1 INTRODUCTION

Soft tissues are diverse biological materials in which the cells are separated by extracellular material. They connect, support, and protect our body and form structures such as organs. Soft tissues include blood vessels, heart tissues, ligaments, tendons, skin or articular cartilage just to name a few. Soft tissues are complex fiber-reinforced composite structures. In a microscopic sense they are non-homogeneous materials because of their composition. Most of them exhibit an anisotropic behavior because of their embedded fibers, which tend to have preferred directions. The tensile response of soft tissues is nonlinear stiffening and the tensile strength depends on the strain rate. In contrast to hard (mineralized) tissues such as bones, soft tissues may experience large deformations. Some soft tissues appear to behave nearly incompressibly and in a markedly viscoelastic manner. Their mechanical behavior is strongly influenced by the concentration and structural arrangement of constituents, the topography, risk factors, age, species, physical and chemical environmental factors, and respective function in the organism.

What is the biomechanics of soft tissue? In a foreword for the journal *Biomechanics and Modeling in Mechanobiology*, Y.C. Fung suggests that biomechanics is the “middle name” between biological structure and function. Hence, the biomechanics of soft tissue seeks to explain the function of soft tissues on the basis of their structure and their mechanics. Understanding, and thus controlling better the mechanics in relation to the structure of any soft biological tissue, how mechanical information is transduced by the cells, and how changes in the cellular and molecular structure of tissues thereby affect tissue function, is a central research goal in soft tissue mechanics.

For simplicity, soft tissues are frequently assumed to behave as hyperelastic materials, and therefore described with the constitutive theory of finite elasticity for which nonlinear continuum mechanics provide the fundamental framework. However, observations of soft tissues indicate that their mathematical description cannot be regarded as simply applied finite elasticity. For example, physiological functions of soft tissues involve fluid-structure interaction, include electrical, thermal, and transport processes and calcium-dependent muscle activation. Soft tissues grow and remodel via mechanotransduction mechanisms.

Because of the inherent geometric, structural, and material complexities of soft tissues, and the spatially non-uniform and time-varying boundary conditions, closed-form
solutions of relevant initial boundary-value problems are (almost) impossible to obtain. Hence, these types of problems demand the finite element (FE) method, sufficient computational resources and graphics capability to display three-dimensional results.

It is important to note that the reliability of computational approaches strongly depends on appropriate three-dimensional mathematical descriptions of the material behavior of soft tissues and their interactions with surrounding tissues. Reasonable constitutive models must be designed within the context of associated comprehensive experimental data for tissue, cellular, and molecular structures. Computational models offer, however, the potential to simulate multifield coupled processes encountered in the micro-heterogeneous soft tissues, and to realistically predict physiological functional interactions. An appropriately developed (large-scale) FE model may provide an ideal tool to enable us to predict the outcome of varying any parameter, and to provide information that would otherwise be difficult to obtain from experiments. Computational biomechanics of soft biological tissue is increasing our ability to address multi-disciplinary problems of academic, industrial, and clinical importance. Clinical applications of computational biomechanics to soft biological tissue may lead to better prevention of injury, improved diagnostics, treatment of disease, surgical planning and intervention, and to optimize the biomedical engineering design for tissue engineering or, for example, vessel implants such as stents.

The purpose of this chapter is to review a few of the many achievements in the biomechanics of soft biological tissue and the computational methods used to analyze it. Of course, as no review can cover all aspects of this broad field, many topics are not discussed here at all. We hope that our choice, which is of course subjective, will be found to be acceptable. The review is concerned with the arterial wall and the heart wall with the heart valves, which are parts of the cardiovascular system, and with the ligament, which is an example of a supportive tissue. The general structure of each section is as follows. We start by describing the biological structure and function of the tissue. We then provide an overview of constitutive models, describe one particular three-dimensional model in more detail, continue with an account on residual stress growth and remodeling, and close with a selection of three-dimensional FE models.

Numerous references are suggested and discussed briefly throughout the chapter; however, because of space limitations, it is not possible to give a comprehensive bibliography of the field. For a general overview of the subject the reader is referred to the seminal books by Fung (1990, 1993, 1997a), or the collection of selected papers by Fung (1997b), which are presented for various topics in more or less chronological order of their publication. The focus of the review by Sacks (2000) is to describe the application of biaxial testing techniques to soft planar tissues and their relation to biomechanical constitutive theories. For mechanical properties and general mechanical characteristics of soft tissues see, for example, Abé et al. (1996), Holzapfel (2001) and Hayashi (2003). The biomechanics of growth, remodeling, and morphogenesis in living systems is particularly addressed in the comprehensive review article by Taber (1995). Computer methods in membrane biomechanics are summarized by Humphrey (1998), while clinical application of computational mechanics to the cardiovascular system is presented in the book edited by Yamaguchi (2000). Surveys of the subject from the experimental, theoretical, and computational point of view are provided in the articles by Weiss and Gardiner (2001), Hunter et al. (2003), Humphrey (2003a), and Holzapfel and Ogden (2010), in the excellent textbook by Humphrey (2002a), and in the books edited by Cowin and Humphrey (2001), Holzapfel and Ogden (2003, 2006, 2009a, 2017), and Holzapfel and Kuhl (2013). For the correspondence between nonlinear continuum mechanics and nonlinear constitutive models as essential prerequisites for FE formulations see the books by Ogden (1997) and Holzapfel (2000).

2 MECHANICS OF THE ARTERIAL WALL

Arteries are vessels that transport blood from the heart to the tissues and organs and supply them with nutrition and oxygen. They are prominent organs composed of soft tissues that transform the pulsatile heart output into a flow of moderate fluctuations serving as an elastic reservoir (“windkessel”). Theoretical, experimental, and clinical principles of arteries may be found in the book by Nichols and O’Rourke (2005), while for the underlying biomechanics including physical and computational perspectives, the reader is referred to Cowin and Humphrey (2001), Holzapfel and Ogden (2003), and Holzapfel and Kuhl (2013). The most comprehensive and updated source on cardiovascular solid mechanics, in particular, on arterial wall mechanics, is still attributed to Humphrey (2002a).

2.1 Structure

Arteries are roughly subdivided into two types: elastic and muscular (see, Rhodin, 1980). Elastic (proximal) arteries have relatively large diameters, are located close to the heart and show pronounced elastic behavior (see, for example, Holzapfel et al., 2000a, and references therein). Muscular (distal) arteries are located at the periphery and show
pronounced viscoelastic behavior with hystereses that are relatively insensitive to strain rates, that is, nearly constant damping, independent of frequency (see, for example, Holzapfel et al. (2002a), and references therein). Some arteries exhibit morphological structures of both types.

Arterial walls consist of three primary layers, the intima (innermost layer of the artery), media (middle layer), and adventitia (outermost layer). The intima is a biologically functional “membrane” that serves as a direct interface between the thrombogenic media and the blood. In healthy young arteries the intima is very thin and stiffens with age (arteriosclerosis) and so their contribution to mechanical properties may become significant (Schulze-Bauer et al., 2003). It is known that pathological changes of the intimal components may be associated with atherosclerosis, the most common disease of arterial walls. The underlying pathological changes lead to so-called atherosclerotic plaques, which have complex geometries and biochemical compositions leading to significant alterations in the mechanical properties of the arterial wall. Hence, the mechanical behavior of atherosclerotic arteries differs significantly from that of healthy arteries. The media consists of a complex micro- and nanostructure of the lamellar unit (O’Connell et al., 2008), and a network of smooth muscle cells, collagen fibrils, elastin, and ground substance matrix. For the transmural organization of the arterial media see the paper by Clark and Glagov (1985). According to Rhodin (1980), the fenestrated elastic laminae separate the media into a varying number of well-defined concentrically fiber-reinforced medial layers. The orientation of and close interconnection between the elastic and collagen fibrils, elastic laminae, and smooth muscle cells together constitute a continuous fibrous helix (Faserschraube). This structured arrangement gives the media high strength and resilience and the ability to resist loads in both the longitudinal and circumferential directions. From the mechanical perspective, the media is the most significant layer in a healthy artery. The adventitia is surrounded continuously by loose perivascular tissue. The thickness of the adventitia depends strongly on the type (elastic or muscular) and the physiological function of the blood vessel, and its topographical site. Adventitias demonstrate high tensile strengths (> 1 MPa) and have significant load-carrying capabilities at higher pressures at which it changes to a stiff “jacket-like” tube that prevents the smooth muscle from acute overdistension (Schulze-Bauer et al., 2002).

For a more detailed description of the morphological structure of the interrelated arterial components and the overall functioning of arteries see, for example, Humphrey (2002a), and references therein.

2.2 Constitutive models

2.2.1 Overview

The passive mechanical behavior of arterial walls is governed mainly by the intrinsic properties of elastin and collagen fibers (see, for example, Cox, 1978). Most constitutive models proposed for arteries are valid for the passive state of smooth muscles and are based on a phenomenological approach that describes the artery as a macroscopic system. Most of these models were designed to capture the response near the physiological state and in this respect they have been successfully applied in fitting experimental data. The most common potentials (energy functions) are of exponential type (Fung et al., 1979; Kas’yanov and Rachev, 1980; Chuong and Fung, 1983; Deng et al., 1994; Delfino et al., 1997), although polynomial (Vaishnav et al., 1972), logarithmic forms (Takamizawa and Hayashi, 1987), and mixed forms (see, for example, Fung et al. 1993; Holzapfel et al., 1996, 2000a, 2015; Holzapfel and Weizsäcker, 1998; Gasser et al., 2006) are also used. For a systematic evaluation of several of the most commonly used passive arterial wall models see Holzapfel et al. (2000a), Horgan and Saccomandi (2003), Schulze-Bauer et al. (2003), and Holzapfel et al. (2015).

Most of the constitutive models treat the arterial wall as a single layer, but a number of models assume the wall to be composed of two or three structurally important homogeneous layers. These models include anisotropy and are documented by von Maltzahn et al. (1981), Demiray and Vito (1991), Rachev (1997), and Holzapfel et al. (2000a); for a review see Holzapfel and Ogden (2010). Some of the constitutive models proposed use the biphasic theory to describe arterial walls as hydrated soft tissues; see, for example, Simon et al. (1998a,b). Less frequently used are models that account for the specific morphological structure of arterial walls. One attempt to model the helically wound fibrous structure is provided by Tözeren (1984), which is based on the very simplified histological assumption that the only wall constituent is the fiber structure. Another structural model proposed by Wuys et al. (1995) assumed that the wavy collagen fibrils are embedded in concentrically arranged elastin/smooth-muscle membranes, which is in agreement with the histological situation (Roach and Burton, 1957). This model allows the deformation behavior of axially symmetric thick-walled vessels to be represented. Following Fung (1967), Holzapfel et al. (2000a) proposed a fully three-dimensional material description of healthy arterial walls suitable for implementation in a FE program. Thereby, the wall is considered as a heterogeneous composite structure composed of three layers, with layer-specific histological features (for a description see Section 2.2.3).
There is evidence that the collagen fibers in artery walls are dispersed (see, for example, Canham et al., 1989; Finlay et al., 1998; Schriefl et al., 2012a). As far as the layers of human aortas are concerned, collagen fibers are helically and almost symmetrically arranged with respect to the cylinder axis, while there is often a third and sometimes a fourth family present in the intima with respect to the axial and circumferential directions. The main existing continuum mechanical models take fiber dispersion into account are summarized in the paper by Holzapfel et al. (2015), with a more recent account by Li et al. (2016, 2017) on the computational implementation of the dispersion model proposed by Holzapfel and Ogden (2015), which also allows the exclusion of fibers under compression without the need for a Heaviside function (the exclusion of the compressed fibers makes a significant difference to the tissue response compared with the situation where they are not excluded).

Basically, there exist two different approaches to consider fiber dispersion: (i) fiber dispersion is represented directly by incorporation in a free-energy function via a probability density function (PDF), called “angular integration” (AI) approach, or (ii) by a “generalized structure tensor” (GST), called GST approach. In the AI approach the strain energy $w(\lambda)$ of a single collagen fiber is considered as a function of the fiber stretch $\lambda$ and integrated over a unit sphere $S$ to obtain the total free-energy function, say $\Psi_f$, of the fibers per unit reference volume, that is,

$$\Psi_f = n \int_S \rho(N) w(\lambda) dS$$  \hspace{1cm} (1)

where $N$ is a unit vector describing the orientation of an individual fiber, and $\rho$ denotes the relative angular density of fibers normalized by $(1/4\pi) \int_S \rho(N) dS = 1$, while $n$ denotes the numbers of fibers per unit reference volume. Hence, fibers are in tension for which $\lambda > 1$, where $\lambda = [(CN) \cdot N]^{1/2}$ is the stretch in the direction $N$, $C = F^T F$ is the right Cauchy-Green tensor and $\mathbf{F}$ denotes the deformation gradient (see, for example, Ogden, 1997; Holzapfel, 2000). Note that (1) requires integration over the unit sphere at each point. It was probably the study by Lanir (1983) that first considered fiber dispersion in the free energy via an orientation density function to capture the response of fibrous tissues. In the GST approach, the total free-energy function is related to a generalized structure tensor, say $\mathbf{H}$, and is given by

$$\Psi_f = \Psi_f(C, \mathbf{H})$$  \hspace{1cm} (2)

where $\mathbf{H}$ is defined by

$$\mathbf{H} = \frac{1}{4\pi} \int_\Omega \rho(N) \otimes N d\Omega, \text{ with } \text{tr}\mathbf{H} = 1$$  \hspace{1cm} (3)

The symbol $\otimes$ denotes the dyadic product defined in index notation by $(\mathbf{A} \otimes \mathbf{B})_{ij} = A_i B_j$. One of the first studies that used the GST approach was probably by Freed et al. (2005) and Gasser et al. (2006). In particular, the model proposed by Gasser et al. (2006) is an extension of the constitutive framework for arterial wall mechanics by Holzapfel et al. (2000a) to the case of (rotationally symmetric) fiber dispersion, which is based on the structure tensor $\mathbf{S}$. Another more recent natural extension to consider non-symmetric dispersion of collagen fibers is documented by Holzapfel et al. (2015). That model allows to capture the significantly different out-of-plane and in-plane dispersion (for a description see Section 2.2.4). By comparing the energy functions (1) with (2) we see that for the latter no integration is needed once $\mathbf{H}$ has been determined by (3). Hence, GST models are simpler to implement and the related computational effort is much lower. Recently, Holzapfel and Ogden (2017) have also shown that GST and the AI models are equivalent with regard to their predictive capabilities.

A structurally based model suitable for predicting reliably the passive time-dependent three-dimensional stress and deformation states of arterial walls under various loading conditions is proposed by Holzapfel et al. (2002a), see also references therein. The viscoelastic model admits hysteresis loops that are known to be relatively insensitive to strain rate, an essential mechanical feature of arteries of the muscular type. Instead of modeling the loading and unloading curves by two different laws of elasticity, that is, pseudo-elasticity (see Fung et al., 1979), the concept of internal variables is introduced in order to replicate the characteristic dissipative mechanism of muscular arteries. Evolution equations and associated closed-form solutions in the form of convolution integrals are provided for the internal variables. An efficient update algorithm, suitable for implementation, allows the algorithmic stress and elasticity tensors to be computed (Simo, 1987; Holzapfel, 1996, 2000). A more general constitutive framework for fiber-reinforced composites incorporating viscoelastic effects, and associated computational aspects may be found in Holzapfel and Gasser (2001).

If arteries are subjected to very high loads, far beyond the physiological domain, they may undergo non-recoverable deformations (see, for example, Holzapfel et al., 2000b). The structural mechanisms during this type of deformation, however, remains unclear. Only a few constitutive descriptions are known in the literature, which include non-recoverable phenomena of arterial walls, see, for example, Tanaka and Yamada (1990), Tanaka et al. (1996), Hokanson and Yazdani (1997), Gasser and Holzapfel (2002), Weisbecker et al. (2012), and Fereidoonmehraz et al. (2016).
In contrast to the passive response of arterial walls, the active mechanical behavior of arterial walls is quite different. It is governed by the elastin and collagen fibers and by the degree of activation of smooth muscle cells. Mechanical models of smooth muscle contraction are documented in, for example, Murphy (1980) and Gestrelius and Borgström (1986). An adequate mathematical (more phenomenological) model, which allows the study of the effects of smooth muscle contraction and relaxation on the strain and stress distribution in the vascular wall, was proposed by Rachev and Hayashi (1999). Using nonlinear continuum mechanics, a few other studies have documented phenomenological models that capture smooth muscle contraction (Rachev and Hayashi, 1999; Zulliger et al., 2004; Schmitz and Böl, 2011). However, such models fail to relate the sequence of coupled physiological processes to the underlying biophysical (microscopic) structure of the cell. Recently, more integrated continuum models for smooth muscle have been proposed that consider chemical, electrical, and mechanical stimuli. A comprehensive model that incorporates mechanical, chemical and electrical components of smooth muscle cell function during the generation was proposed by Yang et al. (2003). For a brief review of such coupled models describing the basic features of active vascular smooth muscle cells using a continuum mechanical framework see Murtada and Holzapfel (2014), with a more recent account in Murtada et al. (2016). In these models the active stress is generated by phosphorylated myosin reflected by the four-state kinetic model proposed by Hai and Murphy (1988). Sharifimajd and Stålhand (2014) documented a continuum model for smooth muscle contraction that includes cell membrane excitability and the kinetics of myosin phosphorylation. The recent study by Stålhand et al. (2016) attempted to treat the contraction of smooth muscle cells from the continuum thermodynamics point of view considering them as an open system where matter passes through the cell membrane.

2.2.2 Basic building block for a structure-based model

Here, a basic building block for a structural model is presented. It is the simplest representation of material anisotropy called transversely isotropic. The material response along directions orthogonal to this preferred direction is isotropic. It represents the foundation of a model to mechanically analyze several types of biological materials such as arteries in health and disease (see, for example, Holzapfel and Ogden, 2003, 2006, 2010; Holzapfel et al., 2015, and with the related references mentioned in subsequent sections), heart valves (Prot et al., 2007, 2010), corneas (Alastrué et al., 2006; Pandolfi and Manganiello, 2006), lens capsules (David et al., 2007), ligaments (Peña et al., 2007a), temporomandibular joint disc cartilage (Peña et al., 2007b), intervertebral discs (Eberlein et al., 2001), just to name a few. The basic building block has also served the basis for the analysis of mechanical responses of, for example, engineered materials such as textile composites (Nam and Thinh, 2006; Milani et al., 2007), and anisotropic hyperelastic solids in general (Lu et al., 2007).

We start by considering a mapping \( \chi \) that defines the deformation from a reference (or unloaded) configuration to a current (or deformed) configuration of the body. We assume that arterial walls maintain a constant volume within the physiological range of deformation (Carew et al., 1968). This is characterized by the incompressibility constraint \( J = 1 \), where \( J = \left| \det F \right| = \left( \det C \right)^{1/2} \) is the local volume ratio. By \( \Psi \) we denote the (Helmholtz) free-energy function for an isothermal hyperelastic process relative to the reference configuration (per unit volume). By incorporating the incompressibility constraint through a Lagrange multiplier \( p \) we then have

\[
\Psi = \Psi(C, M) - p(J - 1)
\]  

where \( \Psi(C, M) \) is defined for \( J = 1 \) and describes the constitutive response of an incompressible elastic material. Note that the scalar multiplier \( p \) introduced in (4) can be identified as an indeterminate hydrostatic pressure arising as a reaction to the incompressibility constraint. The (three-dimensional) statistical distribution of collagen fiber directions can be characterized by a family of collagen fibers whose mean direction is represented by the unit vector \( \mathbf{M} \), and it is this direction that renders the material’s properties anisotropic. The mean direction is provided in the reference configuration of the material and serves as an essential set of input data for both the material and the numerical model.

According to Holzapfel and Weizsäcker (1998), we use an additive split of the free-energy function \( \Psi \) into a part \( \Psi_g \) associated with the non-collagenous ground-matrix (indicated by the subscript \( g \)) and a part \( \Psi_f \) associated with the embedded families of collagen fibers (indicated by the subscript \( f \)). Hence, for a tissue, \( \Psi \) may be written as

\[
\Psi(C, M) = \Psi_g(C) + \Psi_f(C, M)
\]

The integrity basis for the two symmetric second-order tensors \( C \) and \( M \otimes M \) consists of the five invariants \( I_1, \ldots, I_5 \). Since \( I_3 = 1 \), the function (5) may be expressed in the form

\[
\Psi(I_1, I_2, I_4, I_5) = \Psi_g(I_1, I_2) + \Psi_f(I_1, I_2, I_4, I_5)
\]

where the invariant \( I_4 = (CM) \cdot M \) is the square of the stretch in the direction \( M \), and it, therefore, has a clear physical
interpretation. For simplicity, and in order to minimize the number of material parameters, we provide a reduced form of (6) as

\[ \Psi(I_1, I_4) = \Psi_g(I_1) + \Psi_f(I_4) \]  

(7)

where the anisotropy arises only through \( I_4 \).

Finally, we particularize the two functions \( \Psi_g \) and \( \Psi_f \). For the low loading domain the (wavy) collagen fibers of soft collagenous tissues are not active (they do not store strain energy). Results from the study by Gundiah et al. (2007) show that the (classical) neo-Hookean model is a satisfactory description for arterial elastin, see also the analysis by Watton et al. (2009). Hence, for \( \Psi_g \) the following function may be taken, that is,

\[ \Psi_g(I_1) = \frac{c}{2}(I_1 - 3) \]  

(8)

where \( c > 0 \) is a stress-like material parameter. The characteristic stiffening effect of the collagenous tissue motivates the use of an exponential function for the description of the energy stored in the collagen fibers. Thus (Holzapfel et al., 2000a),

\[ \Psi_f(I_4) = \frac{k_1}{k_2} \left\{ \exp[k_2(I_4 - 1)^2] - 1 \right\} \]  

(9)

where \( k_1 > 0 \) is a stress-like material parameter and \( k_2 > 0 \) is a dimensionless parameter. Due to the wavy structure it is generally assumed that collagen is not able to support any compression. These fibers would buckle under the smallest compressive load. Therefore it is assumed that the fibers contribute to the strain energy in extension and do not contribute in compression. Hence, in (7) the anisotropic term should only contribute when the fibers are extended, that is, when \( I_4 > 1 \). If, for example, \( I_4 \) is less than or equal to 1, then the response of the tissue is purely isotropic. This modeling assumption is not only physically based, but is also essential for reasons of stability, see Holzapfel et al. (2004) for the related analysis.

### 2.2.3 A three-dimensional constitutive model for elastic arterial walls

In this section a fully three-dimensional material description of healthy arteries in the passive state of the smooth muscles is provided (Holzapfel et al., 2000a; Holzapfel, 2001). The model is structural in the sense that it takes account partly of the architecture of the wall, that is, each individual layer is treated as a fiber-reinforced material with the fibers corresponding to the collagenous component of the tissue, and information about the orientations of the collagen fibers, which render the material orthotropic, is incorporated. Only the response of elastic arteries is considered and for this purpose the theory of nonlinear elasticity is used.

Since arteries are composed of (thick-walled) layers, each of these layers is modeled with a separate free-energy function. From the engineering point of view each layer may be considered as a composite reinforced by two families of collagen fibers that are arranged in symmetrical spirals. It is assumed that each layer has a similar mechanical response, and therefore the same form of \( \Psi \) (but a different set of material parameters) is used for each layer. Hence, the appropriate extension of (5) is

\[ \Psi(C, M, M') = \Psi_g(C) + \Psi_f(C, M, M') \]  

(10)

where the families of collagen fibers are characterized by the two (reference) direction vectors \( M, M' \), with \( |M| = |M'| = 1 \). In order for \( \Psi \) to satisfy the usual objectivity requirement it must be an isotropic invariant of \( C, M \otimes M \) and \( M' \otimes M' \) (Spencer, 1984; Holzapfel, 2000). Hence, it may be expressed as a function of seven deformation-dependent invariants denoted \( I_1, I_2, I_4, I_6, \ldots, I_8 \). Since we are considering an incompressible material, the invariant \( I_1 = \det C \equiv 1 \) is omitted.

At low pressures, the energy contribution of the (wavy) collagen fibers within arterial walls is assumed to be negligible, and the mechanical response is largely due to the non-collagenous matrix material, which we assume to be isotropic and modeled by \( \Psi_g \). At higher pressures, the collagenous fibers are recruited and provide the main contribution to the resistance to loading (Roach and Burton, 1957). This response is modeled by the anisotropic function \( \Psi_f \). When this is specialized in terms of invariants equation (10) takes on the form

\[ \Psi(I_1, I_4, I_6) = \Psi_g(I_1) + \Psi_f(I_4, I_6) \]  

(11)

and replaces (7).

One possible particularization of \( \Psi_g \) that determines the isotropic response in each arterial layer is the (classical) neo-Hookean model. The strong stiffening effect of each layer observed at high pressures may be described by

\[ \Psi_f(I_4, I_6) = \frac{k_1}{2k_2} \sum_{a=3,6} \left\{ \exp[k_2(I_a - 1)^2] - 1 \right\} \]  

(12)

where \( k_1 \) is a material parameter with the dimension of stress, and \( k_2 \) is a dimensionless material parameter. For this model to predict a physically reasonable response these parameters must be positive. For a whole set of material parameters that captures the mechanical response of rabbit carotid arteries (Fung et al., 1979) see the work by Holzapfel et al. (2004).
In view of its wavy structure it is reasonable to consider that collagen is not able to support compressive stresses. We therefore assume that the fibers support stress only under extension. Consequently, the anisotropic term in (11) contributes only when the fibers are extended, that is, when either \( I_4 > 1 \) or \( I_6 > 1 \) or both. For example, if \( I_4 \leq 1 \) and \( I_6 > 1 \), then only \( I_6 \) contributes to \( \Psi_f \). These physically motivated requirements ensure that convexity is guaranteed \textit{a priori} by the form of \( \Psi \) given by (12) for an arbitrary set of (positive) material parameters, as discussed in Holzapfel et al. (2000a). Interestingly, these requirements are reinforced by a discussion in Holzapfel et al. (2004), which shows that fiber extension is consistent with the condition of strong ellipticity.

Noting that in the undeformed configuration \( I_1 = 3 \) and \( I_4 = I_6 = 1 \) it follows from (11) and (12) that \( \Psi(3, 1, 1) = 0 \), \( \psi_1 = c/2 \), \( \psi_{11} = 0 \), and \( \psi_{4}(3, 1, 1) = 0 \) and \( \psi_{66} = k_1 \), where the subscripts 1 and 4 denote differentiation with respect to \( I_1 \) and \( I_4 \), respectively (similarly for the derivatives with respect to \( I_6 \)). Hence, the free energy vanishes in the undeformed configuration, and, provided the pressure term \( p \) is such that in the reference configuration \( p = c/2 \), then so does the stress, while \( k_1 \) is a positive elastic constant. These are three fundamental conditions that the free energy has to satisfy in the absence of residual stresses.

It is important to note that the free-energy function \( \Psi \) involves only three material constants. Additionally, \( \Psi \) involves the unit vectors \( \mathbf{M} \) and \( \mathbf{M}' \) describing the fiber structure. However, these vectors are different for each layer. The overall effect of the structure means that the mechanical response of each layer can be assumed to be similar in that it is essentially orthotropic in character. We may therefore use the same form of free-energy function (11), (12) for each layer but with a different set of material constants and different vectors \( \mathbf{M} \) and \( \mathbf{M}' \) associated with the structure. The functions (12) are sufficiently general to capture the basic features of arterial responses observed in experiments.

### 2.2.4 An extension to model non-symmetric collagen fiber dispersion

In arterial layers, the collagen fiber orientations are non-symmetrically distributed (see, for example, Schriefl et al., 2012b; Niestrawska et al., 2016, with more references therein). We briefly review a model that captures non-symmetric collagen fiber dispersion (Holzapfel et al., 2015) by extending the three-dimensional constitutive model for elastic arterial walls, as presented in Section 2.2.3.

We start by providing a measure for in-plane fiber dispersion (tangential plane of the artery) and out-of-plane dispersion. We describe a general fiber direction \( \mathbf{N} \) (with \( |\mathbf{N}| = 1 \)) in the (unloaded) reference configuration by a coordinate system that is characterized by the unit rectangular Cartesian basis vectors \( \mathbf{e}_1 \), \( \mathbf{e}_2 \), \( \mathbf{e}_3 \) (Figure 1), where \( \mathbf{N} \) is defined by the two angles \( \Phi \in [0, 2\pi] \) and \( \Theta \in [-\pi/2, \pi/2] \) with respect to the unit rectangular Cartesian basis vectors \( \mathbf{e}_1 \), \( \mathbf{e}_2 \), \( \mathbf{e}_3 \). (Reproduced with permission from Holzapfel, G. A., Niestrawska, J. A., Ogden, R. W., Reinisch, A. J., and Schriefl, A. J. (2015). Modelling non-symmetric collagen fibre dispersion in arterial walls. J. R. Soc. Interface 12:20150188. @ The Author(s), 2015.)

\[
\rho_{ip}(\Phi) = \frac{\exp[a \cos(2(\Phi + \alpha))]}{I_6(a)},
\]
\[
\rho_{op}(\Theta) = 2\sqrt{\frac{2}{{\pi}}} \frac{\exp[b(\cos 2\Theta - 1)]}{{\text{erf}}(\sqrt{2b})}
\]  

where \( \rho_{ip}(\Phi) = \rho_{ip}(\Phi + \pi) \) and \( \rho_{op}(\Theta) = \rho_{op}(-\Theta) \) denote the in-plane and out-of-plane dispersions, respectively, \( I_6(a) \) is the modified Bessel function of the first kind of order 0, \( \alpha \) is the angle between the mean fiber direction and the circumferential direction \( \mathbf{e}_3 \), and \( a \) and \( b \) are concentration parameters to be used as fitting parameters. An in-plane fiber dispersion \( \kappa_{ip} \) and out-of-plane dispersion \( \kappa_{op} \) is according to Holzapfel et al. (2015)

\[
\kappa_{ip} = \frac{1}{2} - \frac{I_1(a)}{2I_6(a)},
\]
\[
\kappa_{op} = \frac{1}{2} - \frac{1}{8b} + \frac{1}{4} \sqrt{\frac{2}{\pi b}} \text{erf}(\sqrt{2b})
\]  

where \( I_1(a) \) is the modified Bessel function of the first kind of order 1, with \( 0 \leq \kappa_{ip} \leq 1 \) and \( 0 \leq \kappa_{op} \leq 1/2 \). These two

dispersion parameters are then used in structure tensors which are incorporated into the constitutive model.

Let us now use again two symmetric fiber families with the (in-plane) mean fiber directions, which we denote in this section as $M_4$ and $M_6$ (rather than $M$ and $M'$). Thus,

$$M_4 = \cos \alpha e_1 + \sin \alpha e_2,$$

$$M_6 = \cos \alpha e_1 - \sin \alpha e_2$$

where $M_4$ and $M_6$ make an angle $\alpha$ with the circumferential direction $e_1$. In addition to the invariants $I_1$, $I_4$ and $I_6$, we introduce also the invariant $I_6$ according to

$$I_1 = \text{tr} C, \quad I_i = (CM_i) \cdot M_i, \quad i = 4, 6$$

$$I_n = (CM_n) \cdot M_n$$

where $M_n$ is a unit out-of-plane vector shown in Figure 2.

Next we introduce the two generalized structure tensors $H_4$ and $H_6$, which characterize the material behavior, that is,

$$H_i = A\mathbf{I} + B\mathbf{M}_i \otimes \mathbf{M}_i$$

$$+ (1 - 3A - B)\mathbf{M}_n \otimes \mathbf{M}_n, \quad i = 4, 6$$

where the constants $A$ and $B$ are

$$A = 2\kappa_{\text{op}}\kappa_{\text{ip}}, \quad B = 2\kappa_{\text{op}}(1 - 2\kappa_{\text{ip}})$$

The two structure tensors $H_i$, $i = 4, 6$, are then considered into a free-energy function $\Psi$ according to

$$\Psi(C, H_4, H_6) = \Psi_g(C) + \sum_{i=4,6} \Psi_{f_i}(C, H_i)$$

where $\Psi_g$ is a function describing the non-collagenous ground-matrix according to (8), and $\Psi_{f_i}$ is the contribution of the two embedded fiber families, which is given by

$$\Psi_{f_i}(C, H_i) = \frac{k_1}{2k_2} \left\{ \exp \left[ k_2(I_i^* - 1)^2 \right] - 1 \right\}, \quad i = 4, 6$$

with the stress-like parameter $k_1 > 0$, the dimensionless parameter $k_2 > 0$ and the generalized invariants $I_i^*$ defined as

$$I_i^* = \text{tr}(H_i \mathbf{C}) = AI_i + BI_i + (1 - 3A - B)I_n, \quad i = 4, 6$$

The generalized invariants include the mean fiber directions in terms of $I_i$ and the two dispersion parameters $k_{\text{ip}}$ and $\kappa_{\text{op}}$ in terms of $A$ and $B$. Note that the free-energy function (19) is the analog of (10). In summary, the material model contains three structural parameters ($k_{\text{ip}}$, $\kappa_{\text{op}}$, $\alpha$) obtained from structural analysis, and three material parameters ($c$, $k_1$, $k_2$) obtained from mechanical data.

### 2.2.4.1 Special cases of this fiber dispersion model

This model includes several other dispersion models as special cases of (17). For the subsequent discussion we assume just one family of fibers so that the generalized structure tensor has the form

$$H = A\mathbf{I} + B\mathbf{M} \otimes \mathbf{M} + (1 - 3A - B)\mathbf{M}_n \otimes \mathbf{M}_n$$

For a transversely isotropic dispersion we consider the form (Gasser et al., 2006)

$$H = \kappa \mathbf{I} + (1 - 3\kappa)\mathbf{M} \otimes \mathbf{M}$$

where $\kappa \in [0, 1/3]$ denotes the dispersion parameter related to transversely isotropic dispersion about the direction $\mathbf{M}$. Note that (23) is recovered as a special case of (22) by taking $\kappa = 1 - 2\kappa_{\text{op}}$, which corresponds to $A = \kappa, B = 1 - \kappa$.

If there is no dispersion in either plane both concentration parameters $a$ and $b$ in (13) become infinite, and we obtain the model proposed by Holzapfel et al. (2000a), which is the one presented in Section 2.2.2 of this chapter. With $a \to \infty$, we get an in-plane delta function for $\rho_{\text{ip}}$, and with $b \to \infty$ we have $\kappa_{\text{op}} \to 1/2$ so that the structure tensor is $H = \mathbf{M} \otimes \mathbf{M}$, where $A = 0, B = 1$ in (22). In this special case all fibers are oriented in the in-plane direction of $\mathbf{M}$.

---

**Figure 2.** Two symmetric fiber families with mean fiber directions $M_4$ and $M_6$ with fiber angle $\alpha$. The normal direction to the plane is $M_6$. (Reproduced with permission from Holzapfel, G. A., Niestrawska, J. A., Ogden, R. W., Reinisch, A. J., and Schriefl, A. J. (2015). Modelling non-symmetric collagen fibre dispersion in arterial walls. *J. R. Soc. Interface* **12**:20150188. © The Author(s), 2015.)
If $\rho(\Phi, \Theta)$ is independent of the two angles $\Phi$ and $\Theta$, then the fiber dispersion is isotropic (no preferred direction), with $\rho_{ip} = \rho_{op} = 1$ and $a = b = 0$, while $\kappa_{op} = 1/3$. Thereby, the structure tensor $H$ is $(1/3)I$ and $\kappa = 1/3$ with $A = 1/3$, $B = 0$ in (22).

In the case where a fiber dispersion is oriented only in-plane then we have (Ogden, 2009; Holzapfel and Ogden, 2010)

$$ H = \kappa I + (1 - 2\kappa) M \otimes M $$

(24)

where $I$ is the two-dimensional identity in the considered plane. Thereby, the in-plane function $\rho(\Theta)$ satisfies $\rho(-\Theta) = \rho(\Theta)$. For the von Mises distribution (13), this corresponds to $b \to \infty$ and $\kappa_{op} \to 1/2$. Note that (24) is obtained from (22) by setting $A = \kappa$ and $B = 1 - 2\kappa$.

A dispersion is planar isotropic for perfect out-of-plane alignment, $b \to \infty$ and $\kappa_{op} \to 1/2$, and for fully in-plane dispersion so that $a \to 0$, $\rho_{ip} = 1$. The structure tensor is then simply $H = (1/2)I$, which corresponds to $A = 1/2$, $B = 0$ in (22).

All discussed special cases are summarized in Table 1. Figure 3 visualizes $\rho(N)N$ for (a) the non-rotationally symmetric dispersion for which $H$ is given by (22), (b) the transversely isotropic dispersion with $H$ given by (23), (c) the perfect alignment case, (d) the isotropic case and (e) the planar dispersion case given by (24).

### Table 1. Special cases of the present dispersion model based on the von Mises distributions (13).

<table>
<thead>
<tr>
<th>Case</th>
<th>Conc. parameter</th>
<th>Dispersion parameter</th>
<th>Structure tensor $H$</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>TI</td>
<td>$a \to \infty, b \to \infty$</td>
<td>$\kappa = 1 - 2\kappa_{op}$</td>
<td>$\kappa I + (1 - 3\kappa)M \otimes M$</td>
<td>Gasser et al. (2006)</td>
</tr>
<tr>
<td>PA</td>
<td>$a \to \infty, b \to \infty$</td>
<td>$\kappa_{op} \to 1/2, \kappa = 0$</td>
<td>$M \otimes M$</td>
<td>Holzapfel et al. (2000a)</td>
</tr>
<tr>
<td>ID</td>
<td>$a = b = 0$</td>
<td>$\kappa_{op} = \kappa = 1/3$</td>
<td>$(1/3)I$</td>
<td>Holzapfel et al. (2005), Gasser et al. (2006)</td>
</tr>
<tr>
<td>PD</td>
<td>$b \to \infty$</td>
<td>$\kappa_{op} \to 1/2$</td>
<td>$\kappa I + (1 - 2\kappa)M \otimes M$</td>
<td>Ogden (2009), Holzapfel and Ogden (2010)</td>
</tr>
<tr>
<td>PI</td>
<td>$a \to 0, b \to \infty$</td>
<td>$\kappa_{op} \to 1/2$</td>
<td>$(1/2)I$</td>
<td>Holzapfel and Ogden (2010), Gasser et al. (2012)</td>
</tr>
</tbody>
</table>

TI, transversely isotropic dispersion; ID, isotropic dispersion; PA, perfect alignment; PD, planar dispersion; PI, planar isotropic dispersion.
was therefore non-homogeneous. Uniform material parameters over the adventitial strips \((c, k_1, k_2)\) were used as summarized in Table 2. Two symmetric fiber families are assumed to make an angle \(\alpha\) of ±47.99° with the circumferential direction (Figure 2), and have a dispersion \(\kappa_{ip} = 0.116\) and \(\kappa_{op} = 0.493\), as also provided in Table 2. We have used 3200 hexahedral elements, and applied the mixed \(Q1/P0\) element throughout the simulation. Figure 4 shows the FE results of the circumferential and axial specimens, subjected to a stretch of 1.3.

![Figure 4. Finite element results of circumferential and axial specimens from the adventitia, subjected to a stretch of 1.3. The Cauchy stress is plotted in the direction of the applied displacement. The solid lines indicate the undeformed (initial) configuration. (Reproduced with permission from Holzapfel, G. A., Niestrawska, J. A., Ogden, R. W., Reinisch, A. J., and Schriefl, A. J. (2015). Modelling non-symmetric collagen fibre dispersion in arterial walls. J. R. Soc. Interface 12:20150188. © The Author(s), 2015.)](image)

### Table 2. Summary of material and structural parameters.

<table>
<thead>
<tr>
<th>Material parameters</th>
<th>Structural parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>(c) (kPa)</td>
<td>(k_1) (kPa)</td>
</tr>
<tr>
<td>Value</td>
<td>10.07</td>
</tr>
</tbody>
</table>

### 2.3 Combined bending, inflation, extension, and torsion of an arterial segment

The exemplary constitutive models described in Section 2.2 are designed to capture the deformation behavior in the central part of an arterial segment so as to exclude end effects. Therefore, axial dependence of the deformation is not considered. This reflects the typical setting used in experiments (see, for example, Schulze-Bauer et al., 2003, among others).

#### 2.3.1 Basic kinematics

We consider the artery as an incompressible thick-walled cylindrical tube subjected to various loads. It is known that the load-free configuration, \(\Omega_{res}\), say, in which the artery is excised from the body and not subjected to any loads is not a stress-free reference configuration \(\Omega_0\). Thus, the arterial ring springs open when cut in a radial direction (Vaishnav and Vossoughi, 1983). We assume that the open sector is the undeformed (stress-free and fixed) reference configuration \(\Omega_0\), as depicted in Figure 5.

Thus, in terms of cylindrical polar coordinates \((R, \Theta, Z)\), the geometrical region \(\Omega_0\) of the tube is defined by

\[
R_i \leq R \leq R_o, \quad 0 \leq \Theta \leq (2\pi - \alpha), \quad 0 \leq Z \leq L
\]

where \(R_i, R_o, \alpha\) and \(L\) denote the inner and outer radii, the opening angle and length of the undeformed (split) tube, respectively. Note that the opening angle \(\alpha\) identified in Figure 5 differs from the definition normally used (see, for example, Fung and Liu, 1989). The angle \(\alpha\) introduced here should not to be confused with the one introduced in Section 2.2.4 describing the angle between the mean fiber direction and the circumferential direction.

The deformation \(\chi\) takes \(\Omega_0\) into the current configuration \(\Omega\). For the considered problem \(\chi = \chi_p \cdot \chi_{res}\) is the composition of the deformations \(\chi_{res}\) and \(\chi_p\), as indicated in Figure 5, where \(\chi_{res}\) generates the load-free configuration \(\Omega_{res}\) associated with residual stresses, while \(\chi_p\) is associated with inflation, axial elongation, and torsion of the tube, and leads to the final configuration \(\Omega\). It is important to note that the residually stressed state is in reality more complex than considered here.
In terms of cylindrical polar coordinates \((r, \theta, z)\), the geometry of the deformed configuration \(\Omega\) is given by

\[
 r_i \leq r \leq r_o, \quad 0 \leq \theta \leq 2\pi, \quad 0 \leq z \leq l
\]  

(26)

where \(r_i\), \(r_o\) and \(l\) denote the inner and outer radii and the length of the deformed tube, respectively.

The deformation \(\chi\), which is taken to be isochoric, may then be written in the form \(\chi = re_r + ze_z\) with reference to the (unit) basis vectors \(\{e_r, e_\theta, e_z\}\) associated with the cylindrical polar coordinates \((r, \theta, z)\), where

\[
 r = \sqrt{\frac{R^2 - R_i^2}{k\lambda_z} + r_i^2}, \quad \theta = k\Theta + Z\frac{\Phi}{L}, \quad z = \lambda_zZ
\]  

(27)

\(\lambda_z\) is the (constant) axial stretch, the parameter \(k\), defined by \(k = 2\pi/(2\pi - \alpha)\), is a convenient measure of the tube opening angle in the unstressed configuration, \(r_i\) is the inner radius in the deformed configuration, and \(\Phi\) is the angle of twist of the tube arising from the torsion.

In addition to \(\lambda_z\), it is convenient to introduce the notations defined by

\[
\lambda_\nu(R) = \frac{\partial r}{\partial R} = \frac{R}{rk\lambda_z}, \quad \lambda_\theta(R) = \frac{r}{R} \frac{\partial \theta}{\partial \Theta} = \frac{kr}{R},
\]

\[
\gamma(R) = \frac{r}{R} \frac{\partial \Phi}{\partial z} = \frac{r}{l} \Phi
\]  

(28)

Here, \(\lambda_\nu(R)\), \(\lambda_\theta(R)\) and \(\lambda_z\) are the principal stretches of the deformation associated with the radial, circumferential, and axial directions when there is no twist, while \(\gamma(R)\), which is associated with the twist, represents locally the amount of shear in a \((\theta, z)\)-plane. Since each of these quantities depends only on the radius \(R\), the one-dimensional character of the problem is apparent. When \(\gamma \neq 0\), \(\lambda_\nu\) is the principal stretch in the radial direction but \(\lambda_\theta\) and \(\lambda_z\) are not then principal stretches. The condition that the volume is preserved during the deformation is independent of \(\gamma\) and requires simply that

\[
\lambda_\nu\lambda_\theta\lambda_z = 1
\]  

(29)

Note that

\[
r_i = \lambda_{\theta i} \frac{R_i}{k}
\]  

(30)

where \(\lambda_{\theta i}\) denotes the value of \(\lambda_\theta\) at the inner surface of the tube.
The first term \( k \Theta \) in (27) represents the deformation from configuration \( \Omega_0 \) to \( \Omega_{\text{re}} \) while the second term \( Z \Phi / L \) describes the influence of the torsion. In terms of the parameters \( k, \lambda_\theta, \lambda, \) and \( \Phi \), equations (27), (30) define the combined bending, inflation, axial extension, and torsion of a thick-walled tube.

### 2.3.2 Equilibrium equations

In the absence of body forces the equilibrium equations are

\[
\text{div} \sigma = 0 \quad (31)
\]

where \( \text{div} (\bullet) \) denotes the spatial divergence of the spatial tensor field \( (\bullet) \). Note that there may be a need to include fluid-induced shear in mechanobiological calculations, and there may be a need, in some cases, to include elastodynamics; for a discussion see Humphrey (2002b).

In cylindrical polar coordinates \((r, \theta, z)\), because of the geometrical and constitutive symmetry, the only non-trivial component of (31) is

\[
\frac{\text{d} \sigma_{rr}}{\text{d} r} + \frac{(\sigma_r - \sigma_\theta)}{r} = 0 \quad (32)
\]

(see, for example, Ogden, 1997). From this equation and the boundary condition \( \sigma_{rr} \rvert_{r=r_o} = 0 \) on the outer surface of the tube, the radial Cauchy stress \( \sigma_r \) may be calculated as

\[
\sigma_r(\xi) = \int_\xi^{r_o} (\sigma_{rr} - \sigma_\theta) \frac{\text{d} r}{r}, \quad r_i \leq \xi \leq r_o \quad (33)
\]

The internal pressure \( p_i = -\sigma_{rr} \rvert_{r=r_i} \) is then obtained in the form

\[
p_i = \int_{r_i}^{r_o} (\sigma_{r\theta} - \sigma_{rr}) \frac{\text{d} r}{r} \quad (34)
\]

This equation plays an important role in the numerical solution of the problem considered.

When the state of deformation is known, expressions for the axial force \( N \) and the torsional couple \( M_t \) can be calculated via the definitions

\[
N = 2\pi \int_{r_i}^{r_o} \sigma_{zz} r \text{d} r, \quad M_t = 2\pi \int_{r_i}^{r_o} \sigma_{r\theta} r^2 \text{d} r \quad (35)
\]

Use of the expressions (33) and (34) leads to the general formula

\[
F = \pi \int_{r_i}^{r_o} (2\sigma_{zz} - \sigma_{r\theta} - \sigma_{rr}) r \text{d} r \quad (36)
\]

for the reduced axial force \( F = N - r_i^2 p_i \), with the axial force provided in (35)\(_1\). This expression for \( F \) is very important since it gives precisely the force that is measured during inflation tests on arteries. A specific form of (36) is given in equation (15) of Chuong and Fung (1983).

Note that for a thin-walled cylindrical tube we make the simplification \( \sigma_{rr} = 0 \) for the radial stress (the membrane approximation). Relations (34), (35)\(_2\) and (36) then enable the reduced equations for the internal pressure \( p_i \), the torsional couple \( M_t \) and the reduced axial force \( F \) to be given simply as

\[
p_i = \frac{h}{r} \sigma_{r\theta}, \quad M_t = 2\pi r^2 h \sigma_{r\theta}, \quad F = \pi rh (2\sigma_{zz} - \sigma_{r\theta}) \quad (37)
\]

where \( r \) and \( h \) denote the radius and wall thickness of the deformed tube, respectively. It is important to note that with this membrane approximation the contribution \( \chi_{\text{res}} \) to the deformation is inadmissible and residual stresses cannot be included.

### 2.3.3 Numerical technique to solve the boundary-value problem

By assuming a particular state of residual strain (characterized by the parameter \( k \)), the fixed axial stretch \( \lambda \), and fixed angle of twist \( \Phi \) of the tube, the isochoric part of the strain (and hence the stress) can always be expressed in terms of the two variables \( \lambda_{\theta i} \) and \( r_i \), that is, the circumferential stretch at the inner surface of the tube and the radius, respectively. Hence, the equation of equilibrium (34) may be written in the general form

\[
p_i = \int_{r_i}^{r_o} F(\lambda_{\theta i}, r) \frac{\text{d} r}{r} \quad (38)
\]

where \( r_i \) is given in terms of \( \lambda_{\theta i} \) by (30). Since closed-form evaluation of equation (38) is only possible for very simple constitutive equations, we employ a Gaussian integration scheme (Hughes, 1987), that is,

\[
p_i \approx \sum_{j=1}^{n} F(\lambda_{\theta i}, r_j) w_j r_j^2 \quad (39)
\]

where \( w_j \) and \( r_j \) (\( j = 1, \ldots, n \)), denote the weights and the Gaussian points, and \( n \) is the order of integration. Equation (39) is, in general, nonlinear in the single unknown \( \lambda_{\theta i} \), and, for given \( p_i \), can be solved for \( \lambda_{\theta i} \) using, for example, a standard Newton iteration with the initial value \( \lambda_{\theta i} = 1.0 \).

Since the deformation is now determined, the torsional couple \( M_t \) and the reduced axial force \( F \) follow directly from equations (35)\(_2\) and (36), respectively. This computation is carried out by employing another Gaussian integration. It
functions for the considered two-layer problem may be
overall response of the tissue. The constants 
\( c \) of the material, which describes the strains), as illustrated in Figure 6.

The model uses six material parameters, that is, \( c_M, k_{1M}, k_{2M} \) for the media and \( c_A, k_{1A}, k_{2A} \) for the adventitia. With respect to of equations (11) and (12) the free-energy functions for the considered two-layer problem may be written as

\[
\Psi_M = \frac{c_M}{2} (I_1 - 3) + \frac{k_{1M}}{2k_{2M}} \sum_{j=4,6} \exp \left[ k_{2M}(I_{1M} - 1)^2 \right] - 1, \\
R_1 \leq R \leq R_1 + H_M
\]

\[
\Psi_A = \frac{c_A}{2} (I_1 - 3) + \frac{k_{1A}}{2k_{2A}} \sum_{j=4,6} \exp \left[ k_{2A}(I_{1A} - 1)^2 \right] - 1, \\
R_1 + H_M \leq R \leq R_o
\]

turns out that for the considered range of deformations a three-point integration (\( n = 3 \)) with the accuracy of order five gives sufficiently accurate solutions.

2.3.4 Example: Artery modeled as a two-layer thick-walled tube with residual strains

In order to report the performance of the constitutive model described in Section 2.2.3 we study the mechanical response of a healthy young arterial segment (with no pathological intimal changes). For this case the innermost layer of the artery is not of (solid) mechanical interest, and we therefore focus attention on modeling the two remaining layers, that is, the media and the adventitia. It is then appropriate to model the artery as a two-layer thick-walled tube (with residual strains), as illustrated in Figure 6.

The model uses six material parameters, that is, \( c_M, k_{1M}, k_{2M} \) for the media and \( c_A, k_{1A}, k_{2A} \) for the adventitia. With respect to of equations (11) and (12) the free-energy functions for the considered two-layer problem may be written as

\[
\Psi_M = \frac{c_M}{2} (I_1 - 3) + \frac{k_{1M}}{2k_{2M}} \sum_{j=4,6} \exp \left[ k_{2M}(I_{1M} - 1)^2 \right] - 1, \\
R_1 \leq R \leq R_1 + H_M
\]

\[
\Psi_A = \frac{c_A}{2} (I_1 - 3) + \frac{k_{1A}}{2k_{2A}} \sum_{j=4,6} \exp \left[ k_{2A}(I_{1A} - 1)^2 \right] - 1, \\
R_1 + H_M \leq R \leq R_o
\]

for the media and adventitia, respectively. The constants \( c_M \) and \( c_A \) are associated with the non-collagenous matrix of the material, which describes the isotropic part of the overall response of the tissue. The constants \( k_{1M}, k_{2M} \) and \( k_{1A}, k_{2A} \) are associated with the anisotropic contribution of collagen to the overall response. In the high-pressure regime the stress–strain response depends significantly on the fiber angles (as should be expected). The fiber angles are associated with the stress-free configuration, as indicated in Figure 6, and we have assumed that they are the same in the load-free configuration.

The invariants, associated with the media M and the adventitia A, are defined by \( I_{ij} = (CM_j) \cdot M_j \) and \( I_{ij} = (CM'_j) \cdot M'_j, j = M, A \). In a cylindrical polar coordinate system, the components of the direction vectors \( M_j \) and \( M'_j \) have, in matrix notation, the forms

\[
[M_j] = \begin{bmatrix} \cos \beta_j \\ \sin \beta_j \end{bmatrix}, \quad [M'_j] = \begin{bmatrix} 0 & \cos \beta_j \\ -\sin \beta_j & 0 \end{bmatrix}, \quad j = M, A
\]

and \( \beta_j, j = M, A \), are the angles between the collagen fibers (arranged in symmetrical spirals) and the circumferential direction in the media and adventitia, as indicated in Figure 6. Note that Finlay et al. (1995) reported that in, for example, human brain arteries, the (collagenous) fiber orientations also have small components in the radial direction. However, we neglect this feature in the present work. The reference thickness of the media \( H_M \) and of the adventitia \( H_A \) is provided according to Figure 6.

We use geometrical data from Chuong and Fung (1983) for a carotid artery from a rabbit (experiment 71 in Fung et al., 1979) and make the assumptions that the media occupies 2/3 of the arterial wall thickness (Schulze-Bauer et al., 2003), and that the wall thickness of each layer in the unloaded configuration (\( \alpha = 0.0^\circ \)) is the same as for the case without residual stress (\( \alpha = 160.0^\circ \)). In order to identify the material parameters of the two-layer model for healthy arterial walls, we fitted the parameters to the experimental data

<table>
<thead>
<tr>
<th>Material</th>
<th>Geometry</th>
</tr>
</thead>
<tbody>
<tr>
<td>Media</td>
<td>Material</td>
</tr>
<tr>
<td>( c_M = 3.0000 ) (kPa)</td>
<td>( H_M = 0.26 ) (mm)</td>
</tr>
<tr>
<td>( k_{1M} = 2.3632 ) (kPa)</td>
<td>( \beta_M = 29.0^\circ )</td>
</tr>
<tr>
<td>( k_{2M} = 0.8393 ) (–)</td>
<td></td>
</tr>
<tr>
<td>Adventitia</td>
<td>Geometry</td>
</tr>
<tr>
<td>( c_A = 0.3000 ) (kPa)</td>
<td>( H_A = 0.13 ) (mm)</td>
</tr>
<tr>
<td>( k_{1A} = 0.5620 ) (kPa)</td>
<td>( \beta_A = 62.0^\circ )</td>
</tr>
<tr>
<td>( k_{2A} = 0.7112 ) (–)</td>
<td></td>
</tr>
</tbody>
</table>

from experiment 71 documented by Fung et al. (1979), and used the standard nonlinear Levenberg-Marquardt algorithm. The material parameters obtained are summarized in Figure 6.

The mechanical response of the carotid artery during bending, inflation, axial extension, and torsion is shown in Figure 7. The solid curves show numerical results based on a load-free, but not stress-free, configuration \( \alpha = 160.0^\circ \), while the dashed curves are based on a load-free and stress-free configuration \( \alpha = 0.0^\circ \). The internal pressure \( p_i \) and the angle of twist \( \Phi \) are varied within the ranges

\[
0 \leq p_i \leq 21.33 \text{ kPa and } -0.10 \leq \Phi \leq 0.10 \text{ rad}
\]

The predicted response is in good qualitative agreement with the experimentally observed mechanical behavior of arteries; see, for example, Humphrey (2002a). In particular, as can be seen from Figure 7(a), the model replicates the typical

---

**Figure 7.** Deformation behavior of a carotid artery during inflation and torsion using the constitutive model (40), (41). Solid curves are numerical results with residual strains included \( \alpha = 160.0^\circ \) and the dashed curves are results without residual strains \( \alpha = 0.0^\circ \). Dependence of (a) the internal pressure \( p_i \) and (b) the reduced axial force \( F \) on inner radius \( r_i \), without shear deformation \( \gamma_i = 0 \). Dependence of (c) the torsional couple \( M_t \) and (d) the reduced axial force \( F \) on the shear \( \gamma_i \) at fixed internal pressure \( p_i = 13.33 \text{ kPa} \). The shaded circles indicate the approximate central region of the physiological state. (Reproduced with permission from Holzapfel, G. A., Gasser, T. C., and Ogden, R. W. (2000a). A new constitutive framework for arterial wall mechanics and a comparative study of material models. *J. Elasticity* **61**:1–48. © Springer, 2000.)
stiffening effect at high pressures and the experimentally observed sigmoidal form of the pressure/radius relationship; see Figure 2(a) of Weizsäcker and Pinto (1988). Note that residual strains have a strong influence on the global pressure/radius response of the artery.

Figure 7(b) shows the typical evolution of the reduced axial force \( F \) with inflation (increase of the inner radius) of the artery; see Figure 2(b) of Weizsäcker and Pinto (1988). This means that \( F \) is a decreasing function of \( r_i \) at axial stretches \( \lambda \), less than some value above the physiological stretch and an increasing function for \( \lambda \) greater than this value.

The response of the artery during torsion at the internal (physiological) pressure \( p_i = 13.33 \) kPa is plotted in Figure 7(c,d). As can be seen from Figure 7(c), the torsional couple \( M_t \) increases more slowly than the shear \( \gamma_i = \Phi r_i / l = \Phi r_i / \lambda L \) on the inner boundary increases (i.e., the slope of the curve decreases). In Figure 7(d) the reduced axial force \( F \) during torsion is plotted against the shear \( \gamma_i \). For an axial pre-stretch \( \lambda = 1.5 \) the reduction in the inner radius \( r_i \) due to torsion is about 5.8% \( (\gamma_i = 0.119) \) and 7.8% for \( \lambda = 1.9 \) \( (\gamma_i = 0.085) \). This behavior is in qualitative agreement with the (rare) data on shear tests of arteries provided by Deng et al. (1994).

The fully three-dimensional formulation of the convex potential (40), (41) allows the characteristic anisotropic behavior of healthy arteries under combined bending, inflation, axial extension, and torsion to be predicted. It is not, however, restricted to a particular geometry such as axisymmetry, and is accessible to approximation techniques such as the finite element method. For an extension of the anisotropic model to the finite viscoelastic domain, see Holzapfel and Gasser (2001), which also describes the implementation of the model in a FE program.

### 2.4 Residual stress, growth and remodeling

#### 2.4.1 Residual stress

One of the most important findings with regard to wall mechanics was that a (load-free) arterial ring is not stress free. It springs open when cut in a radial direction, forming an open sector and releasing residual stresses (it appears that Vaishnav and Vossoughi, 1983, were the first to publish this discovery). In general, however, even this open sector is residually stressed since the opening angles of the separate arterial layers are different (Vossoughi et al., 1993; Greenwald et al., 1997; see also the theoretical work by Taber and Humphrey, 2001). The study by Holzapfel et al. (2007) documents layer-specific 3D residual deformations of human aortas in their passive state. It particularly shows that residual deformations are three dimensional, and that related modeling requires consideration of both stretching and bending, which are highly layer-specific and axially dependent.

One important aspect of the influence of residual stress is the effect that it has on the stress and strain distributions through the deformed arterial wall in the physiological state. This is illustrated in Figure 8, in which the distributions of the principal Cauchy stress components \( \sigma_{\theta \theta}, \sigma_zz \) and \( \sigma_{rr} \) through the deformed wall thickness (media and adventitia layers) are plotted against \( r - r_i \), where \( r \) is the deformed radial coordinate and \( r_i \) the deformed inner radius. The data were adopted from the example discussed in Section 2.3.4, and the solution of the three-dimensional boundary-value problem was obtained by using the (mixed) FE method.

Figure 8(a) shows the Cauchy stress distributions for the case in which there are no residual stresses \( (\alpha = 0.0^\circ) \), while Figure 8(b) shows the corresponding plot with residual stresses included \( (\alpha = 160.0^\circ) \). The plots demonstrate the relatively high values of the circumferential stress \( \sigma_{\theta \theta} \) in the media compared with that in the adventitia, which was also found, for example, in von Maltzahn et al. (1984). Interestingly, the maximum stress values \( \sigma_{\theta \theta} \) and \( \sigma_{zz} \) (which occur at the inner side of the media), and the gradients of \( \sigma_{\theta \theta} \) and \( \sigma_{zz} \) in the media are significantly reduced by the influence of the residual stress, an effect which has also been reported for a single layer by, for example, Fung (1990), see Section 11.3 and references therein. Hence, the existence of residual stress seems to homogenize the stress field in the arterial wall, and the stress gradients would be reduced further by larger values of \( \alpha \), as has also been described by Fung (1990). Note that the residual stress also influences the deformed wall thickness and the strains in the physiological state. In particular, at the inner wall, for example, the circumferential strain (measured relative to the stress-free configuration) is reduced by the residual stress (see also the overview article by Rachev and Greenwald, 2003). Note, however, that the assumption of uniform strain is sometimes adopted (Takamizawa and Hayashi, 1987); for a discussion see Ogden and Schulze-Bauer (2000) and Ogden (2003).

It seems that vascular smooth muscle contraction affects the residual stresses and strains, although a detailed quantification is still missing. In particular, the work by Rachev and Hayashi (1999) shows that the incorporation of a model of the basal muscular tone would further reduce (in parallel to residual stress) the computed stress gradients in the wall, which is in agreement with the experimental findings of Matsumoto and Hayashi (1996), and which is also confirmed by Humphrey (2002b). According to Humphrey (2003d) it seems that “... with each increasing level of complexity that we include in the stress–strain relation (material heterogeneity, residual stress, muscle activation, etc.), we find that
The local mechanical environment at any point, which is sensed by the cells of the arterial wall, is represented by the (pulsatile) pressure-induced wall stress and the flow-induced shear stress at this point. This may be characterized by the mean circumferential stress $\overline{\sigma}_\theta$ in the wall (Laplace law) and the mean wall shear stress $\tau$ at the inner surface according to

$$\overline{\sigma}_\theta = \frac{p_i r_i}{h}, \quad \tau = \frac{4\eta Q}{\pi r_i^3} \tag{45}$$

where $p_i$ is the mean arterial pressure, $r_i$ is the deformed inner radius, $h$ is the deformed wall thickness, while $Q$ is the mean blood flow rate, and $\eta$ is the blood viscosity assuming the blood to be a Newtonian fluid and to develop Poiseuille flow.

It is well accepted that endothelial cells, smooth muscle cells, and fibroblasts are regulated in part by mechanical factors such as $\overline{\sigma}_\theta$ and $\tau$.

Pathological changes such as hypertension (characterized by a chronic increase in pressure), aneurysms (focal dilatations of the vascular wall), or atherosclerosis (leading to narrowing of the arterial lumen – stenosis, and to a reduction or even total arrest of blood flow), lead to changes in the mechanical environment, that is, changes in pressure and/or flow. If these changes persist over several days and...
even weeks, the artery responds by a gradual change in mass, internal structure and composition. The process of added mass is called growth, while negative growth is termed atrophy. Any irreversible alteration in internal structure and, consequently, material properties of the arterial tissues caused by mechanical factors is called remodeling (Taber, 1995). Remodeling processes are achieved either by reorganizing existing constituents or by synthesizing new constituents that have a different organization resulting in a different composition of the tissue.

The residually stressed configuration $\Omega_{\text{res}}$ of an artery (compare with Figure 5) arises from growth mechanisms and remodeling of the different layers, and that the arterial wall adapts in response to sustained changes in the mechanical environment so that the circumferential stresses are uniform within each layer. For example, in hypertension, the wall thickness increases in order to maintain/restore stresses to normotensive levels (Matsumoto and Hayashi, 1996). For a constitutive model that accounts for mechanical adaptation of arteries to sustained hypertension see the work by Rachev et al. (1998). The quantification of the biomechanical effects of cell-mediated vascular adaptation (including growth, remodeling, etc.) is crucial to prevent disease or augment healing. Several examples of vascular adaptations are documented by Langille (1993), a model of arterial adaptation to alterations in blood flow is provided by Rachev (2000), and for an extensive overview see Humphrey (2002a), Chapter 9.

In addition, a detailed understanding of the effects of residual stresses on the mechanical behavior of arteries requires the consideration of growth and remodeling effects; see, for example, Fung (1990), Rodriguez et al. (1994); Taber (1995, 1998); Rachev (1997), Rachev et al. (1998), or the overview article by Rachev (2003). The two most important features of biological growth and remodeling appear to be the local rates of turnover (production and removal) of the individual constituents that comprise the tissue, and the configurations in which this turnover occurs; see the constrained mixture model by Humphrey (2003b) suited to describe the underlying biomechanics.

By comparing computed opening angles with experimental data of Greenwald et al. (1997), for the bovine carotid artery, Taber and Humphrey (2001) implied that the material properties change continuously across the vessel wall and that mechanical stress, not strain, correlates with growth in arteries. The stress-based growth law used has the form (Taber, 1998)

$$
\dot{\lambda}_{rg} = \frac{1}{t_r} \left( \frac{\sigma_{\theta}}{(\sigma_{\theta})_m} - \tilde{\sigma}_{\theta} \right),
$$

$$
\dot{\lambda}_{\theta g} = \frac{1}{t_{\theta}} \left( \frac{\sigma_{\theta}}{(\sigma_{\theta})_m} - \tilde{\sigma}_{\theta} \right) + \frac{1}{t_{\tau}} \left( \frac{\tau}{(\tau_0)_m} - \tilde{\tau}_0 \right)
$$

and assumes that (i) the circumferential stress $\sigma_{\theta}$ is maintained at a normal value uniformly across the wall, (ii) the lumen radius is controlled by the mean wall shear stress $\tau$ on the endothelium due to blood flow, approximated by Poiseuille’s formula (45), and that (iii) longitudinal growth $\dot{\lambda}_{rg} = 0$ is ignored to keep the number of free parameters to a minimum.

The subscript 0 indicates (specified) homeostatic stresses, which occur at normal (stable) biological states. At maturity, indicated by the subscript m, these stresses are taken as $(\sigma_{\theta})_m = 200 \text{ kPa}$ (rat) or $300 \text{ kPa}$ (cow); and $(\tau_0)_m = 1.5 \text{ Pa}$ (rat and cow), see Taber (1995). According to Taber (1998), it is assumed that the non-dimensional stresses $\tilde{\sigma}_{\theta}$ and $\tilde{\tau}_0$ depend linearly on the changing blood pressure during development and then remain constant, that is, $\tilde{\sigma}_{\theta}(t) = \tilde{\tau}_0(t) = p(t)/p_m$, where $(p_m)$ is the pressure when maturity is reached. At maturity, therefore $\tilde{\sigma}_{\theta}(t) = \tilde{\tau}_0(t) = 1$. The time constants are $(t_r, t_\theta, t_\tau) = (0.3, 3, 5)$ days for the rat and $(t_r, t_\theta, t_\tau) = (5, 10, 50)$ days for the cow. This form of growth law gives solutions that converge robustly to growth equilibrium under a variety of loading conditions.

### 2.5 Finite element models in vascular solid mechanics

Numerous computational analyses have been performed with the aim to better assess the biomechanics of arterial walls with respect to health and disease. Because of the inherently complex geometries and loading conditions associated with most initial boundary-value problems in vascular mechanics, the FE method seems to be the only tool suitable for predicting realistic mechanical behavior. By providing appropriate references, here we select and discuss five challenging clinically relevant areas of arterial mechanics, that is, (i) arterial clamping, (ii) aneurysm, (iii) artery bifurcation, (iv) balloon angioplasty and (v) aortic dissection which is described in more detail. A brief account is provided on the first four topics while modeling and simulation of aortic dissection is discussed in more detail.

#### 2.5.1 Finite element models for arterial clamping

Arterial clamps are used to compress arteries during surgery so that blood flow is arrested. Arterial compression may lead to injuries of the vessel wall, which are associated with severe short-term and long-term complications. Hence, surgeons require arterial clamps that allow efficient compression causing only minimal injury. For a three-dimensional FE model, designed to optimize the arterial clamping process and to perform detailed parameter studies on a virtual clamped artery, see Gasser et al. (2002), and references therein. In this computer model the artery is treated
as a two-layer tube (media and adventitia) accounting for the presence of residual strains. The model is based on the constitutive equation, as summarized in Section 2.2.3. Nonlinear FE analyses have been performed with the mean dilatation \( Q_1/P_0 \)-element (Simo et al., 1985; Simo and Taylor, 1991). Frictionless contact is assumed between the arterial boundary (master) and the boundary of the clamp (slave), using a point to surface strategy. The control of the penetration between the clamp (modeled as a rigid body) and the artery is performed by means of the penalty method. For more details on the FE model and the loading process see Gasser et al. (2002). Figure 9 illustrates different deformed states of the artery, which occur during the clamping process. State A represents the physiological configuration (before contact with the clamp), while states B–F show the decrease of the arterial lumen due to clamping. In addition, Figure 9 shows the local evolution (change) of normalized Cauchy stresses in the axial and circumferential directions of the artery during clamping. In particular, the stress plots refer to a representative point \( P \), which is located at the inner surface of the media. The axial stress \( s_z \) increases significantly, while the circumferential stress \( s_\theta \) decreases with progressive clamp displacement. Remarkably, in state F the value of \( s_z \) at \( P \) is about four times higher than that in the associated state A.

In a more recent study by Fereidoonnezhad et al. (2016) the process of arterial clamping is solved in a more realistic way. Arterial clamping that involves non-physiological tissue loading leads to damage-induced inelastic phenomena (i.e., stress softening and permanent deformation), which was considered as an additional modeling feature. The aortic clamping problem was simulated using a specifically developed FE framework, thereby non-symmetric blood pressure after clamping was also analyzed.

### 2.5.2 Aneurysm

Aneurysms are focal dilatations of the vascular wall that appear to enlarge over years but can rupture suddenly, often without warning. The majority form in the cerebral arteries and the thoracic and abdominal aortas. Numerical analyses of wall stresses may be helpful to study the biomechanics of aneurysmal genesis and growth, and to predict the susceptibility of a particular aneurysm to rupture, thereby providing an aid in the clinical management of patients. The majority of all intracranial aneurysms are saccular lesions, which usually develop at the apex of a bifurcation in or near the circle of Willis located at the base of the brain. They are typically thin-walled and balloon-like in shape. Based on (idealized) axisymmetric lesions, Kyriacou et al. (1996) and Shah et al. (1997) have developed fully nonlinear (materially and geometrically) FE models with a Fung-type constitutive law. They investigated a range of (quasi-static) stress–strain behaviors from homogeneous and isotropic to heterogeneous and anisotropic. For more details on the mechanics of intracranial saccular aneurysms see, for example, Humphrey...
arotic aneurysms occur, however, in the abdominal aorta and involve most of the circumference of the vessel over a finite axial length. A fully nonlinear FE model for abdominal aortic aneurysms, with the assumption of isotropy, homogeneity, and incompressibility, has been proposed by Raghavan and Vorp (2000). This study seems to be the first report to develop and evaluate a finite strain material model specific to abdominal aortic aneurysm. It is based on known experimental data and the use of shell elements. Residual stresses were not considered. The study indicates that a variation in the computed wall stress distribution due to a variation in material parameters over a reasonable range is little. The coupled fluid-structure interaction model by Di Martino et al. (2001) accounts for CT-based three-dimensional geometry of a patient’s abdominal aortic aneurysm and the presence of a thrombus. Additional information on the mechanics of aortic aneurysms may be found in the book by Humphrey (2002a), Section 8.4, or in the more recent book edited by McGoughlin (2011), with more references therein.

2.5.3 Artery bifurcation

Bifurcation regions of an artery are the most important sites pathologically, because atherosclerosis and intracranial saccular aneurysms often occur therein. Hence, the need for developing an appropriate constitutive theory and for determining wall stresses in bifurcations is clear. Delfino et al. (1997, 1998) constructed a realistic three-dimensional FE model of the human carotid bifurcation that included the varying thickness of the arterial wall and residual strains, which were characterized by experimental observations. They proposed an (isotropic) rubber-like constitutive model, which is able to model the typical stiffening effects in the high pressure domain. Although the model is not able to reproduce the pronounced anisotropic mechanical behavior of arteries observed in several experimental investigations, its predictions for the kinematics and loading conditions, as described in the example of Section 2.3, are in some respect qualitatively similar to those for the anisotropic energy function (40) and (41). Perktold and Rappitsch (1995) developed a skilled numerical model of local blood flow and vessel wall mechanics in a carotid artery bifurcation.

2.5.4 Balloon angioplasty

Balloon angioplasty is a well-established interventional procedure aimed at dilating stenotic or occluded arteries in order to restore blood flow. It is the most frequently used therapeutical intervention worldwide and attracts great and steadily growing medical, economic, and scientific interest (Mozaffarian et al., 2016). The knowledge that balloon angioplasty is a mechanical solution for a clinical problem implies that there is a necessity for a detailed understanding of the biomechanics and mechanobiology of the types of soft tissues and calcifications involved. It is exactly this understanding that is needed to improve such procedures (procedural protocols, interventional instruments such as balloons and stents etc.), which often fail due to restenosis. The work by Holzapfel et al. (2002b) reviews existing computational models and proposes a new method for the simulation of balloon angioplasty using a realistic three-dimensional FE model. On the basis of an individual human stenotic post-mortem artery, three-dimensional stress states during balloon expansion and stent deployment were analyzed. The layer-specific geometrical model is based on in vitro magnetic resonance imaging of the considered artery, and is represented by non-uniform rational B-splines surfaces (Holzapfel et al., 2000b). Eight different arterial tissues are considered. Data from mechanical tests were used to establish large strain constitutive laws, which model the typical anisotropic, highly nonlinear, and inelastic mechanical characteristics under supra-physiological loadings (Holzapfel et al., 2000a; Holzapfel and Gasser, 2001; Gasser and Holzapfel, 2002). In addition, the model incorporates balloon–artery interactions and accounts for vessel-specific axial in situ pre-stretches. A new and very efficient strategy to parameterize contact surfaces of arbitrary mesh topology in three dimensions, as occurring in the complex contact problem of balloon angioplasty, was proposed by Stadler and Holzapfel (2004).

The study by Gasser and Holzapfel (2007b) proposed physical and computational 3D models to trace fissuring/dissection in atherosclerotic plaques that occur during balloon angioplasty interventions. Thereby, tissue failure is captured by a strong discontinuity kinematics and a cohesive zone model, while the numerical implementation is based on the partition of unity FE method and the interface element method. The geometry of an atherosclerotic-prone human external iliac artery is generated from images and tissue-specific material properties are considered. Numerical results suggest that the plaque fissures at both shoulders of the fibrous cap, and that local dissections between the intima and the media develop at the fibrous cap location with the smallest thickness. The analysis documented by Gasser and Holzapfel (2007a) shows a computational approach to capture balloon-induced over-stretch of remnant non-diseased tissues in atherosclerotic arteries. The inelastic model is able to capture experimentally observed wall changes that occur during balloon inflation. In particular, the different 3D stress states at physiological loading conditions before and after balloon inflation are discussed. The work by Kiousis et al. (2008) introduced
2.5.5 Modeling and simulation of aortic dissection

Aortic dissection is a vascular pathology that may occur spontaneously or non-spontaneously. The annual occurrence of aortic dissection is about 5–30 cases per million of the population (Knipp et al., 2007). An aortic dissection may initiate from an intimal tear and continue propagating toward the middle layer of the aorta, and may subsequently cause a delamination of the media or could delaminate the media from the adventitia. Such a delamination may create a “false lumen” which changes the hemodynamics and the stress pattern of the underlying wall. Aortic dissection may also lead to an acute rupture of the wall which is rare (Criado, 2011). Mechanically, dissections can be attributed to intra-lamellar failure of the microstructural components within the wall, that is, elastin and collagen fibers (Pal et al., 2014). For a schematic sketch of an aortic dissection see Figure 10 (taken from Holzapfel, 2009). It is key to better understand the mechanism of a dissection through an aortic tissue, which is basically a biomechanical process. For a recent review of the mechanics of tissue dissection in health and disease from the experimental and modeling point of view, see Tong et al. (2016).

In this section, we provide a continuum model for aortic dissection using the phase-field approach with an energy-based anisotropic failure criterion, and we discuss the FE simulation of a simple shear test in 3D, which is according to Gültekin et al. (2016a).

2.5.5.1 Modeling failure in an aortic dissection using the phase-field approach

We describe a diffusive crack topology and start by introducing a material body \( B \subset \mathbb{R}^3 \) at time \( t_0 \subset \mathbb{R} \), the reference configuration, where we denote \( \mathbf{X} \in B \) as the material point. The placement of the body at \( t \subset \mathbb{R} \) we call spatial configuration \( \mathbf{S} \subset \mathbb{R}^3 \) so that \( \mathbf{X} \in B \) is mapped to the spatial point \( \mathbf{x} \in S \) by the deformation map \( \varphi(\mathbf{X}, t) \), subsequently considered as a primary field variable. In addition, we let \( \partial B \subset \mathbb{R}^2 \) be the surface of \( B \subset \mathbb{R}^3 \). Finally, we introduce the crack phase-field \( d(\mathbf{X}, t) \in [0, 1] \), an additional primary field variable, where \( d = 0 \) characterizes an intact material, while \( d = 1 \) the ruptured state of a material.

Next we introduce the field equation for \( d \) in 1D and assume an infinitely long 1D bar with a crack at \( x = 0 \). The crack phase-field \( d(x) \in [0, 1] \) characterizes the crack topology according to

\[
d(x) = \delta(x) : \begin{cases} 1 & \text{for } x = 0 \\ 0 & \text{otherwise} \end{cases}
\]

(47)

where \( \delta(x) \) is the Kronecker delta, see Figure 11(a). The sharp crack topology can be approximated by a diffusive crack topology as

\[
d(x) = \exp\left(-|x|/l\right)
\]

(48)

where \( l \) is the length-scale parameter regularizing the sharp crack topology. Hence, the crack is spread over the whole length of the bar, see Figure 11(b). The exponential function (48) is the solution of the homogeneous ODE (Miehe et al., 2010), that is,

\[
d(x) - \bar{l}^2 d''(x) = 0
\]

(49)

subjected to the Dirichlet-type boundary conditions \( d(0) = 1 \) and \( d(\pm \infty) = 0 \). An equivalent functional form may be given as \( I(d) = (1/2) \int_B (d' + \bar{l}^2 d'')^2 \mathrm{d}x \), where a scaling with \( l \) may lead to the definition of the crack surface density per unit length according to

\[
\gamma(d, d') = \frac{1}{2l} (d'^2 + \bar{l}^2 d''^2)
\]

(50)

The analog of equation (49) in 3D reads \( d - \bar{l}^2 \Delta d = 0 \) (in \( B \)) and \( \nabla d \cdot \mathbf{N} = 0 \) (on \( \partial B \)), where \( \Delta d \) is the Laplacian of \( d \), and \( \mathbf{N} \) is here the unit surface normal oriented outward in the
where \( \rho_0 \), \( \bar{\varphi} \), and \( \bar{T} \) are the density, the prescribed body force, and the surface traction in the reference configuration, respectively.

Next the crack energy functional \( D_c \) is defined by using the volume-specific crack surface density \( \gamma \) (51). Thus,

\[
D_c(d) = \int_B g_c \gamma(d, \nabla d) dV
\]

where \( g_c \) is the critical fracture energy required to convert an un-cracked tissue into a cracked tissue. The crack dissipation functional \( D \) is then obtained from (58) as

\[
D(d) = \int_B g_c [\delta_d \gamma(d, \nabla d)] dV
\]

where \( \delta_d \gamma \) denotes the variational derivative of the crack surface density \( \gamma \) (Miehe et al., 2010), with the explicit form

\[
\delta_d \gamma = \frac{1}{\ell} (d - \Delta d) \]

and \( D \geq 0 \) according to the second law of thermodynamics.

Finally, with the stated functionals (55), (57), and (59), we obtain the power balance \( \Pi \) according to

\[
\Pi(\dot{\varphi}, \dot{d}) = E(\dot{\varphi}, \dot{d}) + D(\dot{d}) - P(\dot{\varphi}) = 0
\]

Hence, a rate-type mixed variational principle can be constructed via a minimization principle for the quasi-static process as

\[
\{ \dot{\varphi}, \dot{d} \} = \arg \left\{ \inf_{\varphi \in \mathcal{W}_\varphi} \inf_{d \in \mathcal{W}_d} \Pi(\varphi, d) \right\}
\]

with the admissible domains for the state variables

\[
\mathcal{W}_\varphi = \{ \varphi \mid \varphi = 0 \ \text{on} \ \partial B_{\varphi} \},
\]

\[
\mathcal{W}_d = \{ d \mid \dot{d} = 0 \ \text{on} \ \partial B_d \}
\]

The variation of the functional leads to the two Euler–Lagrange equations

\[
\text{Div}(\mathbf{F}S) + \rho_0 \ddot{\varphi} = \mathbf{0}, \quad (f - g_c \delta_d \gamma) \dot{d} = 0
\]
along with the loading-unloading conditions ensuring the principal of maximum dissipation during evolution of $d$, that is,

$$
d \geq 0, f - g_c \delta \gamma \leq 0, (f - g_c \delta \gamma)\dot{d} = 0 \tag{65}
$$

The first condition ensures irreversibility of the evolution of $d$, the second condition is an equality for evolving a crack and it is negative for a stable crack, while the third condition describes the balance law for the evolution of $d$ subject to the former conditions.

Before discussing the computational analysis of tissue dissection we refer now to the used constitutive equations and provide the failure criterion. In particular, we use dissection we refer now to the used constitutive equations and itis negative for a stable crack, while the third condition describes the balance law for the evolution of $d$ subject to the former conditions.

Before discussing the computational analysis of tissue dissection we refer now to the used constitutive equations and provide the failure criterion. In particular, we use $A = 0$ and $B = 1$ in (21) so that $I^* = I_4$ and $I^* = I_6$, a case with perfectly aligned collagen fibers as already discussed in Section 2.2.3. Hence, to describe the mechanical response of the intact aortic tissue the free-energy function $\Psi_0$ in (52) is specified as

$$
\Psi_0 = \Psi_{0g}(J, I_4) + \Psi_{0f}(I_4, I_6) \tag{66}
$$

where the isotropic function, which represents the mechanical behavior of the non-collagenous ground-matrix, is here characterized by

$$
\Psi_{0g}(J, I_4) = \tilde{\kappa}(J - \ln J - 1) + \frac{\mu}{2}(I_4 - 2 \ln J - 3) \tag{67}
$$

and $\Psi_{0f}(I_4, I_6)$ is the exponential anisotropic free-energy function taking into account the contributions of the collagen fibers, which is according to (12). In (67) $\tilde{\kappa}$ denotes the penalty parameter whereas $\mu$ is the shear modulus.

Finally we provide an energy-based anisotropic failure criterion that captures the tissue state at which the cracking starts and propagates. In order to describe anisotropic failure, we further elaborate on the equation for the evolution of $d$ by using (64) with (60), and (56) with (52), (53) for $d \geq 0$, that is,

$$
f - \frac{g_c}{l}(d - l^2 \Delta d) = 0 \quad f = 2(1 - d)\Psi_0 \tag{68}
$$

By assuming distinct failure processes for the ground-matrix and the collagen fabric we may write

$$
2(1 - d)\Psi_{0g} - \frac{g_{cg}}{l}(d - l^2 \Delta d) = 0,
$$

$$
2(1 - d)\Psi_{0f} - \frac{g_{cf}}{l}(d - l^2 \Delta d) = 0 \tag{69}
$$

which are dual to the free-energy functions for the isotropic and the anisotropic parts, respectively, see (66). In (69) we have introduced the critical fracture energies $g_{cg}$ and $g_{cf}$ which relate to the isotropic ground-matrix and the anisotropic fiber contribution, respectively. We now introduce a (dimensionless) crack driving function, say $\hat{H}$, which we also additively decompose as

$$
\hat{H} = \hat{H}_g + \hat{H}_f, \quad \hat{H}_g = \frac{\Psi_{0g}}{g_{cg}/l}, \quad \hat{H}_f = \frac{\Psi_{0f}}{g_{cf}/l} \tag{70}
$$

where $\hat{H}_g$ relates to the isotropic part (ground-matrix) and $\hat{H}_f$ to the anisotropic part (collagen fibers).

By superposing the failure processes (69) and using (70), we get

$$
d - l^2 \Delta d = (1 - d)\hat{H} \tag{71}
$$

where the left-hand side is the geometric resistance to crack growth and the right-hand side is the local source term for crack growth (Raina and Miehe, 2016). To enforce the irreversibility condition and prevent healing effects, the dimensionless source term (70) is recast as

$$
H(t) = \max_{s \in [0,t]}[(\hat{H}(s) - 1)] \tag{72}
$$

with the Macaulay brackets $(\langle \bullet \rangle) = [(\bullet) + |(\bullet)|]/2$. Hence, $d$ does not evolve for a dimensionless crack source term $\hat{H}(s) < 1$. The specific choice for $H(t)$ in (72) ensures irreversibility of the crack evolution.

2.5.5.2 Operator-splitting algorithm, finite element simulation of aortic dissection

From the strong forms of the coupled set of equations we obtain a staggered set of algebraic equations using a Galerkin type FE formulation. The weak form of the balance of static equilibrium is derived and consistently linearized along the deformation map $\varphi(X, t)$ and the crack phase-field $d(X, t)$. A temporal and spatial discretization scheme is employed for $\varphi$ and $d$. All field variables are discretized with isoparametric shape functions yielding a set of algebraic equations to be solved by a one-pass operator-splitting algorithm. A discrete time increment $\tau = t_{n+1} - t_n$ is considered, where $t_{n+1}$ and $t_n$ stand for the current and the previous time steps, respectively. The operator-splitting algorithm yields a decoupling within the time interval, and is the composition of the mechanical sub-problem and the crack-growth sub-problem, that is,

$$
ALGO_{CM} = ALGO_{C} \cdot ALGO_{M} \tag{73}
$$

The algorithm of each sub-problem is obtained as

(M): \[
\begin{align*}
\text{Div}(\mathbf{F}S) + \rho_0 \dot{\gamma} &= 0 \\
\dot{d} &= 0 \\
\end{align*}
\]

(C): \[
\begin{align*}
\dot{\varphi} &= 0 \\
d - l^2 \Delta d - (1 - d)H &= 0 \\
\end{align*}
\]
where the algorithm (M) is the mechanical predictor step at a frozen crack phase-field parameter $d = d_n$, and the algorithm (C) is the crack evolution step at a frozen deformation map $\varphi$. For the discrete residual vector and the (coupled) stiffness matrix the reader is referred to Gültelen et al. (2016a). The operator-splitting algorithm as outlined in Table 3 forms the basis for the numerical scheme in which $d$ is driven by the local history field $H(t_{n+1})$. The phase-field model was implemented in the FE analysis program (Taylor, 2008).

Finally, we present an aortic fracture simulation using the FE method. In particular, a simple shear test of a media obtained from a human thoracic aorta is analyzed and compared with experimental data, as documented by Sommer et al. (2016), see specimen AVIII. The aortic specimen was sheared along the circumferential $\theta$-direction (referred to as $\zeta\theta$ mode) and the longitudinal $z$-direction ($\theta z$ mode). The computational analysis is performed with a monotonic shear load applied to the specimen with symmetric incisions; for the related geometries see Figure 12(a,c). The geometry of the specimen sheared along the $\theta$-direction is discretized with 23,525 four-node tetrahedral elements, with a length-scale parameter $l = 0.167$ mm, see Figure 12(b), while the specimen sheared along the $z$-direction is discretized with 22,657 elements, with $l = 0.25$ mm, see Figure 12(d). The parameter $l$ is chosen to satisfy $l > 2h$ in order to resolve the crack surface properly, see Miehe et al. (2010). The FE meshes are refined in the regions where the crack is expected to propagate. With respect to the Dirichlet-boundary conditions the nodes at $z = 0$ are constrained in three directions for the $\zeta\theta$ mode, while those located at $\theta = 0$ are constrained in three directions for the $\theta z$ mode. The elastic material parameters are obtained using a least-squares analysis. The critical fracture energies $g_{c\theta}$ and $g_{c\zeta}$ are predicted for each mode by comparing the Cauchy stress versus the amount of shear curves of the numerical results with those obtained from the experiments. The parameters are summarized in Table 4.

Figure 13 shows the FE results in terms of the Cauchy stress values $\sigma_{\zeta\theta}$, $\sigma_{\theta z}$, and the amount of shear $\gamma$. The FE results are in good agreement with the anisotropic experimental response. The numerical results in Figure 13 are obtained by considering the average of all nodal stresses at the edge $z = \theta = 3$ mm for the $\zeta\theta$ mode, and at the edge $\theta = 3$, $z = 5$ mm for the $\theta z$ mode. The onset of the cracks is at the two tips of the symmetrically incised region where the stress concentration, and, therefore, the energy of the intact tissue satisfies the failure condition. The two distinct crack patterns meet in the middle of the refined region at which the complete failure phenomenon manifests itself. This is accompanied by a sudden loss of the load-bearing capacity. Figure 14 illustrates the spatial distributions of the crack phase-field $d$ and the Cauchy shear stress $\sigma_{\theta z}$ at the locations A, B, C, and D, as indicated in Figure 13(b).
Figure 12. (a,c) Geometries of the specimens sheared in the circumferential $\theta$-direction ($z\theta$ mode) and in the longitudinal $z$-direction ($\theta z$ mode) by the displacement $3\gamma$ (thickness times amount of shear). The structure of the media is characterized by two families of fibers, oriented in the directions $\mathbf{M}_4$ and $\mathbf{M}_6$ in the reference configuration, and they are symmetrically arranged with respect to the cylinder axis. The angle between the fibers and the circumferential direction is $\alpha$; (b,d) finite element meshes. Dimensions are provided in millimeters. (Reproduced with permission from Gültekin, O., Dal, H., and Holzapfel, G. A. (2016a). A phase-field approach to model fracture of arterial walls: theory and finite element analysis. Comput. Meth. Appl. Mech. Eng. 312: 542–566. © Elsevier, 2016.)

Figure 13. Simple shear test data (triangles) and finite element results (solid curves): (a) Cauchy shear stress $\sigma_{\theta z}$ versus amount of shear $\gamma$ for the $z\theta$ mode; (b) Cauchy shear stress $\sigma_{\theta z}$ versus $\gamma$ for the $\theta z$ mode. (Reproduced with permission from Gültekin, O., Dal, H., and Holzapfel, G. A. (2016a). A phase-field approach to model fracture of arterial walls: theory and finite element analysis. Comput. Meth. Appl. Mech. Eng. 312: 542–566. © Elsevier, 2016.)
3 MECHANICS OF THE HEART WALL

The primary function of the heart is to pump blood to the tissues of the body. A detailed exposition of cardiac function within the context of the mechanics of ventricular walls is provided in the review article by McCulloch (1995). An account of the heart from the modeling viewpoint is found in the book edited by Cowin and Humphrey (2001). A comprehensive overview on the mechanics of the cells and tissues that constitute the heart is presented by Humphrey (2002a), Chapter 10, while the review article by Hunter et al. (2003) contains an account of modeling the total heart function. For a more recent review on the biomechanics of cardiac function see Voorhees and Han (2015).

3.1 Structure

The heart consists of four chambers: the left ventricle (LV) and right Ventricle (RV), separated by the interventricular septum, and the left and right atria, separated by the interatrial septum. The ventricles are three-dimensional pressure vessels (pumping muscular chambers) whose thickness and curvatures depend on space and time. The thick-walled (LV) pumps blood at (physiologically) high pressures up to approximately 17.0 kPa (130 mmHg) during the normal heart cycle throughout the arteries, while the much thinner RV pumps blood at low pressures of about 1/7 of the pressure of the LV. The thin-walled atria serve as low pressure blood reservoirs for the ventricles. For a detailed assessment of normal and abnormal cardiac function see the article by Little (2001).

Like arterial walls, the wall of the heart is composed of three distinct layers, the endocardium (innermost layer of the heart), myocardium (middle layer), and epicardium (outermost layer). The endocardium is a serous biologically functional “membrane” (∼100 μm thick) inside of each of the cardiac chambers, which protects the myocardium from direct contact with the blood. The myocardium, that is, the parenchymal, is a highly structured orthotropic soft tissue. It consists primarily of myocytes that are arranged into locally parallel muscle fibers embedded in an extracellular matrix, which consists largely of collagen. In contrast to the arterial wall, the transmural orientations of muscle fibers typically vary continuously within the myocardium from about −60° in the sub-epicardial region to near 0° in the mid-wall region to about 60° in the sub-endocardial region, which is with respect to the circumferential direction (see, for example, LeGrice et al., 1995, and Hunter et al., 1997b, for a data-based model see LeGrice et al., 2001). It is the transmural splay of muscle fiber directions that causes the heart to twist during the cardiac cycle; for more on the structure of the myocardium see, for example, Section 2 by Holzapfel and Ogden (2009b). From the mechanical perspective, the myocardium is the most significant layer in normal
heart, endowing the heart with its ability to pump blood. The outermost layer is the epicardium (or visceral pericardium), which is a serous membrane with a thickness of approximately 100 μm, like the endocardium. Torsional deformation at the epicardium is smaller than at the endocardium. The heart is surrounded by a fibrous sac that encompasses the heart to resist rapid increases in cardiac size and that isolates the heart from other structures in the thorax. The inner wall of this sac is the epicardium, while the outer wall is the (parietal) pericardium, which is another membrane, thicker than the endocardium and epicardium, composed of an inner serous layer and an outer fibrous layer. Both membranes, the epicardium and pericardium, create a small space within the sac filled with a small amount of “lubricating” (pericardial) fluid (produced by the pericardium), which provides lubrication for the continuous movement of the heart within the thorax. Like the adventitia, it is thought that the pericardium serves to limit overdistension of the heart. For a more comprehensive survey on cardiac anatomy the reader is referred to Hunter et al. (1997b), Chapter 6.2, and references therein.

3.2 Constitutive models

3.2.1 Overview

Myocardial tissue is composed of discrete layers (or “sheets”) of muscle fibers tightly bound by endomysial collagen and relatively loosely connected by perimysial collagen (LeGrice et al., 1995). Since myocardial deformations during the cardiac cycle are large (fiber strains typically reach 10% at end-diastole), finite deformation theory is required, with constitutive laws based on the anisotropic and inhomogeneous fibrous structure of the myocardium. Previous three-dimensional constitutive models for the passive LV assumed that the myocardium is transversely isotropic (Humphrey and Yin, 1987; Horowitz et al., 1988a; Humphrey et al., 1990a,b; see also the reviews by Hunter and Smaill, 1989; Smaill and Hunter, 1991). However, biaxial tension tests for thin sections of passive myocardial tissue along the fiber axis (coinciding with the muscle fiber direction at each point), the sheet axis (defined to lie in the plane of the sheet and perpendicular to the fiber direction), and the sheet-normal axis (defined to be orthogonal to the first two) have shown highly nonlinear and quite different stress–strain responses (Smaill and Hunter, 1991). Additional biaxial tension tests on thin sections of the passive LV tissue have been carried out by Demer and Yin (1983), Yin et al. (1987), Humphrey et al. (1990b) and Novak et al. (1994). Figure 15 exhibits a schematic diagram of typical stress–strain behavior of myocardium when stretched along each of the three axes (Hunter et al., 1997a). As can be seen, the limiting stretch for an elastic response along the three axes differs significantly. The limiting stretch along the fiber axis is about 1.28 and along the sheet axis about 1.5. Below a stretch of about 1.5 the tension along the sheet-normal axis is very small. However, the tissue responses with an (exponential) stiffening effect at higher stretches and damage occurs when this stretch exceeds about 1.72 (Hunter et al., 1997a). Morphological and structural explanations of the low sheet-normal stiffness and the high fiber stiffness are offered by LeGrice et al. (1995) and MacKenna et al. (1994), respectively. It remains, however, uncertain how the passive biaxial mechanical properties of isolated myocardial tissue are related to the properties of the intact ventricular wall.
A powerful orthotropic and microstructurally based constitutive model for the myocardium, which, in particular, considers the characteristic stress–strain curves illustrated in Figure 15, has been proposed by Smaill and Hunter (1991), and is examined in Section 3.2.2. Another constitutive model, which treats the passive myocardium as nonlinear and orthotropic, has the exponential Fung-type form (Usyk et al., 2001). postulated to have the decoupled form

\[ \Psi = \frac{1}{2}C(\exp(Q - 1) - p(J - 1)) \]

\[ Q = b_{ff}E_{ff}^2 + b_{cc}E_{cc}^2 + b_{ss}E_{ss}^2 + b_{cs}(E_{cc}^2 + E_{ss}^2) + b_{fs}(E_{fs}^2 + E_{sf}^2) + b_{fc}(E_{fc}^2 + E_{cf}^2) \]

where \( E_{ij} \) are components of the Green-Lagrange strain tensor referred to a local orthogonal coordinate system having fiber, crossfiber, and sheet coordinates (f, c, s). The function \( p(J - 1) \) is in accord with (4). The seven material parameters have been estimated for the intact canine ventricular myocardium at end-diastole, and are proposed to be \( C = 0.88 \text{kPa}, b_{ff} = 18.5, b_{cc} = b_{ss} = 3.58, b_{fc} = b_{fs} = b_{cs} = 2.8 \).

The models of Huyghe et al. (1991a) and Yang and Taber (1991) consider the contribution of extracellular fluid flow of the myocardium to the nonlinear viscoelastic and poroelastic behavior of the passive myocardial tissue. Nash (1998) introduced a simple model of the fluid movement throughout the ventricular walls to account for regional myocardial compressibility via changes in the vascular volume. A coupled constitutive model of cardiac cellular electro-mechanics was proposed by Nickerson et al. (2001). It combines passive and active muscle mechanics (Hunter et al., 1998) to cardiac myocyte electrophysiology (Noble et al., 1998) via the calcium transient in a computationally efficient manner so that this model can be used in anatomically and biophysically based tissue and organ models. For more details on modeling cardiac mechanical properties the reader is referred to the review article by Costa et al. (2001).

### 3.2.2 The pole-zero strain-energy function for myocardium

Based on biaxial test results of the passive ventricular myocardium, as described above (see also Figure 15), and on microstructural observations, Smaill and Hunter (1991) developed a three-dimensional orthotropic constitutive model, which entered the literature as the so-called pole–zero strain-energy function for the myocardium. The passive heart tissue is considered to be incompressible and perfectly elastic. The energy \( \Psi \) stored in the myocardium is

\[ \Psi = k_{11}\left(\frac{E_{11}^2}{(a_{11} - E_{11})^{b_{11}}} + k_{22}\left(\frac{E_{22}^2}{(a_{22} - E_{22})^{b_{22}}} + 1\right) + k_{33}\left(\frac{E_{33}^2}{(a_{33} - E_{33})^{b_{33}}} + 1\right) + k_{12}\left(\frac{E_{12}^2}{(a_{12} - E_{12})^{b_{12}}} + 1\right) + k_{13}\left(\frac{E_{13}^2}{(a_{13} - E_{13})^{b_{13}}} + 1\right) + k_{23}\left(\frac{E_{23}^2}{(a_{23} - E_{23})^{b_{23}}} + 1\right) \right) - p(J - 1) \]

where \( E_{ij}, i, j = 1, 2, 3, \) are the components of the Green-Lagrange strain tensor referred to the coordinates (1, 2, 3), while \( a_{ij}, b_{ij}, k_{ij} \) are 18 material parameters, as discussed and provided below. The first three terms in (77) relate to the axial modes of deformation, and hence the subscripts 11, 22, and 33 indicate the three microstructural axes, that is, the fiber, sheet, and sheet-normal axes, respectively. The next three terms relate to modes of shear deformation, where the subscripts 12, 13, and 23 denote fiber/sheet, fiber/sheet-normal and sheet/sheet-normal, respectively. The function \( p(J - 1) \) is in accord with (4). Biaxial tension tests on thin sections of passive myocardium show that the stress-strain behavior along one axis is nearly independent of the degree of lateral strain (Smaill and Hunter, 1991). Therefore, the strain-energy function (77) is separated into individual expressions in terms of the strain along each of the axes.

The constitutive parameters are explained as follows: the “Pole” parameters \( a_{ij} \) with the conditions \( a_{ij} > E_{ij} \), represent the limiting strain for a particular type of deformation. They are physical properties of the tissue that may be measured directly from microstructural observations. The parameters \( b_{ij} \) govern the curvature of the stress–strain curves for each mode of deformation, while \( k_{ij} \), with the dimension of stress, give the relative contribution of the corresponding mode of deformation to the total strain energy of the material. Note that the parameters \( k_{11}, k_{22}, k_{33} \) are defined to be zero if the components \( E_{11}, E_{22}, E_{33} \) of the Green-Lagrange strain tensor, respectively, are negative. The constitutive parameters of (77) have been estimated using biaxial experiments (Nielsen et al., 1991a; Smaill and Hunter, 1991) and shear tests (Dokos et al., 2002) on myocardial tissue, and are listed in Table 5 (Stevens et al., 2003). Hunter et al. (1997a) introduced an elastic constitutive model for the cardiac muscle to help understand and quantify the correlation between the parameters of the “pole-zero” constitutive law (77). The authors assumed that there are three families of (collagen) fibers with preferred orientations in addition to the locally parallel muscle fibers. Each family is normally distributed about a mean direction, which is aligned with one of the
Table 5. Parameter values of myocardium for the pole-zero constitutive law, that is, equation (77).

<table>
<thead>
<tr>
<th>Type</th>
<th>Axial properties</th>
<th>Shear properties</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coefficients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$k_{11}$</td>
<td>2.0 kPa</td>
<td>$k_{12}$</td>
</tr>
<tr>
<td>$k_{22}$</td>
<td>2.0 kPa</td>
<td>$k_{13}$</td>
</tr>
<tr>
<td>$k_{33}$</td>
<td>2.0 kPa</td>
<td>$k_{23}$</td>
</tr>
<tr>
<td>$a_{11}$</td>
<td>0.523</td>
<td>$a_{12}$</td>
</tr>
<tr>
<td>$a_{22}$</td>
<td>0.681</td>
<td>$a_{13}$</td>
</tr>
<tr>
<td>$a_{33}$</td>
<td>1.037</td>
<td>$a_{23}$</td>
</tr>
<tr>
<td>Curvatures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$b_{11}$</td>
<td>1.351</td>
<td>$b_{12}$</td>
</tr>
<tr>
<td>$b_{22}$</td>
<td>5.991</td>
<td>$b_{13}$</td>
</tr>
<tr>
<td>$b_{33}$</td>
<td>0.398</td>
<td>$b_{23}$</td>
</tr>
</tbody>
</table>

3.2.3 A structurally based model for the passive myocardium

We start by briefly reviewing the relevant kinematics. By recalling the specific structure of the myocardium (fiber, sheet (cross-fiber), sheet-normal (normal) directions), and the definition of the invariant $I_4 = (C_M) \cdot M$ in Section 2.2.2, we can consider the invariant $I_4$ associated with each of these directions by using the notation

$$I_{4i} = f_0 \cdot (Cf_0), \ I_{4s} = s_0 \cdot (Cs_0), \ I_{4n} = n_0 \cdot (Cn_0) \quad (78)$$

with the fiber axis $f_0$, the sheet axis $s_0$, and the sheet-normal axis $n_0$ in the reference configuration. We note that

$$\sum_{i=1, s, n} I_{4i} = C : (f_0 \otimes f_0 + s_0 \otimes s_0 + n_0 \otimes n_0) = C : I = I_1$$

(79)

where $I_1 = \text{tr} C$ is the first invariant. Consequently, only three of the invariants $I_{4f}, I_{4s}, I_{4n}$, and $I_1$ are independent so that we may omit one of these in the functional dependence of the free energy.

We may also define the invariants $I_{5f}, I_{5s}, I_{5n}$ for each direction, which are related by $I_{5f} + I_{5s} + I_{5n} = I_1^2 - 2I_2$. In addition, we have the coupling invariants according to

$$I_{8fs} = I_{8sf} = f_0 \cdot (Cs_0), \ I_{8sn} = I_{8ns} = s_0 \cdot (Cn_0)$$

$$I_{8sn} = I_{8sn} = s_0 \cdot (Cn_0)$$

(80)

It can be shown that $I_{5f}, I_{5s}, I_{5n}$ are expressible in terms of the other invariants via $I_{5i} = I_{5s} + I_{5fs}^2 + I_{5fs}^2$, $I_{5s} = I_{5s} + I_{5fs}^2 + I_{5sn}^2$ and $I_{5n} = I_{5sn}^2 + I_{5sn}^2$, and that the third invariant $I_3$ can be expressed by the invariants $I_{4f}, I_{4s}, I_{4n}, I_{8fs}, I_{8sn}$ and $I_{8sn}$. Consequently, if the material is compressible there are seven independent invariants, while for an incompressible material there are six.

For an incompressible material that depends only on the invariants $I_1, I_4, I_5$, and $I_4, I_5$, for example, the Cauchy stress tensor $\sigma$ is

$$\sigma = 2\psi_1 B + 2\psi_4 f \otimes f + 2\psi_4 s \otimes s - pI$$

(81)

where we have omitted the invariant $I_{4n}$; there is a good physical reason for this choice. In (81) $B = F F^T, f = F f_0, s = F s_0$, and $\psi_1 = \partial p / \partial V, \psi_4 = \partial \psi_1 / \partial V_i, i = f, s$.

Next we review a specific model, in particular, we provide a free-energy function and the related Cauchy stress tensor in the most general form with the assumption that the myocardium is in its passive state. In order to capture the orthotropic response of the tissue, it is necessary to make use of one or more of the invariants $I_{8ij}$. By choosing the invariant...
Figure 16. Diastolic pressure-volume relations resulting from three experimental studies of canine LV. The prediction of the pressure-volume relation, which is based on the ventricular mechanics model of the LV (◊), considering the “pole-zero” constitutive law (77), shows a sufficiently realistic behavior in comparison to experimental data. Error bars indicate standard deviations. (Reproduced with permission from Nash, M. P., and Hunter, P. J. (2000). Computational mechanics of the heart. J. Elasticity 61: 113–141. © Kluwer Academic Publishers, 2000.)


We now fit the model to experimental data of simple shear tests on passive ventricular myocardium from pig hearts (Dokos et al., 2002). This is illustrated in Figure 17, which is based on Figure 6 from the latter paper. However, the

\[\Psi = \frac{a}{2b} \left\{ \exp \left[ b(I_1 - 3) \right] - 1 \right\} \\
+ \frac{a_i}{2b_i} \left\{ \exp \left[ b_i(I_{4i} - 1)^2 \right] - 1 \right\} \\
+ \frac{a_{fs}}{2b_{fs}} \left[ \exp \left( b_{fs}I_{8fs}^2 \right) - 1 \right] - p(J - 1) \quad (82)\]

where \(a, b, a_i, a_s, b_i, b_s, a_{fs}\), and \(b_{fs}\) are eight positive material constants, the parameters \(a\) have dimension of stress and the parameters \(b\) are dimensionless. The function \(p(J - 1)\) is in accord with (4). It is now straightforward to derive the related Cauchy stress as

\[\sigma = a \exp \left[ b(I_1 - 3)\right] B + 2a_i(I_{4i} - 1) \times \exp \left[ b_i(I_{4i} - 1)^2\right] \mathbf{f} \otimes \mathbf{f} \\
+ 2a_i(I_{4s} - 1) \exp \left[ b_i(I_{4s} - 1)^2\right] \mathbf{s} \otimes \mathbf{s} \\
+ a_{fs}I_{8fs} \exp \left( b_{fs}I_{8fs}^2 \right) \left( \mathbf{f} \otimes \mathbf{s} + \mathbf{s} \otimes \mathbf{f} \right) - p I \quad (83)\]

This stress relation consists of the isotropic term in \(I_1\), the transversely isotropic terms in \(I_{4i}\) and \(I_{4s}\), and the orthotropic term in \(I_{8fs}\).
ordering of the labels fn and fs in Figure 6 of Dokos et al. (2002) is inconsistent with the data shown in the other figures in that paper. Hence, we have switched the roles of fs and fn in Figure 17 (compare with Figure 6 of Dokos et al., 2002). The fit of the model 83 to the experimental data for the loading curves are shown in Figure 17. The values of the material parameters for the fit are: \( a_1 = 18.472 \text{kPa}, b_1 = 16.026, a_2 = 2.481 \text{kPa}, b_2 = 11.120, a_{fs} = 0.216 \text{kPa}, b_{fs} = 11.436 \). The fit indicates very good agreement between the model and the experimental data. The distinct shears in the different directions exemplify the orthotropic response. Recently, Balaban et al. (2016) used a gradient-based optimization algorithm to solve the nonlinear parameter estimation problem with relatively few iterations. The authors tested the algorithm with a least squares fitting problem, and they provided also estimates for the material parameters of the invariant-based model (82).

The model (82), with only four invariants, has the advantage that it is geometry independent and it requires knowledge only of the local preferred directions in the material. In addition, it is straightforward to implement the three-dimensional orthotropic model within a FE environment, and that is already done in several codes including Abaqus 6.13 Analysis User’s Guide, 2013. The model is structurally based and considers the morphological structure through the muscle fiber direction, the myocyte sheet orientation and the sheet normal direction, and it takes account of the resulting macroscopic nature of the myocardium. The presented model uses a set of eight material parameters whose interpretations can be based partly on the underlying histology. While in a healthy heart the fiber alignment follows very closely a helical structure with only a small angular dispersion (AD), the AD may locally increase by as much as 65% (at foci points within the septal wall) (see, for example, Usyk et al., 2001) or \( \approx 50\% \) (at the site of infarction) (see, for example, Strijkers et al., 2009) in a diseased heart such as hypertrophic cardiomyopathy or myocardial infarction, respectively. The model by Eriksson et al. (2013) is an extension of the model (82) to consider dispersion of fiber and sheet orientations in the myocardium. In particular, two dispersion parameters are used to fit experimentally observed AD data of myocardial tissues. It is shown that the use of fiber dispersions relating to a pathological myocardium has a rather big effect on the mechanical response.

Until very recently, insufficient experimental data on the (human) myocardium were available. The study by Sommer et al. (2015) aimed to systematically determine biaxial extension and triaxial shear properties and the underlying microstructure of the passive human ventricular myocardium. The results show that the passive response of the human left ventricular myocardium under quasi-static and dynamic multi-axial loading is a nonlinear, orthotropic, viscoelastic and history-dependent soft biological material undergoing large deformations. In particular, the viscoelastic behavior of the tissue during biaxial extension and triaxial shear is clearly visible, not sufficiently discussed in the literature. The recent study by Gültekin et al. (2016b) deals with the viscoelastic modeling and the respective FE analysis of the human myocardium by considering elastic, cyclic, and relaxation test data as documented by Sommer et al. (2015).

### 3.2.4 Active cardiac muscle mechanics

Muscle cells within the cardiac walls are excited in turn as a wave of electrical activation propagates throughout the myocardium. As the wave of excitation propagates, individual myocardial cells generate tensile forces and contract. At a macroscopic level, this causes the ventricles to contract and pump blood to the body. The active mechanical properties of cardiac muscle are obtained primarily from experiments on small isolated papillary muscles or trabeculae. The myofilaments are activated in a graded manner by micromolar concentrations of calcium, which binds to troponin-C according to a sigmoidal relation (Rüegg, 1988).

Many different formulations of contractile mechanics of cardiac muscle have been proposed. Several are based on the assumption that the Cauchy stress tensor \( \sigma \) is the sum of the passive stress \( \sigma_p \), derived from a strain-energy function for the passive material, and the active stress \( \sigma_a = \sigma_a m_t \otimes m_t \). Here, \( \sigma_a \) denotes the active tensile stress generated along the current muscle fiber direction, characterized by the unit vector \( m_t \) with \( \hat{m}_t = \hat{F} m \), where \( \hat{\lambda} \) is the muscle fiber stretch and \( \hat{M} \) is the reference direction of the muscle fiber.

According to Hunter et al. (1997a) a simple active model, which was developed for the simulation of the steady state mechanical properties of cardiac muscle at a constant level of activation, is briefly presented. The level of activation of a cardiac muscle cell is taken to mean the concentration of free intracellular calcium \( \text{Ca}^{2+} \). Thus, under steady state conditions, the change in the active stress \( \sigma_a \) with the muscle fiber stretch \( \lambda \) and \( [\text{Ca}^{2+}] \) is described by

\[
\sigma_a(\lambda, [\text{Ca}^{2+}]) = \frac{[\text{Ca}^{2+}]^p}{[\text{Ca}^{2+}]^p + [\text{Ca}^{2+}]_{S_0}^p} \sigma_{a, max}[1 + \beta(\lambda - 1)]
\]

(84)

where \( \sigma_{a, max} \approx 100 \text{kPa} \) is the isometric, actively developed maximum tensile stress at \( \lambda = 1 \), and \( [\text{Ca}^{2+}]_{S_0} \) is the value of the intracellular calcium concentration \([\text{Ca}^{2+}] \) for 50% of \( \sigma_{a, max} \). The value \( n \) is the Hill coefficient, governing the shape of the sigmoidal curve, while the material parameter \( \beta = 1.45 \) is a non-dimensional slope \( \beta = (1/\sigma_{a, max})(d\sigma_a/d\lambda) \), describing myofilament cooperativity.
The most comprehensive model of passive and active cardiac muscle mechanics, suitable for use in continuum mechanics models of the intact heart, was proposed by Hunter et al. (1998). It is a model in four state variables, where the free calcium concentration \([\text{Ca}^{2+}]\) and the muscle fiber stretch \(\lambda\) are regarded as inputs to the system. The major biophysical events are represented via appropriate rate constants and binding curves, considering (i) the passive properties of myocardial tissue, (ii) kinetics of calcium binding to troponin-C, (iii) tropomyosin kinetics, and the length dependence of steady state tension, and (iv) the cross-bridge kinetics associated with myofilament mechanics.

The review article by Niederer and Smith (2008) provided a brief overview of the numerical methods employed to simulate electrophysiology, active contraction and mechanics, and proposed an improved approach to solve strongly coupled excitation/contraction models on the heart. Nordsletten et al. (2011) reviewed the coupling of multi-physics models to cardiac mechanics; in particular, they focused on the mathematics and physics behind the coupling of tissue mechanics to electrophysiology. More recently Trayanova and Rice (2011) and Pfeiffer et al. (2014) extensively reviewed cardiac electromechanical models.

### 3.3 Residual stress, growth and remodeling

From experimental observations it is well known that the ventricular myocardium is not stress free in its unloaded state. Omens and Fung (1990) demonstrated residual strain in the rat LV by radially cutting an equatorial cross-sectional ring and observing how the ring changes its shape when the residual stress is relieved. Costa et al. (1997) quantified three-dimensional distributions of residual strain in arrested canine LVs referred to the anatomical fiber coordinates. On the basis of a three-dimensional analysis they concluded that the unloaded myocardium was pre-stretched in the sub-epicardial region and compressed in the sub-endocardial region, while shear components of residual fiber strains were observed to be small. They argued that myocardial laminae may be the principal residual-stress-bearing structures in the LV. An experimental and theoretical study on cross-sectional rings of arrested mouse ventricles by Omens et al. (2003) showed that further stress is relieved by making a circumferential cut after the radial cut. The cutting experiments were analyzed by a cylindrical shell model with incompressible hyperelastic material properties. It was Guccione et al. (1991) who proposed that residual stresses are one mechanism by which the normal LV maintains its optimal function in terms of fiber stress. A few studies suggest that the residual stresses give rise to (more) uniform transmural distributions of end-diastolic myocardial stress (Guccione et al., 1991; Rodriguez et al., 1993; Nevo and Lanir, 1994), which was suggested in parallel to the work in arterial mechanics (compare also with Section 2.4). Rodriguez et al. (1993) claimed that residual strain leads to pre-stretched myofibers at the epicardium and to compressed myofibers at the endocardium. In four porcine hearts (Jöbsis et al., 2007) demonstrated the significant role of the visceral pericardium with respect to residual stresses and the passive stiffness of the heart.

Like in arterial walls, residual stresses in the heart may be an indicator of patterns such as myocardial growth and remodeling (Omens, 1998). Changes in the mechanical environment of the heart due to, for example, altered hemodynamic loads, may cause remodeling of the ventricles (changes in geometry, microstructure, material properties), and may alter cardiac output. Hence, different adaptation mechanisms may occur in the structure and function of the heart, which can hypertrophy in response to increased load, it can form collagenous scars or it can dilate considerably. Consequently, continual turnover of constituents within the heart wall occurs including turnover of proteins within the myocytes and the extracellular matrix. Heart models to illustrate the developmental processes of growth, remodeling, and morphogenesis, and theoretical models of the embryonic heart as it transforms from a single tube into a four-chambered pump, are presented by Taber and Perucchio (2000) and Taber and Chabert (2002). The study by Kroon et al. (2007) developed a method to simulate 3D-inhomogeneous volumetric growth of cardiac tissue. Thereby, the tissue turnover on growth was analyzed by incrementally updating the reference configuration.

### 3.4 Finite element models

#### 3.4.1 Overview of finite element models

Early nonlinear and three-dimensional FE analyses of ventricular walls enforcing incompressibility were published in the 1980s by Hamid et al. (1986) and Horowitz et al. (1988b). Realistic ventricular geometry and muscle fiber organization using three-dimensional FEs by means of a prolate spheroid coordinate system has been studied by Nielsen et al. (1991b) and Vetter and McCulloch (1998), among others. Prolate spheroid coordinates reduce the number of degrees of freedom required to represent ventricular geometry but also limits the accuracy with which the geometry can be modeled. A geometric model of the LV and RV of the pig heart using a rectangular Cartesian coordinate system including fiber and sheet orientations was proposed by Stevens et al. (2003). Cartesian coordinates provide a more flexible, though less compact, description of ventricular geometry. It was the work by Bovendeerd
et al. (1992) that considered a transversely isotropic model to simulate the active and passive behavior of the LV, with varying muscle fiber direction. The nonlinear FE analysis was based on 20-noded elements and incompressibility was enforced using the augmented Lagrange-multiplier method. Residual stresses were not considered.

The FE models of Guccione and McCulloch (1993), Guccione et al. (1993, 1995), Costa et al. (1996a,b), and Hunter et al. (1997a) are based on a formulation of the virtual work in the material description, and include a comprehensive description of the fibrous-sheet structure of the myocardium (Nielsen et al., 1991b; Hunter et al., 1997b). These models use high-order Hermite basis functions for discretizing the heart as a transversely isotropic material or as a material with collagen fibers statistically distributed in the matrix material. Huyghe et al. (1991b) proposed a two-phase FE model of the diastolic LV, and Huyghe et al. (1992) presented a poroelastic medium FE model of the beating LV including torsion around the axis of symmetry of the ventricle, transmural variation of fiber angle, and redistribution of intracoronary blood in the myocardial wall. Smith et al. (2000, 2002) provided a first approach toward fluid-structure mechanics in which the pressure-area relation, characterizing the elasticity of the ventricular wall, is coupled to the equation governing blood flow and pressure in the heart, that is, the (one-dimensional) Navier-Stokes equation. Zhang and Hisada (2001) coupled an arbitrary Lagrange–Euler fluid mesh with nonlinear shell elements, which describe the membrane in pulsatile ventricular assist devices.

Finite element models of the electrical and mechanical behavior of the whole heart were proposed by Hunter and Smaill (1989), McCulloch (1995), and Hunter et al. (1997a,b). The latter work presents a computational framework for solving the mechanical field (considering the pole-zero law (77)), in parallel with the ionic current field of myocardial activation (considering the modified van Capelle–Durrer current-voltage relation, see van Capelle and Durrer, 1980), which is influenced by a constantly changing heart geometry. The solution technique for the coupled electromechanical problem of the heart is based on the solution of the mechanical equations, which involves the Galerkin method, followed by the solution of the electrical activation equations, which involves a collocation mesh. To study the role of electrical propagation on the mechanical activation during the cardiac cycle, Usyk et al. (2002) proposed a computational framework of three-dimensional ventricular electromechanics. A model of impulse propagation was coupled with an anatomically based FE model of regional ventricular mechanics, muscle fiber architecture, and Purkinje fiber network anatomy. The Purkinje fiber system was shown to be important in determining the mechanical activation sequence during normal sinus rhythm. A data-parallel implementation of a passive heart filling model on a parallel processing computer was described by Vetter and McCulloch (2000). They demonstrated excellent correspondence between predicted and measured epicardial strains.

Since the first edition of this chapter numerous computational models were published to study either the electrical or the mechanical behavior, or also the coupled response of the individual chambers. However, for the first time, the study by Baillargeon et al. (2014) presented the integrative electromechanical response for a four-chamber human heart model generated from computer topography and magnetic resonance images using the constitutive model of the passive myocardium as described in Section 3.2.3. The electrical potential and the mechanical deformation across the human heart throughout its cardiac cycle are visualized by using a single, unified FE framework. In addition, the pressure–volume relationship is analyzed agreeing well with clinical observations. The development of the integrative simulator is a joint work between Stanford University (Ellen Kuhl and co-workers) and the team of the Living Heart Project (launched in May 2014: https://www.3ds.com/products-services//simulia/solutions//life-sciences//the-living-heart-project) at the FE company Dassault Systèmes Simulia Corp., see Abaqus 6.13 Analysis User’s Guide (2013). Figure 18 shows a prototype of the living heart model.

3.4.2 A three-dimensional finite element model of the heart

A three-dimensional FE model of the heart, as proposed by Stevens et al. (2003), aims to accurately predict the mechanical changes in the left and right ventricular myocardium during the cardiac cycle. The model was developed in rectangular Cartesian coordinates and uses tricubic Hermite basis functions for the geometric coordinates. The full ventricular model considers (i) ventricular geometry (anatomy) and tissue structure (fiber and sheet orientations), (ii) passive material properties of the extracellular matrix, (iii) the orientation and magnitude of the actively developed muscle forces, and (iv) the boundary conditions associated with the ventricular cavity pressures and pericardial constraints.

The geometry and tissue structure in the ventricles constitute the starting point for the FE model. One-dimensional cubic Hermite polynomials were fitted to the measured coordinate points of the four valve ring geometries at the base of the ventricles. Next, two-dimensional (bicubic Hermite) FE surface meshes were fitted to measurements from the endocardial and epicardial surfaces (Figure 19(a)), which incorporate the previously fitted valve rings (fitting procedures
Figure 18. Prototype models of the human heart: (a) anatomic model displaying characteristic features, generated from computer tomography and magnetic resonance images; (b) circulatory model displaying characteristic circulatory features; (c) solid model including the aortic arch, the pulmonary artery, the superior vena cava, the atria, and the ventricles; (d) finite element model discretized with 208,561 linear tetrahedral elements; (e) mechanical deformation across the human heart at a certain state of the cardiac cycle (red color indicates a deformation in the range of 10 mm, while blue color indicates a low deformation). (Reproduced with permission from Baillargeon, B., Rebelo, N., Fox, D. D., Taylor, R. L., and Kuhl, E. (2014). The Living Heart Project: a robust and integrative simulator for human heart function. *Eur. J. Mech. A/Solids* 48: 38–47. © Elsevier, 2014.)

Figure 19. Fitted surfaces of a pig heart model: (a) endocardial (bicubic Hermite) finite element surfaces of the left and right pig ventricles are shown through the translucent epicardial surface. Note the very thin wall at the apex; (b) epicardial surface of a finite element model for the LV and RV using 88 elements. The software used here to display the finite element models is available from www.bioeng.auckland.ac.nz. (Reproduced with permission from Stevens, C., Remme, E., LeGrice, I., and Hunter, P. (2003). Ventricular mechanics in diastole: material parameter sensitivity. *J. Biomech.* 36: 737–748. © Elsevier, 2003.)

for the Hermite surface meshes are as described by LeGrice *et al.*, 1997). The fitted three-dimensional mesh of the whole ventricular myocardium is then generated by joining up the two-dimensional surface meshes, as shown in Figure 19(b). In contrast to earlier prolate spheroidal models, the mesh was generated by 88 elements using tricubic Hermite basis functions in the rectangular Cartesian coordinates, which ensures derivative continuity across element boundaries. Note that the model captures the anatomical detail of the thin collagenous structure at the apex of the heart. Since the element basis functions are tricubic Hermite, the heart model uses one element through the wall. The fitted undeformed myocardial volume is 83.1 mm³, the undeformed base-apex length is 56 mm, while the undeformed left and right ventricular cavity volumes of the pig heart are 22.7 mm³ and 15.9 mm³, respectively.

The distribution of the three-dimensional muscle fiber field was obtained by means of tricubic Hermite basis functions. The measurement and the fitting procedure of the fiber field is that of LeGrice *et al.* (1995). The model of the fibrous-sheet
structure of the myocardium assumes that the fibers lie in planes tangent to the epicardial and endocardial surfaces.

To model the mechanics of the passive myocardial tissue the orthotropic “pole-zero” constitutive law is used according to Section 3.2.2, with material parameter values listed in Table 5. Material axes are defined in the muscle fiber direction (fiber axis), orthogonal to this in the plane of the sheets (sheet axis), and orthogonal to the fiber and sheet axes (sheet-normal axis). These axes establish a (spatially varying) rectangular Cartesian reference system. Active stress components generated along the muscle fiber directions during systole may be added to the stress tensor according to the model by, for example, see Hunter et al. (1998). Residual strains were incorporated in the model by creating a trilinear fiber stretch field $\lambda_f$ in the reference configuration (for prescribed data see Stevens et al., 2003).

To compute the mechanical response of the heart at end-diastole, ventricular pressure boundary conditions are applied (0.8 kPa to the left and 0.16 kPa to the RV) and the Galerkin method is used. All degrees of freedom at the base nodes were fixed (all other nodes were free). The numerical integration of the element equations is performed with $3 \times 3 \times 3$ Gauss points. The mid-wall distributions of fiber (♦), sheet (■) and sheet-normal (▲) stretches around the LV and the septum are shown in Figure 20. These values have been obtained by averaging over 6 Gauss points across two elements. As can be seen, these plots show significant variation of stretches, which can be attributed mainly to the varying wall thickness. The peak fiber stretch occurs at the locations marked as 10 and 11, which corresponds to the thinnest part of the wall. The minimum fiber stretch occurs at location 33, where the wall is thickest at the margins of the RV as it merges with the LV. Sheet stretches are compressive (except for point 3) because the sheets are primarily oriented in the radial direction, which is compressed during diastole. Sheet-normal stretches are tensile (except for point 3) because the sheet-normal direction is primarily in the base–apex direction, which is extended during diastole.

3.5 Mechanics of the heart valves

The four heart valves, that is, tricuspid, mitral, pulmonary, and aortic valves, maintain the flow in one direction within the heart. The mitral and tricuspid valves connect the atria to their respective ventricles and consist of two and three leaflets, respectively. The pulmonary and aortic valves serve
to prevent retrograde blood flow from the great arteries back into the ventricles. The aortic valve consists of three cusps each of which with a three-layer structure adapts to the hemodynamic stress state. The aortic valve exhibits low flexural rigidity to allow valve opening, and high tensile strength to resist transvalvular pressures. The mechanical response of the cusps, subjected to equi-biaxial tension, is highly anisotropic and strongly coupled between the circumferential and radial directions. A quantitative study of the gross fiber architecture of the aortic valve was performed by Sacks and Smith (1998). Evidence of residual stresses in the aortic valve cusp have been reported by Vesely and Noseworthy (1992). For a detailed account on the aortic valve see the book by Thubrikar (1990); for a survey of the biomechanics of native and engineered heart valve tissues see Sacks (2003).

Several structural models have been developed to capture the response of the aortic valve (see, for example, Krucinski et al., 1993; De Hart et al., 1998; Cacciola et al., 2000). Based on the quantified fiber architecture (Sacks and Smith, 1998) and a complete set of biaxial mechanical data (Billiar and Sacks, 2000a,b) proposed a structurally based constitutive model for the aortic valve cusp behavior following the approach by Lanir (1983).

The function of heart valve systems, however, involves fluid–structure interaction, which is best simulated with computational approaches. De Hart et al. (2003) proposed a computer model to simulate the mechanical behavior of the valve and the blood through it. The fictitious domain method, used to describe the interaction of the large motion of the thin leaflets within the computational fluid domain, is applied to a three-dimensional FE model of a stented aortic valve, assumed to behave isotropically, with a rigid aortic root. The fictitious domain method circumvents fluid mesh update strategies such as remeshing or arbitrary Lagrange–Euler techniques. Hence, this approach allows independent discretizations of the computational domains. The set of discretized linear algebraic equations is solved in a fully coupled manner. The authors investigated the effect of the interaction on the valve behavior for a low Reynolds number (Re = 500) and a non-physiological Strouhal number (Sr = 0.3) during systolic functioning.

Rausch et al. (2013) provided a critical review on the mechanics of the mitral valve. In particular, in vivo material parameters are identified for three (common) hyperelastic models for mitral valve tissue using an inverse FE approach. It is also shown that the identified parameter values are highly sensitive to pre-strain. In the more recent review article by Sun et al. (2014) the advances in valve geometry reconstruction, tissue property modeling, and loading and boundary definitions are outlined for the purpose of realistic computational structural analysis of cardiac valve function and intervention.

### 4 MECHANICS OF THE LIGAMENT

Ligaments bind bones together across joints or support viscera. Skeletal ligaments are short bands of fibrous connective tissue that comprises a dense (cablelike) network of collagen fibrils. They have been designed to assist in maintaining stability by guiding normal joint movement, to restrict abnormal joint movements and to transmit mainly uniaxial loads along (or close to) the ligament axis. Ligaments also experience shear and transverse loading in vivo. An extensive review of the efforts made to model ligament mechanics from the physical and computational point of view is provided by, for example, Weiss and Gardiner (2001).

#### 4.1 Structure

Ligaments consist of relatively few cells (primarily fibroblasts) surrounded by aggregates of collagen, elastin, proteoglycans (<1% of the dry weight), glycolipids, and water (65–70% of the weight of ligaments). The major constituent of ligaments is (type I) collagen (70–80% of the dry weight), primarily responsible for their tensile strength. Collagen fibers form bundles that are oriented primarily in the direction of the axis of loading in vivo, while many other tissues have an intricate disordered network of collagen fibers embedded in a gelatinous matrix of proteoglycans. In the absence of load the collagen fibers are in relaxed conditions and exhibit a wavy and “crimped” appearance that may contribute to the high compliance observed at initial loading. All biochemical constituents, except the collagen, are referred to as the ground substance. For a detailed account on ligament anatomy, see, for example, Woo et al. (1999).

#### 4.2 Constitutive models

##### 4.2.1 Overview

Ligaments are highly specialized tissues that govern complex joint functions. Their biochemical constituents vary in concentration, microstructural organization, and their interaction with each other throughout the body. Hence, the mechanical properties of ligaments are enormously diverse. Within the physiological loading range they display both time-dependent and rate-dependent properties due to the intrinsic viscoelastic nature of the solid phase and the interaction between the solid and fluid phases. Here we mention a few elastic, viscoelastic, and poroelastic models; in particular, we focus on three-dimensional models, because these types of models are necessary for accurate and reliable stress
predictions. A more complete list and critical discussion of available constitutive models is provided by, for example, Weiss and Gardiner (2001).

After the “pre-conditioned” state, where the typical stress softening effects are no longer evident (Humphrey, 2002a), ligaments exhibit very small hysteresis. The study by Sverdlik and Lanir (2002) has shown that pre-conditioning in sheep tendon material is an irreversible phenomenon that is strain level dependent. By neglecting the irreversible (dissipative) effects many constitutive laws focus on the modeling of the nonlinear elastic response of ligaments. Three-dimensional constitutive models to capture the elastic response of soft connective tissues were developed by, for example, Lanir (1983), Ault and Hoffman (1992a,b), Weiss et al. (1996, 2002), Hurschler et al. (1997), and Hirokawa and Tsuruno (2000). The continuum model of Lanir (1983), developed on the basis of microstructural and thermodynamic considerations, describes an incompressible composite of undulating collagen fibers (which contribute to the strain energy only in tension), embedded in a fluid matrix assumed to contribute to the stress only through a hydrostatic pressure term. Ault and Hoffman (1992a) modeled the connective tissue as a composite of crimped collagen fibers embedded in a glycosaminoglycan matrix, which they assumed to be an isotropic and linearly elastic material over a representative volume element (RVE). The fiber-reinforced geometry of the RVE led to a transversely isotropic response. Application of the model to rat tail tendon and joint capsule is described in Ault and Hoffman (1992b). Hurschler et al. (1997) proposed a complex model based on both microstructural and tissue level aspects. At the microstructural scale, a constitutive law for collagen fibers, which considers the three-dimensional orientation of the collagen fibrils, is derived. At the tissue level, an average stress versus strain relation is computed by assuming a probability distribution for fiber straightening. A stretch-based failure criterion is applied at the fibril and fiber levels. Although a simplified form of the model is discussed to characterize the nonlinear response of healing medial collateral ligaments (MCLs), the model approach suffers because of the large number of material parameters needed. The model of the anterior cruciate ligament (ACL), published by Hirokawa and Tsuruno (2000), features an isotropic and homogeneous ground substance in which two families of densely distributed extensible fibers are embedded. The model is similar to the one developed earlier by Weiss (1994) and Weiss et al. (1996) (the constitutive model by Weiss et al., 1996, is discussed in Section 4.3). On the basis of a transversely isotropic material with an exponential strain-energy function for the ground substance, Weiss et al. (2002) modeled the ligament material behavior under shear loading. The study suggests that the gradual loading of transversely oriented microstructural features such as intermolecular collagen crosslinks or collagen-proteoglycan crosslinking may be responsible for the stiffening response under shear loading.

When ligaments undergo cyclic loading or high-rate loading, complex interactions of the collagen and the ground substance occur, which lead to a viscoelastic behavior of the material characterized by small hystereses. Viscoelasticity has been incorporated into several constitutive models for ligaments. As for other types of soft tissues, the theory of quasi-linear viscoelasticity (QLV) has commonly been applied for modeling the viscoelastic behavior of ligaments (see, for example, Fung, 1993). This theory assumes that the stress at a given time can be expressed as a convolution integral formula, separating the nonlinear elastic response function and the relaxation function. Thus,

$$S(t) = G(t) : S^r(E)$$  \hspace{1cm} (85)

where the time-dependent second Piola-Kirchhoff stress tensor $S(t)$ is the double contraction of $G(t)$, in general a fourth-order tensor providing direction-dependent relaxation phenomena, and $S^r(E)$, which describes the elastic response. Fung suggested the need for a continuous relaxation spectrum since the hysteresis loops are relatively insensitive to strain rate.

From the computational point of view, however, this approach is not appropriate since information must be stored at each time step in order to compute the stress–strain response at the current time step. A numerical calculation based on the QLV theory requires storage which quickly exceeds available computer storage, even for small problems. One way to overcome this difficulty is the efficient discrete spectrum approximation for the QLV relaxation function, as proposed by Puso and Weiss (1998). By assuming that the relaxation function is the same in all directions, which reduces $G(t)$ to a scalar $G(t)$, the approximation is used as a series of exponentials according to

$$G(t) = G_e + \frac{G_0 - G_e}{N_d + 1} \sum_{i=0}^{N_d} \exp\left(\frac{-t}{10^{I_0 + i}}\right)$$  \hspace{1cm} (86)

where $G_e$ is the equilibrium modulus, $G_0$ is the initial modulus, $N_d$ is the span of the transition region in decades, and $10^{I_0}$ is the lowest discernible relaxation time (a particular set of data for the discrete series approximation is, according to Puso and Weiss, 1998, $G_e = 0.429$ MPa, $G_0 = 1.0$ MPa, $N_d = 6$ and $I_0 = 0$).

Nevertheless, the QLV theory, when used to model the time-dependent behavior of MCLs, has certain limitations. For example, Thornton et al. (1997) documented experimental data on ligaments showing that relaxation proceeds more rapidly than creep, a behavior that cannot be explained
by linear viscoelasticity. Based on continuum concepts, Lakes and Vanderby (1999) attempted to improve the QLV theory with inter-relating coefficients for creep and relaxation in a single-integral form of a nonlinear superposition model. Another approach to circumvent the limited QLV theory is documented by Thornton et al. (2001).

Johnson et al. (1996) used a single integral finite strain model, and Provenzano et al. (2002) the modified superposition model to describe the nonlinear viscoelastic behavior of ligaments. By assuming isotropy, Pioletti et al. (1998) proposed a viscoelastic model for large deformations including short-term and long-term memory effects. A microstructurally based model of a collagen sub-fascicle to simulate oriented collagen fibrils with elastic-orthotropic continuum elements was proposed by Atkinson et al. (1997), in which a poroelastic representation was used to represent the central core of each fascicle. Wren et al. (1998) proposed a model for load-dependent growth, development, and adaptation of tendons and ligaments.

### 4.3 A three-dimensional elastic model for ligaments

#### 4.3.1 Constitutive model

In this section the structurally motivated continuum model of Weiss (1994), Weiss et al. (1996) and Quapp and Weiss (1998) is described. The model uses a strain energy approach and represents ligaments (and tendons) as fiber-reinforced composites with incompressible and transversely isotropic behavior. The use of incompressibility is justified due to the large amount of trapped water in the tissue. The mathematical structure of the constitutive framework allows an easy determination of coefficients from material testing, and a straightforward finite element implementation.

The particular strain-energy function has the form

\[
\Psi = F_1(I_1, I_2) + F_2(\lambda) + F_3(I_1, I_2, \lambda) - p(J - 1) \tag{87}
\]

where \( I_1, I_2 \) are the invariants of the right Cauchy-Green tensor, and \( \lambda \) is the stretch along the local fiber direction. The function \( p(J - 1) \) is in accord with (4). The function \( F_1 \) represents the behavior of the ground substance, which is isotropic (characterized by, for example, a one-parameter neo-Hookean material or a two-parameter Mooney-Rivlin material), while \( F_2 \) represents the strain energy contribution from the collagen fiber family. For most biological soft tissues, an exponential function may be appropriate for \( F_2 \). The function \( F_3 \) considers the interactions between the collagen fiber family and the ground substance such as a shear coupling. Because of the lack of sufficient data the interaction term \( F_3 \) is frequently omitted.

The specific form of \( F_2 \) is chosen on the basis of several observations of the mechanical response of collagen fibers. In view of their wavy structure it is reasonable to consider that collagen is not able to support compressive stresses. Therefore, it is assumed that the fibers support stress only under extension. In addition, the tensile stress–stretch relation for ligaments is approximated by an exponential in the low-load region and subsequently by a linear portion. Consequently, the response function \( \partial F_2/\partial \lambda \) of the collagen fiber family may be written in the form (Gardiner and Weiss, 2003)

\[
\begin{align*}
\lambda \frac{\partial F_2}{\partial \lambda} &= 0, \lambda \leq 1, \\
\lambda \frac{\partial F_2}{\partial \lambda} &= C_3[\exp(C_4(\lambda - 1)] - 1], 1 < \lambda < \lambda^*, \\
\lambda \frac{\partial F_2}{\partial \lambda} &= C_5\lambda + C_6, \lambda \geq \lambda^*.
\end{align*}
\]

Here \( \lambda^* \) denotes a level of fiber stretch before which the fiber stress–strain behavior is exponential and after which the fiber stress–strain curve is linear. The constant \( C_3 \) scales the exponential stress response, \( C_4 \) is the rate of collagen uncrimping, and \( C_5 \) scales the linear stress response. The parameter \( C_6 \) is determined from the condition that the fiber stress is at least \( C^0 \)-continuous at \( \lambda^* = \lambda \), that is, \( C_6 = C_5 \{\exp[C_4(\lambda^* - 1)] - 1]\} - C_5\lambda^* \). By taking the neo-Hookean material for the ground substance, particular sets of material coefficients \( C_1, C_3, C_4, C_5 \) and the fiber stretch \( \lambda^* \) are summarized in Table 6. The parameters, adopted from Gardiner and Weiss (2003), were obtained by a curve-fitting procedure of the constitutive model to stress–strain data of eight specimens.

The model has been implemented efficiently in a FE program to allow for fully incompressible material behavior. It has been used successfully to describe and predict the quasi-static response of human fascia lata, both parallel and transverse to the collagen fiber direction.

#### 4.3.2 Application in a finite element model for knee joints

Several computational models of diarthrodial joints have been developed to quantify their quasi-static mechanical responses for given external loads and kinematic constraints, which depend on the material properties, in situ strains, topographical site and respective function of the ligaments, and their interactions with the surrounding connective tissues and bone. For example, a powerful three-dimensional computational model may allow the study of different variables responsible for joint functions after ligament reconstruction under various loading conditions. The human knee joint has been one of the most commonly modeled joints due
to the high incidence of injury. A powerful finite element model of the knee joint that has incorporated the MCL as a three-dimensional and transversely isotropic material is reviewed.

Weiss and co-workers used a subject-specific approach to create a FE model of the knee consisting of three structures, that is, the femur, the tibia, and the MCL, which runs from the femur to the tibia. Its orientation allows the collagen fibers within the long axis of the ligament to be aligned along the direction of loading. The model is based on inputs determined from experimental testing. Surfaces of the three structures were extracted from data obtained from CT slices taken at 1.0 mm intervals with the knee at 0° flexion. Polygonal surfaces of the femur and tibia were extracted, cross-sectional contours of the superficial MCL digitized from each CT slice and a polygonal surface of the MCL generated from the contours. Finally, eight-node hexahedral element meshes were constructed for each of the three structures. Both the femur and tibia were modeled using rigid elements, and their six-degree-of-freedom motion was completely prescribed using measured 3D kinematic data. The MCL attachments to the bones were modeled by specifying the final row of elements at the proximal and distal ends of the ligament to be part of the same rigid body as the corresponding bone. Frictionless contact and load transfer was allowed between the MCL and both bones, and accommodated using the penalty method. The MCL material properties are assumed to be homogeneous, and the function $F_3$ was excluded in the FE analyses.

The FE formulation is based on the work of Simo et al. (1985) and Simo and Taylor (1991), employing a three-field variational principle. Besides the displacement and pressure fields, a third additional kinematic field variable is treated independently within FE discretizations. To prevent volumetric locking, trilinear interpolations are used for the displacement and constant interpolations for the volumetric variables. Since the volumetric variables can be eliminated on the element level, the procedure leads to a reduced displacement-based method. The augmented Lagrangian method is used to fully enforce incompressible behavior to a user-specified accuracy (Simo and Taylor, 1991). A detailed description of this mixed finite element method in tensor and matrix forms, suitable for direct FE implementation, is found in Holzapfel (2003).

Three-dimensional video analysis was performed to study the stress-free position from which the in situ stretch has been determined (Gardiner et al., 2001). This information was then used to apply in situ stretch to the MCL in the computational model. To apply a continuous range of in situ stretch over the entire MCL FE mesh, the experimental values were interpolated between discrete points over the MCL mesh. An iterative update algorithm was used to ensure that the experimentally measured in situ stretches were satisfied exactly at each integration point in the mesh. The knee motion corresponding to valgus rotation, obtained from experimental kinematic testing was then applied to the tibia with the femur held fixed. The secant method with the BFGS-update was applied to solve the nonlinear boundary-value problem.

Figure 21 illustrates the computed results for the distribution of the fiber direction strain throughout the entire ligament after application of 10 Nm valgus torque at 0° flexion and following knee flexion of 30° and 60° using the rotational degrees of freedom of the rigid femur. In general, the numerical results correlate reasonably well with experimentally measured MCL strains, as shown in Figure 21. During passive flexion and valgus rotation, the MCL strains were highly inhomogeneous at all flexion angles. At 0° flexion, the three-dimensional model predicts the highest MCL strains in the posterior region of the MCL proximal to the joint line during valgus loading, while the smaller fiber strains are in the anterior region. Following knee flexion, the strains in the posterior and central MCL regions decrease,

### Table 6. Material coefficients $C_1, C_3, C_4, C_5$ and fiber stretch $\lambda^*$ for the constitutive model (87), (88), determined by curve-fitting the stress–strain data of eight specimens.

<table>
<thead>
<tr>
<th>Specimen</th>
<th>$C_1$ (MPa)</th>
<th>$\lambda^*$</th>
<th>$C_3$ (MPa)</th>
<th>$C_4$ (–)</th>
<th>$C_5$ (MPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.50</td>
<td>1.055</td>
<td>0.493</td>
<td>47.9</td>
<td>356.8</td>
</tr>
<tr>
<td>2</td>
<td>1.29</td>
<td>1.080</td>
<td>0.120</td>
<td>48.3</td>
<td>327.4</td>
</tr>
<tr>
<td>3</td>
<td>1.28</td>
<td>1.100</td>
<td>0.352</td>
<td>31.1</td>
<td>352.4</td>
</tr>
<tr>
<td>4</td>
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</tr>
<tr>
<td>5</td>
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<td>1.045</td>
<td>0.539</td>
<td>66.8</td>
<td>823.7</td>
</tr>
<tr>
<td>6</td>
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<td>1.060</td>
<td>0.854</td>
<td>38.0</td>
<td>401.6</td>
</tr>
<tr>
<td>7</td>
<td>1.41</td>
<td>1.060</td>
<td>1.303</td>
<td>40.6</td>
<td>462.3</td>
</tr>
<tr>
<td>8</td>
<td>2.05</td>
<td>1.050</td>
<td>0.387</td>
<td>65.2</td>
<td>649.1</td>
</tr>
</tbody>
</table>

(Data from Gardiner and Weiss, 2003.)
Figure 21. Experimental measurements and FE predicted distribution of the fiber direction strain in the human MCL during a valgus torque of 10 Nm and knee flexion angles of 0°, 30°, and 60°. The discrete experimental values have been interpolated onto the FE mesh to generate a continuous spatial representation of results. (Reproduced with permission from Gardiner, J. C., and Weiss, J. A. (2003). Subject-specific finite element analysis of the human medial collateral ligament during valgus knee loading. *J. Orthop. Res.* **21**:1098–1106. © Orthopaedic Research Society, 2003.)

while the strains along the anterior border remain relatively constant. The predicted MCL strain distribution may be a valuable indicator for joint configurations and loading conditions where the MCL is (most) vulnerable to injury under certain loading conditions.

On the basis of the constitutive relation (87), the viscoelastic model of Puso and Weiss (1998) was implemented in a FE program in an efficient way. The ability of the formulation to analyze large three-dimensional problems such as the mechanical response of the human femur-MCL-tibia complex is shown by Puso and Weiss (1998).

The FE model of Hirokawa and Tsuruno (2000), designed to simulate the three-dimensional finite deformation and stress distributions, which occur in the ACL during passive knee flexion, uses a similar version of model (87), and ACL geometry and kinematics from experimental studies. For the analyses, the authors have estimated values that were based on previous theoretical and experimental works, and the initial stress state in the ligament was generated arbitrarily by moving the ACL insertion sites from a non-physiological position into their position at full extension. Based on magnetic resonance images of a cadaveric human knee and biomechanical experimental data of the same specimen, Li et al. (2002) presented a three-dimensional computational knee model for parametric studies of knee biomechanics after ACL injury or reconstruction.

5 RELATED CHAPTERS

(See also Finite Element Methods, Mixed Finite Element Methods, Computational Fracture Mechanics, Damage, Material Instabilities, and Failure, Computational Modeling of Damage and Failures in Composite Laminates, Identification of Material Parameters for Constitutive Equations)

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