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An irreversible constitutive model for fibrous soft biological tissue: A 3-D microfiber approach with demonstrative application to abdominal aortic aneurysms

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ABSTRACT

Understanding the failure and damage mechanisms of soft biological tissue is critical to a sensitive and specific characterization of tissue injury tolerance and its relation to biological responses. Despite increasing experimental and analytical efforts, failure-related irreversible effects of soft biological tissue are still poorly understood. There is still no clear definition of what "damage" of a soft biological material is, and conventional macroscopic indicators, as known from damage of engineering materials for example, may not identify the tissue's tolerance to injury appropriately. To account for the complex three-dimensional arrangement of collagen, a microfiber model approach is applied, where constitutive relations for collagen fibers are integrated over the unit sphere, which in turn defines the tissue's macroscopic properties. A collagen fiber is represented by a bundle of proteoglycan cross-linked collagen fibrils that undergoes irreversible deformations when exceeding its elastic tensile limit. The proposed constitutive model is able to predict strain stiffening at physiological strain levels and does not exhibit a clear macroscopic elastic limit, two typical features known from soft biological tissue testing. An elastic-predictor/plastic-corrector implementation of the model is followed and constitutive parameters are estimated from in vitro test data from a particular abdominal aortic aneurysm (AAA). Damage-based structural instabilities of the AAA under different inflation conditions are investigated, where the collagen orientation density has been estimated from its in vivo stress state.

1. Introduction

Understanding damage mechanisms of soft biological tissue is critical to the sensitive and specific characterization of tissue injury tolerance, including its implications on biological (physiological and pathological) responses. Such knowledge may help us to develop concepts, among others, that allow an accurate rupture risk assessment of abdominal aortic aneurysms (AAAs) and vulnerable plaques, as it is crucial for clinical treatment planning, or to optimize the design of medical devices based on a proper understanding of short-term and long-term mutual interactions with biological tissues. The challenge is to relate tissue chemical morphology to engineering concepts and constitutive models that integrate the tissue's microhistology may help to enrich our current understanding regarding the damage of soft biological tissues.

Collagen is the most abundant protein in mammals and provides soft biological tissue, like the vasculature, with mechanical strength, stiffness and toughness; specifically, fibrillar collagen with diameters ranging from 50 to a few hundred nanometers, is biomechanically most important [65]. Collagen fibrils are regarded as a basic building block of collagenous tissue and their organization into suprafibrillar structure determines macroscopic tissue properties. To date, relatively few observations have been made that relate to the specificity of intrafibrillar or large-scale interactions, and, although collagen fibrils are densely packed, they do not make mutual contact. It has been suggested that interfibrillar proteoglycan (PG) bridges, as found in every extracellular matrix (ECM) in all animals, keep collagen fibrils in register [53].

The close packing and cross-linking of collagen molecules in fibrils defines a virtually inextensible fiber, such that the strain within collagen fibrils is always much smaller than the macroscopic strain in collagenous tissues, which points towards the existence of gliding processes occurring at the interfibrillar and/or the interfiber levels [28].

Over 50 years ago, Roach and Burton [50] suggested that collagen had a main impact on the mechanical properties of arterial tissue at higher strain levels, i.e. where mechanical failure is supposed to appear. Since then, a direct correlation between the collagen content and the stiffness and strength has become generally accepted. Earlier work from observations indicated that the

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collagen-rich abdominal aorta was stiffer than the collagen-poor thoracic aorta [6,39] and later regional variations of aortic properties were specifically documented (e.g. [58]). Numerous further references are provided by the seminal works of Fung [19] and Humphrey [34]. In this respect, it is also important to note that the collagen fiber orientation of vascular tissues is significantly dispersed [17] and that this structural property significantly affects the macroscopic mechanical properties [25].

Exposing biological soft tissue to supraphysiological mechanical stresses rearranges the tissue's microstructure through irreversible deformations. Damage-related effects (e.g. for tendon and ligament [47,41] and for vascular tissue [14,13,46]) and plasticity-related effects (e.g. for skin [49], tendon and ligament [1,47,59] and vascular tissues [46,51]) have been documented, where experimental data were analyzed using macroscopic metrices like stress and strain. However, damage to soft biological tissue is defined by spatial localization of structural collagen damage, and microfailure well below ultimate failure at the tissue level (51 ± 12%) of the ultimate strength for tendon tissue has been reported [48]. Specifically, changes from small-angle X-ray scattering spectra suggested that macroscopic tendon and ligament failure is preceded by damage from intrafibrillar sliding [38]. Consequently, a macroscopic (single scale) view may be questionable in order to investigate and/or describe damage of soft biological tissue appropriately.

Constitutive modeling of vascular tissue is an active field of research and numerous models, such as for the arterial wall [12,20,60,35,33,25], have been reported. Different modeling assumptions accounting for inelastic phenomena have been suggested, where specifically viscoelastic modeling has been fostered (see [34] and references). However, a few models for soft biological tissue damage [32,4,63,9] and plasticity [61,22] have also been reported, and despite the general lack of information regarding failure mechanisms, fracture models [36,23,24,16,18] are known as well. Microstructural-based constitutive models reasonably assume collagen fibers to be unloaded in compression, i.e. they have a negligible bending stiffness. This assumption is also justified from the context of convex constitutive formulations [52,15]. However, it is difficult to implement within a macroscopic (single scale) metric and when dispersed collagen fiber orientations are being considered.

In conclusion, despite increasing experimental and analytical efforts to investigate failure-related irreversible effects of soft biological tissue, the underlying mechanisms are still poorly understood. There is still no clear definition of what damage is and conventional indicators of mechanical injury (such as visible failure and loss of stiffness) may not identify the tissue's tolerance to injury appropriately. Likewise, a macroscopic (single scale) view of tissues does not allow for an explicit description of individual collagen fibers (thought to be continuously distributed in orientation), and hence may fail to account for the localized structural rearrangement of collagen fibrils under supraphysiological mechanical stress.

The present work proposes a novel constitutive model for collagenous soft biological tissue, aimed specifically at capturing supraphysiological stress states. To this end, a microfiber model approach is considered and macroscopic tissue properties are in turn derived by integrating over the unit sphere [40,15]. Such an approach reflects salient features of the microstructure and supports the application of challenging constitutive models for collagen fibers, i.e. it allows the integration of biochemical information of the microarchitecture of collagenous tissues. A simple straightening mechanism of collagen fibers is considered to account for their tension–compression nonlinearity, and a viscoplastic sliding mechanism is coupled with failure of collagen cross-links. The model is limited to strain stiffening, i.e. it cannot be applied to investigate macroscopic localization without additional regularization techniques.

2. Method

2.1. Modeling assumptions

The late stage of AAA disease is characterized by irreversible pathological remodeling of the aortic wall connective tissue, which, among many others, involves degradation of the elastin and compensatory increased collagen synthesis and content (see Ref. [10] and references therein). Consequently, the passive mechanical response of a larger AAA can be modeled as fibrous collagenous tissue with negligible contribution from the degraded and fragmented elastin. Specifically, AAA wall tissue is considered at finite deformations, where an orientation density function $\rho(\mathbf{M}) = \rho(-\mathbf{M})$ defines the spatial alignment of collagen fibers (bundles of collagen fibrils interconnected by collagen cross-links), i.e. the density of collagen along the direction $\mathbf{M}$ with $|\mathbf{M}| = 1$ [25]. Although the subsequently detailed approach can be applied to any orientation density function $\rho(\mathbf{M})$, a transversely isotropic distribution of collagen is considered here. Specifically, the main collagen orientation is defined by the unit direction vector $\mathbf{A}$, and along a particular direction $\mathbf{M}$ the orientation density reads [25]

$$\rho(\Theta) = \gamma \exp[b(\cos(2\Theta) + 1)] \quad \text{with } \gamma = 4\sqrt{b/(2\pi)}/\operatorname{erfi}(\sqrt{2b}) \tag{1}$$

where Θ denotes the angle between $\mathbf{A}$ and $\mathbf{M}$. In Eq. (1) the dispersion of the collagen fibers around the main direction $\mathbf{A}$ is defined by the concentration parameter b, i.e. $b = 0$ and $b = \infty$ characterize isotropic and Dirac-delta orientation density distributions, respectively.

Collagen fibers are embedded in an otherwise isotropic matrix material, thought to capture the mechanics of the non-collagenous tissue components, i.e. mainly elastin. It is assumed that a particular collagen fiber is assembled by a bundle of collagen fibrils, which successively straightens under stretch before it can carrying a load. PG bridges serve as inter-fibrillar cross-links and provide load transition across the fibrils (see Fig. 1). Specifically, small proteoglycans like decoran bind noncovalently but specifically to the collagen fibril and cross-link adjacent collagen fibrils at about 60 nm intervals [53]. PG bridges have been identified in several collagenous tissues and it has been suggested that they are present in every ECM in all animals [54].

The present model aims at capturing supraphysiological stress states and it is assumed that, at the straightening stretch λ_{st}, all collagen fibrils that constitute a collagen fiber straighten simultaneously, i.e. there is no continuous recruitment considered, as has been suggested in the literature [66,67,44].

Stretching a collagen fiber beyond λ_{st} involves stretching of the collagen fibrils and shearing of interfibrillar material, as is schematically illustrated in Fig. 1. Such a deformation mechanisms involves sliding of collagen fibrils relatively to each other, which, to a great extent, is defined by the elastic properties of the PG bridges. Reversible deformability of the PG bridges is crucial to serve as shape-maintaining modules [53] and fast and slow deformation mechanisms have been identified [54]. The fast (elastic) deformation is supported by the sudden extension of about 10% of the L-iduronante (an elastic sugar) at a critical load of about 200 pN [31]. The slow (viscous) deformation is based on a sliding filament mechanisms of the twofold helix of the glycan [53].

Sliding of the PG bridge becomes irreversible if the overlap of the glycan chains decreases beyond a critical level (see Ref. [53] and references therein). Consequently, the physiological shape-maintaining deformation range of the PG bridge is exceeded and the collagen fibrils (within a collagen fiber) will be rearranged irreversibly. Note that this molecular mechanism (irreversible sliding of PG bridges) could explain the irreversible (plastic) effects known