
<td>-</td>
<td>1367 \times 10^6</td>
</tr>
<tr>
<td>R-squared</td>
<td>0.667</td>
<td>0.9955</td>
</tr>
</tbody>
</table>

Table 2.1: Material constants and R-square values of fit for Neo-Hookean and Yeoh models of tendon base material

Despite a higher R-squared value for the Yeoh’s model, since the ratio of base to along-fibre tensile response (i.e. were very small, any choice of the material models Equation 2.21a and Equation 2.21b for the base material would be acceptable. A Neo-Hookean model was selected for the simplicity of the overall MTU model. A bulk modulus value of \( \kappa = 1 \times 10^8 \) Pa was chosen for the tendon tissue to reflect the incompressible nature of the tendon and minimize the change in its volume. Eventually, the tendon base material properties can be written as:

\[ W_{base,tendon} := c_1(I_1 - 3) - 1, \ c_1 = 52.56 \times 10^4 \text{ Pa}. \]  

(2.30)

2.6 Aponeurosis

2.6.1 Aponeurosis: Along-fibre properties

The challenge with developing mathematical models of aponeurosis and similarly thin tissues (epimysium) is that it is not easy to experimentally determine the stress developed in them during loading. This is mainly because the cross-sectional area (CSA) changes along its length. Therefore, there are very few experimental studies of aponeurosis (e.g.
that have reported stress-stretch properties. We estimated the stress-stretch curve for aponeurosis by assuming an estimated average CSA for aponeurosis. This way, the ratio of the tendon force and the estimated aponeurosis CSA will provide us with along-fibre stress. This is consistent with assumptions made by other modelling groups.

Along with estimating the aponeurosis area by a single CSA, based on the few experimental studies of aponeurosis mechanical properties available, many modelling groups (e.g. [59], [70]) have opted to select the same material properties for both tendon and aponeurosis. This assumption, although a simple way of representing muscle-tendon unit (MTU) structure, ignores the effects of different fibres in these tissues. Specifically, collagen fibre directions and the base material stiffness may be different between the aponeurosis and tendon in the same muscle. In order to shed light on the effects of architectural and structural details in studying muscle mechanics, one has to build the structures as carefully as possible; and if possible, not to compromise the accuracy. In this thesis, we include aponeurosis material properties independently.

As explained in previously, the focus in this thesis will be on the human triceps-surae muscle group. Therefore, data on any of the human triceps-surae muscles (gastrocnemius or soleus) aponeurosis is preferred. Magnusson et al [54] reports data on both free Achilles tendon and triceps-surae aponeurosis. The only problem as described above is that aponeurosis data is in force-stretch form. In this thesis, the average CSA for aponeurosis was estimated as half of the free tendon CSA and equal to 36.5 mm$^2$. We assumed that tendon CSA linearly decreases to almost zero as the aponeurosis extends from the muscle-tendon junction towards the centre of the muscle belly. This along-fibre stress-stretch function is formulated (equation 2.31) as a piecewise function similar to the tendon.

It is worth repeating that the reported along-fibre stretch modulus are the sum of fibre and base material contributions. Since there are limited studies that present the difference between these contributions, we have chosen to follow the only study of the longitudinal and transverse tensile response of aponeurosis by Azizi et al. [99] to give us the guidelines. In their study, the gastrocnemius aponeurosis of bipedal wild turkeys was investigated. This is a similar structure as intended to be studied in this thesis. Based on their result the along-fibre stiffness (or modulus of elasticity) was seven times larger than cross fibre stiffness (or modulus of elasticity). This means that the fibres in aponeurosis provide six-seventh of
the contribution to the along-fibre tensile response of the tissue and the rest is due to base material mechanical properties. Note that in theory, a similar calculations should have been done for the tendon but the ratio of the mechanical properties (i.e. moduli) was about one hundred to ninety nine, and this is close to unity. In this case, the accuracy of proposed base material properties for the tendon tissue would not be affected much by choosing a simpler material model and the slight difference was ignored. This difference cannot be ignored for the aponeurosis tissue. The stress-stretch equation in this section and the tensile response of the base material in the following section have been based on the contribution ratio from the Azizi et al. [99] study, and the actual human gastrocnemius aponeurosis tensile response from Magnusson et al. [54].

$$\sigma_{apo}(\lambda) = \begin{cases} 
3.053 \times 10^6(\lambda^{124.6} - 1) & 1 \leq \lambda \leq 1.025 \\
3.053 \times 10^6(124.6 \times 1.025^{123.6}(\lambda - 1.025) + (1.025^{124.6} - 1)) & 1.025 < \lambda
\end{cases}$$

(2.31)

Here, as before, $\sigma$ is the Cauchy stress and $\lambda$ is along-fibre stretch. Using equation 2.17 the strain energy function for along-fibre tensile response of aponeurosis is represented by:

$$\lambda \frac{\partial W_{apo}}{\partial \lambda} = \sigma_{apo}(\lambda)$$

(2.32)

### 2.6.2 Base isotropic properties

We used the same technique as the previous section to retrieve material constants for the base isotropic aponeurosis material. As mentioned in the previous section, we will assume that the cross-fibre contribution for the tensile response is about one-seventh of the total the along-fibre tensile response of the aponeurosis. The material constants of base aponeurosis for various but simple models can be seen in Table 2.2. We additionally looked at two extra strain energy functions for more nonlinear Mooney-Rivlin [96] and Humphrey [100] material models since the base material properties play a larger role in aponeurosis mechanical behaviour when compared to tendon,

$$W_{Mooney-Rivlin} = c_1(I_1 - 3) + c_2(I_2 - 3),$$

(2.33)

and

$$W_{Humphrey} = c_1(e^{c_2(I_1 - 3)} - 1).$$

(2.34)
Figure 2.2: along-fibre stress-stretch curve for aponeurosis tissue based on the Magnusson et al. 2003 [54] (see equation 2.31).

The uniaxial tension stress for incompressible Mooney-Rivlin and Humphrey models are then,

\[ \sigma_{\text{Mooney-Rivlin}} = 2(\lambda^2 - \frac{1}{\lambda})(c_1 + \frac{c_2}{\lambda}) \]  

(2.35)

and

\[ \sigma_{\text{Humphrey}} = 2(\lambda^2 - \frac{1}{\lambda})c_1c_2e^{c_2(I_1-3)} \]  

(2.36)

<table>
<thead>
<tr>
<th>Constants (Pa)</th>
<th>Neo-Hookean</th>
<th>Yeoh</th>
<th>Mooney-Rivlin</th>
<th>Humphery</th>
</tr>
</thead>
<tbody>
<tr>
<td>( c_1 )</td>
<td>( 58.89 \times 10^6 )</td>
<td>( 54.47 \times 10^6 )</td>
<td>( 3337 \times 10^6 )</td>
<td>( 43510 )</td>
</tr>
<tr>
<td>( c_2 )</td>
<td>-</td>
<td>( 1732 \times 10^6 )</td>
<td>( -3348 \times 10^6 )</td>
<td>( 579.6 )</td>
</tr>
<tr>
<td>( c_3 )</td>
<td>-</td>
<td>( 13820 \times 10^6 )</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>R-squared</td>
<td>0.827</td>
<td>0.8646</td>
<td>0.9886</td>
<td>0.9985</td>
</tr>
</tbody>
</table>

Table 2.2: Material constants and R-square values of fit for four material models of aponeurosis base material

Here the accuracy of estimates (goodness of fit) is very important since the difference between longitudinal and transverse tensile response of the aponeurosis is smaller. Only Mooney-Rivlin and Humphrey models seem to be highly accurate (based on R-squared
value of the fit). The Humphrey model has the advantage of a slightly better R-square
and only using the first invariant of Cauchy-Green tensor to reduce computational cost.
This model was implemented for the strain energy of aponeurosis base material. The bulk
modulus value of $\kappa = 1 \times 10^8$ was also chosen for this material to keep the the tissue
nearly incompressible under convergence criteria. Finally, the strain energy function for
the aponeurosis base material looks like:

$$W_{\text{base,apo}} := c_1(e^{c_2(I_1-3)} - 1), \quad c_1 = 4.351 \times 10^4 \text{ Pa}, \quad c_2 = 5.796 \times 10^2 \text{ Pa}. \quad (2.37)$$

### 2.6.3 Different stiffness levels for aponeurosis

Chapters 3 to 5 presents simulations for muscles with different aponeurosis stiffness
properties. The three levels of stiffness used in this thesis were named as compliant, normal and stiff aponeurosis tensile properties and would develop maximum strains of 10, 5 and 2% when the muscle was developing maximum isometric force. The compliant
aponeurosis tensile properties were those of the Achilles tendon as described before (equation 2.19 and Table 2.1). For normal aponeurosis, the material properties described
in this section (equation 2.31 and Table 2.2) were used in the simulations. For the stiff
aponeurosis, the base and along-fibre material properties of the normal aponeurosis was
scaled so that the 2% strain level at maximum isometric force of the muscle is reached.
The following describe the along-fibre stress-stretch curve and base material strain
energy for stiff aponeurosis used throughout this thesis:

$$\sigma_{\text{sapo}}(\lambda) = \begin{cases} 
2.442 \times 10^{7}(\lambda^{124.6} - 1) & 1 \leq \lambda \leq 1.01, \\
2.442 \times 10^{7}(124.6 \times 1.01^{123.6}(\lambda - 1.01) + (1.01^{124.6} - 1)) & 1.01 < \lambda.
\end{cases} \quad (2.38)$$

$$W_{\text{base,apo}} := c_1(e^{c_2(I_1-3)} - 1), \quad c_1 = 3.481 \times 10^5 \text{ Pa}, \quad c_2 = 4.637 \times 10^3 \text{ Pa}. \quad (2.39)$$

### 2.7 Muscle

Unlike tendon and aponeurosis, muscle tissue can be loaded actively as well as in
passive condition. Therefore separate sections are devoted to passive and active
properties of the muscle tissue as follows. Based on this, muscle mechanical properties are decomposed into passive and active components. While active properties are modelled here as along-fibre tensile properties only, passive properties of skeletal muscles were divided into the along-fibre and base material properties similar to other passive tissues. The base materials are considered to hold the fibres in active or passive conditions; therefore, there is no need to remodel them when discussing active properties of the muscle tissue. Passive along-fibre stress-stretch function ($\sigma_{\text{Passive}}(\lambda)$) was added to active along-fibre tensile properties ($\sigma_{\text{Active}}(\lambda)$) to form the along-fibre material properties of the muscle tissue. Here the active and passive along-fibre stresses were normalized by the maximum isometric stress $\sigma_0 = 200$ KPa at the optimal length of the fibre and given a "∧" superscript:

$$\sigma_{\text{Muscle}}(\lambda) = \sigma_0(\hat{\sigma}_{\text{Active}}(\lambda) + \hat{\sigma}_{\text{Passive}}(\lambda)),$$  \hspace{1cm} (2.40)

and the along-fibre strain energy for the muscle tissue will look like:

$$\lambda \frac{\partial W_{\text{Muscle}}}{\partial \lambda} = \sigma_{\text{Muscle}}(\lambda).$$ \hspace{1cm} (2.41)

### 2.7.1 Muscle: Passive properties

Among the experimental studies on skeletal muscle material properties, there are few (e.g.[86], [101] and [87]) which report both longitudinal (along-fibre) and transverse (cross fibre) measurements. The results are occasionally contradictory. Morrow et al. [86] in 2010 measured longitudinal and transverse tensile as well as longitudinal shear properties of rabbit extensor digitorum longus muscle and reported that longitudinal module of elasticity is twenty time higher then transverse module. Takaza et al. [87] in 2013 measured the longitudinal and transverse elastic modulus of pig longissimus dorsi muscle. Although their result were very similar but there was a significant difference in the ratio of longitudinal to transverse modulus in their work compared to Morrow et al. [86]. Their results show that transverse modulus is slightly larger than longitudinal modulus of the tissue. Structurally, the passive properties can be thought of a combination of titin filaments, intracellular and extracellular connective tissue passive properties. A review by Gillies and Lieber [102] in 2011 narrated the ratio between bundle of fibre (fibre plus extracellular) modulus to fibre modulus from many experimental studies. This ratio was
between 1.6-2.7 for most of the human muscles studied. These results [102] stand somewhere between the two reported group of results mentioned before [86, 87] and adds to the confusion. In modelling studies there has been a tendency to have large ratios of longitudinal to transverse modulus. For example, in the Blemker et al. [59], the muscle tissue longitudinal modulus is approximately two orders of magnitude higher than the transverse modulus. We considered that along-fibre tensile response [i.e. modulus ($E$)] of the muscle tissue are a combination of fibre and base isotropic materials. Also, the mechanical properties of the base material is what we consider the transverse tensile properties of a transversely isotropic material. Therefore, the ratio of longitudinal to transverse tensile properties (i.e. $\frac{E_L}{E_T}$) represent the ratio between fibre tensile properties plus base material tensile properties to base material tensile properties (i.e. $\frac{E_{fibre}+E_{base}}{E_{base}}$).

Based on the uncertainty of the ratio of the longitudinal to transverse modulus, this thesis tested different ratios to find an appropriate representation for both passive along-fibre and base passive muscle materials. The passive properties of skeletal muscle tissue were adopted from the classic Zajac 1989 [53] study.

1. **Longitudinal to transverse modulus ratio $\sim 100$**

   It was assumed that 99% of stresses in the passive curve presented by Zajac [53] are results of the fibres and only 1% is due to base material. However the curve for along-fibre tensile response was fitted to original data rather than 99% of data. It was assumed the difference in the model output would be insignificant based on this difference. The passive stress-stretch properties when present $\lambda > 1$ can be shown by an exponential function. This function can be shown as:

   $$\hat{\sigma}_{\text{Passive}}(\lambda) = \begin{cases} 0 & \lambda \leq 1.0 \\ (42.76 \times 10^{-5})e^{5.339\lambda} - 8825 \times 10^{-5} & 1.0 < \lambda \end{cases}$$

   (2.42)

   For transverse tensile properties again the effort was mostly dedicated to fit a simple and computationally cost efficient model to one-hundredth of along-fibre stress-stretch properties. Therefore, similar to the tendon base material property (section 2.5.2), we only fitted the base muscle tissue to Neo-Hookean and Yeoh’s models. The summary of different material constants for the passive base material for this modulus ratio is shown in Table 2.3. Because of the high ratio of longitudinal to transverse modulus in this part, only the constants for simplest models are
presented.

<table>
<thead>
<tr>
<th>Constants</th>
<th>Neo-Hookean</th>
<th>Yeoh</th>
</tr>
</thead>
<tbody>
<tr>
<td>$c_1$</td>
<td>$292.4 \times 10^{-5}$</td>
<td>$67.5 \times 10^{-8}$</td>
</tr>
<tr>
<td>$c_2$</td>
<td>-</td>
<td>$278.05 \times 10^{-5}$</td>
</tr>
<tr>
<td>$c_3$</td>
<td>-</td>
<td>$-19.765 \times 10^{-5}$</td>
</tr>
</tbody>
</table>

R-squared | 0.864 | 0.9985 |

Table 2.3: Material constants and R-square values of fit for for Neo-Hookean and Yeoh models of passive skeletal base material with modulus ratio of $\sim 100$.

Eventually, despite the higher R-squared values for Yeoh’s model fit, there is not much difference in total response between the two models when compared to longitudinal tensile response. If a longitudinal to transverse modulus ratio of $\sim 100$ is to be used for modelling the muscle tissue, than it would be recommended that the Neo-Hookean representation is used, due to its mathematical simplicity. Note that the base passive materiel for stretches less than 1.0 is set to zero. The respective $\kappa = 1 \times 10^6$ was chosen for this case. The model converges well in small and medium range strains (up to 40%) but it is incapable of converging at extreme (up to 65%) strains. All these cases have to be revisited when the active response is simulated.

2. **Longitudinal to transverse modulus ratio $\sim 10$**

In this case, 90% of the longitudinal tensile properties are due to fibres passive response and the other 10% due to base materials. The function for along-fibre stress-stretch was fitted as below.

$$\hat{\sigma}_{\text{Passive}}(\lambda) = \begin{cases} 
0 & \lambda \leq 1.0 \\
(38.495 \times 10^{-5})e^{5.339\lambda} - 7945 \times 10^{-5} & 1.0 < \lambda 
\end{cases}$$ (2.43)

Since transverse tensile properties are now a considerable amount of 10% compared to whole passive properties of the tissue, material constants for four models were calculated for comparison. The results are in Table 2.4.

Between the four options the Yeoh’s model has a slightly better R-squared value and is a polynomial with only the first invariant as a parameter. This makes Yeoh’s model simpler compared against Mooney-Rivlin with two invariants and exponential nature of Humphrey’s model. Therefore Yeoh constants along with a $\kappa = 1 \times 10^6$ was used for this case. The model converged up to 65% in strain values.
### Table 2.4: Material constants and R-square values of fit for four material models of passive skeletal base material with modulus ratio of $\sim 10$.

<table>
<thead>
<tr>
<th>Constants</th>
<th>Neo-Hookean</th>
<th>Yeoh</th>
<th>Mooney-Rivlin</th>
<th>Humphery</th>
</tr>
</thead>
<tbody>
<tr>
<td>$c_1$</td>
<td>0.02924</td>
<td>$675 \times 10^{-5}$</td>
<td>0.13255</td>
<td>$634 \times 10^{-5}$</td>
</tr>
<tr>
<td>$c_2$</td>
<td>-</td>
<td>0.0278</td>
<td>-0.14525</td>
<td>1.943</td>
</tr>
<tr>
<td>$c_3$</td>
<td>-</td>
<td>$-197.45 \times 10^{-5}$</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>R-squared</td>
<td>0.864</td>
<td>0.9985</td>
<td>0.9928</td>
<td>0.9959</td>
</tr>
</tbody>
</table>

3. **Longitudinal to transverse modulus ratio $\sim 1$**

In the third case an equal portion of passive tensile properties was assumed to represent the along-fibre and base responses. The stress-stretch function for along-fibre in this case is:

$$
\hat{\sigma}_{\text{Passive}}(\lambda) = \begin{cases} 
0 & \lambda \leq 1.0 \\
(21.39 \times 10^{-5})e^{5.339\lambda} - 4413 \times 10^{-5} & 1.0 < \lambda 
\end{cases}
$$

(2.44)

Similar to other cases the material constants for base materials can be seen in Table 2.5.

<table>
<thead>
<tr>
<th>Constants</th>
<th>Neo-Hookean</th>
<th>Yeoh</th>
<th>Mooney-Rivlin</th>
<th>Humphery</th>
</tr>
</thead>
<tbody>
<tr>
<td>$c_1$</td>
<td>0.1462</td>
<td>$3375.5 \times 10^{-5}$</td>
<td>0.6625</td>
<td>$3171.5 \times 10^{-5}$</td>
</tr>
<tr>
<td>$c_2$</td>
<td>-</td>
<td>0.139</td>
<td>-0.726</td>
<td>1.943</td>
</tr>
<tr>
<td>$c_3$</td>
<td>-</td>
<td>$-0.9875 \times 10^{-2}$</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>R-squared</td>
<td>0.864</td>
<td>0.9985</td>
<td>0.9928</td>
<td>0.9959</td>
</tr>
</tbody>
</table>

Table 2.5: Material constants and R-square values of fit for four material models of passive skeletal base material with modulus ratio of $\sim 1$.

Here again, Yeoh’s model was selected because it is one of the simplest and at the same time a very well fitted model. The value of $\kappa$ in this case was also selected to be $1 \times 10^6$ for convergence up to 65% strain. There might be room to change the ratio of longitudinal to transverse modulus to less than 1.0. However, the stiffer the base material properties the lower the amount of the muscle bulge and fibre force transfer to aponeurosis and tendon.

#### 2.7.2 Selection of an appropriate ratio

As mentioned before, the muscle tissue is modelled as a transversely isotropic material. The assumption of transverse isotropy means the base materials are...
Figure 2.3: Plots of stress vs the first invariant of the Cauchy-Green tensor. Comparison of fitted Yeoh's models (dashed black) for longitudinal to transverse ratio of $\sim 1$ (A), $\sim 10$ (B) and $\sim 100$ (C) with fitted Yeoh's models to experimental data on compressive response of the muscle tissue (gray). Gray curves represent the Yeoh's models for the data from Bosboom et al. (dotted gray; [103]), Zheng et al. (dashed gray; [104]), Van Loocke et al. (solid gray; [105]) and Grieve and Armstrong (dash-dotted gray; [106]).
isotropic and have to show similar responses in both in compression and extension. In contrast, the fibres will show little to no resistance under compression, while in extension, the majority of the whole tissue’s response is due to the mechanical response of the fibres. As a result, the experimental data on the compression tests on muscle tissue can be used to estimate the transverse (base) material properties of the muscle tissue. On this basis, we compared the fitted Yeoh’s models for the three longitudinal to transverse modulus ratios of 1, 10 and 100 (as described above), to Yeoh’s models that we fitted to experimental data collected from muscle tissue under compression (Figure 2.3; [103, 105, 106, 104]) to find the better ratio out of the three ratios of longitudinal to transverse tensile response. Yeoh’s model was chosen for the comparison since it had a good fit for all the three ratios. In other words, we have assumed that the compressive response of the muscle tissue is a good estimate of passive base material in the muscle tissue. Yeoh’s model for the longitudinal to transverse ratio of 10, showed closer similarity to many of the previously measured experimental data [105, 106, 104] than the 100 and 1 ratios when plotted for $I_1$ values between 3 and 4 that represent a range of 0.54 to 1.68 for along-fibre stretch. In one case, the data from Bosboom et al. [103] on rat tibialis stood out by showing higher stiffness in compression than most of the other studies. (Figure 2.3)

For this thesis, we chose the material properties reflecting a ratio of 10 for the longitudinal to transverse tensile properties as the passive base material properties for the skeletal muscle tissue. This was mainly because most of the experimental data were similar to this selection. Based on this, the base material strain energy function we used in this thesis can be presented as:

$$W_{\text{base,muscle}} := \sum_{i=1}^{3} c_i (I_1 - 3)^i, \quad c_1 = 6.75 \times 10^{-3} \text{ Pa}, \quad c_2 = 2.78 \times 10^{-2} \text{ Pa}, \quad c_3 = -1.9745 \times 10^{-3} \text{ Pa}.\quad (2.45)$$

It should be remembered that this strain-energy is normalized (in a similar way to equation 2.40) and will be adjusted by multiplying $\sigma_0$ when combined with the other normalized components of the muscle tissue strain energy function. Also equation 2.43 represents the functional form of passive along-fibre stress-stretch curve (Figure 2.4).
2.7.3 Muscle fibre: Active properties

Muscle tissue differs from other soft tissues in that it can produce elevated forces when activated. The production of this force in skeletal muscles is initiated when myo-filaments (actin and myosin) attach by forming cross-bridges. The developed force is transferred via intracellular and extracellular connective tissues to whole fibres, bundles of fibres and finally to the aponeurosis and tendon of a muscle. Eventually, the tendon pulls on the skeleton and possibly moves the limbs. The total force is dependent on the extent of myo-filaments overlapping at the onset of activation (force-length property), how fast they can slide past each other (force-velocity property) and finally how many cross-bridges are attached based on calcium concentration inside the cell (activation level). These properties of skeletal muscle fibres has frequently been measured and reported in literature and are the three parameters needed for developing a Hill-type [20] model. The normalized stress-stretch function for active along-fibre mechanical properties of skeletal muscle as describe
in equation 2.40 is defined as:

\[
\dot{\sigma}_{Active} = \alpha(T)\dot{\sigma}_\lambda\dot{\sigma}_\lambda
\]

(2.46)

where \(\alpha(t)\) is the activation function in time and has a value between 0 and 1, \(\dot{\sigma}_\lambda\) in the normalized isometric stress-stretch function and \(\dot{\sigma}_\lambda\) is the the normalized stress-stretch rate function.

If different activation levels in different regions of the muscle were needed, we modified equation 2.46 to make the dependence on location explicit:

\[
\dot{\sigma}_{Active} = \alpha(X,T)\dot{\sigma}_\lambda\dot{\sigma}_\lambda
\]

(2.47)

The three functions describing along-fibre active stress-stretch are defined in the next few sections.

2.7.4 Muscle fibre: Activation function

In this thesis we used a ramp function for activation. Therefore the only parameters for the activation function are the onset of activation, activation slope, maximum level of activity \(\alpha_{max}\) and the region of activity. In the simplest instance, we can set \(\alpha(X,t) = 0\) for inactive regions, and linearly increasing over the simulation time from zero to a selected maximum level of activity in the remaining. However, this may result in abrupt transitions in activity within the muscle, which may not be physiologically accurate. Instead, we used combinations of \(\text{arctan}(X)\) functions to vary activity smoothly between regions which were active and those which were not.

2.7.5 Muscle fibres: Normalized isometric stress-stretch

The normalized isometric stress-stretch in active muscle fibres is commonly known as the force-length property. It is usually described in terms of the tetanic isometric force of a fibre measured in different fixed lengths (stretches) after the passive force has been subtracted. The active force-length property of a muscle fibre is usually described with either a single quadratic [19] or a piecewise quadratic [59] function. The quadratic nature of many of the proposed functions for this property is in contrast to its asymmetric nature or predicts unusual amount of strain for the eccentric (descending limb) section of the
curve. Here, the stress-stretch relation has been approximated (from Gordon et al. [18] 1966 data) fitting a continuous function based on the five first terms of a Fourier series (Figure 2.5). The functional representation of the normalized active stress-stretch property of fibres muscle for $0.55 \leq \lambda \leq 1.75$ is:

$$
\sigma_\lambda = 0.534 + 0.229 \cos(\omega \lambda) - 0.095 \cos(2\omega \lambda) + 0.024 \cos(3\omega \lambda)
- 0.021 \cos(4\omega \lambda) + 0.013 \cos(5\omega \lambda) - 0.421 \sin(\omega \lambda) + 0.079 \sin(2\omega \lambda)
- 0.029 \sin(3\omega \lambda) + 0.013 \sin(4\omega \lambda) + 0.002 \sin(5\omega \lambda)
$$

(2.48)

with $\omega = 4.957$. The value of this function the of stretch values $\lambda \leq 0.55$ and $1.75 \leq \lambda$ was set to be zero.

- **Normalized stress-stretch rate**

A piecewise hyperbolic function was used to describe the normalized stress-stretch property of muscle fibres. Since $\lambda = \epsilon + 1$, strain rate ($\dot{\epsilon}$) is equal to stretch rate ($\dot{\lambda}$). In this thesis normalized stress-strain rate relations were adopted from Wakeling et al. (2012;
where \( \dot{\epsilon} \) is the strain rate, \( \dot{\epsilon}_0 \) is the maximum intrinsic speed and \( m \) is a parameter that defines the curvature based on fibre type. Table 2.6 shows the values for \( \dot{\epsilon}_0 \) and \( m \) for fast and slow fibres of human muscle.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>( m_{\text{fast}} )</td>
<td>0.29</td>
</tr>
<tr>
<td>( m_{\text{slow}} )</td>
<td>0.18</td>
</tr>
<tr>
<td>( \dot{\epsilon}<em>{0</em>{\text{fast}}} )</td>
<td>10 s(^{-1})</td>
</tr>
<tr>
<td>( \dot{\epsilon}<em>{0</em>{\text{slow}}} )</td>
<td>5 s(^{-1})</td>
</tr>
</tbody>
</table>

Table 2.6: Constants for slow and fast normalized stress-strain rate fibres from [107] (ml/s is muscle lengths per second)

In this thesis we have simulated isometric contraction of a muscle. Therefore \( \dot{\sigma}_\lambda \) was set equal to 1 for all the simulations in this thesis. In future work, we intend to study this contribution of effects to MTU response in more detail.
2.7.6 Adipose tissue (fat)

Fat was assumed to be a nonlinear isotropic material. The neo-Hookean strain energy for fat \(W_{fat}\) was adopted based on modelling work on human breast tissue [108] and is defined as:

\[
W_{fat} = 0.13 \times 10^6 (I_1 - 3) \text{ Pa,} \tag{2.50}
\]

The adipose tissue (fat) had a larger stiffness than the isotropic muscle base material for the lean muscle (equation 2.43).

The incompressibility constant, \(\kappa\), for the volumetric part of the strain energy \(W_{vol}\) (equation 2.15) was chosen to be \(\kappa_{fat} = 0.25 \times 10^6\) for fat. This was based on the fat compressibility properties used in modelling the human heel pad [109]. \(\kappa_{fat}\) had a smaller value than the muscle tissue (\(\kappa_{muscle} = 1.0 \times 10^6\)) indicating that it is more compressible.

In Chapter 5, we will see in detail some models of fatty tissue, and numerical studies based on these. For reasons described later, it is important for our code to be capable of simulating regions with blended tissue-fat material properties. This functionality is built into our code.

2.7.7 History Dependent Properties

The history dependent material properties are usually used to model physiological changes that are dependent on the duration of activation, stimulation rate history and the history of length changes. An example of history dependent material properties of the skeletal muscle is force enhancement after muscle stretch [110]. The effect of these properties in single tetanic contractions of a muscle are considered negligible. In this thesis we have not included such effects, and leave this for future studies.

2.8 Discrete formulation and code.

We recall the three-field elasticity formulation derived in Section 2.2.4
\[ \text{div} (\sigma(\mathbf{T}(\mathbf{u}))) + \mathbf{f}_b = \rho \frac{\partial^2}{\partial t^2} \mathbf{u} \]  \hspace{1cm} (2.51a)  

\[ J(\mathbf{u}) = \tilde{J} \]  \hspace{1cm} (2.51b)  

\[ \tilde{p} = \frac{\delta W_{\text{vol}}(\tilde{J})}{\delta \tilde{J}} \]  \hspace{1cm} (2.51c)  

The first of the three equations is the elasticity or equilibrium equation where \( \rho \) is body mass density and \( t \) in \( \frac{\partial^2}{\partial t^2} \) represents time. In this study the applied body force \( \mathbf{f}_b \equiv 0 \). Also we will solve for quasi-static contractions of the muscle and therefore \( \frac{\partial^2}{\partial t^2} \mathbf{u} \equiv 0 \). Since the partial differential equation is not time-dependent \( (\mathbf{f}_b \equiv 0) \), we didn’t use a time-stepping scheme.

We meshed the MTU using hexahedral elements in 3D. We used a discontinuous Galerkin method for \( \mathbf{u}, \tilde{p} \) and \( \tilde{J} \). The finite element system consisted of three continuous displacement degrees of freedom (DOFs) where elements had a polynomial degree of 1 \( (Q_1) \), and discontinuous pressure and dilation DOFs where elements had a degree of 0 \( (DGQ_0) \). The resultant non-linear system was solved using Newton-Raphson iterations, and the linear solves within each Newton step were performed using a conjugate gradient method.

### 2.8.1 Discrete form of equations

The residual for the set of unknown fields \( \Xi := \{ \mathbf{u}, \tilde{J}, \tilde{p} \} \) is equal to the differential of the total potential energy (equation 2.10) and has the following form:

\[ R(\Xi; \delta \Xi) = D_{\delta \Xi} U(\Xi) = \frac{\partial U(\Xi)}{\partial \mathbf{u}} \delta \mathbf{u} + \frac{\partial U(\Xi)}{\partial \tilde{J}} \delta \tilde{J} + \frac{\partial U(\Xi)}{\partial \tilde{p}} \delta \tilde{p} \]  \hspace{1cm} (2.52)  

We have to solve for the residual equation iteratively (Newton-Raphson method). Therefore we assume that the system is known in an \( i_{\text{th}} \) iteration and we want to find \( d\Xi \) so that

\[ R(\Xi_{i+1}) = R(\Xi_i) + D^2_{d\Xi,\delta \Xi} U(\Xi_i) d\Xi = 0 \]  \hspace{1cm} (2.53)  

Then by setting \( \Xi_{i+1} = \Xi_i + d\Xi \) the slope of the residual will have the form of

\[ \frac{R(\Xi_{i+1}) - R(\Xi_i)}{d\Xi} = D_{d\Xi} R(\Xi; \delta \Xi) = D^2_{d\Xi, \delta \Xi} U(\Xi_i) := K(\Xi; \delta \Xi, \delta \Xi) \]  \hspace{1cm} (2.54)  

where \( K(\Xi; \delta \Xi, \delta \Xi) \) is the tangent matrix of the linearized problem and can be written as:

\[ K(\Xi; \delta \Xi, \delta \Xi) = D_{d\mathbf{u}} R(\Xi; \delta \Xi) d\mathbf{u} + D_{d\tilde{J}} R(\Xi; \delta \Xi) d\tilde{J} + D_{d\tilde{p}} R(\Xi; \delta \Xi) d\tilde{p} \]  \hspace{1cm} (2.55)
Therefore, for the \( i \text{th} \) iteration, the linearized equation will be:

\[
K(\Xi_i)d\Xi = F(\Xi_i)
\] (2.56)

The explicit forms of \( D_{du} R(\Xi; \delta \Xi) du, \ D_{d\tilde{J}} R(\Xi; \delta \Xi) d\tilde{J}, \ D_{d\tilde{p}} R(\Xi; \delta \Xi) d\tilde{p}, \ K(\Xi_i) \) and \( F(\Xi_i) \) can be found in (http://www.dealii.org/developer/doxygen/deal.II/step_44.html). Since there are no gradient (derivative) of \( \tilde{J} \) and \( \tilde{p} \) in the \( D_{d\Xi} R(\Xi; \delta \Xi) \) these two fields can be condensed out and will make it easier to solve for the displacements.

The discretization and solution was performed within the deal.II finite element library [111]. Our code is based on a modification of a code (http://www.dealii.org/developer/doxygen/deal.II/step_44.html) by Pelteret and McBride. This code was developed to compute the material response of a constant-parameter neo-Hookean material. The complexity of MTU of course far exceeds that of a simple block of neo-Hookean material. The code developed as part of this thesis includes, as discussed, tissues of different constitutive properties, capable of supporting activated fibres, and varying material properties; the code is available as a supplementary electronic document to the thesis (see appendix A).

### 2.8.2 Mesh generation

For this thesis, we meshed the "STL" geometry surfaces generated by a mechanical design software. For example, designed simplistic geometry for human gastrocnemius muscle was meshed in IA-FEMesh (3D meshing software developed in the university of Iowa). We could also use STL files that have been measured and reconstructed from real tissue scanning by a coordinate-measuring machine. However, due to the nature of the questions that were studied we only used the simplistic geometries in this thesis. Mesh-generation can also be performed within the deal.II environment if desired.

The meshed geometry (Figure 2.7) was exported as an ABAQUS input file. The file was then changed with a deal.II script to a grid file that is importable into the main code. Upon importing the grid in the main script, there are tools in deal.II C++ libraries where it is possible to further refine or change the mesh.
2.8.3 Assignment of material properties at the discrete level

Since the entries of the (nonlinear) matrix equations in Equation 2.55 consist of integrals of nonlinear functions, they are approximated by quadratures over the hexahedral elements. The data for the strain energy, therefore, needs to be specified at these quadrature points. For this purpose, detailed information on many parameters such as the fibre orientations, the material description and distribution and the activity distribution and levels along with many functions that estimate along-fibre force, contraction velocity have to be provided for each quadrature point.

Our hope is to use this code to study many questions about the elastic response of muscle. To this end, the code is deliberately designed to be flexible, allowing the user to specify many properties associated with the MTU. Each of these can be independently specified at each quadrature point. We can specify 20 different pieces of information at each quadrature point: a vector with the initial local orientation of the fibre (3 terms), whether the fibre will be activated or not (1), whether the local tissue is muscle, tendon, fat or aponeurosis (4 terms); the local compressibility constant $\kappa$, the initial values of $J$ and $p$; and 9 components of the initial deformation tensor. In addition, we can specify the activation function $\alpha(X, t)$ 2.47 at each point, allowing for fibres of different activity levels through the domain.

In the next few subsections, we describe some the methods we used to define the initial constants needed for the simplified human gastrocnemius geometry (Figure 2.7).
Fibre orientation

The direction of muscle fibres in the muscle belly or collagen fibres in tendon and aponeurosis was accounted for in the strain energy function by having $(a_0)$ in the formulation (e.g. see equation 2.13). As described above, the C++ code developed in this thesis allows the user to input the direction of fibres as unit vectors for each quadrature point. For the problems studied in this thesis we have mostly used simple fibre orientations (see Chapters 3-5 for more details). However, fibre orientations have been measured and reconstructed from ultrasonography (e.g [14, 13, 112]) or DT-MRI images (e.g [113]). In future work, these fibre orientation maps can be used to specify the local orientations within our simulation code. For this purpose we generated a MATLAB script that imports the orientations from the image processing done on ultrasonography images, fits a 3D vectors field to the data and finally estimates fibre orientation in every quadrature point of a grid developed from a realistic geometry. The specific questions of this thesis didn’t require the use of this script but it can be used in future works.

Material constants

In order to select stress-stretch properties representing each tissue at the quadrature points we introduced a constant coefficient for each material property function in the code. These constants can have values between 0 or 1 based on the percentile of the property each part of the geometry inherits from the individual soft tissues modelled in this thesis. For example, for the tendon tissue these constants will have a values of 1 for functions describing tendon material properties and 0 for the rest of material functions defined in the code. If a blended material were to be chosen for a specific region (e.g. muscle-tendon junction) these constants may hold values between 0 and 1. For example a part of the material which has 85% muscle fibre and 15% fat mechanical properties (if physiologically relevant) will hold constant values of 0.80 for muscle material functions and 0.2 for fat (see Chapter 5) while the rest are kept equal to 0. These values are assigned to each integration point in the geometry.
Activation constants

Similar to importing fibre orientation and material constants, activation constants are imported for every integration point. Import of the activation parameters allows for calculating the activity level using the built-in activation function in each muscle integration point. This allows for the activity level in the muscle tissue to be a function of both time and space (region(s) of the muscle belly). In this thesis we used a constant parameter that is a number between 0 and 1 for a ramped activation function through time. For future purposes, however, it is easy within the code to use functions with varying onset times of activation or non-constant and time-dependent changes in activation level.

2.9 Model Validations

2.9.1 Computational validation

In order to validate the mathematical framework and the solver accuracy, we tested our code by calculating the result for the same physical condition under four consecutive element refinements. For this purpose we built a rectangular cube with $8 \times 1 \times 1$ mm$^3$ dimensions as the test geometry. Four sets of simulations with four levels of refinement (8, 64, 512 and 4096 elements) were performed. In each set, a combination of specific material, loading and boundary conditions was considered. The displacement along the length of the cube was used to compare simulation results of the four grid sizes in each set. The following describes each set of simulations and the results are brought in tabular form.

1. **Nonlinear elastic and nearly incompressible isotropic material**: The geometry was fixed at one end (z-direction normal; Dirichlet boundary with $u = 0$) and was pulled with a force ramping up through time (Neumann boundary) at the other end. The displacement along the z-direction was compared after 1 second of simulation (Table 2.7) including 10 time-steps for each of the four levels of mesh refinement. of a nonlinear neo-Hookean material as the material filling the geometry. In this case, the difference between the responses were also quite small as the linear elasticity simulation set.
CHAPTER 2. MATHEMATICAL MODEL: DEVELOPMENT AND IMPLEMENTATION

| Grid size | z-Displacement (mm) | error (|z - z*|) p in $O(h^p)$ |
|-----------|---------------------|-----------------------------|
| 8         | 0.33569             | 0.01369 2.06357             |
| 64        | 0.34640             | 0.02880 2.81323             |
| 512       | 0.34352             | 0.00031 3.88515             |
| 4096      | 0.34321             | -                           |

Table 2.7: Displacement of the pulled end of the $8 \times 1 \times 1$ mm$^3$ cube with Neo-Hookean material (Lamé constants $\mu = 80 \times 10^6$ and $\nu = 0.49$) in z-direction for 10 MPa of extensive load.

2. Transversely isotropic passive muscle tissue material: The second set was also similar to the first set in boundary and loading conditions. However, this set was performed with a passive skeletal muscle material properties for the rectangular block. The z-direction displacements were compared again to evaluate the system performance with passive and transversely isotropic tissue (Table 2.8).

| Grid size | z-Displacement (mm) | error (|z - z*|) p in $O(h^p)$ |
|-----------|---------------------|-----------------------------|
| 8         | 0.70589             | 0.00193 1.89643             |
| 64        | 0.71814             | 0.00713 2.37729             |
| 512       | 0.72307             | 0.00220 2.94145             |
| 4096      | 0.72527             | -                           |

Table 2.8: Displacement of the pulled end of the $8 \times 1 \times 1$ mm$^3$ cube with passive muscle material in the z-direction (along-fibre) for 10 KPa of extensive load.

The difference in z-displacements are once again small. This confirms the mathematical validity of the system for solving problems with transversely isotropic material in passive state.

3. Transversely isotropic active muscle tissue material: In this set of simulations the rectangular cube of muscle used in the previous set was activated by ramping up the activity level in the muscle tissue. The difference here was that beside the fixed end of the cube, the other end was left free of traction so the cube could contract and shorten upon activation. The z-displacement was used to compare the results of the simulations as before (Table 2.9). Additionally, we ran the four simulations with a time-step of half of the original simulations in this set. This was performed to show that muscle contraction is stable when activated with different time-stepping (Table 2.9). The difference within each group of simulations with the same time-step and between same grid sizes of different time-stepping groups were still small. This
CHAPTER 2. MATHEMATICAL MODEL: DEVELOPMENT AND IMPLEMENTATION

| Time-step (s) | Grid size (mm) | z-Displacement (mm) | error $(|z - z_+|)$ | p in $O(h^p)$ |
|---------------|----------------|---------------------|---------------------|----------------|
| 0.01          | 8              | -2.07581            | 0.5883              | 0.25512        |
|               | 64             | -2.19712            | 0.06248             | 1.33348        |
|               | 512            | -2.14112            | 0.00648             | 2.42326        |
|               | 4096           | -2.13464            | -                   | -              |
| 0.005         | 8              | -2.07581            | 0.5883              | 0.25512        |
|               | 64             | -2.19712            | 0.06248             | 1.33348        |
|               | 512            | -2.14112            | 0.00648             | 2.42326        |
|               | 4096           | -2.13464            | -                   | -              |

Table 2.9: Displacement of the free end of the $8 \times 1 \times 1 \text{mm}^3$ cube with activated muscle material in the z-direction (along-fibre).

verifies the robustness of the system for modelling active muscle tissue.

4. **Active muscle tissue material with two regions of activity**: As described in section 2.7 in case of different levels of activity at different regions we used combinations of $\arctan(X)$ functions to vary activity smoothly between regions that were active and those which were not. This was mainly because in presence of two adjacent regions where one could active and the other was completely inactive at all times, upon activation of the activable region, an impulse is created at the boundary of the two regions. This leads to mathematical difficulties. Also, in real tissues activation regions do not vary over infinitesimal length scales. Therefore, to avoid potentially unphysiological behaviour, we chose the $\arctan(X)$ functions for prescribing a smooth transition between the two regions.

In this next set of simulations we tested four different activity transition functions on the rectangular block of 512 elements. Like the previous set of simulations, the block of muscle was fixed at one end but the activity changed half way through the muscle. This means the activity in the half of the cube closer to the fixed end was scaled by the portion of $\arctan(X) \sim 1$ and the activity in the other half (free end) was scaled by $\arctan(X) \sim 0$. The transition period $(0.05 \leq \arctan(X) \leq 0.95)$ could span different number of elements. The effect of this transition span on the output of muscle contraction was tested for an approximately 1, 2, 4 and 16 elements span sizes (Table 2.10).

The results show that when the span size is relatively small compared to the geometry, there is a small difference in converged solution while it allows the model
<table>
<thead>
<tr>
<th>Transition span (mm)</th>
<th>z-Displacement (mm)</th>
<th>Difference (%)</th>
<th>Maximum converged activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 element</td>
<td>-1.67</td>
<td></td>
<td>28</td>
</tr>
<tr>
<td>2 elements</td>
<td>-1.69</td>
<td>1.2</td>
<td>30</td>
</tr>
<tr>
<td>4 elements</td>
<td>-1.73</td>
<td>3.6</td>
<td>33</td>
</tr>
<tr>
<td>16 elements</td>
<td>-1.92</td>
<td>15.0</td>
<td>49</td>
</tr>
</tbody>
</table>

Table 2.10: Displacement of the free end of the $8 \times 1 \times 1 \text{mm}^3$ cube with half the muscle activated in the z-direction (along-fibre) by different transition functions from passive to active regions.

To converge even at higher activation levels. This is not surprising: as the activation levels increase, the difference in strain energy between the activated and non-active regions increases. If this transition happens over small spatial scales, once again we expect impulse-like behaviour at the interface. However if the span of the $\arctan(X)$ increased to cover a high proportion of the length of the geometry, the difference in displacement also increases. This suggest that although using this technique would allow to converge even at higher levels of activity in the muscle model, one should be careful about how the activity transition function is designed to prevent loss of accuracy in prediction.

We additionally ran an instance of the simulations in the chapters 3 to 5 of a muscle belly with different levels of mesh refinement to asses computational robustness in the target domain and when different tissues are combined. The results that we report frequently such as muscle belly force had small changes upon refinement of the mesh. For example the forces for a uniform activity of 50% for a muscle belly with no fat and grid sizes of 840 and 3696 were 204.21 and 201.86 respectively.

### 2.9.2 Physiological

No matter how mathematically accurate a model is, it has to represent the physics of the phenomenon it is modelling. Therefore, the entire Chapter 3 is dedicated to compare the results of this modelling framework of skeletal muscle contraction to previously measured experimental data under similar testing conditions.
2.10 Summary

In this Chapter we described the mathematical formulation for simulating the behaviour of the tissues in a muscle-tendon unit. The choice material properties for different tissues were described and formulated to be used in the next Chapters. In addition, the techniques developed to assign the material constant to each part of the geometry was introduced. Finally, four sets of simulations were performed on a simple geometry to assess the mathematical robustness and accuracy of the proposed system.
Chapter 3

Muscle model: Physiological validation and numerical experiments

3.1 Introduction

Forces developed by contracting skeletal muscle depend on the structure and geometry of the contracting fascicles, and their interaction with the surrounding connective tissues. Recent studies have highlighted the complexity of the internal structure of the muscles in 3D, and the changes to this structure during contraction (e.g., [112]). However, relatively little is known about the mechanisms that relate the structure to function. It is likely that regional variations in muscle structure, tissue properties and activation patterns all contribute to the force output from the muscle. In order to understand such effects it is necessary to use a muscle model that can incorporate these complexities. An efficient way, in terms of both time and cost, to test these effects would be with a 3D finite element simulation platform based on a realistic mathematical model of muscle.

Muscle models and their related simulations have evolved over the last decade to incorporate 3D structural and architectural parameters such as fascicle orientations and connective tissue properties (e.g., [69, 59, 70]). Features such as fascicle activation patterns, structural changes (for instance changes in fascicle curvature and orientation)
under isometric and dynamic contractions and their effects on the force and power generated by the whole muscle have been investigated in a number of previous works (e.g., see Chapter 4 and [36]). While recent developments in imaging and signal processing techniques are enhancing our ability to measure detailed structure [114, 112] and activation profiles (e.g., [115, 116, 117]) in a muscle, all the intended parameters may be hard or impossible to collect in a single experiment. Therefore, there is a need to use mathematical models to get insight into muscle function where large number of parameters can be manipulated or measured during a simulation of muscle contraction.

Here we present the results of 3D finite element simulations of a skeletal muscle model that has been developed specifically to investigate the relation between the muscle's internal structure and activation patterns and its force output. The model has the ability to include detailed 3D architecture and regionalized submaximal activity in different groups of fascicles. It integrates the effects of different tendon and aponeurosis properties on the force transfer within the muscle-tendon unit from its origin to insertion. Furthermore, we have previously shown that this mathematical modelling framework can predict the deformations of the internal structure within the muscle, and the force vector developed by the whole muscle, while the activity patterns within the muscle can be varied and regionalized (see Chapter 4).

The main purpose of this chapter is to present the validity of this modelling framework using different sets of experimental data. A validated computational model of muscle can be used to test mechanisms and investigate the effect of parameters that are difficult or impossible to measure. The second purpose of this chapter is to demonstrate some of the effects of the tendon and aponeurosis properties on the structural properties of the muscle during contraction.

3.2 Methods

The mathematical framework for this work was described in Chapter 2. The computational model was validated by comparing the force-length properties of the whole muscle to experimental measures, and also by comparing the shape, orientation and curvature of the modelled muscle fascicles to similar measures that have recently been made available through ultrasound imaging studies. The comparisons will be done on the
data from human gastrocnemius muscle, one of the muscles in the calf that acts to flex the knee and extend the ankle joint in humans. Gastrocnemius muscle has two heads: medial (MG) and lateral (LG). Each head can be considered a unipennate muscle that insert onto common Achilles tendon.

A unipennate muscle belly geometry of human gastrocnemius (Figure 3.1) was created for the numerical experiments (Dimensions mostly from Randhawa et al., 2013 [118]). The model geometry had a regularized shape to help constrain model variants and results to the conceptual questions which are the focus of this thesis, rather than allowing the model to respond to idiosyncrasies of individual geometries. The dimensions, as well as the structural and material properties of the model were styled to be consistent with those of the gastrocnemius (lateral or medial head) in humans. The soft tissues were treated as transversely isotropic hyperelastic materials. The muscle-aponeuroses complex was meshed by a grid of hexahedral elements. The model coordinate system had the z-axis running proximal-distal the line of action of the muscle, the y-axis ran from the deep to the superficial direction and the x-axis ran across the medial-lateral width of the muscle. This model had the same constitutive law that we described in Chapter 2. For this Chapter, specific activation patterns and structural parameters along with mathematical boundary and initial conditions were used. The end planes of the aponeuroses were defined as the transverse planes where the aponeuroses would join onto the external tendons, and mark the proximal and distal ends of the muscle belly. Some simulations were run for isometric contractions of the muscle belly where the end planes of the aponeuroses were fixed. Other simulations were run for the whole muscle-tendon unit with the external tendons included: for these, the proximal and distal ends of the muscle-tendon unit were fixed during contraction.

Simulations in this study were done using a set of C++ libraries for finite element modelling (DEAL.II; [111]). Each simulation was run with an increasing and uniform level of activation across all fascicles. The simulations were terminated when the nonlinear iterations did not converge and specified tolerances within given number of steps; this point depended on the initial state and boundary conditions for each simulation. Where groups of simulations are compared together, they were compared up to the highest activation level that was commonly achieved across the set. Each simulation took approximately 10 minutes to run [on a standalone 8-core (16 thread) computer], and this
3.2.1 **Simulation vs. Experiments - Validation of a muscle model**

Two sets of simulations were carried out on a muscle belly geometry (Figure 3.1). Initially the muscle belly was a parallelepiped with 65 mm initial fascicle length, 15 degree pennation angle, and for simplicity each aponeurosis was a rectangular cuboid of $210 \times 55 \times 3 \text{ mm}^3$. The initial stretch values for both the muscle and aponeuroses fascicles were set to one. This stretch corresponds to the optimal length for the muscle fascicles. A set of simulations was run to map the force-length relation for the muscle belly, and a second set of simulations was run to test the trajectories of the muscle fascicles and the strains within the tissues during contraction.

- **Force-length test for isometric contractions of a muscle belly**

The model of the muscle belly was adjusted to different lengths by fixing one end at its aponeurosis end plane, and passively displacing the other aponeurosis end plane to a new position. When the length of the muscle belly reached the desired length, both end planes for the aponeuroses were fixed to maintain the muscle belly at an isometric length, and the activation level in the muscle fascicles was then ramped up. The range over which the muscle belly length changed was selected so that pre-activation fibre stretch in the muscle was between 0.75 and 1.35. This is close to the range for stretches in human medial gastrocnemius that have been reported when the ankle is passively moved from 30 degrees plantarflexion to 15 degrees dorsiflexion [15]. To achieve this, the muscle belly was shortened about 6% for the lower bound of the fascicle stretch range. However, lengthening of the belly was selected to surpass the natural range so the force-stretch curve could be...
plotted for a longer range. The simulations at different lengths reached a common activity level of 30%. The magnitude of the passive and total belly forces were computed along with the muscle fascicle lengths at which those forces were developed. The active muscle force was taken as the difference between the total force and the passive force for a set of common muscle fascicle lengths.

- **Internal structural changes during isometric contractions of the muscle belly**

Both end planes of the aponeuroses for the initial geometry were fixed and the activation was uniformly ramped up. Geometrical properties of fascicles both in 2D (fascicle curvature) mid-longitudinal and transverse planes (Figures 3.2, 3.3) and 3D (fascicle path, along-fascicle and transverse strains) were measured at different activity levels (Figure 3.4 and Table 3.1). Undeformed fascicles (Figures 3.2, 3.4) were chosen as groups of points that fit along lines that connect the two aponeuroses and have 15 degrees inclination (pennation) in the initial geometry. These fascicles were then tracked throughout all simulations to measure the structural deformations at the fascicle level. The mean pennation and curvature of the fascicles along with the along-fascicle (longitudinal) and transverse strains were extracted from the deformed fascicle data after the contractions had been simulated. The extent of fascicle curvature across the whole muscle belly in its mid-longitudinal plane was quantified by its root-mean-square (RMS) value for each activity level (% MVC). Fascicle sheets were defined as the 3D faces that run longitudinally through muscle and contain fascicles that were originally in the same YZ-plane of the undeformed geometry. Figure 3.2B shows the intersection of these sheets with the mid-transverse plane.

- **3.2.2 The effect of tendon and aponeurosis properties on structural changes of the muscle tendon unit**

Proximal and distal tendons were attached to the geometry of the muscle belly, where the distal tendon mimics the Achilles tendon. Both tendons had the same thickness and width as aponeuroses, but had lengths of 20 and 160 mm for the proximal and distal tendons, respectively. Initial tests showed considerable rotations of the muscle belly during contraction as the aponeuroses end planes aligned along the line-of-action of the whole muscle tendon unit (Figure 3.5). To minimize this rotation, the deep aponeurosis (that was attached to the distal tendon) was constrained to not move any more in a deep direction.
Figure 3.2: Geometry of the muscle fascicles within the muscle belly (A), shown for their mid-transverse (B) and mid-longitudinal (C) planes. The frames with black fascicle lines are in a relaxed state and the frames with red fascicle lines belong to muscle fascicles at a 40% activity level. The active fascicles show a decrease in thickness and an increase in width in the longitudinal and transverse sections, respectively. Note that the fascicles in the longitudinal section (fascicle plane) are mostly curved to S-shapes in the active state.

during contraction. The free end of proximal tendon was fixed and the free end of the distal tendon was pulled about 0.2% of the total muscle-tendon unit length as an initialization step to settle the system into a initially stable structure. It was then fixed to keep the muscle-tendon unit isometric. Two situations were investigated: (1) the tendon and aponeurosis had the same material properties that were equal to the tendon properties, and (2) the tendon and aponeurosis had distinctive material properties as seen in Chapter 2. These simulations achieved a common activation level of 10%, and the patterns of aponeurosis and tendon strains were compared for the two material formulations.

3.3 Results

The force-length properties for the contracting muscle belly are shown in Figure 3.6 along with selected data from experimental studies on human muscle. As the muscle was activated, the stretch in the connective tissues allowed the fascicles to shorten, and so the fascicle lengths were different between the active and passive states. Plots shown in Figure 3.6 are all for equivalent fascicle lengths, and so the active force was calculated by subtracting the passive force at a slightly longer belly length away from the total force for
a contracting muscle. The total and active muscle belly force showed a peak for fascicle stretch of 1, however, the overall shapes of the active and passive plots for the muscle belly were different from the plots for purely muscle fascicles due to the effects from the aponeurosis, muscle structure and pennation.

This modelling shows that the belly force and fascicle pennation becomes larger when the activation state of the muscle belly increases. In the current study the pennation also increased when the belly was passively shortened, and decreased when the belly was passively lengthened. The range of pennation for passive and 30% active belly were 11.6-19.3 degrees and 13.4-21.2 degrees, respectively, as the belly length was reduced.

The muscle fascicles in the gastrocnemius belly, changed from their initially straight configuration to a curved state during contraction. The fascicles showed an S-shaped profile in the mid-longitudinal plane (Figure 3.2) with the fascicles intersecting with the aponeurosis at a lower angle than their mean orientation would predict. These curvatures profiles match those that have previously been reported from experimental studies using ultrasound-based imaging [114], and both are shown in Figure 3.3. The magnitude of the fascicle curvatures increased as the contraction level increased, and the increases in curvature matched the increases experimentally observed in contracting MG [114] (Figures 3.3, 3.7).

Strain measures for muscle tissue in the centre of the muscle belly are shown for an isometric contraction at 40% in Table 3.1 along with experimentally measured values [119].
Figure 3.4: 3D paths of three fascicles crossing the mid-transverse plane. Each fascicle is plotted for 0 (green), 30 (blue) and 60% (red) activity levels. The arrows show the normals to a medial/lateral fascicle at 30% activity and are coloured by their azimuthal angle where the azimuthal angle is the angle between the projection of the fascicle path in the xy-plane with the x-axis. The change in azimuthal angle from 80 (yellow) to 99 degrees (red) shows that the fascicle sheets curve away from the centre of the muscle belly.

The transverse strains in the fascicle (mid-longitudinal:yz) plane were much smaller than the strains normal to this plane. The Poisson’s ratio in the fascicle plane was calculated as the magnitude of the ratio between transverse and along-fascicle strains in the mid-longitudinal plane and was 0.089.

The fascicle sheets bulged in both medial and lateral directions when the muscle belly contracted (Figures 3.2, 3.4), and the bulge increased as the activity level rose. The path of the fascicles in 3D showed them running along the fascicle sheets as they bulged, and thus formed a part of a helix (demonstrated by their varying azimuthal angle along their length (Figure 3.4).

When the whole muscle-tendon unit was simulated (with the external tendons included), the muscle belly showed substantial rotations as the aponeurosis end planes aligned to be closer to the line-of-action of the muscle (Figure 3.5). Subsequent simulations of the MTU constrained the deep aponeurosis to not displace any deeper, and this forced the bulging of the muscle belly to be in the superficial direction. This was to
Figure 3.5: Displacement of whole muscle-tendon unit when activated without deep or superficial constraints.

emulate a simplified set of constraints that occur on the MG within the intact leg. The final simulations (Figure 3.8) showed that when a stiffer aponeurosis was used instead of adopting tendon properties, the strains in aponeurosis were smaller. Also the strains in the muscle tissue were more uniform when a stiffer material for the aponeurosis was used.

### 3.4 Discussion

Validating a mathematical framework and numerical implementation of it for human muscle is a challenge, due in part to the fact that muscle forces cannot be directly measured in vivo. In this study we have compared the force output from a computational

<table>
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<th>Values</th>
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<tr>
<td>Along-fascicle (longitudinal) strain (%) - simulation</td>
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</tr>
<tr>
<td>Transverse (cross-fascicle) strain (%) - simulation</td>
<td>0.74</td>
</tr>
<tr>
<td>Out of plane (width) strain (%)- simulation</td>
<td>7.83</td>
</tr>
<tr>
<td>Mid-longitudinal plane Poisson's ratio - simulation</td>
<td>0.089</td>
</tr>
<tr>
<td>Poisson's ratio - in-vivo [119]</td>
<td>0.09±0.01</td>
</tr>
</tbody>
</table>

Table 3.1: Along-fascicle and transverse strains for fascicles in the middle of the muscle belly for 40% activity (Fig.3.2). The Poisson's ratio in the mid-longitudinal plane is calculated as the magnitude of the ratio of the transverse (cross-fascicle) to the along-fascicle strain. The last row shows the measured Poisson's ratio from 2D ultrasound images in the mid-longitudinal plane of the MG during dynamic contractions [119].
3D FEM model with the forces estimated from studies of ankle joint flexion-extension experiments. The general pattern of the force-length relationship generated by the model matches those from the experimental studies. Experimental measures can identify the overall shape of the muscle with MRI [122] and even the internal trajectories of the muscle fascicles using diffusion-tensor MRI [123, 124, 125]. While this information is very important, the relatively long scan times of MR imaging preclude such measurements for active contractions [13]. However, the aim of the presented muscle model is to understand the mechanisms occurring during muscle contractions. It is therefore important to validate the muscle model in its contracted state. For this study we have used ultrasound-based measures from the literature [114, 112] of the internal structure during contraction (fascicle orientations, curvatures, and strains) to validate the model.

The simulations in this thesis had a simplistic initial geometries that had the overall dimensions and mean fascicle pennation of the MG in man, but without the details of the geometry or internal structure. Furthermore, all the muscle fascicles within the model had the same material properties and thus represented the same fibre-types. Additionally, the activation was uniform across all fascicles: again these are gross simplifications compared to the physiological complexities and variations that occur within muscles in-vivo. Nonetheless, the emergent features from the model showed a remarkable similarity to the experimental measures that are available for comparison. This gives confidence that the model can identify general features and consequences of the muscle structure that were not a result of idiosyncrasies or muscle-specific details of geometry, structure or activation.

Intramuscular pressure develops within muscles during contraction [126, 127, 128], and the fascicles curve around the regions of higher pressure. Previous modelling studies [65, 129] have shown how the curvatures in both the muscle fascicles and aponeurosis must balance the intramuscular pressure, and indeed our current model shows curvatures developing in both of these structures. However, in the previous studies the curvatures of the muscle fascicles were constrained to be constant along their lengths, whereas this was not a constraint in the current model. The muscle fascicles in the current model started straight in their initial configuration, but developed S-shaped profiles when quantified in the mid-longitudinal plane. Both the S-shaped profiles and the magnitude of the increases in curvature that occurred with increasing activity and muscle force mirror
those that we have previously been imaged for the MG using B-mode ultrasound [114, 112]. A consequence of the S-shaped trajectories is that the angle at which the fascicles insert onto the aponeurosis can be reduced, allowing for a greater component of traction in the line of action of the whole muscle along the direction of the aponeuroses.

When tracked in 3D, the muscle fascicles followed curved paths on their fascicle sheets indicating that change in architecture is not simply due to a bulge of the sheets. The active configuration of these fascicles indicate that S-shaped fascicles in 2D curvature maps (Figure 3.3) are not only the result of projecting the fascicles on a 2D plane (e.g. [130]) but comes from curling of the fascicles in a helical path. These 3D helical paths are curved around the centre of the muscle (Figure 3.4) where the intramuscular pressure is higher.

It is generally assumed that muscle fascicles are isovolumetric [84], and isovolumetric assumptions dictate the relation between longitudinal and transverse strains. Poisson’s ratio is the absolute value of ratio of the transverse to the longitudinal strain, and should be 0.5 for small strains in an incompressible and elastic material. The simulations in this study showed that as the activation increased, the transverse strain (in the mid-longitudinal plane) was lower than expected, resulting in a Poisson’s ratio of 0.089, however this was compensated for by greater transverse strains in the orthogonal direction (Table 3.1). The muscle fascicles were represented as transversely isotropic materials in this model, and so the asymmetry in their transverse bulging must reflect asymmetries in the transverse stresses acting on the fascicles. Being a unipennate model, there would have been a larger compressive force in the mid-longitudinal plane that was bounded by the aponeuroses that were being squeezed together by the pennate fascicles, than in the medial-lateral direction where there was no aponeurosis bounding the muscle. Indeed, the model showed muscle belly bulging to its sides, but decreasing in its thickness between the aponeuroses during contraction, in a similar manner to the decreases in thickness observed for the MG in vivo [118]. Recently the transverse bulging of the muscle fascicles in the MG has been quantified from B-mode ultrasound images [119], showing a Poisson’s ratio of 0.09; this matches the simulated results and provides confidence that emergent features of the model explain realistic features of muscle contraction.

When the model was evaluated with external tendons, there was a need to constrain displacements of the geometry since the unconstrained simulation (Figure 3.5) showed a
large displacement of the muscle in the y-direction. This illustrates that a range of additional boundary constraints may need to be applied to finite element models of muscle-tendon units in order to result in more realistic deformation.

In the case that the aponeurosis and tendon were given the same material properties a pattern of non-uniform strains resulted in the aponeurosis. This non-uniformity in strain is similar to that observed in previous experiments [131, 132], but our modelling study shows this can be an emergent feature of the muscle, and not necessarily due to differences between active and inactive motor units in submaximally activated muscle, as has been previously suggested [131]. The aponeurosis strains were smaller than the tendon strains for both formulations of material property (Figure 3.8). Although there is an obvious jump in strain between the tendon and aponeurosis when a stiffer material is used for the aponeurosis, the difference in strains was less than 2%. A benefit of using a stiffer aponeurosis material compared to tendon, would be that a more uniform distribution of strains occurs in the fascicles, and this would allow the fascicles to have more uniform sarcomere length.

The simulated results from this finite element model match the general patterns from experimental and imaging results. Whole muscle force is partly shaped by the internal geometry of the muscle fascicles, and their interactions with the aponeuroses, and so cannot be explained entirely by modelling a muscle as a scaled-up muscle fibre [133]. As the fascicles shorten, they must increase in cross-sectional area in order to maintain their volume, but asymmetric bulging occurs due to asymmetries in the compressive stress acting on the fascicles during contraction. The fascicles curve and adopt S-shaped profiles that align their traction to be closer to the aponeurosis direction, and they curl across fascicle sheets that in turn bulge around the intramuscular pressure that develops during contraction. Material properties of the aponeuroses affect the strains in the fascicles and thus their force generating potential. The muscle model that we have validated in this Chapter will provide a useful tool for understanding the mechanisms that relate muscle structure to its contractile function.
Figure 3.6: Measured (gray) and modelled (black) force-length properties of human calf muscles. The simulations reached a 30% activation, and the forces have been normalized to achieve a maximum active force of 1. The black lines without symbols show the active (solid line) and passive (dashed line) force-length properties that were input for the fascicles (see Chapter 2). The black lines with symbols show normalized active (inverted triangles), passive (squares) and total (circles) forces for the whole muscle belly. The normalized active (diamonds) human gastrocnemius force was measured from twitch contractions [120]. Normalized passive (stars) forces from gastrocnemius are a combination of experimental values upto 1.1 stretch and beyond that are extrapolated numerical values. The active human soleus (triangles) forces were measured from tetanic contractions [121].
Figure 3.7: The change in root-mean-square curvatures of the fascicles in mid-longitudinal plane increased with activation for both simulation (black) and experimental (gray solid line; [114]) results. The dashed gray lines show the range of deviation from mean change in RMS curvature (±S.D.) from the experimental study.
Figure 3.8: Total strain in the muscle tendon unit tissue at a 10% activity level for two material conditions: equal material properties for aponeurosis and tendon (A), tissue specific properties (Chapter 2) for aponeurosis and tendon (B).
Chapter 4

Regionalizing muscle activity causes changes to the magnitude and direction of the force from whole muscles

4.1 Introduction

Skeletal muscles can contain subunits called neuromuscular compartments that are spatially distinct regions that contain specific motor units and motor drive from the nervous system [28]. In muscles with broad attachments, a relationship between anatomical compartments and function may appear logical, and this has shown to be the case for both the biceps femoris in the cat [33, 26] and the masseter muscle in the pig [134, 135]. However, functional regionalization in muscles with long tendons has also been reported [36], leading to the suggestion that activation of motor units in different compartments may result in differences to both the direction and the magnitude of force applied at the tendon [28]. It is likely that asymmetry in the fascicle architecture combines with the location of the neuromuscular compartments to result in varied force vectors from a contracting muscle.

A unipennate muscle is asymmetrical in its architecture, and muscle fibres in different locations have different moment arms and may exert different torques about a joint. The
way in which forces are transmitted from the contractile fibres to the tendon can involve myofascial pathways [136], that in turn may modify the resultant force vector from the individual fibres. It has been shown that activity can differ between the neuromuscular compartments and spatial regions in the gastrocnemii in the cat during walking [137], and in man during both cycling and postural tasks [138, 139]. Changes in activity between the neuromuscular compartments in the cat lateral gastrocnemius led to changes in the direction of the force vector along the tendon, altering the moments of yaw, pitch or roll about the ankle [36]. However little has been reported about the mechanisms that link the varied forces developed by individual fibres to the net mechanical output of the whole muscle.

The different stiffnesses of connective tissues such as aponeurosis and tendon add to the complexity of muscle-tendon unit (MTU) behaviour. In-vitro measurements of mechanical properties of tendon and aponeurosis [99, 91, 51], and ultrasound-based in vivo measurements of these properties [95, 54] suggest that tendon and aponeurosis may have different tensile elastic moduli which can be altered with age [140], training [141] and injury [142]. The elastic properties of the aponeurosis can affect the extent to which muscle fibres rotate as they contract [118], and can thus affect the magnitude and direction of the forces developed by the whole muscle. However, it is beyond current experimental techniques to measure the effect of aponeurosis stiffness on the force outputs from muscle.

Some of the limitations in experimental studies can be addressed using in silico models of muscles. These models need to contain a realistic architecture and physiologically relevant connective tissue properties. Further, they should be able to support different activation levels in different regions. Implementing fundamental physiological concepts and material properties within sophisticated mathematical frameworks has moved muscle simulations from one-dimensional models [53, 61] to more architecturally and functionally detailed two- [68, 65] and three-dimensional models [69, 59, 70]. Despite the level of architectural details that current models include, such models rarely include other heterogeneities within the muscle such as material distribution (e.g. fiber-type or connective tissue properties) or differential patterns of activation. In this chapter we investigate how uneven patterns of activation across a unipennate muscle affect the magnitude and direction of the force developed by the whole
muscle, using a conceptual *in silico* muscle model. The *in silico* model has a simple geometry but is asymmetric in architecture, and regionalized in activity. This model was also used to investigate how the aponeurosis properties affect the force development in the fibres and its transmission to the external tendon.

### 4.2 Material & Methods

#### 4.2.1 Geometry, mesh, boundary and fibre architecture

A unipennate muscle belly model was created *in silico* to test the effects of the activation being regionalized on the direction and magnitude of the force developed by the whole muscle. This model had the same constitutive law (Chapter 2) and geometry (Chapter 3) that we have previously used. However, for this chapter the activation patterns and structural parameters along with mathematical boundary and initial condition were altered. The muscle-aponeuroses complex was meshed by a grid of hexahedral elements. Displacements, stresses and forces were calculated using a three-field finite element formulation. The activation levels of the different muscle regions within the model could be independently varied.

#### 4.2.2 Numerical simulations

A set of simulations were designed to investigate the effect of regionalized activation, as well as different aponeurosis stiffnesses, on the magnitude and the direction of force developed by an isometrically activated muscle. The average activation of the whole muscle tissue was set to be 10% but the distribution of activation was changed between the simulations. For initial undeformed (relaxed) state, the muscle fibres were considered to be at optimal length and the along-fibre strain in aponeurosis was set to zero.

The different distributions of activation are shown in Table 4.1. All activation distribution scenarios were repeated for three different elasticity moduli of aponeurosis. The aponeurosis was considered with maximum strains of 2, 5 and 10 % when the muscle was developing maximum isometric force, where the 5 % case is given in equation 2.31.

The model was run on an eight-core computer with multi-threading over the cores (16...
CHAPTER 4. REGIONALIZING MUSCLE ACTIVITY CAUSES CHANGES...

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<th>Medial-Lateral (Shifted)</th>
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<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
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</table>

Table 4.1: Activity level ($\alpha_{max}$) and regionalization of activation in different simulations. For heterogeneous patterns, the light gray region was activated to the prescribed maximum level (last row), while the dark gray region(s) were inactive. Note that for the medial-lateral activity pattern, the region of activity was not symmetric about the mid-plane ($x=27.5$ mm) but instead was offset to one side, to be symmetrical about the plane $x=32.1$ mm.

threads). The average CPU time for each simulation was approximately 10 minutes. This included the time needed to initialize the mesh, assemble matrices and iteratively solve the system.

### 4.3 Results

During the isometric contractions simulated in this study, the aponeuroses stretched, allowing the muscle fibres to shorten and rotate to greater pennation angles (Figure 4.1) than the initial pennation angle of 15 degrees. A common end-point for the contractions was defined as the time where there was a mean 10% activation across the muscle tissue. The end-point of a contraction can be seen in Figure 4.2A for the condition with a uniform activation and compliant aponeurosis; this figure shows the total strain for each element in the tissues. However, note that the maximum strain in the muscle was 26%. For this condition the aponeurosis stretched up to 1.5%, and the greatest shortening of the muscle fibres occurred in the centre of the muscle belly. The muscle belly bulged in its width ($x$-direction) by approximately 12%, and decreased in the thickness between the aponeuroses. The muscle fibres curved during contraction, with the greatest curvatures occurring close to the aponeusoses, and the fibres following S-shaped paths. The initial condition had the fibres arranged in plane (parallel to the $yz$ plane), and these curved outwards as the muscle belly width increased during contraction.

The results comparing all 12 simulations can be seen in Figure 4.3. The force vectors
Figure 4.1: Deformed (active) and undeformed (relaxed) geometries for (A) the uniform activation pattern and (B) the proximal-distal activation pattern. These geometries are shown with pale areas and blue lines for the undeformed states, and darker areas and gray lines for the deformed states. Note that in the deformed states the pennation angle for the proximal-distal activation pattern (18.37°) is larger than for the Uniform activation pattern. Transverse sections through the muscles are shown for the (C) Midline activation pattern, and (D) Medial-lateral activation pattern. In these panels the undeformed shape is shown by the rectangular and dark red area. The coloured elements show the magnitude of the strain in the model tissues in their deformed state, ranging from low strains (blue) in the aponeurosis to greatest strains (red) in the muscle belly. Note how the muscle belly thickness between the aponeuroses is least over the active region of fibres, and the width of the muscles has increased beyond the undeformed state. Also note that in the Medial-lateral activation pattern the maximum strains have moved laterally (to the left) within the muscle.

For the whole muscle were calculated from the shear and tensile stresses developed across the transverse plane bounding the deep aponeurosis (z=0, for contour details see Figure 4.2B). The force vectors were described by the x-, y- and z- direction cosines of the force vector ($\delta x$, $\delta y$ and $\delta z$, respectively), and the resultant force magnitude (for details see Figure 4.2C).

In general, an increase in aponeurosis stiffness caused an increase in the magnitude of force and a change to its direction (see $\delta y$ in Figure 4.3). The stretch in the aponeurosis was reduced for increased aponeurosis stiffness, and this led to a reduction in the shortening of the muscle fibres and a reduction in their rotation to higher pennation angles. Additionally, as the aponeurosis stiffness increased, the changes in muscle belly thickness and width became smaller. For the example of the uniformly activated muscle with a stiff aponeurosis, the width increased by only 7% during contraction.
Figure 4.2: Simulation results for the uniform activation condition with compliant aponeurosis and 10% activation. (A) Magnitude of strain. (B) "xz" and "yz" shear and "zz" tensile stress contours on the plane connecting the aponeurosis and tendon (z=0). (C) The direction cosines (dark gray) and force magnitude for the resultant force (light gray) acting on the z=0 plane.
CHAPTER 4. REGIONALIZING MUSCLE ACTIVITY CAUSES CHANGES ...

<table>
<thead>
<tr>
<th></th>
<th>COFx (mm)</th>
<th>COFy (mm)</th>
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<td>31.4</td>
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</table>

Table 4.2: x and y components of the centre of force (COF) on the z=0 plane.

The conditions with uniform activation had each muscle fibre activated to 10%. For the other three conditions with regionalization of the activity, the mean activity level across the muscle was kept at 10%, but this was concentrated in half the fibres each being activated to 20%. The magnitude of the muscle force was similar for the simulations with uniform, midline and medial-lateral distributions of activity, however the proximal-distal activation pattern resulted in greater muscle force. The active fibres in the conditions with heterogeneous activation patterns (proximal-distal, midline and medial-lateral) contracted to a shorter length and rotated to a greater pennation angle than the uniform pattern. Additionally, in the conditions with proximal-distal activation patterns the thickness of the belly changed non-uniformly along the length of the muscle with a greater reduction in thickness in the active region.

For the conditions with compliant aponeurosis, the y-component of the centre of force moved from a position midway down the aponeurosis to a level closer to the deep surface for the stiff aponeurosis condition (Table 4.2). Conditions with the uniform, proximal-distal and midline activation patterns are all symmetrical about the midplane of the muscle (x=27.5 mm). For these conditions there was a negligible x-component to the whole-muscle force, with $\delta x < -10^{-6}$. The medial-lateral condition had the region of activity displaced to one side (Table 4.2), with the activity centred about the plane x=32.1 mm. The x-component for the whole-muscle force was increased for this condition ($\delta x \approx -3 \times 10^{-3}$): this value was still small, however, there was a more substantial increase in the
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Figure 4.3: Stress contours and force magnitudes and directions for the 12 test conditions. The scales are shown in Figs. 4.2 (B) and (C).
x-component of the centre of force (Table 4.2) acting at the end of the aponeurosis (to $x=31.3$ mm).

### 4.4 Discussion

The *in silico* isometric contractions of human gastrocnemius in this study show decreases in muscle fibre length and increases in pennation (Figure 4.2 A-B) in a similar manner to *in vivo* reports [15]. In addition, the *in silico* muscle belly thickness decreased during contraction in a manner more representative of *in vivo* measurements from the medial gastrocnemius [15]. The simulated muscle belly thickness decreased because a component of the contractile force of the muscle fibres acts to compress the muscle between the aponeuroses, and this was balanced by increases in the width of the muscle belly (Figure 4.2 C-D) to maintain the nearly incompressible behaviour of the muscle tissue. Compressing the muscle belly would cause increases in intramuscular pressure, and this in turn drives increases in the curvature of the muscle fibres (Chapter 3 and [65]). Indeed, in our simulations the initial configurations of the fibres were straight, and this changed to curved S-shapes during contraction. The width of the simulated muscle belly increased at its mid-point during contractions more than the width of the aponeuroses (Figure 4.2 C-D), and so the belly bulged outwards to the sides. A consequence of this bulging was that the planes across which the fibres were initially aligned (parallel to the yz plane) transformed to curved sheets during contraction. Sejersted and co-workers [127] observed curved fascicle sheets in the vastus lateralis of human cadavers and have suggested the arrangement of fascicle sheets in an onion-like arrangement, and recent 3D reconstructions of fibre curvatures have also demonstrated that the fibre trajectories in both the medial and lateral gastrocnemius curve around concentric sheets during contraction [112]. Despite the simplistic initial geometry (Figure 3.1) of the muscle in these simulations with straight fibres and rectangular aponeuroses, an emergent feature from the simulations for the fibres was to develop curved trajectories in 3D, and this has been suggested to be an important property to maintain mechanical stability within the muscle [65].

All the *in silico* conditions in this study had an equivalent level of muscle activity with an average of 10% activity across the muscle fibres (see Table 4.1) in the contracting state.
However, both the magnitude and direction of the force (Figure 4.3) varied with the different regionalizations of the muscle activity. All conditions with regionalized activity resulted in greater muscle forces than for the condition with uniform activity across all fibres, and they also showed localized decreases in thickness, fascicle length and larger pennations around their active regions. These results are consistent with findings by [68] that compared the level of force in a uniformly fully active muscle with muscles where half the fibres were fully active: they activated the fibres in one end of the muscle and noted that the muscle force was 14% greater than expected from the average activity level. There was a pronounced increase in the muscle force for the non-uniform pattern of activation in the proximal-distal model (Figure 4.3); this could be due to specific changes in the shape of the muscle belly compared to other activity patterns, where the active region decreased in thickness more than the inactive region, and the muscle bent around the region where the activity levels transitioned. Here, we additionally show that changing the regionalization of the activity results to changes in the direction of the force vector from the whole muscle (Table 4.2), and this would result in different directions of the muscle torque in the joints that it spans, explaining experimental observations for the lateral gastrocnemius in the cat [36].

The increases in aponeurosis stiffness in these in silico contractions resulted in decreased aponeurosis stretch and muscle fibre strain, and smaller increases in pennation of the fibres. These changes resulted to increases in the magnitude of the force (Figure 4.3) developed by the whole muscle. These results are consistent with previous finite element models of the biceps femoris in which aponeurosis dimensions were changed with conditions that had stiffer aponeuroses, resulting in reduced fibre strains [77]. In another study, a finite element model of the medial gastrocnemius from the cat demonstrated that increased aponeurosis stiffness resulted in greater muscle forces for isometric contractions [143], again consistent with our results. The combined findings from these three modelling studies show that the interactions between the muscle fibres and the connective tissue are important for shaping the mechanical output from the whole muscle. Our simulations additionally demonstrate how the direction of the muscle force is affected by the stiffness of the aponeurosis (Figure 4.3), presumably due to the changes in the shape of the muscle belly and force transmission that are caused by the different aponeurosis properties.

In our simulations the aponeurosis was included in an unrealistically thick (3 mm) state.
for computational simplicity, however the material properties of the aponeurosis was scaled so that its overall stiffness matched that expected for the \textit{in vivo} condition. The thickness in the aponeurosis in our simulations allowed us to observe gradients of stress in the thickness direction (y-direction) that change with the aponeurosis stiffness. The simulations showed a reduced muscle fibre strain near the ends of the muscle where the fibres are structurally close to the fixed-end boundary condition and pull against the stiff aponeurosis. It is possible that removing the fixed boundary constraints, for instance by including the external tendon, would reduce this effect in future studies. Our \textit{in silico} results show that the stress in the aponeurosis increased for the stiffest conditions, with the highest stress being more concentrated towards the outer layers of the aponeurosis (Figure 4.3), and it is possible that this indicates increases in the risk of injury initiation at areas closer to the outer surface of the aponeurotic sheets.

The results from this study highlight that the mechanical output of a whole muscle should not simply be considered to be a scaled-up muscle fibre that matches the size of the whole muscle [133], or a simple sum of actions of all the individual muscle fibres [144], but instead depends on the complex interactions between the muscle fibres and connective tissues that is brought about by the 3D structure of the muscle. In particular we show how the effect of regionalizing the muscle activity to a particular volume of muscle fibres causes changes to both the magnitude and direction of the whole muscle force, even when the mean level of muscle activity remains unchanged.

In summary, our simulations indicate that muscles with stiffer aponeuroses would result in smaller aponeurosis stretches and muscle fibre shortening. This effect would place the muscle fibres at a longer length on the ascending limb of their force-length curves, allowing them to develop greater stress and force. Additionally, as the stretch in the aponeurosis is reduced, the muscle fibres did not increase in their pennation angle as much during contraction. The simulations of regionalized and non-uniform activation patterns caused local differences in the shape of the muscle belly, strains and orientations of the muscle fibres. These factors affect both the magnitude and direction of the resultant muscle force.
Chapter 5

The effect of intramuscular fat on skeletal muscle mechanics: implications for the elderly and obese

5.1 Introduction

Skeletal muscle provides the forces that are necessary for the maintenance of body posture and for driving body movements for our activities of daily living. Muscle forces depend partly on the structural features [7] of the muscle that include fibre length, the pennation angle of the fibres relative to the line of action, the number of fibres and their physiological cross-sectional area [121]. Muscles forces additionally depend on the base material properties of the muscle tissue, but much less is know about this. The structural and material properties of muscle vary between muscles and individuals [9, 145] but can also change through our lifespan [4] and can be affected by disease (e.g., [6]). The purpose of this study was to investigate how the inclusion of fat within a muscle belly can affect its force output.

Intramuscular fat accumulates both in (intramyocellular) and out (extramyocellular) of the muscle fibres. Healthy muscle contains about 1.5 % of intramyocellular fat and this can increase to over 5 % in the obese [146]. The total intramuscular fat additionally
contains extramyocellular components, and so the total intramuscular fat may exceed these values. Additionally in the obese, the muscles may remodel by hypertrophy to a larger size [147], and experience a transition to faster fibre-types [146]. It has previously been shown that obesity can result in reductions in joint specific-torque (relative to lean or total body mass [148, 149]), but we do not know the effect of intramuscular fat and its distribution on individual muscle mechanics, or the mechanisms that may cause deterioration of such performance.

Intramuscular fat can also increase as we age, and can reach about 11 % in the elderly [150]. Ageing also results in progressive muscle wasting called sarcopenia [151] that results in reductions in size, strength and a transition to slower fibre-types [4]. Additionally, the lower levels of physical activity that accompany obesity in the elderly have been shown to accelerate muscle atrophy [152]. Also, connective tissue (tendon and aponeurosis) properties change as well. Despite earlier experimental studies suggesting no effect [153] or an increase [154] in tendon stiffness with ageing, recent studies have reported a decrease in stiffness [155, 140, 156] of human tendons in the elderly. However, less is known about age-related changes to the aponeurosis stiffness.

Experimental measures of intramuscular fat have been achieved with a variety of imaging [150, 157, 158] and biochemical techniques [146, 159]. However, in order to understand the mechanisms that may affect the fat-dependent loss of contractile performance, it is helpful to model the mechanical effect of fat inclusions within a muscle. Here, we test the effect of fat on skeletal muscle performance within a 3D finite-element model that is based on the physics of continuum mechanics and represents the muscle as a composite biomaterial. A range of model variants were tested that represent the inclusion of intra- and extracellular fat. We additionally report on the influence of muscle structure and connective tissue properties on the deterioration of performance.

5.2 Methods

5.2.1 Geometries, boundary conditions and muscle activations

The effect of fat inclusions was studied for the gastrocnemii. These ankle plantarflexor muscles were chosen because the plantarflexors have been shown to have greater loss of
Figure 5.1: Sample geometries of simplified human lateral gastrocnemius (LG) muscle with initial pennation of $10^\circ$ (A) and $20^\circ$ (B). Note that the change in cross sectional area is only due to initial pennation because the fibre length and belly length are constant. Muscle tissue is shown in light gray and aponeuroses in dark gray. The belly and aponeuroses extended out of plane to a width of 55 mm.

A simplified geometry of the human gastrocnemius (lateral or medial head) belly was used. Based on a recent study [118] using ultrasound imaging of young and elderly plantarflexor muscles, the initial fibre length (65 mm), initial belly width (55 mm) and length (273 mm) were kept constant for all the simulations (Figure 5.1). The same study also showed that the initial pennation decreases with age and results in smaller physiological cross-sectional area (PCSA) of the muscle. However, muscle pennation may increase with obesity [147]. Here we have chosen a parallelepiped geometry for the muscle (similar to Chapter 3) with a range of pennation angles representing sarcopenic ($10^\circ$), healthy ($15^\circ$) and obese ($20^\circ$) states. The finite element grid had 2772, 3696 and 4620 elements (muscle and aponeurosis combined) for geometries with $10^\circ$, $15^\circ$ and $20^\circ$ pennation, respectively. Each element had 27 integration (quadrature) points and fibre bundles passed through sets of integration points within the muscle tissue. Despite the change in the number of muscle tissue elements between different geometries, the number of muscle fibre bundles was the same and equal to 4158.
The muscle belly was fixed at the muscle-tendon junctions before uniformly activating
the muscle fibres. The activation was ramped up from zero towards a fully active muscle.

5.2.2 Material properties

The base- and along-fibre properties of the fibre reinforced composite muscle and
aponeuroses and nonlinear isotropic properties of fat tissue are previously described in
Chapter 2.

For the case of $X\%$ intracellular fat infiltration the isochoric (volume preserving)
component of the strain energy $W_{\text{iso}}$ (equation 2.16) for fatty muscle can be written as:

$$W_{\text{iso,fatty muscle}} = W_{\text{muscle}} + (1 - \frac{X}{100}) \times W_{\text{base,muscle}} + \frac{X}{100} \times W_{\text{fat}}. \quad (5.1)$$

Here $W_{\text{muscle}}$ is the muscle along-fibre strain-energy and $W_{\text{base,muscle}}$ is the base muscle
strain-energy. Also, whenever assuming an $X\%$ loss of contractile elements of the fibres,
the $W_{\text{muscle}}$ component of isochoric strain energy was reduced by a factor of $1 - \frac{X}{100}$.

The incompressibility constant, $\kappa$, for the volumetric part of the strain energy $W_{\text{vol}}$
(equation 2.15) was chosen to be $\kappa_{\text{fat}} = 0.25 \times 10^6$ for fat. This was based on the fat
compressibility properties used in modelling the human heel pad [109]. $\kappa_{\text{fat}}$ had a smaller
value than the muscle tissue ($\kappa_{\text{muscle}} = 1.0 \times 10^6$) indicating that it is more compressible.
In this study, the volumetric part of the strain energy for $X\%$ intracellular fat accumulation
had the form of:

$$W_{\text{vol,fatty muscle}} = [(1 - \frac{X}{100}) \times \kappa_{\text{muscle}} + \frac{X}{100} \times \kappa_{\text{fat}}] \left[ J^2 - 1 - 2 \log(J) \right], \quad (5.2)$$

where $J$ is the determinant of the deformation gradient tensor and represents dilation
(see Chapter 2). The implementation of combined tissue (e.g. fatty muscle) in the
modelling framework is explained in section 2.8.3. The deep and superficial aponeuroses
were assumed to have the same material properties in these simulations and had a
stiffness level that was either compliant, normal or stiff (Chapters 2 and 4).

5.2.3 Distributions (model variants) and intensities of intramuscular fat
accumulation

The properties of the transversely isotropic muscle tissue were changed in six model
variants. Lean muscle (M1-M2) had no fat in the muscle base material or between the
fibres. For the other four model variants an $X\%$ accumulation was introduced into muscle, where the effects of fat were simulated differently. Variations of the model are: (M1) Lean muscle (no fat) with 100% along-fibre properties (AFPs) in muscle fibres; (M2) lean muscle with $X\%$ reduction in AFPs; (M3) muscle with $X\%$ fat in the base muscle material and 100% AFPs; (M4) muscle with $X\%$ of fat in the base muscle material and $X\%$ reduction in AFPs; (M5) muscle with a random and sparse distribution of $X\%$ pure fat ($W_{iso} = W_{fat}$, $κ = κ_{fat}$) at the integration points dispersed within the lean muscle tissue; and (M6) muscle with a random and sparse distribution of $X/2\%$ pure fat points, $X/2\%$ of fat in the base muscle material and an $X/2\%$ reduction in AFPs. M1 represented a control condition for lean muscle. M2 was a lean muscle with a loss of AFPs, M3 and M4 were models with intracellular fat, M5 represented extracellular fat and; M6 contained a combination of intracellular and extracellular fat. The different variations of the model are summarized in Table 5.1. The sparse distributions of fat in the M5 and M6 models were chosen such that fat was not contained in adjacent integration points, and we assumed that the sparse distribution had a negligible effect on the fibre orientations in the belly.

<table>
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<th>Model</th>
<th>Base Muscle Properties (%)</th>
<th>Fat properties (%)</th>
<th>Contractile Elements (%)</th>
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<tr>
<td>M1</td>
<td>100</td>
<td>-</td>
<td>100</td>
<td>-</td>
</tr>
<tr>
<td>M2</td>
<td>100</td>
<td>-</td>
<td>100-X</td>
<td>-</td>
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<td>100-X</td>
<td>X</td>
<td>100</td>
<td>IMC</td>
</tr>
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<td>M4</td>
<td>100-X</td>
<td>X</td>
<td>100-X</td>
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<tr>
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<td>100-X/2 (muscle points)</td>
<td>100 (for $X/2$ fatty points)</td>
<td>100-X/2 (muscle points)</td>
<td>IMC &amp; EMC</td>
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Table 5.1: The model variants for $X\%$ fat infiltration in the muscle. Fatty variants (M3-M6) represent possible intramyocellular (IMC) and extramyocellular (EMC) fat distributions.

Three levels of fat were used for the models M3-M6, having 2, 10 or 20%. The 2% fat represents a healthy condition, with higher levels reflecting the increased intramuscular fat in the elderly and obese. As an example, Figure 5.2 shows a muscle with 15° pennation angle and 20% sparse fat distribution (M5 variant). The dots show the positions of the integration points with aponeuroses (gray), muscle (red) and fat (yellow) properties.
which is a M5 variant at a 20% fat level.

5.2.4 Calculated parameters and analysis method

The resultant force ($F$) at the muscle-tendon junction, mean pennation angle relative to aponeuroses and mean fibre length were calculated to assess structural changes and performance of the muscle in the simulated scenarios.

To accommodate the effect of different initial pennation on the force that muscles with different physiological cross-sectional area (PCSA) can develop, the force ($F$) was normalized by the PCSA of the muscle to give the specific-force. Here the PCSA is defined as:

$$\text{PCSA} = \frac{V_{\text{muscle}}}{l_{\text{fibre}}} = w \times \sin(\beta) \times \left[l_{\text{belly}} - l_{\text{fibre}} \times \cos(\beta)\right],$$

(5.3)

where $\beta$, $V_{\text{muscle}}$, $l_{\text{fibre}}$, $l_{\text{belly}}$ and $w$ are the initial values for pennation, muscle tissue volume, fibre length (65 mm), muscle belly length (273 mm) and muscle width (55 mm), respectively.

5.2.5 Data Analyses

We ran ten iterations of the M5 randomized distribution for a particular combination of the other three factors, namely $15^\circ$ pennation, 10% fat and normal aponeuroses stiffness. At 20% activity level, the coefficients of variations (standard deviation/mean) for the force, specific force, fibre stress, final fibre length and pennation were 0.2, 0.2, 0.2, 0.01 and 0.03%, respectively. Since the values for coefficients of variation were small for the randomized variants of the model (M5-M6), we used the result of only one instance of each combination of randomized model variants, fat level, pennation and aponeuroses stiffness.

The effects of fat level ($X$), model variant (M1-M6), initial pennation ($\beta$) and aponeurosis stiffness ($k$) (factors) on the force, specific force, fibre stress, final fibre length and final pennation (response variables) were compared by their least square means (adjusted means) of the deterministic muscle model responses (JMP 11.0, SAS Institute Inc., Cary, NC, USA).
Figure 5.3: The clump fat simulation. The integration points for a 15° muscle geometry (A) with cutting planes corresponding to transverse (B) and longitudinal (C) sections of the muscle. The muscle points are shown in red, fat points are in yellow and aponeurosis points are shown in gray. The deformed shape of the muscle belly at 20% activity (D) is coloured with a contour showing the magnitude of the displacement of the integration points. Comparison of the muscle belly force for simulations with the same initial geometry and connective tissue properties, and X=10 between the clumped-fat simulation, the lean variants M1-M2 and variant M5 that had a sparse distribution of extracellular fat (E).
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5.2.6 Fat clump simulation

A further model was simulated that included 10% fat as a concentrated clump inside the muscle belly. The clump of fat in the muscle belly was a tube extending for 16 elements along the length of the belly and had a symmetric and polygonal cross-sectional area (Figure 5.3A-C). Fibre orientations at integration points up to two elements from the fatty clump were changed so that the fibres curved smoothly around the fatty clump. This simulation was run with a 15° pennation muscle belly and normal aponeuroses stiffness. It was similar to M5 apart from the fat being clumped into the centre of the muscle belly and the minor deviations to the neighbouring muscle fibre directions.

5.3 Results

The simulations were for an isometrically contracting muscle belly. As the activation level increased the fibres shortened and expanded in their transverse direction, rotating to greater pennation angles and causing the aponeuroses to stretch as they became loaded. The maximum activation level that could be simulated varied between conditions (Figure 5.4), and so the data analyses were performed at a 20% activation that was common to all simulations (Figure 5.5). The fibre stresses at 20% activation reached up to 17% of the maximum isometric stress of 200 KPa, but were reduced in cases of low initial pennation, reduced aponeurosis stiffness and increased fat accumulation.

The increased initial pennation of the muscle was a major factor for greater muscle force. The geometries with higher pennation angle, and therefore larger PCSA, developed higher forces at each level of activity. For instance, the mean force for 10° pennated muscle geometry was 41% less than the 15° pennated geometry. When the effect of increased PCSA was removed, by calculating the specific-force (force/PCSA) of the whole muscle and the stress of the muscle fibres, it was seen that changes in specific-force and fibre stress showed similar patterns to the changes in muscle force (Figure 5.5). Therefore, despite normalizing the force by the PCSA, the effects of pennation change still persisted on the specific force and fibre stress. The extent of fibre rotation and shortening as well as the muscle belly force depended on the aponeurosis stiffness. A stiffer aponeurosis resulted in smaller rotation and shortening of the fibres and an increase in the force and stress (Figure 5.5).
Figure 5.4: Force-activation plots for the different variants M1-M6. Lines show variant M1 (black circles), M2 (red diamonds), M3 (blue squares), M4 (green triangles), M5 (purple inverted triangles) and M6 (orange stars) at 2% (A), 10% (B) and 20% (C) fat levels.
There was an effect of the model variant (fat and muscle distribution) used in the simulations on the muscle force and stress of the muscle fibres. However, there was no effect of the model variants on the final pennation angle of the muscle fibres. A reduction in the along fibres properties showed a decrease in the belly force: for example the M2 variant with 15° pennation muscle, normal aponeurosis stiffness and a 10% reduction in AFPs (X=10%) showed an 11.3% decline in force compared to the lean M1 variant (Figure 5.3E) at 20% activity. The longer fibre lengths for the fatty models would predispose them to greater forces due to their force-length properties (see Chapter 2), however, the force and stress were reduced due to the intramuscular fat despite this effect (Figures 5.4-5.5). For example, a 15° pennation muscle with normal aponeuroses stiffness showed an average of 25% and 45% decrease in force for 10% and 20% of fat accumulation, respectively. Despite the substantial effect of fat on muscle force, specific-force, fibre stress and final fibre length, there was no effect of the percentage of fat on the final fibre pennation.

The simulation with 10% fat clumped in the centre of the muscle belly showed a lower force (60.1 N) compared to the lean variants M1-M2 (80.4 N and 72.2 N, respectively), however the force from the clumped fat simulation was greater than for the M5 variant (48.8 N) that had 10% of extracellular fat distributed across the muscle belly (Figure 5.3D).

## 5.4 Discussion

Fat accumulation in skeletal muscles is a common phenomenon in ageing and obese populations. Studying the effect of fat infiltration on the mechanical performance of human skeletal muscles is an experimental challenge since muscle forces cannot be measured directly. In addition, it is impossible to experimentally manipulate factors such as connective tissue stiffness, fibre pennation and the percentage and distribution of fat that affect muscle performance in the elderly and obese populations. In this work we used a model to uncouple the effect of such factors on muscle belly force output. This study focused on the human plantarflexor gastrocnemii muscle group as a major contributor to human balance and locomotion.

Skeletal muscle models have previously used to study the effects of ageing and obesity on human locomotion. Thelen in 2003 [161] introduced a framework for
comparing young and elderly dorsi- and plantarflexor muscles performance during isometric and isokinetic contractions. He showed that elderly muscle with 30% decrease in maximum isometric strength, 20% decline in maximum contraction velocity and an increased deactivation rate of 20% compared to young models had about 40% or more decline in ankle torque and power. In another study [162], a decline in maximum contraction velocity and maximum isometric force, an increase in muscle stiffness and altered shape of force-length curve were predicted when mechanical properties of the elderly muscle were estimated using an inverse dynamics optimization technique. In case of the obese population, a recent modelling study [163] estimated that an increase in gastrocnemii force and a decrease in vasti muscle group force would occur with altered gait patterns of obese people. Despite the similarities of our results such as increase muscle tissue stiffness due to fat accumulation and increase in gastrocnemii muscle force in obese muscle with larger PCSA, the previous modelling studies addressing muscle performance in ageing and obesity used point to point muscle models that had no base-material representation, and this limits the study of muscle structural parameters and the effect of fat accumulation. In previous three-dimensional finite element modelling frameworks for active skeletal muscle (e.g. [59, 70, 69]), the heterogenetic effects of fat accumulation have not been considered. However, Hodgson et al. [164] used a finite elements model to show that increases to the stiffness of the base material resulted in decreased muscle force. This model was essentially 2D and unable to account for the transverse bulging of the fibres that is known to occur [119], and the base material was not modelled using known fat properties; however they parallel our modelling results.

In this study, the simulations tested three different muscle geometries that varied by their pennation. The geometries with higher initial pennation had more muscle fibres acting in parallel, and thus they had greater physiological cross-sectional areas. It is known that muscle force increases with PCSA [7, 165], and indeed the models with higher PCSA generated greater force (Figure 5.5). The force was normalized by the PCSA to result in the specific-force, and this is similar to the term “muscle quality” that is the force a muscle can produce per unit of its size [166, 167]. The specific-force showed changes to the simulation parameters that mirrored the changes in absolute force (Figure 5.5), although at a lower magnitude, and indeed these patterns were also reflected at the level of the fibre stress. Thus, the inclusion of intramuscular fat and changes to aponeurosis stiffness
<table>
<thead>
<tr>
<th>Fat %</th>
<th>Model variants</th>
<th>Initial pennation (°)</th>
<th>Aponeuroses stiffness</th>
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<tbody>
<tr>
<td></td>
<td>M1</td>
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<td>M2</td>
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<td>M6</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Specific force (Pa)</th>
<th>Final fibre length (mm)</th>
<th>Force (N)</th>
<th>Fibre stress (Pa)</th>
</tr>
</thead>
<tbody>
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<td>57</td>
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<td>59</td>
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<td>61</td>
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Figure 5.5: Main effects of the fat level, model variant, pennation and aponeurosis stiffness on the final pennation, muscle fibre length, stress and force. Points show the least-squares means, with their standard errors.
changed the muscle quality independent of the effect of the muscle size or PCSA. Thus, intramuscular fat and aponeurosis stiffness are important factors that affect the contractile performance of muscle. The fatty models (M3-M6) generated specific-forces that were lower than for the lean models (M1-M2). However, the fatty models generated these forces at longer fibre lengths (Figure 5.5). The fibre lengths for the fatty models were closer to their optimum length of 65 mm (Figure 5.1). Due to the force-length properties of the contractile elements (see Chapters 1-2 and also [18]), these longer fibre lengths would predispose the fatty models to generate higher forces, but this was not the case. Thus, the fatty models generated lower specific-forces despite, and not because of, their longer fibre lengths.

A reduction in the number of contractile components within the muscle caused a decrease in the muscle force, and this can be seen in the change from M1 to M2 (Figure 5.5). However, not only does the muscle force depend on the contractile components but also on the nature of the interaction between the contractile components and the base material within the muscle. Fat has stiffer material properties than muscle [108, 109], and thus the introduction of fat into the muscle resulted in a stiffer base material, and this increase in stiffness would act to resist the muscle fibre shortening and transverse bulging. The fatty models all showed lower specific force than the lean models, even for equivalent along-fibre properties (Figure 5.5), and this is due to the increase in stiffness of the base material due to the inclusion of fat. These results support experimental findings that report a loss of muscle quality in both the elderly [166, 167] and obese [168], and show that one of the causes for such a loss in contractile performance is the increase in muscle belly tissue stiffness as the concentration of intramuscular fat increases.

The simulation with a single clump of fat (Figure 5.3) within the muscle belly showed a reduced force compared to the lean muscle, but the reduction was not as pronounced as when the same amount of fat was dispersed throughout the muscle, as in model M5. The clump of fat acted to separate the medial and lateral aspects of the muscle within the middle of the muscle belly: if the muscle were totally divided into two halves, then it would be expected that the force from each half would be half the value for the lean muscle, and that the two halves combined would then be the same as for the lean condition, but this was not the case. This results shows that the distribution of fat through the muscle will alter the muscle force. The actual distribution of fat would likely be somewhere between
the extremes that we have tested here: between a fine but uniform distribution to a single clump containing the entire amount of intramuscular fat. There are currently little data to inform the exact nature of fat distribution within skeletal muscle, and for this reason we did not focus on testing a range of possible intermediate fat distributions. It will be important to experimentally quantify fat distributions in different populations if we are to fully understand the impact of intramuscular fat on the contractile mechanics of muscle.

The simulations show that muscles with more compliant aponeuroses generate lower forces (Figure 5.5) and this is consistent with the simulations reported in Chapter 4. For the more compliant aponeuroses, the aponeurosis would stretch more allowing the fibres to rotate to greater pennation angles and shorten to shorter lengths. These simulations all started with the muscle fibres at their optimal length, and so the reduction in fibre length would result in lower fibre stress as seen in Figure 5.5. The whole muscle force would be further reduced by the greater pennation for the fibres in their active state, although this effect is relatively minor. It is not totally clear if there are general changes to the aponeurosis stiffness as we age, although the consensus would suggest that the aponeurosis stiffness is reduced in the elderly [155, 140, 156]. Thus, this effect of increased aponeurosis compliance causing reductions in muscle force may be a contributing factor to the reduction in muscle forces that occur in the elderly.

In conclusion, a mathematical modelling framework was used to simulate the effect of intramuscular fat on muscle force, to predict its effect for the elderly and obese. Both the concentration of intramuscular fat, and the stiffness of the aponeusoses were shown to have an important effect on the muscle fibre stress and the whole muscle force. The effect is partly due to the increased stiffness of the base material properties that affect the extent of fibre shortening, lateral expansion of the fibres and thus their interaction with the aponeuroses. The simulations in this study (M1-M6) were for muscle with uniform distributions of activity and intramuscular fat. It should be remembered that muscle force additionally depends on regional variations in muscle activity (Chapter 4 and [36]), fat distribution (Figure 5.3) and fibre-type composition [23, 169], and that the muscle contribution to joint torque also depends on its moment arm that can vary with ageing and obesity [170, 171]. Nonetheless, the results from this study show that the inclusion of intramuscular fat and the base material properties of the muscle tissue have an important effect on muscle force.
Chapter 6

Conclusion and future work

The purpose of this thesis was to study some aspects of the structural and functional mechanisms that affect the mechanical behaviour of muscle-tendon units. Phenomena such as regionalization of muscle activity, changes in connective tissue stiffness and changes in muscle architecture and tissue compositions were studied in this work. These studies were performed by utilizing a three-dimensional (3D) finite element modelling framework, specifically developed for this thesis. This chapter summarizes the work presented in the previous chapters, discusses the similarities and differences of this work with previous studies, the novel methods and approaches used and current difficulties in studying skeletal muscle using similar frameworks. Finally, suggestions will be presented for possible future studies based on the experience gained in this work.

6.1 Summary of the thesis

The physiological and biomechanical properties of muscle contractions such as force development, muscle activation, and the intrinsic properties of muscle, tendon and aponeurosis tissues were discussed in Chapter 1. This chapter also included a review of some of the structural parameters that are known to influence muscle function. The relationships between the structural and functional characteristics of skeletal muscles and their mechanical output were briefly explained and supported with experimental evidence from literature. A separate section in Chapter 1 was used to summarize existing biomechanical modelling approaches for studying skeletal muscle function. The versatility in the skeletal muscle modelling approaches, achievements and deficits in simulating
Chapter 6. Conclusion and Future Work

Starting from a continuum description of a nearly-incompressible fibre-reinforced biomaterial in Chapter 2, we presented constitutive laws that encapsulate many of the commonly known properties of the muscle-tendon unit. The tissue stress tensors were defined based on strain-energy functions that possess the transverse symmetry associated with muscle, tendon and aponeurosis. We explicitly included the fibre orientation into the strain energy functions using the invariants of the Cauchy-Green deformation tensor. These invariants also provided other contributions to the strain energy functions that encode information on the local tissue properties. Eventually, we used the principle of stationary strain energy to introduce a discrete form of the three field formulation (equation 2.11) with displacement, pressure and dilation as the independent fields. This resultant nonlinear equations were iteratively solved at each time-step using a Newton-Raphson scheme. The introduced computational framework was then used to study the physiological problems of interest in this thesis in Chapters 3 to 5.

The purpose of Chapter 3 was to validate the represented biomechanics of the muscle-tendon unit (MTU) using the 3D finite element modelling framework introduced in Chapter 2. We simulated contractions for an idealized medial/lateral gastrocnemius muscle in human. Simulations were performed to test the force-length relation of the whole muscle, to evaluate the changes in internal fascicle geometry during contractions, and to assess the importance of material formulations for the aponeurosis and tendon. The simulation results were compared to previously published experimental values. The force-length curve for the whole muscle showed a realistic profile. As the muscle contracted, the fascicles curved into S-shaped trajectories and curled around 3D paths, both of which matched previous experimental findings. As the fascicles shortened they increased in their cross-sectional area, but this increase was asymmetric with the smaller increase occurring within the fascicle-plane: the Poisson’s ratio in this plane matched that previously shown from ultrasound imaging. The distribution of strains in the aponeurosis and tendon were shown to be a function of their material properties. This chapter demonstrated that the model could replicate realistic patterns of whole muscle-force, and
changes to the internal muscle geometry, and so will be useful for testing mechanisms that affect the structural changes within contracting muscle.

Skeletal muscle can contain neuromuscular compartments that are spatially distinct regions that can receive relatively independent levels of activation. The study in Chapter 4 tested how the magnitude and direction of the force developed by a whole muscle would change when the muscle activity was regionalized within the muscle. The 3D finite element framework introduced in Chapter 2 was used to develop a model of a human gastrocnemius muscle with its bounding aponeuroses, and isometric contractions were simulated for a series of conditions with either a uniform activation pattern, or regionally distinct activation patterns. In all cases, the mean activation from all fibres within the muscle reached 10%. The models showed emergent features of the fibre geometry that matched physiological characteristics: fibres shortening, rotating to greater pennation, adopting curved trajectories in 3D and changes in the thickness and width of the muscle belly. Simulations were repeated for muscles with compliant, normal and stiff aponeurosis. The aponeurosis stiffness affected how the fibre geometry changed, as well as the resultant muscle force. Changing the regionalization of the activity resulted in changes in the magnitude, direction and centre of the force vector from the whole muscle. Regionalizing the muscle activity resulted in greater muscle forces than when uniform activity was simulated across the muscle belly. The chapter shows how the force from a muscle depends on the complex interactions between the muscle fibres and connective tissues and the region of muscle that is active.

Skeletal muscle accumulates intramuscular fat through age and obesity. Muscle quality is a measure of muscle strength per unit size and decreases in these conditions. It is not clear how fat influences this loss in performance. Changes to structural parameters (e.g. fibre pennation and connective tissue properties) affect the muscle quality. The study presented in Chapter 5 investigated the mechanisms that lead to deterioration in muscle performance due to changes in intramuscular fat pennation and aponeurosis stiffness. A finite element model of the human gastrocnemius was used for the purpose of this study. The base-material properties were modified to include intramuscular fat in five different ways. All the model variants with fat generated lower fibre stress and muscle quality than their lean counterparts. This effect is due to the higher stiffness of the muscle tissue in the fatty models. The fibre deformations influence their interactions with the aponeuroses, and
these change with fatty inclusions. Muscles with more compliant aponeuroses generated lower forces. The muscle quality was further reduced for muscles with lower pennation. This study shows that whole muscle force is dependent on its base-material properties and changes to the base-material due to fatty inclusions result in reductions to force and muscle quality.

### 6.2 Discussion on research contributions

We reviewed some of the state-of-the-art continuum models of skeletal muscle in Chapters 1 and 2. We will now discuss the key differences in the physiological and mathematical aspects of the work presented in this thesis in comparison to those models. In addition, we will compare our findings in the area of muscle mechanics with previous experimental studies.

In this thesis we used a three-field formulation for the nonlinear elastic response of a quasi-incompressible material, based on the work of Simo et al. [172]. Their method has been in use in last twenty years as the basis of some of the continuum mechanics models of soft tissue (e.g. [59, 88]). While different models use modified or completely different approaches to solve the problem, the difference between the outcomes of the many models [59, 70, 69, 164] are mostly due to their definitions of strain-energy functions for the transversely isotropic material. As described in Chapter 2, the strain-energy functions represent the along-fibre, base and nearly incompressible properties of the soft tissue. The differences arise in the representation of these functions. The first major difference is whether they are presented as functions of the invariants of the Cauchy-Green deformation tensor (e.g. Chapter 2, [59]) or not (e.g. [70]). The second difference is based on the choice and use of invariants in representing the strain energy: the physically-motivated invariants used by Criscione et al. [85], [59]) or the classical invariants (e.g. [96, 97]).

Here, we chose simple models based on the classical invariants (e.g. the Neo-Hookean, Yeoh and Humphery models) for the base properties. Indeed, we allowed for different tissue to have different models. This approach is unique to this thesis. Additionally, we derived the derivatives of the along-fibre strain-energy using stress-stretch curves fitted to experimental data (similar to [59, 88]). We used the
simplicity of the base material models to our advantage when we selected the fitting curves for along-fibre properties of the modelled biomaterials. The curves were fitted to the experimental data that were collected from the specific muscle-tendon unit (human gastrocnemius) under study in this thesis. Extra care was taken to have accurate and continuous fits of the data. While we recognize the importance of the physically based invariants [85] in connecting the experimental data directly to the mathematical description of the tissue properties, we also believe there are insufficient data for specifically muscles along- and cross-fibre stretch as well as along-fibre shear to fully implement them.

While our model was shown to mathematically predict the deformations of a nonlinear quasi-incompressible material accurately, we also needed to show that the chosen material properties are able to predict the changes in structure and function of skeletal muscles when activated similar to experimental studies. A comparison between the simulation results with experimental results is presented in Chapter 3. Similar steps have been done for other modelling frameworks (e.g. [59]). This is a crucial validation step in mathematical modelling of skeletal muscles and must be repeated when models are developed for different muscle-tendon units in the body. In other words, while any validated model would most probably be mathematically valid when used for a different muscle-tendon unit, the simulation results for biomechanical response of the new specific MTU need to be reevaluated; and if necessary, adjustments should be made to material properties describing the tissues.

We introduced an activation transition function between the active and inactive regions of the muscle tissue in Chapter 2. This novel approach allowed the use of a simple grid and enabled simulations of submaximal activity in different regions in a skeletal muscle model (Chapter 4). In addition to a previous experimental study that showed regionalized activities would change muscle function by producing different torques around a joint [36], our simulation results showed that substantial differences can arise in the magnitude of force of a single muscle, when the activity is regionalized. While a previous modelling study had shown the differences in force for the regionalized activation patterns [68], our work additionally benefits from a three-dimensional and architecturally detailed framework. We suspect that the greater difference in force levels across activation patterns, compared to the previous modelling study [68], was due to the differences in modelling techniques.
between the two works.

To demonstrate the capacity of the current framework to encompass mixed material properties (fat and muscle) and to investigate the effect of fat accumulation on the skeletal muscle function, we developed lean and fatty variants of the human gastrocnemius muscle (Chapter 5). The results show not only that the fatty muscles in the elderly and obese humans have smaller output force than the lean muscles but the distribution of fat also plays a role in the amount of this force deficit. The fat accumulation added an intrinsic stiffness to the muscle tissue that interfered with force transmission to the aponeurosis and eventually the tendon. This finding explains one of the reasons that measured human plantarflexor muscle torques in the elderly and obese are reported to be lower than in healthy young adults.

The preparation, development and results of this thesis has brought insight into the role of modelling in biology and physiology of skeletal muscle. The modelling not only answers questions that are hard to measure in experiments such as regionalizing activity in skeletal muscles (see Chapter 4), it can also point out the beneficial effects of different tissues possessing different material properties. For example, we showed that the difference in aponeurosis and tendon stiffness is a possible mechanism for the transmission of a higher force from the muscle belly to the tendon (see Chapters 3 to 5). The lack of established experimental data to develop more realistic models is a major constraint for current modelling frameworks. This was the case for this study as well, where parameters related to some of the mechanical behaviours of different tissues were chosen based on experimental data where available, and physiologically-based assumptions otherwise.

A major outstanding challenge is the incorporation of dynamic contraction effects, and this will be addressed in future work. The challenges in incorporating the fast and slow fibre properties include the common problem of lack of information on the distribution fibre types in the muscle belly, the need for accurately calculating the along-fibre contraction velocity by differentiation of the displacement field and the large difference in the force of fast and slow fibres when the belly is contracting at a certain velocity. The velocity calculations depend on the ability to solve the more complex nonlinear system which arises for small time-steps.

This thesis brought novel contributions such as:
• Development of a fully flexible computational modelling platform (C++ code) that allows manipulations of detailed structural and functional parameters of a muscle at each (quadrature) point in that muscle

• Implementing a novel combination of material models uniquely developed for this platform that represents an accurate mechanical properties for the human gastrocnemius muscle.

• Validating the physiology represented by the gastrocnemius muscle model by comparing the curvature and strain ratios of the simulated fibres (in a fascicle plane) with those recently reported from experimental studies.

• Creating activation transition functions that allowed modelling of different distributions of activity in a muscle belly and predicted the force distributions associated with those activities for the first time in a 3D muscle model.

• Using a combined material description to model fatty muscle tissue for the muscle of the elderly and obese people

6.3 Perspectives

Modelling skeletal muscles based on continuum mechanics knowledge is at its beginning. This is in part due to the structural and functional complexities of skeletal muscles that are yet to be incorporated in these modelling schemes. The capacity to include different fibre-types in a single muscle model and to recruit those fibres in any acceptable pattern is one of the many physiological characteristics that need to be incorporated in the future models. Such physiological details not only allow for a more accurate study of muscle-tendon units in order to answer conceptual or clinical questions, but will also be useful when studying the function of muscle groups in musculoskeletal simulations. Other physiological concepts such as muscle fatigue, history dependent properties and spasticity in skeletal muscle can also be the focus of the future studies.

While there is lack of experimental information (both structural and functional) to develop more physiologically detailed muscle models, it is possible to predict some of this information using inverse methods. For example, it has been common to predict the
activity (force) in the individual muscles of the lower extremities during human locomotion using inverse dynamics and optimization techniques (e.g. [63]). Developing a similar approach for architecturally detailed continuum models can help in understanding muscle function by predicting their regionalized activity when the kinematics of the muscle geometry is used as the input. This is particularly useful when dealing with limitations in experimental studies such as difficulties in accurate measures of individual muscle excitation in human neck during swallowing [173].

Whether we choose to run future muscle models in forward or inverse simulations for their specific purpose, it is clear that the mathematics describing the models should also be revisited. This could be due to additional physiological details a model must posses to answer the specific questions it was designed for, or the fact that in larger scale simulations or multiscale models, the computational cost has to be highly reduced. In addition, development of more advanced software (codes) that not only handle the parameters more efficiently but also can be used in parallel processing schemes, will reduce the time-frame of the future simulations.

In conclusion, modelling and experimental studies complement each other to allow for the further understanding of any physiological phenomenon. The role of modelling is to build on the data provided from experiments to predict the possibly hard to measure parameters. Also, models can simulate cases that have not been measured before or to test the generality of mechanisms that may even be impossible to elicit physiologically, to challenge experimentalists and inspire scientific innovations.
Appendix A

Supplementary electronic document

The code developed as part of this thesis is available as a supplementary electronic document to the thesis.

Filename: muscle-model.txt
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