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A Forward Incremental Prestressing Method with Application to Inverse Parameter Estimations and Eye-Specific Simulations of Posterior Scleral Shells

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Abstract

Numerical simulations or inverse numerical analyses of individual eyes or eye segments are often based on an eye-specific geometry obtained from in vivo medical images such as CT scans or from in vitro 3D digitizer scans. These eye-specific geometries are usually measured while the eye is subjected to internal pressure. Due to the nonlinear stiffening of the collagen fibril network in the eye, numerical incorporation of the pre-existing stress/strain state may be essential for realistic eye-specific computational simulations. Existing prestressing methods either compute accurate predictions of the prestressed state or guarantee a unique solution. In this contribution, a forward incremental pre-stressing method is presented that unifies the advantages of the existing approaches by providing accurate and unique predictions of the pre-existing stress/strain state at the true measured geometry. The impact of prestressing is investigated on (i) the inverse constitutive parameter identification of a synthetic sclera inflation test and (ii) an eye-specific simulation that estimates the realistic mechanical response of a preloaded posterior monkey scleral shell. Evaluation of the pre-existing stress/strain state in the inverse analysis had a significant impact on the reproducibility of the constitutive parameters but may be estimated based on an approximative approach. The eye-specific simulation of one monkey eye shows that prestressing is required for accurate displacement and stress/strain predictions. The numerical results revealed an increasing error in displacement, strain and stress predictions with increasing pre-existing pressure load when the pre-stress/strain state is disregarded. Disregarding the prestress may lead to a significant underestimation of the strain/stress environment in the sclera and overestimation in the lamina cribrosa.

Keywords

Prestressing; Sclera; Eye-specific models; Inverse problems; Inflation Experiments

1 Introduction

Reliable biomechanical models of individual human eyes require detailed knowledge of the nonlinear and anisotropic constitutive response of these soft connective tissues. Recent advances in speckle interferometry allow for high resolution recording of scleral surface

displacements during inflation tests. The inverse analysis of such scleral inflation test presents a promising technique to estimate eye-specific intrinsic constitutive properties. In our earlier studies, an inverse finite element approach was utilized to obtain scleral constitutive properties from inflation experiments on posterior scleral shells subjected to pressure levels from 5 to 45 mmHg (Girard et al. 2009a,b). The experimental procedure could neither record displacements nor the shell geometry at intraocular pressures (IOP) below 5 mmHg, mainly because the scleral shells are very compliant at low pressure levels (< 5 mmHg). Scleral shell segments of primates or young human donors can not maintain their spherical shape and buckle at low pressure levels. Previously, the pre-existing stress/stretch state at the loaded reference configuration (5 mmHg) has only been rudimentarily taken into account by adjusting the external loading to reflect effective pressure increases. Consequently, the constitutive parameters estimated in our previous study characterize the inflation response of the sclera shells from 5 to 45 mmHg IOP but not for pressure levels below 5 mmHg. To estimate intrinsic constitutive properties that characterize the complete material response starting at zero pressure, a forward incremental prestressing method is introduced in this paper. The forward incremental pre-stressing method is used to estimate the pre-existing stress/strain state at the true measured geometry obtained at 5 mmHg IOP. The impact of an pre-existing stress/stretch state on the inverse finite element characterization of scleral inflation tests is investigated by means of a synthetic inflation experiment.

Previous experimental and numerical studies investigated the changing biomechanical response of the eye-specific posterior sclera and in particular of the lamina cribrosa (LC) for normal aged and glaucoma eyes subjected to acute IOP elevation based on histologic, histophometric and other geometric measurements of pre-loaded monkey eyes perfusion fixed at IOP levels between 10 and 45 mmHg (Yang et al. 2007, 2009, 2011b,c,a; Sigal et al. 2011; Roberts et al. 2010c,a, 2009; Downs et al. 2008; Strouthidis et al. 2009; Ren et al. 2009). The realistic characterization of the biomechanical environment within the LC is of often of special interest as present evidence indicates that optic nerve axons are damaged at the level of the LC during the development of glaucoma (Quigley and Addicks 1980). To our knowledge, all existing eye-specific studies were based on geometric measurements obtained from pressurized eyes. However, the pre-existing stresses or strains at these reference configurations were not previously investigated. We investigate the impact of the pre-existing stress/stretch state in an eye-specific simulation of a posterior monkey scleral shell. The macro-geometry and the meso-structure of the collagen architecture was experimentally measured while the monkey eye was subjected to IOP.

Several numerical techniques have been suggested to calculate the stress/strain state that corresponds to an experimentally obtained configuration under known external loading conditions. Most approaches are based on an *inverse elastostatic* approach, wherein the unknown unloaded (stress-free) configuration is explicitly calculated first (Govindjee and Mihalic 1996, 1998; Chadwick 1975; Carlson and Shield 1969; Lu et al. 2007, 2008). Thereafter, the prestressed configuration is computed by applying the pre-existing external load to the previously calculated unloaded configuration. The numerical implementation of the inverse elastostatic approach is rather complex. Inverse elastostatic analyses are known

to accurately compute the pre-existing stress/strain state including biological membrane-like structures such as abdominal aortic aneurysms (Lu et al. 2007, 2008). However, the inverse elastostatic analysis leads to non-unique solutions if buckling effects occur during the backward calculation of the unloaded configuration (Govindjee and Mihalic 1996, 1998; Gee et al. 2010). Thin walled structures, such as scleral shells of non-human primates or young human donors, may tend to exhibit bifurcation during the backward calculation of the zero pressure geometry. This is a major drawback of the inverse elastostatic approach, which makes this prestressing technique unsuitable for our purposes.

Recently, two prestressing methods have been proposed that are based on the multiplicative split of the deformation gradient (de Putter et al. 2007; Gee et al. 2010). The deformation gradient is split into the deformations experienced by a body up to the reference time point at which the geometry was experimentally measured and the deformations experienced thereafter. Both methods are based on an updated Lagrangian formulation. Consequently, these methods require significantly less effort to implement compared to the inverse elastostatic approach. The *backward incremental method* presented by de Putter et al. (2007) is able to accurately estimate the prestressed state, however, the accuracy depends on the incremental application of the pre-existing load. The backward calculation of the unloaded configuration remains in the backward incremental prestressing procedure, leading to the same problem of non-uniqueness that is common with the inverse elastostatic approach. This problem was finally resolved by Gee et al. (2010) who proposed the *modified updated Lagrangian formulation* (MULF). This method estimates the pre-existing state by means of a forward calculation of the pre-existing deformation gradient solely. The calculation of the unloaded configuration is thereby not needed and a unique solution is guaranteed, as the reference configuration is not updated during prestressing. However, equilibrium at the pre-stressed state is achieved with respect to a *virtual* reference configuration and not with respect to the experimentally obtained configuration. Consequently, the accuracy of this method also depends on the incremental application of the pre-existing load and is known to overestimate the pre-existing stress state.

The presented prestressing approach is based on the MULF method developed by Gee et al. (2010). The formulation was modified from its original form to unify the advantages of the existing backward and forward prestressing methods: being accurate, easy to implement and robust. The prestressing method was implemented into an inverse finite element approach to estimate eye-specific intrinsic constitutive properties from scleral inflation tests. The finite element formulation is based on a micro-structural constitutive formulation that incorporates the collagen fibril crimp response at low IOP levels and the dispersion of collagen fibril orientations (Grytz and Meschke 2009, 2010).

Former prestressing methods have generally not been applied to anisotropic constitutive formulations. While the prestressing formulation is basically independent of the constitutive formulation, it needs special attention when dealing with large strains and anisotropic material laws that are formulated with respect to the (unknown) unloaded configuration. Fachinotti et al. (2008) proposed a method to approximate the preferred directions of anisotropy in a distorted configuration which is applicable to small strains. In contrast, a orthonormal pull-back operation for characteristic material directions is proposed here,

which accounts for prestressing hyperelastic material formulations at large strains that incorporate distributed collagen fibril orientations through generalized structure tensors.

In Section 2, the forward incremental prestressing method is derived and its implementation into finite element simulations is explained. The prestressing of soft tissues with distributed collagen fibril orientations is discussed at the end of Section 2. A synthetic inflation experiment of a generic posterior scleral shell model is presented in Section 3.1. The synthetic example is used to verify the prestressing method and to investigate the impact of a pre-existing stress/strain state on an inverse parameter estimation analysis. Conclusions are finally drawn in Section 4.

2 Numerical consideration of pre-loaded reference configurations

In individual-specific numerical simulations of tissue segments or organs, the geometry of the specimen is usually measured while the specimen is subjected to an external load. Consequently, the specimen is subjected to a stress state that is in equilibrium with the external load at the time the geometry of the specimen was captured. Previous studies showed that in the case of large strain analysis the knowledge about the pre-existing stress and strain state at the recorded geometric configuration is a prerequisite for realistic computational simulations of pre-loaded tissues (Gee et al. 2010). This is especially true for soft tissues such as the sclera, which are characterized by a nonlinear constitutive response due to the nonlinear stiffening of its collagen fibrils. In this section we present a numerical method to estimate this pre-existing stress/strain state.

2.1 Theoretical Framework

Let $\mathcal{B}_r$ be the *reference configuration* of a body in a 3D Euclidean space $\mathcal{E}^3$ at the time t_r , its geometry was captured experimentally. In $\mathcal{B}_r$, the body is supposed to be subjected to an external load (e.g. pressure) that is in equilibrium with the internal stress state. From $\mathcal{B}_r$ the body deforms at a certain time t to its *actual configuration* $\mathcal{B}_t$ due to e.g. changes in the external loading conditions (Fig. 1). At the time t_0 the body was in its *unloaded configuration* $\mathcal{B}_0$ in which the external load (pressure) was zero and the body was unstressed. Residual stresses are not considered in the present work.

Let $\mathbf{x}_r$ be the position vector of a point $\mathcal{P}_r$ in $\mathcal{B}_r$. The motion of this point to its unloaded $\mathbf{X}$ or actual position $\mathbf{x}$ may be expressed as a function of time and the reference position

$$\mathbf{X} = \mathbf{X}(\mathbf{x}_r, t_0), \quad \mathbf{x} = \mathbf{x}(\mathbf{x}_r, t). \quad (1)$$

The two deformation gradients that are related to these motions are defined as

$$F_r^{-1} = \frac{\partial \mathbf{X}(\mathbf{x}_r, t_0)}{\partial \mathbf{x}_r}, \quad F_t = \frac{\partial \mathbf{x}(\mathbf{x}_r, t)}{\partial \mathbf{x}_r}. \quad (2)$$

The total deformation gradient related to the motion from the unloaded to the actual configuration can be decomposed into these two tensors (de Putter et al. 2007; Gee et al. 2010)

$$F = F_t F_r. \quad (3)$$

Our target is to compute the motion $\mathbf{x}(\mathbf{x}_r, t) = \mathbf{x}_r + \mathbf{u}_t(\mathbf{x}_r, t)$ of the body from the loaded reference configuration $\mathcal{B}_r$ to its actual configuration $\mathcal{B}_t$ by using the finite-element method. This can be done by solving the weak form of the balance equation according to the principal of virtual work. In the absence of body forces, the virtual work reads with respect to the unloaded material configuration

$$\begin{aligned} \delta \Pi &= \delta \Pi_{\text{int}} - \delta \Pi_{\text{ext}} \\ &= \int_{\mathcal{B}_0} \frac{1}{2} \mathbf{S}(\mathbf{F}) : \delta \mathbf{C} dV_0 - \int_{\partial \mathcal{B}_0} \mathbf{t}_0 \cdot \delta \mathbf{u} dA_0 \stackrel{!}{=} 0 \end{aligned} \quad (4)$$

with the external load vector $\mathbf{t}_0$ and the variation of the right Cauchy-Green tensor $\delta \mathbf{C} = \delta(\mathbf{F}^T \mathbf{F})$. Let us assume that the mapping from the unloaded to the reference configuration is known such that $\delta \mathbf{F}_r = 0$ and $\delta \mathbf{x}_r = \mathbf{0}$. In this case and by considering the multiplicative split (3), the variation of the right Cauchy-Green tensor can be restated to

$$\begin{aligned} \delta \mathbf{C}|_{\delta \mathbf{x}_r = 0} &= \delta(\mathbf{F}^T \mathbf{F}) = \delta(\mathbf{F}_r^T \mathbf{F}_t^T \mathbf{F}_t \mathbf{F}_r) = \mathbf{F}_r^T \delta(\mathbf{F}_t^T \mathbf{F}_t) \mathbf{F}_r \\ &= \mathbf{F}_r^T \delta \mathbf{C}_t \mathbf{F}_r. \end{aligned} \quad (5)$$

Equation (5) together with the identities $\mathbf{t}_0 dA_0 = \mathbf{t}_r dA_r$ and $\det \mathbf{F}_r = dV_r/dV_0$ can be used to reformulate the virtual work (4) with respect to the reference configuration to

$$\begin{aligned} \delta \Pi|_{\delta \mathbf{x}_r = 0} &= \int_{\mathcal{B}_0} \frac{1}{2} \mathbf{S} : (\mathbf{F}_r^T \delta \mathbf{C}_t \mathbf{F}_r) dV_0 - \int_{\partial \mathcal{B}_0} \mathbf{t}_0 \cdot \delta \mathbf{u}_t dA_0 \\ &= \int_{\mathcal{B}_r} \frac{1}{2} (\mathbf{F}_r \mathbf{S} \mathbf{F}_r^T) : \delta \mathbf{C}_t (\det \mathbf{F}_r)^{-1} dV_r \\ &\quad - \int_{\partial \mathcal{B}_r} \mathbf{t}_r \cdot \delta \mathbf{u}_t dA_r \\ &= \int_{\mathcal{B}_r} \frac{1}{2} \Sigma : \delta \mathbf{C}_t dV_r - \int_{\partial \mathcal{B}_r} \mathbf{t}_r \cdot \delta \mathbf{u}_t dA_r \stackrel{!}{=} 0 \end{aligned} \quad (6)$$

where Σ represents the reference stress tensor at $\mathcal{B}_r$.

Assuming a hyperelastic constitutive response throughout the deformation history of the body and according to (6), the reference stress can be expressed as a function of total $\mathbf{F}$ and the pre-existing deformation gradient $\mathbf{F}_r$.

$$\sum(F, F_r) = (\det F_r)^{-1} F_r S(F) F_r^T. \quad (7)$$

Consequently, the deformation $\mathbf{u}_t$ can only be computed from (6) if the pre-existing deformation gradient F_r is known. One can also see that the explicit calculation of the unloaded configuration $\mathcal{B}_0$ and the related motion $\mathbf{X}(\mathbf{x}_r, t_0)$ (1)₁ are not needed to solve (6). However, most of the prestressing approaches available are based on the backward solution of the motion $\mathbf{X}(\mathbf{x}_r, t_0)$. Note that the Cauchy stress relates to the reference stress through $\sigma = (\det F_t)^{-1} F_t \sum F_t^T$.

2.2 Forward Incremental Prestressing Method

The presented method is based on the *modified updated Lagrangian formulation* proposed by Gee et al. (2010). The basic idea of Gee et al. (2010) was to estimate the pre-existing stress/strain state by computing the pre-existing deformation gradient F_r (2)₁ with a forward calculation and not by calculating the backward motion $\mathbf{X}(\mathbf{x}_r, t_0)$ (1)₁.

Let $\mathcal{B}_i$ be a configuration in the close neighborhood of the experimentally obtained reference configuration $\mathcal{B}_r$ at the increment i (Fig. 2). In the following we will call $\mathcal{B}_i$ the *neighboring reference configuration*. At $\mathcal{B}_i$, the total deformation gradient is split into pre-existing deformations F_r representing the mapping from the unloaded to the true reference configuration and subsequent deformations F_r^i to the neighboring reference configuration

$$F^i = F_r^i F_r. \quad (8)$$

In $\mathcal{B}_i$, the stress state $\Sigma(F^i, F_r) = \mathbf{0}$ is required to be in equilibrium with the known external load $\mathbf{t}_r$. Following the assumptions made in the previous subsection, the weak form of the balance equation at an increment i can be derived similar to (6)

$$\delta \Pi^i|_{\delta \mathbf{x}_r} = \int_{\mathcal{B}_r} \frac{1}{2} \Sigma(F^i, F_r) : \delta C_{\bar{r}} dV_r - \int_{\partial \mathcal{B}_r} \mathbf{t}_r \cdot \delta \mathbf{u}_{\bar{r}} dA_r \stackrel{!}{=} 0,$$

where $\delta C_{\bar{r}} = \delta(F_{\bar{r}}^T F_{\bar{r}})$.

(9)

where $\delta C_{\bar{r}} = \delta(F_{\bar{r}}^T F_{\bar{r}})$.

The aim of the forward incremental prestressing method is to incrementally reduce the subsequent deformations $\mathbf{u}_{\bar{r}}^i$ until the neighboring reference configuration $\mathcal{B}_i$ coincides with the true reference configuration $\mathcal{B}_r$. Let us assume that a limit state $i \rightarrow \infty$ exists, where the subsequent deformations vanish

$$\mathbf{u}_{\bar{r}}^i|_{i \rightarrow \infty} = [\mathbf{x}_{\bar{r}}^i - \mathbf{x}_r]_{i \rightarrow \infty} = \mathbf{0}, \quad F_{\bar{r}}^i|_{i \rightarrow \infty} = I. \quad (10)$$

In this case, equation (9) can only be true if a non-trivial deformation gradient $F_r = I$ exists that results in a non-trivial stress tensor $\Sigma(F_r, F_r) = 0$. At this limit state the total deformation gradient (8) and the stress tensor, consequently, represent the pre-existing strain/stress state

$$\begin{aligned} F^i|_{i \rightarrow \infty} &= [F_r^i F_r]_{i \rightarrow \infty} = F_r, \\ \Sigma(F^i, F_r)|_{i \rightarrow \infty} &= \Sigma(F_r, F_r) \neq 0. \end{aligned} \quad (11)$$

To achieve the limit state (10) we use relation (11)₁ to motivate the incremental update of the pre-existing deformation gradient in accordance to Gee et al. (2010)

$$F_r \leftarrow F_r^i F_r. \quad (12)$$

If $\mathcal{R}_i$ and $\mathcal{R}_r$ are in a close neighborhood, the iterative application of solving (9) and subsequently updating F_r according to (12) will lead to the limit state outlined in (10) and (11).

The forward incremental prestressing procedure is summarized in Table 1. To ease the understanding of the forward incremental prestressing method we illustrate the procedure in the following: First, the pre-existing deformation gradient $F_r = I$ is initialized. In the first increment, the pre-existing load $\mathbf{t}_r$ is applied to the reference configuration as it would be the unloaded configuration $\mathcal{R}_i = \mathcal{R}_r$. A usual iterative finite element calculation is performed and the body deforms to the neighboring reference configuration $\mathcal{R}_i$ (see Fig. 2), where external and internal forces are at equilibrium based on (9). During the first increment, the total deformation gradient does not include pre-existing deformation $F_r = 0$ but consists solely of subsequent deformations $F^1 = F_r^1$.

At the end of the first increment, the pre-existing deformation gradient is explicitly updated according to (12). Consequently, the total deformation gradient of the second increment $F^2 = F_r^2 F_r$ is now partially related to pre-existing deformations F_r and subsequent deformations F_r^2 . As F^2 is utilized to compute the constitutive equation $\Sigma(F^2, F_r)$ to solve (9), the pre-existing deformations F_r will contribute to the internal forces. In turn, the subsequent deformations $\mathbf{u}_r^2$ need to be smaller than $\mathbf{u}_r^1$ to lower the contribution of F_r^2 to the internal forces, such that equilibrium can be achieved at $\mathcal{R}_i$. At the end of the second increment, the pre-existing deformation gradient is again updated according to (12). Further iterations of solving (9) followed by the update of the pre-existing deformations (12) will eventually lead to vanishing subsequent deformations as anticipated in (10). The prestressing procedure is deemed converged once the subsequent displacements are below a given tolerance $|\mathbf{u}_r^i| < tol$.

One can picture the iterative procedure outlined above as the incremental decrease of the distance between the neighboring and the true reference configuration while the unloaded configuration related to the neighboring reference configuration virtually moves from the true reference configuration $\mathcal{R}_i = \mathcal{R}_r$ to the true unloaded configuration $\mathcal{R}_i^{unl} = \mathcal{R}_0$ (see Fig. 2). However, the forward incremental prestressing method does not require the computation of

the unloaded configuration $\mathcal{B}_0$ or the backward motion $\mathbf{X}(\mathbf{x}_r, t_0)$. This is a major advantage of prestressing methods that are based on the forward calculations of $\mathbf{F}_r$ such as the present and the MULF method (Gee et al. 2010) compared to inverse elastostatic approaches.

In the original MULF method (Gee et al. 2010), the neighboring reference configuration $\mathcal{B}_r$ was not updated during the prestressing process. Instead, the Jacobian matrix was updated to perform an equivalent step. Consequently, equilibrium between the pre-existing external load and the internal stress state was not achieved with respect to the true reference configuration $\mathcal{B}_r$ but with respect to an ‘unconverged’ neighboring reference configuration $\mathcal{B}_r$. Due to this inconsistency, the results of the original prestressing method depend on the load step size and the estimation of the prestressed state can only be considered as an approximation. (Gee et al. 2010) noted that the MULF method overestimates the pre-existing stresses. This is not the case for the present method as $\mathcal{B}_r$ is incrementally updated until it coincides with the true reference configuration $\mathcal{B}_r$ with respect to a given tolerance ($|\mathbf{u}_r^i| < tol$). The vector field $\mathbf{x}_r^i$ is consistent with the neighboring reference configuration $\mathcal{B}_r$, where equilibrium between external and internal forces is achieved at the end of each prestressing increment i . Accordingly, the converged numerical results of the present prestressing method are independent of the applied load step size. However, the present method requires reasonably small load increments during prestressing to guarantee convergence similar to explicit integration schemes.

Note that the boundary value problem defined in (9) is practically identical to (6) except for the incremental update of the pre-existing deformation gradient $\mathbf{F}_r$ through (12). Consequently, the implementation of the presented prestressing approach into a standard finite element code is relative simple. There are basically two adjustments to be done compared to a standard nonlinear finite element calculation: (i) throughout the simulation (during prestressing and afterwards) the total deformation gradient (3) which includes the pre-existing deformation gradient has to be used to compute the constitutive equation $\Sigma(\mathbf{F}, \mathbf{F}_r)$ and (ii) during a prestressing increment the pre-existing deformation gradient $\mathbf{F}_r$ has to be incrementally updated according to (12). The implementation can be performed at the material point level, where the components of $\mathbf{F}_r$ can be stored as state variables. In contrast, the original MULF method required for an implementation at the finite element level to perform the update of the Jacobian matrix. However, the present approach requires additional increments to calculate the pre-existing deformation gradient and is therefore computationally more expensive than the original approach by Gee et al. (2010).

2.3 Prestressing Soft Tissues with Distributed Collagen Fibrils

In general, the forward incremental prestressing method outlined in the previous subsection is independent of the constitutive formulation. However, special care must be exercised when dealing with anisotropic constitutive models in which (generalized) structure tensors account for predominant collagen fibril orientations. These models usually define preferred fibril orientations at the unloaded configuration, which is an unknown configuration in our case.

In this work, we use the microstructure-oriented constitutive formulation initially derived in Grytz (2008). The model is based on the assumption that, at the micro-scale, collagen fibrils crimp into the shape of a helix and are solely subjected to an axial load in fiber direction $\mathbf{e}$ (Grytz and Meschke 2009). At the meso-scale, collagen fibrils are assumed to form a collagen network which can be characterized by a planar distribution of its fibril orientations $\mathbf{e}$ (Grytz and Meschke 2010). The constitutive model contains two material parameters (the elastic modulus of the fibril per macroscopic tissue volume E and the stiffness parameter of the standard Neo-Hookean model c), two microstructural parameters (the crimp angle θ_0 and the ratio R_0/r_0 between the radii of the helical wave form and of the fibril cross section) and three meso-structural parameters (the collagen fibril dispersion parameter $\kappa \in [0; 1/2]$ and two vectors $\mathbf{M}_\alpha (\alpha = 1, 2)$ that span the plane in which collagen fibrils are dispersed around the mean fibril orientation $\mathbf{M}_1$). The meso-structural parameters were used to formulate a generalized structure tensor similar to the work of Gasser et al. (2006)

$$H_{2D} = (1 - \kappa)\mathbf{M}_1 \otimes \mathbf{M}_1 + \kappa\mathbf{M}_2 \otimes \mathbf{M}_2, \quad (13)$$

where $\mathbf{M}_\alpha$ were assumed to form a orthonormal basis $\mathbf{M}_i$ with $\mathbf{M}_3 = \mathbf{M}_1 \times \mathbf{M}_2$. The tensor H_{2D} links the macro- to the micro-scale in the constitutive model, representing the dispersion of the collagen fibril orientations in an integral sense.

In contrast to the concept of the generalized structure tensor, Roberts et al. (2009) used the MIL method to calculate a fabric tensor

$$H_{\text{MIL}} = \sum_{i=1}^3 H_i \mathbf{M}_i \otimes \mathbf{M}_i \quad \text{with} \quad \sum_{i=1}^3 H_i = 1 \quad \text{and} \quad H_1 \geq H_2 \geq H_3 \quad (14)$$

representing the predominant beam orientations of the regional connective tissue architecture in the LC. Note that the generalized structure tensor (13) can be represented by the fabric tensor (14) by setting $H_1 = 1 - \kappa$, $H_2 = \kappa$ and $H_3 = 0$. Accordingly, we propose that the fabric tensor (14) can be used as an alternative to the generalized structure tensor (13) to represent the collagen fibril network in our constitutive formulation.

Together with the macroscopic Cauchy-Green tensor $\mathbf{C}$ the generalized structure tensor (13) or the fabric tensor (14) is used to compute the average fibril stretch of the collagen fibril network $\lambda_{\text{col}} = \sqrt{H_* : \mathbf{C}}$ ($*$ = 2D, MIL), which is then used to compute the strain energy contribution of the collagen network from the one-dimensional strain energy density function originally derived for one crimped collagen fibril at the micro-scale $W_{\text{fib}}(\lambda_{\text{col}})$. For the complete derivation and a detailed explanation of the constitutive model, please see Grytz (2008); Grytz and Meschke (2009, 2010). Note that in contrast to our previous work the collagen fibril dispersion is represented here by one instead of two generalized structure tensors of the form (13).

Note that tissue deformation changes the micro- and meso-structure of the collagen network including the collagen fibril orientations $\mathbf{e}$ (see Fig. 1). As the constitutive model was formulated with respect to the unloaded configuration, so were the micro- and meso-

structural parameters related to the unloaded configuration of the collagen fibril network. Here, however, the macro-structure of the specimen is assumed to be known from experimental observations only at a preloaded reference configuration $\mathcal{B}_r$ while the unloaded configuration $\mathcal{B}_0$ is unknown. While this presents no problem for the scalar parameters in our constitutive formulation, it is more practical to introduce a second orthonormal basis $\mathbf{M}_i^r$ to define predominant orientations of the collagen network at the pre-loaded reference configuration. However, to construct the generalized structure tensor (13) the orthonormal basis $\mathbf{M}_i$ at the unloaded configuration needs to be estimated from $\mathbf{M}_i^r$. This cannot be accomplished by a standard pull-back operation using the pre-existing deformation gradient F_r , where the orthonormality of a pulled-back basis is generally not preserved. Therefore we introduce a orthonormal pull-back operation of the vector basis $\mathbf{M}_i^r$ as proposed by Grytz and Meschke (2010)

$$\begin{aligned} \mathbf{M}_1 &= \frac{F_r^{-1} \mathbf{M}_1^r}{\|F_r^{-1} \mathbf{M}_1^r\|}, \quad \mathbf{M}_2 = \mathbf{M}_3 \times \mathbf{M}_1 \\ \mathbf{M}_3 &= \frac{F_r^T \mathbf{M}_3^r}{\|F_r^T \mathbf{M}_3^r\|} \quad \text{with} \quad \mathbf{M}_3^r = \mathbf{M}_1^r \times \mathbf{M}_2^r. \end{aligned} \quad (15)$$

The orthonormal pull-back operation (15) ensures that vector basis $\mathbf{m}_r^i = F \mathbf{M}^i$ derived by a standard push-forward application satisfies the following relationship with the orthonormal vector basis $\mathbf{M}_r^i$ at the pre-loaded reference configuration $\mathcal{B}_r$: (i) the mean fibril orientations will point in the same direction ($\mathbf{m}_r^1 / \|\mathbf{m}_r^1\| \stackrel{!}{=} \mathbf{M}_r^1$) and (ii) the plane in which the fibrils are dispersed will coincide ($\mathbf{m}_r^\alpha \cdot \mathbf{M}_r^3 \stackrel{!}{=} 0$). The fulfillment of these requirements can be easily proven as shown here

$$\begin{aligned} \frac{\mathbf{m}_r^1}{\|\mathbf{m}_r^1\|} &= \frac{F_r \mathbf{M}_1}{\|F_r \mathbf{M}_1\|} = \frac{F_r F_r^{-1} \mathbf{M}_1^r}{\|F_r F_r^{-1} \mathbf{M}_1^r\|} = \frac{F_r^{-1} \mathbf{M}_1^r}{\|F_r^{-1} \mathbf{M}_1^r\|} = \mathbf{M}_1^r \\ \mathbf{m}_r^1 \cdot \mathbf{M}_3^r &= F_r \mathbf{M}_1 \cdot \mathbf{M}_3^r = \frac{\mathbf{M}_1^r \cdot \mathbf{M}_3^r}{\|F_r^{-1} \mathbf{M}_1^r\|} = 0 \\ \mathbf{m}_r^2 \cdot \mathbf{M}_3^r &= F_r \mathbf{M}_2 \cdot \mathbf{M}_3^r = \mathbf{M}_2 \cdot F_r^T \mathbf{M}_3^r \\ &= \frac{(F_r^T \mathbf{M}_3^r \times \mathbf{M}_1) \cdot F_r^T \mathbf{M}_3^r}{\|F_r^T \mathbf{M}_3^r\|} = 0 \end{aligned} \quad (16)$$

Note that together with (15) and (13) the stress and elasticity tensor can then be calculated in a standard way using the total deformation gradient F (3) as outlined in detail in Grytz (2008).

3 Numerical Examples

3.1 Synthetic Inflation Experiment

In this section a synthetic inflation experiment of a generic posterior scleral shell is presented. The synthetic example is used to verify the prestressing method and to test its performance. Furthermore, the impact of the pre-existing stress/stretch state on the inverse

problem to estimate the constitutive parameters from the synthetic inflation data set is investigated.

The generic posterior sclera model has the geometry of a 1 mm thick spherical cap with an outer radius of 12 mm at its unloaded configuration $\mathcal{B}_0$ (Fig. 3a). Collagen fibrils are oriented parallel to shell surface and are assumed to be isotropically dispersed ($\kappa = 0.5$) except for three regions: two regions in the periphery of the sclera have a preferred collagen fibril alignment in the circumferential and meridian direction, respectively, and a ring of highly aligned fibrils around the scleral canal (Fig. 3b). These anisotropic regions were chosen to test the prestressing method under complex anisotropic material conditions and not to represent the realistic collagen fibril architecture in the human eye. For the sake of simplicity, the LC is assumed to have the same thickness as the sclera. The microstructural and material parameters of the model are summarized in Table 2. The constitutive parameters of the sclera have been previously estimated by Grytz and Meschke (2010) from scleral inflation tests performed by Woo et al. (1972). While the microstructural parameters θ_0 and R_0/r_0 of the LC were assumed to be identical to the scleral parameters, the material parameters c and E were chosen to be 1/15 times the value of the scleral parameters to compensate for its rather lower stiffness and thickness (Sigal et al. 2009). The synthetic model was discretized into 3328 tri-linear hexahedral finite elements, which are based on a hybrid formulation to account for incompressibility. Nodes at the cut off plane of the spherical cap were clamped.

A synthetic experimental data set was created by applying 10 IOP levels (5, 7, 10, 15, 20, 25, 30, 35, 40, 45 mmHg) to the unloaded configuration $\mathcal{B}_0$. The deformed mesh of the synthetic data set at 5 mmHg IOP was captured and was then used as the reference configuration $\mathcal{B}_r$ for the prestressing and inverse analyses presented in the subsequent subsections.

3.1.1 Prestressing—We now assume that the solution of the synthetic experiment at 5 mmHg IOP represents the reference configuration $\mathcal{B}_r$ that was obtained experimentally and the unloaded configuration $\mathcal{B}_0$ would be unknown. Hence, starting from $\mathcal{B}_r$ the forward incremental pre-stressing technique outlined in Subsection 2.2 is applied to estimate the pre-existing stress/strain state in $\mathcal{B}_r$.

The pre-existing load of 5 mmHg IOP was applied in two load steps and the tolerance for the prestressing algorithm was set to $10^{-8} \mu\text{m}$. During the prestressing calculation the maximal virtual displacement $|\mathbf{u}_r^i|$ is incrementally decreasing as can be seen in Fig. 4. The prestressing algorithm converged after 11 increments. Further iterations decreased the virtual displacements furthermore until machine precision was reached.

After prestressing, the internal pressure was increased up to the maximal pressure level of 45 mmHg. In Fig. 5, the von Mises stress distribution of the analysis using the forward incremental prestressing algorithm is compared to the reference solution at 5 and 45 mmHg IOP. In Table 3, the maximum von Mises stress and the height of the deformed posterior scleral shells are compared for the two solutions. The results show that the application of the

forward incremental prestressing method allows for a very accurate reproduction of the reference solution without computing the unloaded configuration $\mathcal{B}_0$.

The accuracy of the method has been investigated for other parameter constellations, higher reference pressure levels and different inhomogeneities. In all cases, the forward incremental prestressing method was able to reproduce the reference solution with the same accuracy shown above.

3.1.2 Inverse Parameter Estimation—In this subsection, the impact of prestressing on the inverse constitutive parameter estimation of posterior scleral shells from inflation experiments is investigated. Using the synthetic data set, we again assume that the geometry of the specimen was obtained at 5 mmHg IOP and the relative displacements $\mathbf{u}_p^{\text{exp}}$ from 5 mmHg to nine higher pressure levels $p = \{7, 10, 15, 20, 25, 30, 35, 40, 45 \text{ mmHg}\}$ were measured experimentally at the outer surface of the posterior scleral shell. To focus on the impact of the prestress, the collagen fibril architecture was assumed to be known from experimental measurements.

Different inverse finite element analyses were performed to estimate the four constitutive parameters of the sclera material from the synthetic data set. The optimal parameter set was defined to minimize the difference of the displacement error by means of the following objective functional

$$\varepsilon = \sum_{p=1}^9 \left(\frac{\sum_i (\mathbf{u}_{p,i}^{\text{FE}} - \mathbf{u}_{p,i}^{\text{exp}})^2}{\sum_i (\mathbf{u}_{p,i}^{\text{exp}})^2} \right)^2, \quad (17)$$

where $\sum_i$ represents the summation over all nodes of the outer surface of the scleral shell. The search for optimal parameters was carried out using a Genetic Algorithm provided by Altair HyperWorks 10.0.

Four inverse finite element analyses were performed to estimate the constitutive parameters of the sclera material from the synthetic data set with and without incorporating the pre-existing stress/strain state. The inverse analyses differ in the calculation of the displacement field $\mathbf{u}_{\text{FE}}^p$ and the application of the external load p :

- a. The prestressing approach: the forward incremental prestressing method was applied to calculate the pre-existing stress/stretch state at the true reference configuration $\mathbf{x}_r$. The relative finite element displacements $(\mathbf{u}_p^{\text{FE}})_a = \mathbf{x}_p - \mathbf{x}_r$ were calculated after prestressing.
- b. The naive approach: the pre-loaded reference configuration was assumed to be the unloaded configuration and the model displacements were (naively) calculated as $(\mathbf{u}_p^{\text{FE}})_b = \mathbf{x}_p - \mathbf{X}$.
- c. The relative pressure approach: in contrast to analysis (b), the pre-existing pressure (5 mmHg) was subtracted from the nine pressure levels to account for the relative

increase in pressure $p^* = p - 5$ mmHg. The displacements were calculated as $(\mathbf{u}_p^{\text{FE}})_c = \mathbf{x}_{p^*} - \mathbf{X}$. This approach was previously used in Girard et al. (2009a,b).

- d. The relative displacement approach: in contrast to (b), the pre-loaded reference configuration $\mathbf{x}_{p^*}$ was approximated by a normal forward calculation, where the pre-existing pressure (5 mmHg) was applied to the true reference configuration. The relative displacements $\mathbf{u}_p^{\text{FE}} = \mathbf{x}_p - \mathbf{x}_{p^*}$, were calculated with respect to the approximated reference configuration. This approach was previously used in Grytz and Meschke (2010); Grytz (2008).

The quality of the parameter estimation was measured as the averaged difference of the estimated par^{FE} and the reference parameter set par^{exp}

$$\varsigma = \frac{1}{4} \sum_{\text{par}} \left| \frac{\text{Par}^{\text{FE}}}{\text{Par}^{\text{exp}}} - 1 \right| \quad \text{with par} = \{c; E; \theta_0; R_0/r_0\}. \quad (18)$$

The estimated parameters together with the error (17) and quality values (18) are summarized in Table 4. Incorporating the prestress according to the forward incremental prestressing method allowed for the exact reproduction of the given synthetic data set in analysis (a). The naive forward calculation starting from the reference configuration in analysis (b) led to very poor estimates of the parameters ($\varsigma = 139.8\%$) and an inaccurate characterization of the nonlinear deformation response ($\varepsilon = 0.102$). The inverse analysis (c) using modified pressure levels was able to estimate the nonlinear deformation response from 5 to 45 mmHg IOP with reasonable accuracy ($\varepsilon = 4.6\text{e-}6$), but significantly overestimated the material parameter c . The best estimation of the inverse problem without explicitly incorporating the prestress was obtained by analysis (d) with only $\varsigma = 1.7\%$ error in the parameter estimation and a displacement error of $\varepsilon = 1.7\text{e-}7$.

These numerical results show that the given problem can be exactly reproduced by incorporating the pre-existing stress/strain state into the inverse analysis (a). Not considering the prestress can lead to poor numerical predictions (b). The indirect consideration of the prestressed state through relative displacements led to a good approximation of the inverse problem in this case (d). Note that the given error estimates depend on the chosen problem which includes the chosen constitutive properties, pressure levels and the geometry of the subject. The error values might be much higher in the case of real eye-specific data sets.

3.2 Eye-Specific Analysis

In this subsection we investigate the impact of pre-stressing on an eye-specific simulation of a monkey scleral shell. The eye-specific model incorporates an anatomically correct scleral shell surface geometry and tissue thickness and an eye-specific LC. The model geometry shown in Fig. 6a,b was obtained from a monkey eye perfusion fixed at an IOP of 10 mmHg using a high resolution tactile scanner and histomorphometric measurements for the sclera (Roberts et al. 2010b). The geometry of the LC was three dimensionally reconstructed using a high resolution histologic serial sectioning technique (Downs et al. 2007; Burgoyne et al. 2004). The eye geometry was discretized into 12,000 quadratic finite elements with a

reduced integration scheme (Fig. 6c). Symmetry boundary conditions are assumed at the equator of the hemisphere.

The realistic modeling of the biomechanical response of the LC is of special interest when investigating the potential cause of retinal ganglion cell axon damage in glaucoma. To account for a realistic representation of the anisotropic material properties of the LC, meso-structural measurements of the LC connective tissue architecture were introduced to the eye model. Roberts et al. (2009) used a three-dimensional segmentation algorithm to reconstruct the porous LC connective tissue meso-structure. Regional fabric tensors were calculated using the MIL method, where H_{MIL}^r represents the regional, eye-specific connective tissue architecture in the preloaded LC at the reference configuration. In Fig. 7a the predominant collagen fibril orientations M_1^r and a measure for the degree of planar anisotropy derived from the principle values of the fabric tensor $A = (H_1^r - H_2^r) / (H_1^r + H_2^r)$ are plotted. The limit cases $A = 0$ and $A = 1$ represent a planar isotropic collagen fibril architecture and perfectly aligned collagen fibrils with the predominant orientation M_1^r , respectively. A planar isotropic collagen fibril architecture was assumed for the sclera excluding the peripapillary scleral ring region, where highly aligned collagen fibrils surround the scleral canal as predicted in our previous remodeling analysis (Grytz et al. 2011) and observed experimentally (Quigley et al. 1991; Winkler et al. 2010).

The regional connective tissue volume fraction n_{CT} of the LC was obtained from the experimental measurements of (Roberts et al. 2009) (Fig. 7b). To incorporate n_{CT} into the constitutive formulation outlined in Sub-section 2.3, the elastic modulus of the collagen network was redefined to $E = n_{\text{CT}}E_0$ with $E_0 = 74.84$ MPa. The other constitutive parameters were set to $c = 0.1$ MPa, $\theta_0 = 5.09^\circ$ and $R_0/r_0 = 1.04$. A connective tissue volume fraction of 50% was assumed for the sclera (Keeley et al. 1984).

Fig. 8 shows the net LC displacements due to IOP elevation from 10 to 45 mmHg. These displacements were computed in the normal direction of a plane fitted to the anterior LC insertion. The results in Fig. 8a were calculated by performing a standard forward calculation first to 10 mmHg and then to 45 mmHg IOP. The results shown in Fig. 8b were obtained by pre-stressing the model at 10 mmHg IOP followed by a standard forward calculation to 45 mmHg IOP. Disregarding the prestress in the eye-specific model led to the underestimation of the LC displacements of up to 6.5%.

In Fig. 9 the impact of prestressing on the collagen fibril strain $\lambda_{\text{col}} - 1$ prediction is investigated. Fig. 9a and Fig. 9b show the collagen fibril strain in the LC at the pre-loaded reference configuration with and without prestressing the model, respectively. Disregarding the prestress led to a small underestimation of the collagen fibril strain (max error 1%). The error increased after IOP elevation to 45 mmHg but remained small (max error 3.5%) as can be seen in Fig. 9c,d.

We also investigated the impact of prestressing on the eye-specific model assuming the meso- and macro-structure were obtained at an elevated IOP of 45 mmHg, which is common in our experimental protocols. Fig. 10a and Fig. 10b show the collagen fibril strain in the LC at 45 mmHg IOP with and without pre-stressing the model, respectively. Fig. 10c,d shows

the collagen fibril strain in the complete posterior scleral shell. Prestressing at high IOP had a significant impact on the prediction of the collagen fibril strain. Disregarding the prestress led to a significant underestimation of the collagen fibril strain in the LC (max error 24%). In contrast, disregarding the prestress led to a significant overestimation of the collagen fibril strain in the scleral shell (max error 9%). This opposed observations are strongly related to the highly aligned ring of collagen fibrils in the peripapillary ring region. While the scleral shell is mainly responding like a pressure vessel that carries the IOP load through membrane stresses (membrane mode), the peripapillary ring of collagen fibrils shields the LC from these membrane stresses in favor of a bending mode. Disregarding the prestress led to an increase in eye volume and as such in total IOP load, which in turn caused the strain overestimation in the scleral shell seen in Fig. 10c. In contrast, to keep the LC at its reference position and preventing its bending required the existence of a high pre-existing stress/strain state as predicted in Fig. 10b. Consequently, the collagen fibril strains were underestimated when the pre-stressing of the LC was disregarded as seen in Fig. 10a.

Note that the reported error estimations are representative for the constitutive parameters, the meso- and the macro-structure used for this particular eye-specific model. For different eye geometries or a different set of constitutive properties the errors may vary significantly in magnitude. In addition to the collagen fibril strains the maximum principal tissue stress and strain were investigated. The results of the tissue stresses and strains did qualitatively not differ from the collagen fibril strain patterns (Fig. 9,10) and were, therefore, not presented here.

4 Conclusions

A forward incremental prestressing method was presented that unifies the advantages of existing prestressing approaches. This method is very robust and very simple to implement within commercial nonlinear finite element code. It delivers highly accurate prestress predictions for three-dimensional structures including anisotropic and nonlinear constitutive properties typically observed in soft tissues. Furthermore, an orthonormal pull-back operation was introduced to pull-back orthonormal vector bases. The orthonormal pull-back operation allows for a consistent incorporation of anisotropic constitutive formulations, which are based on a generalized structure tensor, into pre-loaded finite element models at large strains. A synthetic inflation experiment of a generic sclera model revealed the importance of pre-existing stresses and strains with respect to inverse parameter estimation analyses, where disregarding the pre-existing stress condition might lead to erroneous numerical predictions. However, the indirect consideration of the pre-loaded reference configuration by means of relative pressure levels or displacement values might also give reasonable inverse parameter estimations.

The prestressing method was also applied to an eye-specific model of a pre-loaded posterior monkey sclera that incorporates experimentally obtained meso- and macro-structural measurements of the connective tissue architecture and eye geometry, respectively. The analysis revealed that disregarding the prestress may lead to moderate errors in the strain and displacement predictions if the eye geometry and the connective tissue architecture were measured at 10 mmHg of IOP pre-load. This error increases for higher pre-load levels. At a

high pre-load level of 45 mmHg IOP, disregarding the pre-stress led to significantly different results. In this case, the incorporation of the pre-existing stress/strain state becomes a prerequisite for accurate displacement and stress/strain predictions. The numerical results showed that the strain and stress environment was overestimated without incorporating the prestress in the scleral shell, which was mainly subjected to membrane deformations due to IOP. In contrast, the strain and stress environment was underestimated without prestressing in the LC, which was mainly subjected to bending deformations in our example due to the stiff collagen fibril ring in the peri-papillary sclera. The eye-specific analysis revealed that disregarding the prestress can lead to over- or underestimation of the strain and stress field depending on the tissue boundary conditions.

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Fig. 1.

The unloaded dcll; ($\mathcal{P}_0, \mathbf{e}_0$), the reference $\mathcal{B}_r$ ($\mathcal{P}_r, \mathbf{e}_r$) and the actual configuration of the body $\mathcal{B}_t$ (of a typical point $\mathcal{P}_t$ and of a collagen fibril orientation $\mathbf{e}_t$). Multiplicative split of the deformation gradient $\mathbf{F}$ into pre-existing $\mathbf{F}_r$ and subsequent deformations $\mathbf{F}_t$.

Fig. 2.

Illustration of the forward incremental prestressing method. The true unloaded configuration $\mathcal{B}_0$ ($\mathbf{e}_0$) and the true reference configuration of the body $\mathcal{B}_r$ (of a collagen fibril orientation $\mathbf{e}_r$). The unloaded configuration $\mathcal{B}_0^i$ ($\mathbf{e}_0^i$) and the neighboring reference configuration of the body $\mathcal{B}_r^i$ (of a collagen fibril orientation $\mathbf{e}_r^i$) at increment i of the forward incremental prestressing process.

Fig. 3.

Synthetic inflation experiment of a generic posterior scleral shell with anisotropic inclusions. (a) Geometry and mesh at the unloaded configuration $\mathcal{B}_0$ (IOP = 0 mmHg); (b) collagen fibril dispersion κ and preferred fibril orientations (white lines). The anisotropic inclusions were chosen to test the prestressing method under complex anisotropic material conditions and not to represent the realistic collagen fibril architecture in the human eye.

Fig. 4.

Maximal virtual displacements $\max |\mathbf{u}_r^i|$ against the cumulated number of increments i of the prestressing calculation. $\diamond$ regular prestressing increment; $\blacklozenge$ prestressing increment with increase in external load.

Fig. 5. Von Mises stress (Cauchy) $|\sigma|$ for the reference solution (top) and the forward incremental prestressed solution (bottom) at (a) 5 mmHg and (b) 45 mmHg IOP.

Fig. 6.

Eye-specific posterior pole geometry of a monkey eye perfusion fixed at 10 mmHg IOP (a) with a detailed view of the optic nerve head region (b) and its discretization into 12,000 finite elements (c) showing the eye-specific LC (green) and the posterior scleral shell (blue) with the peripapillary sclera ring region (red). The scleral geometry and thickness were measured using a high resolution tactile scanner and histomorphometric measurements, respectively (Roberts et al. 2010b). The LC geometry was three dimensionally reconstructed using a high resolution histologic serial sectioning technique (Downs et al. 2007; Burgoyne et al. 2004).

Fig. 7.

(a) Preferred collagen fibril orientations M_1^r (black lines) and degree of planar anisotropy $A = (H_1^r - H_2^r) / (H_1^r + H_2^r)$; (b) connective tissue volume fraction n_{CT} in the peripapillary sclera and the LC. For the LC, the connective tissue volume fraction and the fabric tensors were experimentally obtained from a voxel-based representation of the porous LC connective tissue microstructure (Roberts et al. 2009). For the sclera, the fabric tensors were estimated based on a numerical remodeling prediction (Grytz et al. 2011) while the connective tissue volume fraction was taken from the literature (Keeley et al. 1984).

Fig. 8.

Net LC displacements for IOP elevation from 10 mmHg to 45 mmHg IOP: (a) by performing a standard forward analysis to 10 mmHg and afterwards to 45 mmHg IOP; (b) by prestressing the reference configuration at 10 mmHg IOP and afterwards performing a standard forward analysis to 45 mmHg IOP.

Fig. 9.

Collagen fibril strain within the LC at 10 mmHg (a,b) and 45 mmHg IOP (c,d) without prestressing (a,c) and with prestressing (b,d). The reference configuration was experimentally obtained at 10 mmHg IOP.

Fig. 10.

Collagen fibril strain within the LC at 45 mmHg IOP without prestressing (a) and with prestressing (b). Collagen fibril strain within the posterior scleral shell at 45 mmHg IOP without prestressing (c) and with prestressing (d). The reference configuration was assumed to be experimentally obtained at 45 mmHg IOP.

Table 1

Forward incremental prestressing procedure. $\mathbf{t}_r$ the known pre-existing external load vector, which can be applied in multiple load steps $n = 1, 2, \dots, m$; tol anticipated tolerance of the prestressing procedure; $i=1, 2, \dots$ cumulated number of increments.

i.	Initialize $F_r = I$
ii.	Increase external load $\mathbf{t}_r^n$ with $\mathbf{t}_r = \sum_{n=1}^m \mathbf{t}_r^n$.
iii.	Use the total deformation gradient $F^i = F_r^i F_r$ (8) to compute the constitutive equation during the iterative solution of (9) and compute the displacements $\mathbf{u}_r^i$ to the neighboring reference configuration
iv.	Update $F_r \leftarrow F_r^i F_r$ (12).
v.	If $n < m$ goto step ii for next load step $n=n+1$ and next increment $i=i+1$.
vi.	If $ \mathbf{u}_r^i > tol$ goto step iii for next increment $i=i+1$.

Table 2

Microstructural and material parameters of the synthetic model.

Tissue	c [MPa]	E [MPa]	θ_0 [deg]	R_0/r_0 [–]
Sclera	0.01	37.42	5.09	1.04
Lamina cribrosa	0.0007	2.50	5.09	1.04

Table 3

Comparison of maximum von Mises stress (Cauchy) $\max |\sigma|$ and height h of the synthetic posterior scleral shell.

Analysis	IOP [mmHg]	$\max \sigma $ [kPa]	h [mm]
Reference Solution	5.0	18.33	8.42453
Prestressing	5.0	18.36	8.42453
Reference Solution	45.0	184.88	8.60332
Prestressing	45.0	184.88	8.60332

Table 4

Comparison of inverse parameter estimations of the synthetic experiment.

Approach	c [MPa]	E [MPa]	θ_0 [deg]	R_0/r_0 [-]	ε [-]	ζ [%]
(a) The prestressing approach	0.0100	37.42	5.09	1.04	9.1e-14	0.0
(b) The naive approach	0.0401	80.37	11.26	0.81	0.102	139.8
(c) The relative pressure approach	0.0154	43.32	5.05	0.95	4.6e-6	19.8
(d) The relative displacement approach	0.0096	36.74	5.09	1.05	1.0e-7	1.7
Target parameter values	0.01	37.42	5.09	1.04		