Stretching the Limits: From Planar-Biaxial Stress–Stretch to Arterial Pressure–Diameter

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Abstract

Understanding the physiological condition of the vascular system is critical to explain, treat, and manage vascular disease. Numerous experimental and computational studies exist to characterize the mechanical behavior of arterial tissue samples under controlled laboratory conditions. However, translating this laboratory knowledge into physiologically realistic and real-life conditions remains challenging. Key difficulties include the selection of suitable and physiologically relevant test methods, minimizing measurement uncertainty, and ensuring robust model validation. Here, we present a novel integrative approach to translate controlled laboratory experiments on arterial samples into pressure–diameter data that can be recorded inexpensively and non-invasively in the clinic. We perform controlled planar-biaxial tests on carotid arteries under three different stretch ratios and generate axial and circumferential stress–stretch data to calibrate a fiber-reinforced soft tissue model for arterial tissue. Using an analytical thick-walled cylindrical model, we predict subject-specific pressure–diameter behavior, informed by anatomical geometries and arterial prestretch. We systematically compare each prediction against extension-inflation experiments on tubes from the same artery by applying controlled pairs of axial stretch and inner pressure, while recording the outer diameter. We quantify the prediction error in both absolute and relative stretch regimes. The results show that planar-biaxial loading probes fundamentally different stretch regimes compared to extension-inflation deformations, leading to an extrapolation of the model predictions. We quantify the influence of the fitted constitutive material parameters, and assess the sensitivity of the results to the accurate representation of axial stretch and circumferential prestretch. We suggest that translating laboratory measurements into realistic physiological conditions is also highly sensitive to the load-free reference configuration and *in vivo* geometries. Only when those key model parameters are accurately captured, and their uncertainty propagated, planar-biaxial stress–stretch data can be used as a reliable tool to predict arterial pressure–diameter behavior. Our study provides a publicly available dataset, along with comprehensive testing protocols and post-processing workflows, to support reproducibility and further research on this topic.

Keywords: Carotid arteries, Planar-biaxial, Stress–stretch, Constitutive modeling, Extension-inflation, Pressure–diameter

1. Introduction

Biological tissues exhibit complex structural, compositional and mechanical behavior, making it challenging to accurately quantify their biomechanical properties. Inverse modeling informed by experimental data offers a valuable approach for estimating these properties, but its reliability depends on careful selection of the appropriate test method, design of a physiologically relevant test protocol, making appropriate model assumptions, and performing robust validation. Factors such as biological variability, nonlinearity, and anisotropy further challenge reliable evaluation. This work focuses on key challenges in mechanical testing

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and subsequent parameter estimation for the biomechanics of arteries, aiming to contribute to more robust and interpretable material descriptions.

Planar-biaxial testing provides a unique, relatively high-throughput, and physiologically relevant method for characterizing the mechanical response of arterial tissue under controlled multi-axial loading (B. Ramachandra and Humphrey, 2019). Unlike uniaxial tests, biaxial loading replicates the simultaneous circumferential and axial stresses experienced by arteries *in vivo*, offering a more complete picture of wall mechanics. A key advantage of this approach is also its tissue-sparing nature, with only small, flat specimens required (Abbeele, 2014).

While biaxial testing provides detailed insight into material behavior, it does not directly result in a pressure–diameter (P–d) relationship, which remains the clinically most relevant descriptor of arterial compliance and function. This is especially important for cardiovascular tissue under dynamic loading conditions, such as those observed between systolic and diastolic blood pressures. *In vivo*, this pulsatility can be observed through ultrasound, MRI, or 4D-CT imaging (Smoljkić et al., 2015; Liu et al., 2019). *Ex vivo* pressure–diameter can be captured through extension-inflation testing. Although more intuitive from a mechano-clinical point of view, extension-inflation data is less omnipresent than planar-biaxial stress–stretch data, partially because of the need for a larger tissue sample geometry and dimensions, but also because of specific device requirements.

Stress–stretch data in the axial and circumferential direction is often used to identify suitable constitutive models describing the mechanical behavior of the relevant cardiovascular tissue. Depending on the symmetry and directional dependence observed in the material response, these models may assume isotropic or anisotropic characteristics. From the experimental stress–stretch data, specific material parameters can be estimated through model fitting, allowing the strain energy function to capture the nonlinear mechanical behavior of the tissue. Once calibrated, this constitutive model can be implemented in numerical simulations to predict tissue deformation under physiological conditions. In particular, it enables the computation of pressure–diameter (P–d) responses under simulated extension-inflation scenarios, effectively linking experimental mechanics with computer models (Doyle et al., 2010; Korte et al., 2016).

Despite the potential to derive clinically relevant insights from mechanical testing and computational modeling, researchers currently face several important challenges throughout this process. First, selecting the most appropriate mechanical testing method, whether planar-biaxial or extension-inflation, is not straightforward. The choice of the experiment depends on the specific output goals, tissue sample, and infrastructure availability. Second, designing a relevant experimental protocol is critical: planar-biaxial testing requires careful control of the axial and circumferential loading paths, while extension-inflation testing invokes simultaneous axial loading and pressurization, a closer approximation of *in vivo* conditions. Third, minimizing measurement uncertainty is essential, as errors in estimating stress (often due to geometric approximations such as wall thickness and cross-sectional area) and stretch (typically captured via digital image correlation or marker tracking) can significantly affect model calibration. Fourth, selecting appropriate modeling assumptions, including the choice of constitutive model and the boundary conditions applied in simulations, requires a balance between physiological realism and computational tractability. Specifically, axial and circumferential prestretch can be highly sensitive to modeled pressure–diameter outputs. Finally, robust model validation against independent experimental data is necessary to ensure predictive reliability, while remaining a non-trivial step due to variability in biological samples and limited available data. Each of these aspects demands careful consideration to ensure that experimental and computational findings meaningfully reflect true *in vivo* tissue behavior.

In this study, we critically evaluate the results of planar-biaxial tensile testing and compare them against the results of extension-inflation tests, aiming to quantify the effects of measurement uncertainty and experimental and modeling design choices.

2. Materials and Methods

Fig. 1 schematically illustrates the integrated experimental and computational framework. All mechanical tests and measurements were carried out at FIBEr, the KU Leuven Core Facility for Biomechanical Experimentation. The resulting datasets span multiple mechanical tests, processing workflows, and modeling approaches. To promote transparency, reproducibility, and further research, all protocols, raw data, and post-processing code have been made publicly available.

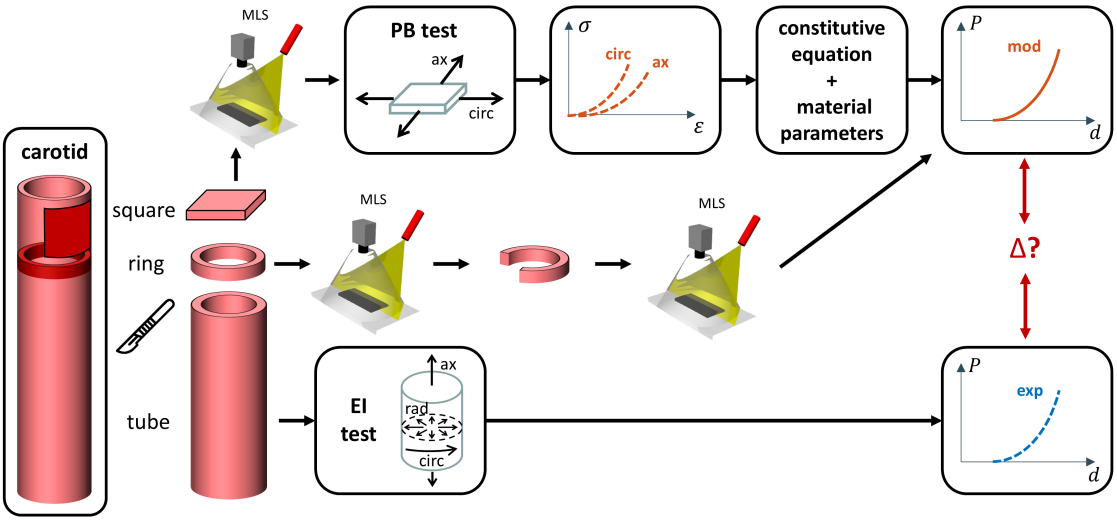

Figure 1: **Experimental and Modeled Biomechanical Characterization Workflow.** Ovine carotid arteries were prepared for planar-biaxial (PB) loading, ring-opening analysis, and extension-inflation (EI) testing. The axial and circumferential stress–stretch (σ–λ) data from PB testing are used to fit material parameters of a chosen constitutive description. These parameters, combined with wall prestretches derived from the ring-opening analysis, enable the modeling (mod) of pressure–diameter (P–d) behavior. The modeled biomechanical response is then compared to the experimental (exp) P–d curve obtained from EI testing on the same artery. All geometrical measurements were acquired using micro laser scanning (MLS).

2.1. Experimental Workflow

Three complementary types of mechanical tests were performed in this study. Planar-biaxial tests were conducted to yield experimental stress–stretch curves, characterizing tissue behavior under controlled axial and circumferential loading conditions. Ring-opening tests were conducted to assess the opening angle, providing insights into the residual stress state and enabling estimation of *in vivo* arterial prestretches (Vander Linden et al., 2022). Extension-inflation tests were performed to generate experimental pressure–diameter data, reflecting the physiological response of the vessels under axial loading and internal pressurization.

2.1.1. Tissue Collection

An overview of the tissue preparation and mounting process is shown in Fig. 2 (López et al., 2010). Five full-length and fresh ovine carotid arteries, labeled A through E, were collected from one-year-old female Swifter sheep weighing between 50 and 70 kg. The study was approved by the UZ Leuven ethical committee for animal experimentation (ECD) under protocol number 189/2021. The tissues were harvested and immediately preserved in phosphate-buffered saline (PBS) at −80°C until further use (O'Leary et al., 2014). Prior to testing, samples were thawed gradually in the fridge at 4°C. Specimen B is shown as a representative example.

2.1.2. Planar-Biaxial Testing: Experimental Stress–Stretch

We performed planar-biaxial tensile tests using a ZwickRoell biaxial testing machine for biomaterials on square samples (Table 1). Five rakes were mounted on each side of the sample, equally spaced, resulting in an initial distance of 7 mm between opposite rake sets in both the axial and circumferential directions. The samples were submerged and tested in a 0.9% saline solution, heated to 37°C. During tensile loading, 30% and 50% stretch levels were applied to the rake holders, calculated relative to their initial positions. Stretches were increased stepwise at a rate of 5%/s until single-rake failure occurred. Four 250 N load cells were used to measure the resulting forces.

For each loading level, we applied three axial-to-circumferential stretch ratios $\{1{:}1, 2{:}1, 1{:}2\}$ using displacement-driven actuators (Fehervary et al., 2018). A 1:2 ratio indicates that half of the 30% or 50% stretch was applied in the axial direction, while the full stretch level was applied in the circumferential direction. Four preconditioning cycles were performed for each loading step and stretch ratio, and the fifth cycle was used for post-processing (Fehervary et al., 2016), with a machine sampling rate of 20 Hz.

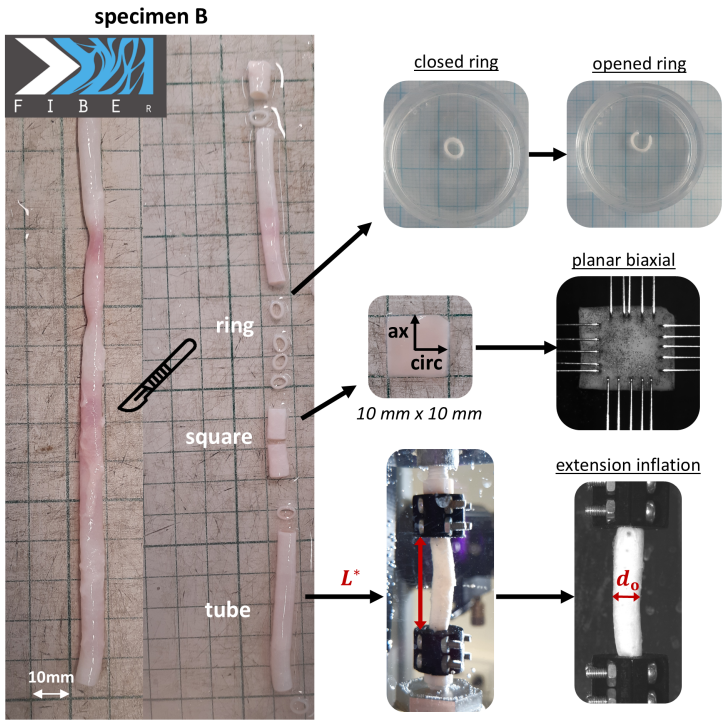

Figure 2: **Schematic Overview of Tissue Harvesting and Experimental Mounting.** Three test samples were prepared from representative specimen B: a square section for planar-biaxial testing, a ring segment for ring-opening analysis, and a tubular segment for extension-inflation testing. The planar-biaxial configuration includes both unmounted and mounted states, with rakes applied in the axial and circumferential directions to impose controlled deformations. The extension-inflation setup illustrates the mounted length $L*$ and the resulting pressurized outer diameter d_o during testing.

Experimentally measured forces were converted to engineering stresses using the initial load-free thickness and areal sample measurements, obtained prior to testing via micro laser scanning (Acacia Technology and Gocator Emulator, LMI Technologies). The results from opposite actuators were averaged to obtain single axial and circumferential stress–stretch curves. Instead of considering stretches and displacements at the level of the rakes, we determined the actual tissue stretches by planar particle tracking of the graphite-powder speckle pattern applied to the sample. Digital image correlation (DIC) was performed using the VIC 2D software (Correlated Solutions, isi-sys) by analyzing the speckle pattern at a 20 Hz camera (Manta G-917, Allied Vision) recording rate (Vander Linden et al., 2023a). The center of the camera was aligned with the zero position of the actuators, imaging orthogonal to the middle of the sample. Note that we consistently speckled and captured the intimal side of the artery. To ensure uniform sample strains, only the central 25% of the loaded area was considered (Sacks, 2000; Fehervary et al., 2016).
The zero-strain state for each planar-biaxial stress-strain curve, defined as the point where both axial and circumferential stretches are zero ($\lambda_{\text{ax}} = \lambda_{\text{circ}} = 0$), can be identified during post-processing by analyzing the 50% loading curve. Specifically, the zero-strain point corresponds to the moment when the measured forces first exceed a predefined threshold specific to each sample. This threshold is determined at the start of the experiment by averaging the force values from the four load cells immediately after all rakes have been inserted into the sample. This mounted configuration is considered the best approximation of a flat, unstressed state. Since the axial and circumferential directions share the same zero-strain state, this method allows the zero point to be determined separately for each loading ratio or test cycle.

2.1.3. Opening Angle Measurements

Due to the release of residual stresses during planar-biaxial tissue specimen cutting, the reference state is different from the *in vivo* state. We performed opening angle tests on estimated 1 mm thick ring cuts to determine any circumferential prestretch in the arterial wall. The intact rings were submerged in 0.9% saline and scanned in a micro laser scanner (Acacia Technology). The rings were then cut axially, submerged to

reduce frictional forces, and ensuring complete residual stress release. A second scan then allowed us to assess the sample-specific ring opening angle. All measurements were performed in the Gocator Emulator software (LMI Technologies).

The closed ring often had an elliptical shape instead of a perfect circle. The major and minor axes of a rectangular region box were then manually adapted to match the inner side of the ring, and averaged to determine a single value for the inner diameter $R_{\mathrm{i}}^{\mathrm{clos}}$, as shown in Fig. 3. The outer diameter of the closed ring ($R_{\mathrm{o}}^{\mathrm{clos}}$) is measured using the same method. For the open ring, inner and outer diameters ($R_{\mathrm{i}}^{\mathrm{open}}$ and $R_{\mathrm{o}}^{\mathrm{open}}$) are measured using a circular sector-shaped bounding box. The sector region is delimited by lines extending from the center to the edges of the arc, with the opening angle β corresponding to the excluded arc angle. The inner diameter is the largest possible diameter within the open ring, and the outer diameter was taken at the same location. Given that flattening has been shown to minimally affect the inferred stress-strain pairs (Jadidi et al., 2019), we do not account for these effects when correlating tubular geometry to planar-biaxial tissue testing.

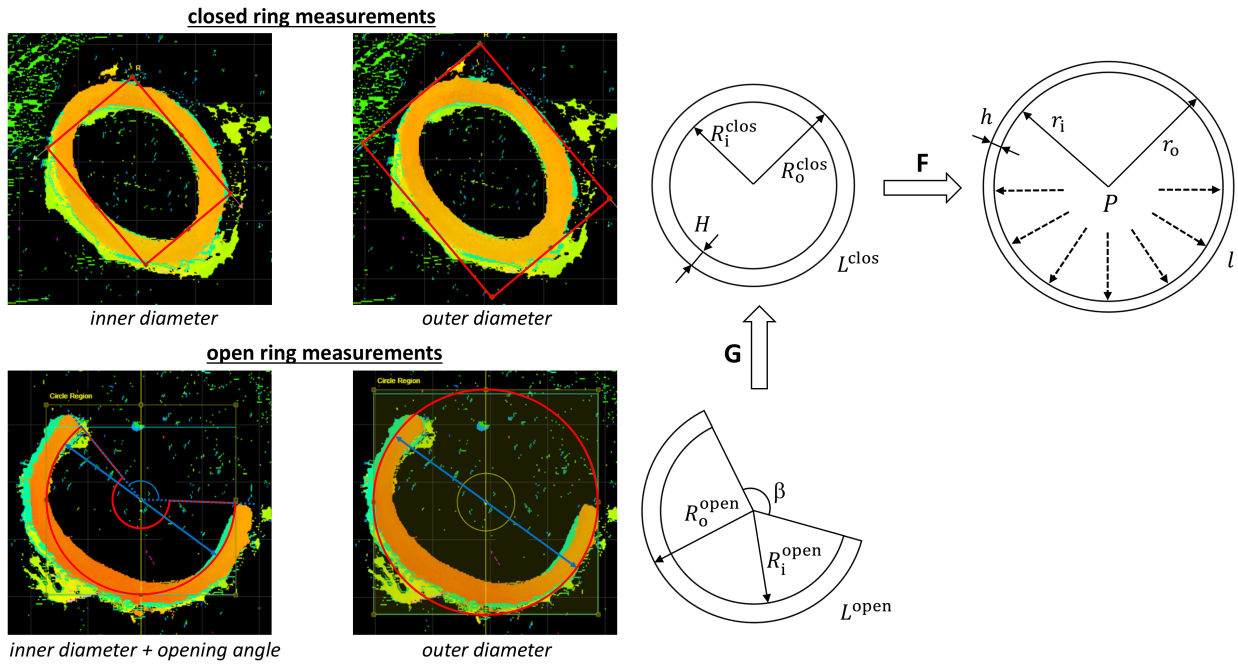

Figure 3: **Ring-Opening Experiments and Sample Deformations.** Experimental methodology used to assess residual stresses and wall prestretches in tubular arterial tissue. The closed ring configuration is analyzed by fitting a rectangular bounding box to the tissue cross-section, from which the inner and outer diameters ($R_{\mathrm{i}}^{\mathrm{clos}}$ and $R_{\mathrm{o}}^{\mathrm{clos}}$) are computed, and the load-free wall thickness H can be derived. In the open ring configuration, β defines the opening angle. The inner diameter ($R_{\mathrm{i}}^{\mathrm{open}}$) is computed as the largest inscribed circle within the open ring, and the outer diameter ($R_{\mathrm{o}}^{\mathrm{open}}$) is measured at the same radial location.The prestretch tensor $\mathbf{G}$ links the reference configuration of length l^{clos} to a deformed configuration via the deformation gradient $\mathbf{F}$. Axial stretch leads to a deformed length l and thickness h, with an inner pressure P inducing deformed diameters r_{i} and r_{o}.

2.1.4. Extension-Inflation Tests: Experimental Pressure–Diameter

The experimental extension-inflation tests were conducted using the ZwickRoell testing machine for *tubular* biomaterials. The device is controlled through a custom test environment created within the TestXpertII software. Two actuators of the machine are employed: (I) the linear displacement mechanism, oriented vertically, used for extending the sample and measuring the axial reaction force via a load cell, and (II) the pump, which is utilized to inflate the tubular sample, by pumping water into it, while simultaneously measuring the applied pressure.

To mount the sample, the top end is first fixed between a mounting pin and two mounting clamps, secured with four screws to ensure an airtight seal. The clamps have an axial length of 12 mm and an inner diameter of 4–6 mm, depending on the considered tube dimensions. The assembly lowered until the distance between the underside of the top clamps and the stud of bottom mounting pin equals the initial axial hanging length

of the tube sample. The bottom end of the sample is then pulled over the bottom pin. The bottom of the tube is then clamped with similar mounting pieces and screws. The whole sample is submerged in a 0.9% saline solution by raising a 37°C heated bath, and the axial load cell is zeroed. The load-free sample length in this reference configuration is measured as the distance between the clamps, assuming no axial forces.

Three consecutive load steps were performed, each applying a different axial stretch corresponding to an additional 30%, 50%, and 75% of the initial mounted length L^* (see also Fig. 2). Note that this mounted length is measured with a caliper before testing, and is different from the initial tube length L due to the 12 mm length of the clamps. The ultimate axial stretch level of 75% represents physiological axial loading conditions for carotid arteries (Blondel et al., 2001). An internal pressure of 90 mmHg was applied during the first two axial stretch steps, while the physiological loading step was conducted at 180 mmHg. The latter reflects the upper limit of systolic blood pressure regimes (Almeida et al., 2014). Lower pressures were used in the initial steps to mitigate the risk of premature tube sealing, loosening, or rupture. Axial loading was applied at a rate of 2.5%/s, and internal pressure was increased at a rate of around 40.0 mmHg/s, depending on the actual pump speed. The relative pressure between the inside and outside of the sample is measured directly by the pressure sensor of the test device.

The experimental outer diameter displacements are captured using a Grasshopper3 camera (Teledyne FLIR). The imaging device is mounted horizontally and aligned with the center of the sample, with respect to both its length and its circumference. The camera, controlled by the VIC Snap software, was configured at a recording rate of 20 Hz (Correlated Solutions, isi sys).

The outer diameter of the sample in the deformed configuration (d_o) is obtained by processing images captured by the camera in Matlab (The MathWorks, Inc.). Note that we differentiate the mounted, load-free outer diameter D_o, from the unpressurized but axially stretch outer diameter $d_\mathrm{o}^{P=0}$, as highlighted for the measured tube in Table 1. We semi-automatically segmented each image to extract the sample and calculate the sample height and width in pixels. We convert pixels to millimeters using the pixel resolution, derived by dividing the known length or height of the mounted sample by the number of pixels in the sample length at the first image of the test protocol.

The converted width or outer diameter is recorded at various points along the sample length. To avoid boundary effects, diameter values in the middle of the sample are reported here. For the experimental pressure–diameter curves, we select the data from the 75% axial stretch loading condition. This step comprises five pressurization cycles, where the first four serve as preconditioning of the sample and minimize viscoelastic effects. Only the stretch or inflation part of the final cycle is used for analysis.

2.2. Modeling Workflow

2.2.1. Kinematics & Assumptions

In what follows, we will use uppercase to represent initial reference configurations through Lagrangian variables $\boldsymbol{X}$. Current or deformed configurations will be represented by lowercase variables $\boldsymbol{x}$, as will model parameters. Tensors are denoted in bold upright font, vectors in bold italic, and scalars in italic. Subscripts and superscripts representing indices are italicized, while other subscripts and superscripts, such as abbreviations, are set in upright font.

We define the deformation gradient as $\mathbf{F} = \partial\boldsymbol{x}/\partial\boldsymbol{X}$, where tissue incompressibility leads to the Jacobian $J = \det(\mathbf{F}) = 1$ (Holzapfel and Weizsäcker, 1998; Ogden, 2017). We will highlight planar-biaxial configurations through subscript PB, while we will refer to extension-inflation setups as EI, resulting in pressure–diameter results (P–d). For consistency, we will write all modeled deformations as $\mathbf{F}^\mathrm{mod}$, and the corresponding modeled First Piola-Kirchhoff stresses as $\mathbf{P}^\mathrm{mod}$. Experimentally measured deformations and stresses will be denoted as $\mathbf{F}^\mathrm{exp}$ and $\mathbf{P}^\mathrm{exp}$, respectively.

In both the planar-biaxial test and the extension-inflation test we ignore shear deformations. In the planar-biaxial test we assume that the artery is consistently stretched in two perfectly orthogonal directions, aligned with the circumferential and axial direction of the artery. Using the stretch definition $\lambda = dx/dX$, we can write $\mathbf{F}_\mathrm{PB} = \mathrm{diag}\{\lambda_\mathrm{circ}, \lambda_\mathrm{ax}, \lambda_\mathrm{rad}\}$, in a Cartesian coordinate system, whereby the three principal directions align with the axial, circumferential and radial direction of the artery, respectively. In the extension-inflation test, we assume an axisymmetric radial pressurization accompanied by an axial elongation, yielding a deformation gradient $\mathbf{F}_\mathrm{EI} = \mathrm{diag}\{\lambda_\mathrm{rad}, \lambda_\mathrm{circ}, \lambda_\mathrm{ax}\}$ in a cylindrical coordinate system. In both tests, the radial stretch will be imposed by incompressibility, $\lambda_\mathrm{rad} = \frac{1}{\lambda_\mathrm{circ}\lambda_\mathrm{ax}}$, whereas the circumferential and axial stretches will be imposed by the testing device.

parameter	definition	value
square		
W_1	average sample width, axial direction	9.9 mm
W_2	average sample width, circumferential direction	10.8 mm
T	average sample thickness	0.30 mm
c_1	neo-Hookean parameter	49.2 kPa
k_1	fiber stiffness coefficient	5.3 kPa
k_2	fiber stiffening coefficient	9.318
κ	fiber dispersion	0.078
α	fiber angle (w.r.t. the circumferential direction)	0.0°
ring		
$R_{\mathrm{i}}^{\mathrm{open}}$	inner radius, open ring	2.40 mm
$R_{\mathrm{o}}^{\mathrm{open}}$	outer radius, open ring	3.15 mm
$R_{\mathrm{i}}^{\mathrm{clos}}$	inner radius, closed ring	2.45 mm
$R_{\mathrm{o}}^{\mathrm{clos}}$	outer radius, closed ring	1.83 mm
β	opening angle	77°
$g_{\mathrm{circ,i}}$	circumferential prestretch, inner wall	0.97
$g_{\mathrm{circ,o}}$	circumferential prestretch, outer wall	0.99
g_{ax}	axial prestretch	1.04
D_{o}	load-free outer diameter	4.90 mm
H	wall thickness	0.62 mm
tube		
L	initial tube length	52 mm
L^*	mounted length, measured	26.49 mm
$l^{P=0}$	unpressurized length, axially loaded	46.14 mm
D_{o}	mounted load-free outer diameter	5.49 mm
$d_{\mathrm{o}}^{P=0}$	unpressurized outer diameter, axially loaded	4.99 mm
λ_{ax}	applied axial prestretch	1.75

Table 1: **Material Parameters for Square, Ring, and Tube Configuration.** We show the data for representative sample B, including the unloaded experimental dimensions for the three geometries (square, ring, and tube), the fitted GOH material parameters, and the calculated prestretches obtained from the ring-opening experiments.

Note that we disambiguate stretch from strain by defining the nominal or engineering strain as $e = (dx - dX)/dX = \lambda - 1$.

2.2.2. Constitutive model

Assuming hyperelastic material behavior, the Cauchy stress may be written as a function of the deformation as

$$\boldsymbol{\sigma} = \frac{\partial \Psi(\mathbf{F})}{\partial \mathbf{F}} \mathbf{F}^T - p\mathbf{I}, \tag{1}$$

where Ψ is the strain energy density function, and p is a Lagrange multiplier enforcing the incompressibility constraint, which will be determined by specific boundary condition assumptions of the planar-biaxial or extension-inflation setup. Subsequently, we can calculate the corresponding first Piola-Kirchhoff stress (i.e. the transpose of the engineering stress) as $\mathbf{P} = J\boldsymbol{\sigma}\mathbf{F}^{-T}$.

We adopt the Gasser–Ogden–Holzapfel (GOH) strain energy density function, which assumes Fung-type strain-stiffening fiber families embedded in an isotropic matrix (Fung et al., 1979; Holzapfel et al., 2000; Gasser et al., 2006; Holzapfel and Ogden, 2025). From the right Cauchy-Green deformation tensor ($\mathbf{C} = \mathbf{F}^T\mathbf{F}$), we can define the first and fourth strain invariants used in the GOH constitutive equation as $I_1 = \lambda_{\mathrm{circ}}^2 + \lambda_{\mathrm{ax}}^2 + (\lambda_{\mathrm{circ}}\lambda_{\mathrm{ax}})^{-2}$ and $I_4 = \lambda_{\mathrm{circ}}^2 \cos^2\alpha + \lambda_{\mathrm{ax}}^2 \sin^2\alpha$, respectively. λ_{ax} and λ_{circ} are again the principal stretches in the axial and circumferential direction. The angle α is defined as the collagen fiber orientation with respect to the circumferential direction in the circumferential–axial plane, assuming two symmetrically oriented fiber families. Due to this symmetry, the fiber angle α is restricted to $0° \leq \alpha \leq 90°$. As such, the GOH model combines an isotropic neo-Hookean contribution based on the first invariant with an anisotropic fiber contribution of the fourth invariant, modeled by a quadratic-exponential function.

The resulting strain energy density function of the GOH constitutive model can be written as

$$\Psi_{\mathrm{GOH}} = \frac{c_1}{2}[I_1 - 3] + \frac{k_1}{2k_2}\left(\exp(k_2[I_4^* - 1]^2) - 1\right), \tag{2}$$

with the shear modulus $c_1 > 0$, the stiffness-like parameter $k_1 > 0$ and the non-dimensional coefficient $k_2 > 0$. The latter modulates the exponential strain-stiffening characteristics of the collagen fibers. The mixed isotropic-anisotropic fiber invariant term expands as $I_4^* = \kappa I_1 + (1 - 3\kappa)I_4$, where the microstructural fiber dispersion parameter κ modulates the degree of isotropy of the collagen fibers. When $\kappa = 0$, we have $I_4^* = I_4$, and the model reduces to non-dispersed collagen fibers along the direction defined by the angle α. When $\kappa = 1/3$, we have $I_4^* = I_1/3$, and the model reduces to a fully isotropic model.

2.2.3. Material Parameter Optimization

To identify the five optimal material parameters $\{c_1, k_1, k_2, \kappa, \alpha\}$ of the GOH model, we perform a parameter optimization using the `lsqnonlin` routine in Matlab (Fehervary et al., 2019; Maes et al., 2019). The optimization minimizes the 2-norm of the residuals between experimental and model-predicted stress components:

$$\min_{\theta} \sum_{r\in\mathcal{R}} \sum_{d\in\mathcal{D}} \left(P^{\mathrm{mod}}_{\mathrm{PB}_{r,d}} - P^{\mathrm{exp}}_{\mathrm{PB}_{r,d}}\right)^2, \quad \text{where} \quad \theta = \{c_1, k_1, k_2, \kappa, \alpha\}. \tag{3}$$

The optimization combines the three loading ratios, $\mathcal{R} = \{1{:}1, 2{:}1, 1{:}2\}$, in the axial and circumferential direction, $\mathcal{D} = \{\mathrm{ax}, \mathrm{circ}\}$, of the fifth loading cycle at 50% stretch. To balance the contributions of each experimental direction and loading ratio, we applied a scaling to normalize their magnitudes. Convergence to local minima was avoided by means of ten different initial guesses in a multi-start strategy. The Lagrange multiplier p in $\mathbf{P}^{\mathrm{mod}}_{\mathrm{PB}}$ was calculated through the assumption of zero radial stresses, $P^{\mathrm{mod}}_{\mathrm{rad}} = 0$.

2.2.4. Simulating Pressure–Diameter Behavior

The analytical framework assumes a thick-walled, axisymmetric, cylindrical artery. The load-free configuration of an extension-inflation, at which $\mathbf{F}_{\mathrm{EI}} = \mathbf{I}$, corresponds to the closed configuration at zero pressure, while the deformed state represents any pressurized configuration of the artery (Peirlinck et al., 2018; Vervenne et al., 2023). However, arterial tissue in its cylindrical shape is still in a prestretched state. Figure 3 shows the link between the deformation gradient $\mathbf{F}_{\mathrm{EI}}$, and the prestretch tensor $\mathbf{G} = \mathrm{diag}\{g_{\mathrm{circ}}, g_{\mathrm{ax}}, (g_{\mathrm{circ}}g_{\mathrm{ax}})^{-1}\}$. $\mathbf{G}$ is used to disambiguate the undeformed load-free configuration from the reference stress-free configuration. From the opening angle β, we can compute

$$g_{\mathrm{circ},j} = \frac{2\pi R_j^{\mathrm{clos}}}{(2\pi - \beta)R_j^{\mathrm{open}}}, \tag{4}$$

at every integration point j through the thickness. A unique value of g_{ax} is then iteratively found by matching the experimentally measured load-free thickness $H = R_{\mathrm{o}}^{\mathrm{clos}} - R_{\mathrm{i}}^{\mathrm{clos}}$ with the modeled radial coordinates through the thickness in the same reference configuration, i.e. for an inner pressure $P = 0$ and an axial stretch $\lambda_{\mathrm{ax}} = 1.0$.

The total deformation of the artery is then equal to $\mathbf{F}^{\mathrm{mod}}_{\mathrm{EI}} = \mathbf{F}_{\mathrm{EI}}\mathbf{G}$, with the prestretch tensor $\mathbf{G}$ determined in the closed, load-free configuration, and the extension-inflation deformation gradient $\mathbf{F}_{\mathrm{EI}}$ dependent on the applied inner blood pressure and imposed axial stretch. Note that, since we assume a thick-walled cylinder, both tensors also vary along the arterial wall thickness.

Indeed, when applying a constant axial stretch $\lambda_{\mathrm{ax}} = l/L^{\mathrm{clos}}$, the remaining unknown in $\mathbf{F}_{\mathrm{EI}} = \mathbf{F}^{\mathrm{mod}}_{\mathrm{EI}}\mathbf{G}^{-1}$ is $\lambda_{\mathrm{circ}} = r/R$, which is dependent on the radial position. R_j and r_j can represent any corresponding undeformed and deformed radial coordinates in the arterial wall thickness. Consequently, we define $\lambda_{\mathrm{circ},j}$, with j referring to a specific integration point through the wall.

A blood pressure P is applied on the inside of the cylinder, with the outside pressure always taken as zero. By considering axisymmetric constraints and ignoring accelerations and body forces in the equation of balance of momentum $\nabla\boldsymbol{\sigma}^{\mathrm{mod}}_{\mathrm{EI}} = 0$, the following equation for stress equilibrium in the radial direction can be derived (Holzapfel and Ogden, 2017):

$$d\sigma_{\mathrm{rad}} = (\sigma_{\mathrm{circ}} - \sigma_{\mathrm{rad}})\frac{dr}{r}. \tag{5}$$

Integration over the wall, i.e. from the inner to the outer radius, and knowing that $\sigma_{\mathrm{rad}}(r_{\mathrm{o}}) = 0$ and $\sigma_{\mathrm{rad}}(r_{\mathrm{i}}) = -P$, yields

$$P_{\mathrm{mod}} = \int_{r_{\mathrm{i}}}^{r_{\mathrm{o}}} (\sigma_{\mathrm{circ}} - \sigma_{\mathrm{rad}}) \frac{dr}{r}. \tag{6}$$

Consequently, the inner circumferential stretch $\lambda_{\mathrm{circ,i}}$ for any applied blood pressure P can be computed using following objective function:

$$\underset{\lambda_{\mathrm{circ,i}}}{\text{minimize}} \;\; \Delta P = P_{\mathrm{mod}} - P = \int_{r_{\mathrm{i}}}^{r_{\mathrm{o}}} (\sigma_{\mathrm{circ}} - \sigma_{\mathrm{rad}}) \frac{dr}{r} - P. \tag{7}$$

An initial guess of $\lambda_{\mathrm{circ,i}}$ is required in the optimization scheme, and should be adjusted to match the expected deformations in order to enhance convergence over the complete pressure range. Volume conservation allows to derive $\lambda_{\mathrm{circ,j}} = r_j/R_j$ at any point in the wall. Indeed, due to incompressibility, it holds that

$$r_j = \sqrt{\lambda_{\mathrm{circ,i}}^2 R_{\mathrm{i}}^2 + \frac{R_j^2 - R_{\mathrm{i}}^2}{\lambda_{\mathrm{ax}}}}. \tag{8}$$

Now, when calculating the modeled extension-inflation Cauchy stresses $\boldsymbol{\sigma}_{\mathrm{EI}}^{\mathrm{mod}}$ through Eq. 1, the Lagrange multiplier p varies throughout the wall too. For the inner wall, it holds that $\sigma_{\mathrm{rad}}(r_{\mathrm{i}}) = -P$. Substitution yields an expression for p at the inner wall. Similarly, $\sigma_{\mathrm{rad}}(r_{\mathrm{o}}) = 0$. Therefore, to find the solution for the Lagrange multiplier within the wall, we consider that Eq. 6 should hold at every radial position. Thus,

$$\sigma_{\mathrm{rad}}(r_2) - \sigma_{\mathrm{rad}}(r_1) = \int_{r_1}^{r_2} (\sigma_{\mathrm{circ}} - \sigma_{\mathrm{rad}}) \frac{dr}{r}, \tag{9}$$

should hold for all radial positions r_1 and r_2 between the inner and the outer arterial wall, r_{i} and r_{o}. This allows us to obtain p at every radial position. Here, the integral was solved through 50 integration points and a trapezoidal method with equal spacing.
Solving equations 7, 8 and 9 allows us to derive the corresponding $\lambda_{\mathrm{circ,o}}^{\mathrm{mod}}$ for any given pressure and applied axial stretch λ_{ax}, from which also the resulting outer diameter d_{o} can be obtained. As such, we report the modeled pressure–diameter behavior for each specimen, over the range 0–200 mmHg.

2.2.5. Extension-inflation optimization

From the modeled and experimental outer diameters, an additional optimization scheme can be performed through

$$\min_{\Theta} \left(d_o^{\mathrm{mod}}(\Theta)/d_{\mathrm{o}}^{P=0}(\Theta) - d_o^{\mathrm{exp}}/d_{\mathrm{o}}^{P=0} \right)^2, \tag{10}$$

over the entire 0–200 mmHg pressure regime. We minimize the relative outer diameters by normalizing each value with respect to its unpressurized diameter. Pressure–diameter data from $\mathbf{F}_{\mathrm{EI}}^{\mathrm{exp}}$ or $\mathbf{F}_{\mathrm{EI}}^{\mathrm{mod}}$ is always considered at axial stretch λ_{ax}, i.e. at deformed length l. In the optimization procedure, an either-or approach is adopted, meaning that only one parameter, or subset of parameters, is optimized at a time, while the remaining variables are held fixed at their initial values listed in Table 1. Accordingly, different optimization schemes can be defined as:

$$\Theta = \begin{cases} \theta & \text{if the GOH parameters are optimized,} \\ \lambda_{\mathrm{ax}} & \text{if the axial stretch is optimized,} \\ \beta & \text{if the opening angle optimized.} \end{cases} \tag{11}$$

Recall that θ is the set of GOH parameters, $\theta = \{c_1, k_1, k_2, \kappa, \alpha\}$.

3. Results and Discussion

In what follows, we will systematically present the results according to our workflow by first reporting the planar-biaxial stress–stretch experimental curves in the axial and circumferential direction. We overlay the experimental results with the simulated planar-biaxial curves computed by the Gasser–Ogden–Holzapfel (GOH) constitutive model fitting. Subsequently, the extracted material parameters are used to simulate the modeled pressure–diameter response of an idealized cylindrical geometry, and to compare the results with experimental extension-inflation data. We then investigate the capacity of the GOH parameters to fit the extension-inflation data directly, and finally assess the sensitivity of the axial stretch λ_{ax} and opening angle β. Due to the large variability between biological subjects and the sample-dependency inherent in our workflow, statistical analysis was deemed inappropriate. Instead, a single sample was selected as use case and proof-of-concept for our data analysis. The Appendix contains the results for all the remaining samples.

3.1. Biaxial Fitting with GOH Material Model

The resulting experimental engineering stress and DIC-derived stretch curves for the three loading ratios, based on the final loading cycle after preconditioning, are presented for representative sample B in Fig. 4. Table 1 reports the undeformed square dimension of the planar-biaxial samples, used to transform measured actuator forces into first Piola-Kirchhoff stresses. According to Section 2.2.2, the material parameters for the GOH constitutive model can then be fitted to calculate the modeled stresses, $\mathbf{P}_{\mathrm{PB}}^{\mathrm{mod}}$, in the corresponding strain regimes. $R^2 = 0.908$ gives an indication of the goodness of fit between the experimental and modeled stress–stretch curves per sample, for the two directions and three loading ratios combined. The model's axial and circumferential predictions for the three loading ratios are overlaid with the corresponding experimental curves, demonstrating the model's ability to capture the anisotropic hyperelastic mechanical behavior of the arterial tissue. From Fig. 4, we note an observably stiffer experimental mechanical behavior in the circumferential direction with respect to the axial direction, consistent with the resulting GOH material parameters. Indeed, both modeled collagen fiber families were found to be oriented predominantly in the circumferential direction, exhibiting a small fiber dispersion. The latter is also in agreement with microstructural fiber analysis in arteries, with a probability density function of collagen orientations towards the circumferential direction, despite a large spread and uncertainty (Rolf-Pissarczyk and Terzano, 2023).

Retrieving high-quality and biofidelic experimental planar-biaxial data is challenging. The observed tissue deformations are considerably lower than the nominal 50% stretch applied at the rakes. This discrepancy arises from two factors: the actual strains at the center of the sample are smaller than those at the rakes (Fehervary et al., 2016), and our methodology to define the zero-strain state. Indeed, the initial starting point of the stress–stretch curve is set at the average force recorded by the four load cells immediately after mounting, prior to the onset of preconditioning. This approach provides the best available approximation of a flat, unstressed planar-biaxial tissue configuration. Using a preload of 0 N to was avoided as positive forces inevitably arise from sample mounting. Defining zero-strain at higher forces would shift the origin of the stress–stretch curve even further along the loading axis, thereby omitting an additional portion of the low-strain response and overestimating tissue extensibility. Note that inelastic deformations can be present in part of the loading protocol, both during preconditioning and the main loading sequence. This is further evidenced by negative force values observed when the rakes return to their initial positions. Occasional discontinuities in the experimental stress–stretch curves are present, particularly in regions where the DIC strain measurements appeared challenging due to lighting, speckle tracking errors, or local sample deformations. The latter is also highlighted by a small but acceptable amount (<10%) of undefined values in the DIC-derived stretches. These limitations underscore the difficulty in obtaining clean, artifact-free biaxial data from soft biological tissues.

The fiber-dispersed GOH material model fits planar-biaxial arterial data well. Through the material parameter optimization of Eq. 3, the fiber-reinforced GOH model achieves an overall fitting performance of $R^2 > 0.8$ for all samples, indicating a consistent good fit between experimental data and the model stress–stretch predictions, across the three different loading ratios. Notably, the isotropic matrix stiffness parameter c_1 appears to scale with the exponential strain-stiffening coefficient k_2 of the collagen fibers, while the fiber stiffness parameter k_1 exhibits an inverse trend. This suggests a compensatory behavior between the isotropic and anisotropic components of the model. The unique circumferential fiber direction (α fitted to the lower limit, 0.0°), combined with a non-zero dispersion parameter ($\kappa > 0$), introduces an

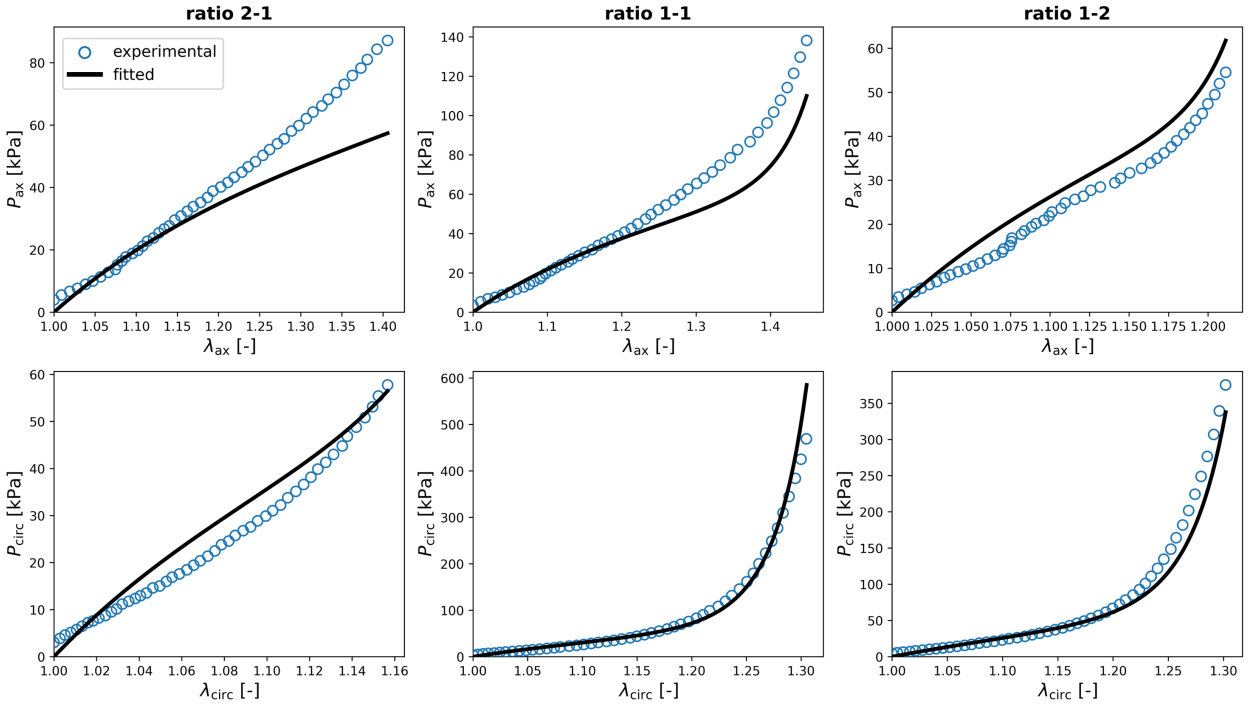

Figure 4: **Experimental and Modeled Planar-Biaxial Stress–Stretch Curves.** Axial and circumferential first Piola-Kirchhoff stresses (P_{ax} and P_{circ}) plotted for biaxial sample B under three loading protocols with stretch ratios of 2:1, 1:1, and 1:2 in the axial and circumferential directions (λ_{ax} and λ_{circ}). Experimental stress–stretch data are shown alongside the modeled stress responses obtained using the fitted material parameters of the GOH constitutive model. The goodness of fit between modeled and experimental biaxial data of the three ratios and two directions is given by $R^2 = 0.908$.

axial stiffness contribution from the two collagen fiber families. While this captures physiologically plausible behavior, it can also reveal over-parametrization of the GOH model in certain cases (Holzapfel and Ogden, 2025). Alternatively to the conventional GOH model, constitutive artificial neural networks can be implemented to autonomously learn material behavior from the biaxial stress–stretch data (Linka and Kuhl, 2023; Linka et al., 2023, 2025; Vervenne et al., 2025). This data-driven framework bypasses predefined model assumptions, and provides additional insights into stress–stretch behavior, offering a powerful alternative for capturing complex arterial mechanics.

3.2. Comparing Pressure–Diameter Responses

In this section, we analyze the pressure–diameter relation, Fig. 5a, as well as the relative circumferential stretch, Fig. 5b. The circumferential stretch in the extension-inflation plot is defined as the relative outer diameter, and is computed as $d_o/d_o^{P=0}$. Note that both the current and initial diameter are computed in a deformed axial stretch state, i.e. with an applied λ_{ax}. Table 1 reports the experimental length and outer diameter of the tube, together with the ring measurements used to retrieve the model's load-free diameters and corresponding wall thickness at zero pressure. The table also shows the measured opening angles and corresponding circumferential prestretch at the inner and outer wall of the rings, together with their corresponding axial prestretch g_{ax}. Unless otherwise stated, the absolute and relative modeled curves are always calculated and plotted with an applied $\lambda_{ax} = 1.75$.

The modeled curves underestimate the absolute pressure–diameter behavior. Fig. 5a highlights how the model underestimates the absolute diameter values for almost all samples, except sample E. To get a sense of biofidelity of our results, the P–d curves could potentially be validated using *in vivo* imaging data, providing diameter measurements at diastolic and systolic pressures. However, such a validation protocol is challenging, as typically only inner diameters can be extracted from standard imaging data, and arterial blood pressures are often not recorded simultaneously with the imaging modality. Intravascular ultrasound has been used to measure both luminal diameters and pressurized arterial wall thicknesses, and may be

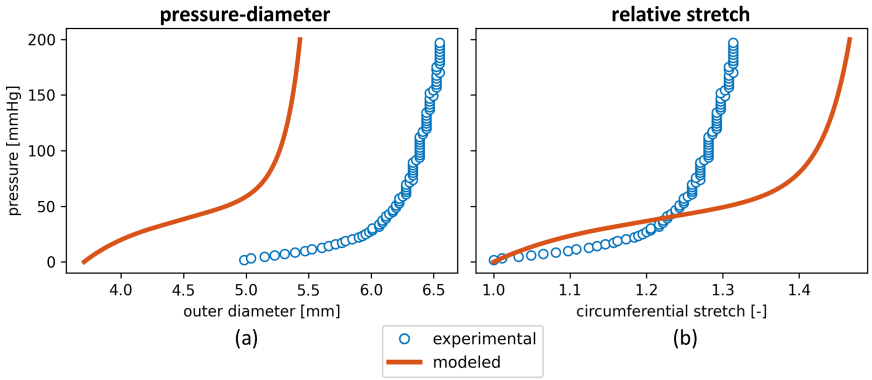

Figure 5: **Modeled and Experimental Pressure–Diameter Behavior.** Comparison of modeled and experimental pressure–diameter behavior for representative sample B, showing (a) the absolute outer diameter, and (b) the relative circumferential stretch. The modeled curves are generated using GOH material parameters fitted from the corresponding biaxial stress–stretch data. Experimental pressure–diameter data is extracted from the extension-inflation test.

further explored and implemented (Wittek et al., 2013; Drews et al., 2020). Pre-operative imaging of the sheep was not performed in this study, but the numerical values of the modeled absolute diameters are in agreement with literature data reported for ovine carotid arteries (James et al., 2019). More specifically, inner diameters between 5 mm and 6 mm have been reported in the literature for systolic and diastolic blood pressures, which aligns well with our results. Normal diastolic and systolic arterial blood pressure values in sheep range from 60–80 mmHg and 90–120 mmHg, respectively (Almeida et al., 2014). This corresponds to the highly non-linear exponential regime in our P–d curves, leading to only minor diameter changes and thus a limited pulsatile effect.

The modeled curves overestimate the relative pressure–circumferential stretch behavior. Fig. 5a also shows that the zero-pressure diameter does not coincide: the axially stretched but pressure-free outer diameter in the model is consistently lower than the experimentally measured outer diameter, even after an axial stretch of $\lambda_{\text{ax}} = 1.75$. The model's initial outer diameter and load-free wall thickness are a potential cause of this mismatch, as the closed-ring configuration is a direct input of the simulations, without taking the tube dimensions into account. To overcome this inherent bias, we also assess the pressure–diameter behavior in a relative manner through the circumferential stretch in Fig. 5b. The latter was obtained by normalizing the diameter profile with its unpressurized but axially loaded value. Here we see that the model generally overestimates the relative diameter change compared to the experimental extension-inflation data. The best relative agreement between model and experiment is observed for samples C and D, see Appendix.

Probing accurate physiological stretches remains challenging. Ideally, we aim to reproduce the physiological stretch regime of arteries during biaxial testing, as this will enhance the biofidelity of the mechanical characterization and any downstream modeling or simulation steps. From in-house experiments at the Experimental Cardiac Surgery lab at KU Leuven on similar ovine carotids, we measured an *in vivo* axial length of approximately 3.5 cm reducing to an *ex vivo* length of around 2 cm, suggesting an axial stretch (λ_{ax}) of about 1.75. Furthermore, *in vivo* echo-ultrasound imaging of a carotid artery under pulsatile pressure showed a loaded inner diameter ranging between 4.5 and 5.5 mm, and a load-free inner diameter between 3.5 and 4 mm, corresponding to estimated circumferential stretches between 1.3 and 1.4. However, achieving such high deformation ranges is limited by experimental constraints, especially the failure of the rakes or clamping system at large displacements. Figure 6 shows how the arterial tissue was loaded in a very different axial-to-circumferential stretch domain when comparing planar-biaxial results with extension-inflation data. The experimental stretches show how $\mathbf{F}_{\text{PB}}^{\text{exp}}$ and $\mathbf{F}_{\text{EI}}^{\text{exp}}$ differ, and none of the biaxial stretch ratios come close to the extension-inflation deformations. The axial and circumferential components of the prestretch tensor in $\mathbf{F}_{\text{EI}}\mathbf{G}$ determine the reference configuration of the extension-inflation data ($\lambda_{\text{ax}} = \lambda_{\text{circ}} = 1$). Extrapolation of the fitted GOH model contributes to the poor pressure–diameter match when predicting extension-inflation data, if the simulation uses constitutive parameters fitted on mechanically non-physiological planar-biaxial tensile tests. Rake failure at increased stresses prevented us from extending the stretch regime, but future planar-biaxial testing protocols and considered loading ratios should be designed to reach appropriate testing

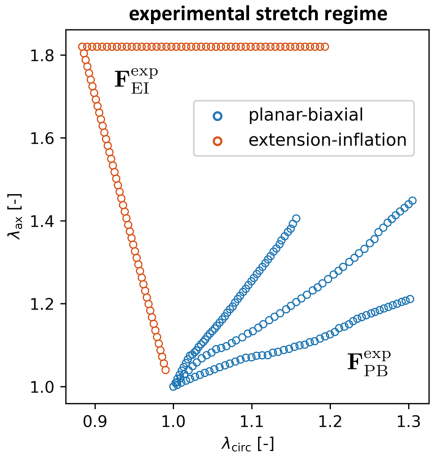

Figure 6: **Experimental Biaxial Stretch Regimes.** Comparison of the three planar-biaxial axial-to-circumferential stretch ratios ($\mathbf{F}_{\mathrm{PB}}^{\mathrm{exp}}$) with the extension-inflation experimental deformations ($\mathbf{F}_{\mathrm{EI}}^{\mathrm{exp}}$). To guarantee an equivalent reference configuration, the stretch domain of the extension-inflation test includes the prestretch tensor $\mathbf{G}$, derived from the corresponding opening angle experiments.

conditions (Avazmohammadi et al., 2018).
In what follows, we will discuss possible solutions to the observed offsets, by refitting the GOH parameters to the extension-inflation data directly, and analyzing the sensitivity of the axial stretch and circumferential prestretch.

3.3. Parameter Optimizations

This section will explore how different modeling strategies and parameter choices can influence the accuracy of simulated pressure–diameter behavior for the representative specimen B. To do so, we performed a least squares optimization of the modeled outer diameters over the whole pressure regime, see Eq. 10. Figure 7 compares several approaches and results. In particular, we will look into an alternative GOH parameter optimization, fitted to the extension-inflation data directly. We will then analyze the sensitivity of the modeled axial stretch and implemented ring opening angle, which influences the circumferential prestretch of the tissue.

3.3.1. GOH Parameter Fitting on Extension-Inflation Data

Because the GOH parameters are fitted to planar-biaxial test data which loads the considered square samples in a very different strain regime compared to the extension-inflation deformations, this leads to non-biofidelic extrapolation of the results. Therefore, we here fit the GOH model directly onto the pressure–diameter data, through the optimization in Eq. 10, for set of GOH parameters $\theta = \{c_1, k_1, k_2, \kappa, \alpha\}$, and with $\lambda_{\mathrm{ax}} = 1.75$.
The GOH model can closely match experimental pressure–diameter relations as well as planar-biaxial data, but not simultaneously. Directly fitting the GOH model to the experimental extension-inflation data (Fig. 7a) greatly improves the agreement between the relative outer diameter of the model and the experiment, originating from notably different fitted material parameters. The shear modulus c_1 decreases drastically, while the fiber stiffness parameter k_1 increases by nearly two orders of magnitude. Additionally, the exponential parameter k_2 increases sharply from 0.0932 to 11.38, indicating a much stronger strain-stiffening effect in the fiber direction. These parameter shifts underscore that planar-biaxial and extension-inflation tests probe fundamentally different aspects of the tissue's mechanical response. This is also in line with previous research relating *ex vivo* triaxial shear testing to *in vivo* pressure–volume loop data (Peirlinck et al., 2019a,b). Nevertheless, both planar-biaxial and extension-inflation approaches here provide valuable insights into the behavior and influence of the GOH parameters under distinct loading scenarios. We could also re-evaluate the modeled planar-biaxial stress–stretch curves with the updated optimized GOH parameters from the extension-inflation data. The latter is shown in Figure C of the Appendix, emphasizing an underestimation of the stress in the low-stretch regime, but an overshoot of modeled stress in the biaxial high-stretch regime. This overestimation is caused by the collagen fiber stiffness

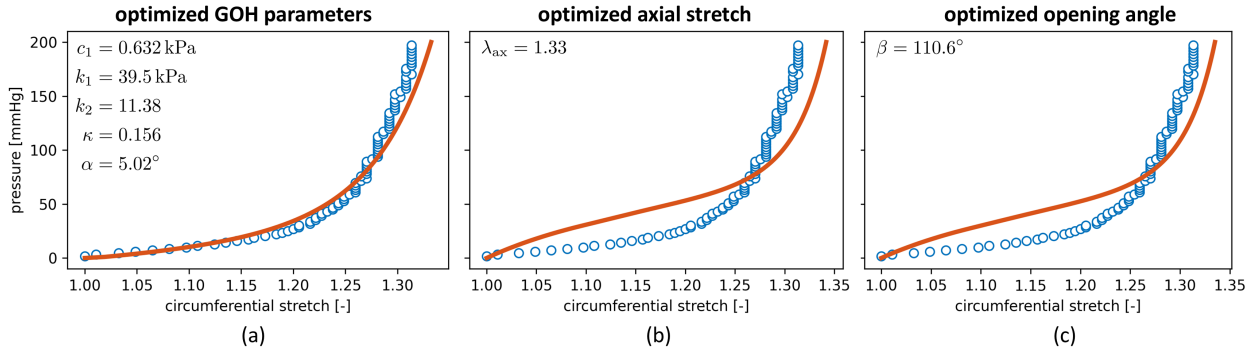

Figure 7: **Parameter Optimizations.** For the representative case of specimen B, we compare different approaches to match experimental pressure–circumferential stretch behavior. (a) GOH model fit directly on the extension-inflation data. (b) Optimization of the axial stretch (c) Optimization of the circumferential prestretch through the opening angle.

and stiffening non-linearity in the updated GOH material properties, dispersed around the circumferential direction, and required to meet the exponential pressure–diameter mechanical behavior.

The (an)isotropic balance of the GOH model has an important influence on the convex or concave shape of the pressure–diameter curve. Interestingly, the modeled GOH curve in Fig. 5a exhibits a pronounced concave slope at low pressures ($P < 50$ mmHg), transitioning into a highly non-linear, convex diameter change as pressure increases, characteristic of strain-stiffening behavior. In contrast, the experimental pressure–diameter curve displays a solely convex shape with an elongated toe region of approximately 20% stretch. When reducing the isotropic parameter c_1 of the GOH model while increasing the fiber-related parameters k_1 and k_2, the initial concave behavior of the P–d curve diminishes, resulting in a fully convex and exponentially increasing mechanical response in circumferential stretch (Fig. 7a).

3.3.2. Axial Stretch Analysis

The influence of the axial stretch is further examined in Fig. 8. By varying λ_{ax} over a physiologically relevant range, we can observe clear changes in predicted pressure–diameter and circumferential stretch behavior. Here, we introduce a third plot showing the mean axial Cauchy stress through the wall thickness and across blood pressures. Subjected to different axial stretches, this axial wall stress profile strongly shifts from decreasing to increasing values, demonstrating how sensitive wall stress estimation is to assumptions on longitudinal loading. The axial stretch analysis highlights the importance of the experimental tube assumptions in the pressure–diameter predictions.

Increasing the axial stretch reduces absolute diameters, but increases the circumferential deformation. Interestingly, increasing the modeled axial stretch leads to a decrease in the absolute modeled outer diameter (Fig. 8a), while simultaneously increasing the relative circumferential stretch regime (Fig. 8b). However, increasing axial stretch values to supra-physiological ranges will ultimately result in a severe increase in tissue stiffness and a reversal of the trend. Indeed, $\lambda_{ax} > 2.5$ will cause the relative diameter curve to shift leftwards again with increasing pressures. Ultimately, and in the specific case of sample B here, $\lambda_{ax} \approx 3.75$ will match the experimental curve again. However, such an axial stretch range is far above the experimentally observed and reasonable *in vivo* λ_{ax} values. In the literature, the most physiological axial stretch is often defined as the value at which the axial stress remains nearly constant, despite an increase in intimal blood pressure (Hu et al., 2007). The latter hypothesis that smooth muscle cells in the arterial wall seek axial steadiness but circumferential pulsatility.

The similar relative outer diameter optimization in Eq. 10 can be performed to find the optimal axial stretch. Figure 7b therefore retains the initial GOH parameters from Table 1, but optimizes λ_{ax}, resulting in a value of $\lambda_{ax} = 1.33$. The remarkable lower axial stretch improves model performance without re-fitting material constants, highlighting that uncertainties in axial boundary conditions of the tubes can have a strong influence on the model's accuracy. Considering also measured axial forces in the optimization scheme of Eq. 10 could enhance biaxial fitting on the extension-inflation tests, and the data could be enriched by minimizing $d_o^{P,\ \lambda_{ax}}/d_o^{P=0,\ \lambda_{ax}=1}$ instead.

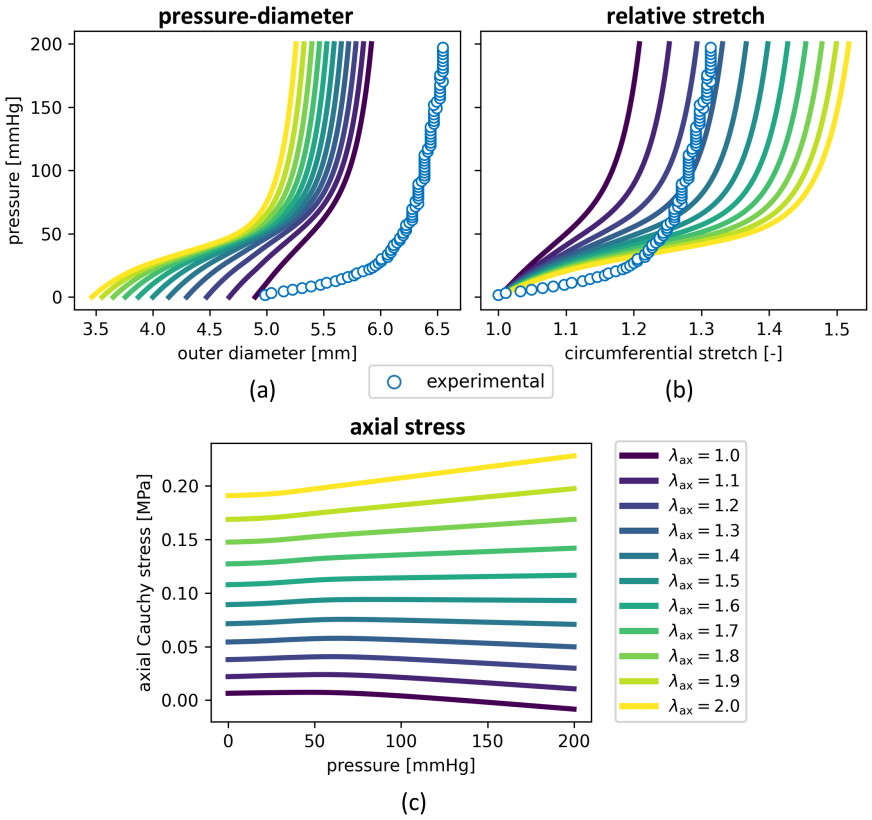

Figure 8: **Axial Stretch Sensitivity.** Effect of varying axial stretch on model predictions for representative specimen B. Axial stretch values range from 1.0 to 2.0 in increments of 0.1. (a) Modeled pressure–diameter curves for each axial stretch value. (b) Corresponding relative circumferential stretch behavior. (c) Mean axial Cauchy stress through the wall thickness across the physiological pressure range. The experimentally applied axial stretch during extension-inflation testing was $\lambda_{\text{ax}} = 1.75$, as imposed by the device actuator.

3.3.3. Opening Angle Analysis

The effect of the opening angle is illustrated in Fig. 9. By systematically varying the opening angle β from $0°$ to $120°$, we assess how residual circumferential prestretch impacts the model's mechanical predictions for absolute and relative outer diameters. The opening angle effect demonstrate the importance of the excised rings in the model workflow and its predictive influence.

Increasing the opening angle stiffens both the absolute and relative pressure–diameter curves. An increasing opening angle causes a stiffening of the pressure–diameter response, both in absolute values and in relative deformation (Figs. 9a,b). A larger opening angle implies greater residual stress at zero pressure, effectively pre-loading the vessel wall in the circumferential direction. As a result, the tissue deforms less under pressurization, leading to a stiffer mechanical response. For sample B, the experimentally measured opening angle was $\beta = 77°$, which aligns well with the model's predicted behavior in this intermediate stiffness range. Importantly, the sensitivity of model predictions to variations in β suggests that incorporating accurate residual stress measurements is essential when simulating vascular mechanics. Unlike the tubular axial stretch, which is externally imposed during testing, the opening angle reflects intrinsic tissue architecture retrieved from ring opening experiments, and should thus carefully be considered during model calibration.

Again, we perform an optimization of the optimal opening angle on the experimental extension–inflation data through Eq. 10. Figure 7c retains the initial GOH parameters of Table 1 with $\lambda_{\text{ax}} = 1.75$, and finds the opening angle and thus circumferential prestretch that minimizes the relative outer diameter difference. This results in a value of $\beta = 110.6°$, leading to circumferential prestretches $g_{\text{circ,i}} = 1.09$ and $g_{\text{circ,i}} = 1.12$, at the inner and outer wall, respectively. Our initial model predictions thus underestimated the opening angle and circumferential prestretches. Note that these were calculated in Eq. 4 and are highly dependent

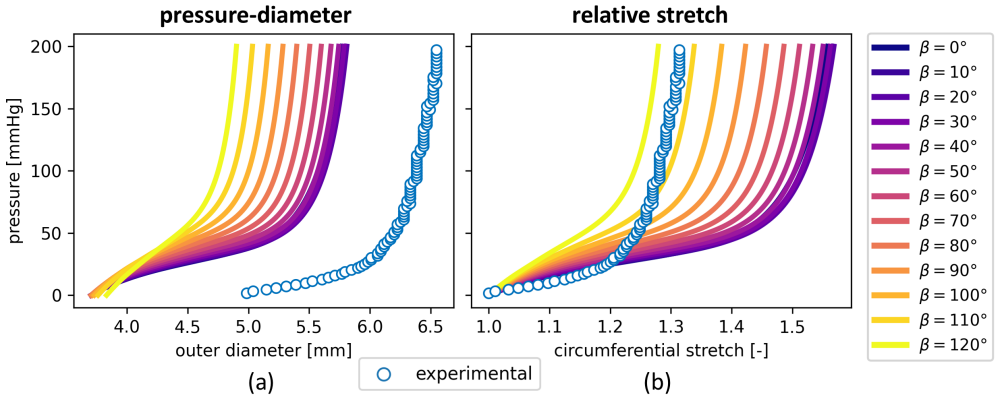

Figure 9: **Opening Angle Sensitivity Analysis.** Effect of a varying opening angle on model predictions for representative specimen B. The opening angle ranges from 0° to 120° in increments of 10°. (a) Modeled pressure–diameter curves for each opening angle value. (b) Corresponding relative circumferential stretch behavior. The experimentally measured opening angle is $\beta = 77°$.

on the open and closed ring diameters, as well as the wall thickness H. They also lead to an updated axial prestretch $g_{\text{ax}} = 0.78$, ensuring a match in the experimental and modeled load-free thickness for $P = 0$ and $\lambda_{\text{ax}} = 1.0$.

3.4. Geometrical Uncertainty

In addition to the GOH material parameters, the axial stretch and circumferential prestretch, several other geometrical quantities remain uncertain across the different load-free and loaded configurations. These uncertainties are briefly discussed in the following section.

The measured load-free thickness and reference diameters are inconsistent in different configurations. Table 1 shows a discrepancy between the mounted outer diameter of the tubes, D_{o}, and the measured outer diameter from the excised rings, $2R_{\text{o}}^{\text{clos}}$. The mismatch could originate from the fact the the ring dimensions were measured at anatomical positions more distal or more proximal to the experimental tubes (Fig. 2), leading to sample-specific biological intravariability. A clinical validation could include a comparison between the *in vivo* arterial wall thicknesses and the modeled values of h, expressed in the deformed configuration, see Fig. 9). The unpressurized wall thickness used in the model, derived from the closed rings and defined as $H = R_{\text{o}}^{\text{clos}} - R_{\text{i}}^{\text{clos}}$, is also notably larger than the experimental thickness T measured from the squared biaxial sample (Table 1), which was used to calculate the planar-biaxial stress tensor $\mathbf{P}_{\text{PB}}^{\text{exp}}$. However, a thinner wall will intuitively result in even larger pressurized diameters, due to reduced resistance to circumferential expansion. Note the concave shape at low pressures remained because of the unaltered GOH parameters in this step.

Experimental pressure–diameter data should be enhanced with *in vivo* measurements. To obtain an exact and sample-specific axial stretch estimation, one should measure the arterial length l before explantation, and the excised length L^{clos} of the same tissue *ex vivo*, resulting in an estimation of λ_{ax}. According to Fig. 3, the same axial measurement could be performed on the open ring L^{open}, in order to obtain the experimental $g_{\text{ax}}^{\text{exp}}$. The experimental axial prestretch could then be compared to the modeled value in Table 1 to verify the workflow. However, in the current model workflow, the optimized g_{ax} guarantees computational consistency by ensuring a match between the experimental load-free closed ring configuration and the modeled geometry at $P = 0$ and $\lambda_{\text{ax}} = 1.0$. However, biological variability might surpass experimental accuracy when measuring the difference between L^{clos} and L^{open}. An extra *in vivo* measurement could assess the diameter $d_{\text{o}}^{\text{exp}}$ at zero pressure, considering the unpressurized artery before sacrifice. The model can predict the same $d_{\text{o}}^{P=0} = 2r_{\text{o}}^{P=0}$ by solely applying the axial stretch λ_{ax} of the deformation gradient. Note that the axially loaded but zero-pressure diameter $d_{\text{o}}^{P=0}$ is also used to normalize the results and compute the relative circumferential stretch curves. Interestingly, for the same unloaded state in Fig. 8a, we see that the experimental outer diameter from $\mathbf{F}_{\text{EI}}^{\text{exp}}$ is close to the modeled $\mathbf{F}_{\text{EI}}^{\text{mod}}$ at $\lambda_{\text{ax}} = 1.0$.

Experimental extension-inflation requires advanced imaging and can suffer from clamping boundary condition effects. The experimental extension-inflation test setup and resulting experimental

pressure–diameter curve could be improved in order to enhance the accuracy and reliability of the measurements. For instance, a dual-camera system could be installed to capture uniform and out-of-plane three-dimensional deformations using 3D-DIC, and to track the actual outer diameter of the pressurized test sample, rather than relying on a two-dimensional plane projection. In addition, the experimentally applied extension and inflation conditions are susceptible to error. The inflation pressure may be affected by leakage or offsets in the pressure regulation system, and the actual axial stretch experienced by the sample may differ from the nominal value of $\lambda_{\mathrm{ax}} = 1.75$ applied at the actuator level. The latter could be experimentally measured by marker tracking of the longitudinal axis extension. Pure pixel tracking of the sample height now shows $l^{P=0}/L^* = 1.74$, see Table 1. During internal pressurization, the measured diameter may vary along the length, typically exhibiting a barrel-shaped profile. This length-dependent diameter evolution originates from the limited sample availability, where the available carotid samples should be free of holes or defects along the required testing length to ensure reliable data. In the current study, only the diameter at the middle of the sample is extracted from the extension-inflation experiments, and the model assumes a straight, perfect cylindrical geometry. Incorporating the length-dependent diameter evolution into the analysis could provide a more accurate description of the deformation. In the optimization described by equation (10), the inclusion of a longitudinal dimension could then be considered to capture length-dependent effects on the diameter evolution. On the modeling side, the behavior of a hollow thick-walled cylinder under internal pressure, axial stretch, and radial constraints could be examined. Such radial boundary conditions introduce longitudinal stress variations and shear stresses in the radial-axial plane, which can induce bulging or deflation of the cylinder and must be accounted for in a comprehensive model of extension-inflation behavior. Altogether, these results highlight the crucial interplay between accurate experimental measurements and endstage pressure–diameter results. While material calibration is essential, mismatches in the assumed wall thickness or vessel dimensions can propagate into model errors and obscure true mechanical behavior. This underscores the need for careful geometric validation in conjunction with mechanical testing for reliable computational modeling of vascular tissues. The total experimental and model uncertainty, together with the variability of the geometries and model parameters, are therefore also always important to consider. Literature presents different techniques to investigate this further (Vander Linden et al., 2023b; Gheysen et al., 2024; Berggren et al., 2024).

4. Conclusions and Outlook

This study presents an integrated experimental and computational framework for characterizing ovine carotid artery biomechanics, bridging the gap between planar-biaxial testing and clinically relevant pressure–diameter behavior. We performed biofidelic extension-inflation experiments to compare model performance with benchtop pressure–diameter measurements. Our results highlight that translating laboratory measurements to realistic physiological conditions critically depends on accurately representing axial stretch and circumferential prestretch, as well as *in vivo* geometries. When these key parameters are well-characterized and their uncertainties properly accounted for, planar-biaxial stress–stretch data can become a reliable input for arterial pressure–diameter predictions.

We systematically combining planar-biaxial loading, ring opening experiments and extension-inflation tests on the same arterial samples. This approach squared, ring and tubular samples of the same specimen allowed us to capture complementary loading conditions and tissue behaviors. To ensure physiological relevance, we designed tailored experimental protocols with controlled axial and circumferential loading in planar-biaxial tests, and axial loading under luminal pressure in extension-inflation setups. To minimize measurement uncertainty, we employed digital image correlation for accurate deformation tracking, and incorporated precise geometric data from micro laser scanning and ring-opening tests. These efforts improved the reliability of stress calculations and deformation measurements, thereby strengthening model input quality.

The modeling framework used the Gasser–Ogden–Holzapfel (GOH) constitutive model to capture the anisotropic hyperelastic material behavior of carotid arteries. Biomechanical predictions were performed through analytical thick-walled cylinder simulations with subject-specific tissue properties, boundary conditions and prestretches. Robust validation was achieved by benchmarking simulated pressure–diameter behavior against experimental extension-inflation data from the same specimens. Systematic comparison of absolute and relative pressure–stretch responses revealed key discrepancies and highlighted the influence of parameter choices on model performance.

Our results confirmed that the *in vivo* stretch in carotid arteries is higher in the axial direction, while the tissue exhibits lower circumferential prestretches. The GOH model fitted the planar-biaxial data well and proved suitable for pressure–diameter simulation. Comparisons between experimental and simulated pressure–diameter curves showed a systematic underestimation of the absolute pressure behavior and overestimation of the relative circumferential stretch, where we found that the anisotropic balance of the GOH model significantly shaped the pressure–diameter curve. We showed that the planar-biaxial stretch regime probes fundamentally different deformations compared to an extension-inflation test. We therefore fitted the GOH parameters directly to the pressure–diameter data, demonstrating the versatility of the constitutive parameters, depending on their biomechanical loading condition. Sensitivity analyses of the tubular axial stretches and ring opening angles emphasized their importance in accurate model calibration. while an increased axial stretch reduced the predicted absolute diameters, it increased the relative outer diameters. An increasing opening angle showed an overall stiffening of the pressure–diameter behavior. Optimizing the axial stretch and circumferential prestretch further enhanced the biofidelity of our simulations.
Despite the robustness of our approach, some limitations remain. Experimental noise, biological heterogeneity, and model simplifications contribute to uncertainty. Standardizing measurement protocols, improving accuracy in thickness and diameter measurements, and automating post-processing workflows will help reduce variability. Future work should focus on (I) expanding datasets to quantify aleatoric and epistemic uncertainties, (II) incorporating clinical imaging data for further validation, (III) exploring 3D optical measurements and inverse modeling to refine experimental and modeling assumptions, (IV) applying constitutive artificial neural networks to autonomously discover novel strain energy density functions for carotid arteries, and (V) implement length-dependent diameter evolutions in the model, in order to consider longitudinal stress variations due to boundary condition effects.

Supplementary Materials - All source data, processing code and results will be available in KU Leuven's research data repository. The full dataset and associated materials will be made openly accessible upon publication.

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Appendix

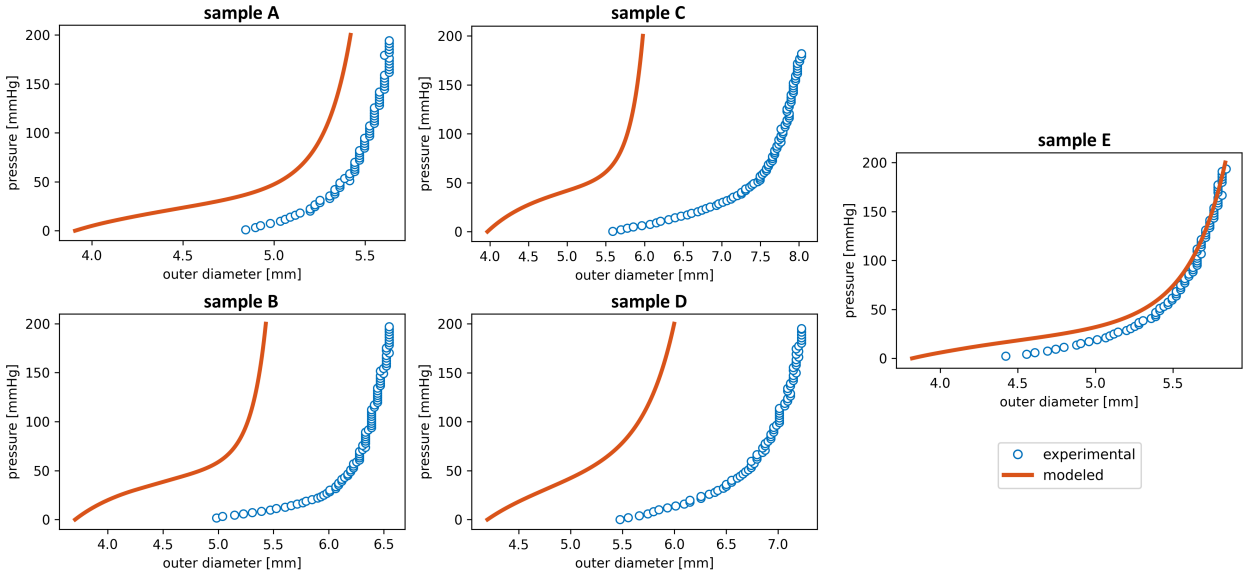

Figure A: **Modeled and Experimental Absolute Pressure–Diameter Behavior.** Comparison of modeled and experimental pressure–diameter (P–d) relationships for the five carotid artery specimens (A–E). The modeled curves are generated using GOH material parameters fitted from the corresponding biaxial stress–stretch data. Experimental pressure–diameter data is extracted from extension-inflation tests performed on each specimen.

sample	squares [mm]			GOH parameters					
	W_1	W_2	T	c_1 [kPa]	k_1 [kPa]	k_2 [-]	κ [-]	α [rad]	R^2 [-]
A	10.5	10.6	0.43	28.4	7.0	6.259	0.112	0.000	0.874
B	9.9	10.8	0.30	49.2	5.3	9.318	0.078	0.000	0.908
C	10.9	9.7	0.23	67.2	3.0	12.268	0.134	0.000	0.796
D	10.3	10.7	0.31	31.2	18.9	6.469	0.186	0.000	0.853
E	10.7	10.9	0.57	20.8	7.8	6.595	0.136	0.000	0.883

Table A: **Biaxial Dimensions and Fitted GOH Material Parameters.** Biaxial square dimensions and Gasser–Ogden–Holzapfel (GOH) material parameters $\theta = \{c_1, k_1, k_2, \kappa, \alpha\}$, fitted to the fifth loading cycle of biaxial tensile tests for samples A to E. Values W_1 and W_2 are the perpendicular widths of the axial and circumferential direction respectively, and T is the average measured wall thickness. The goodness of fit of the modeled and experimental stress-stretch curves are highlighted by R^2.

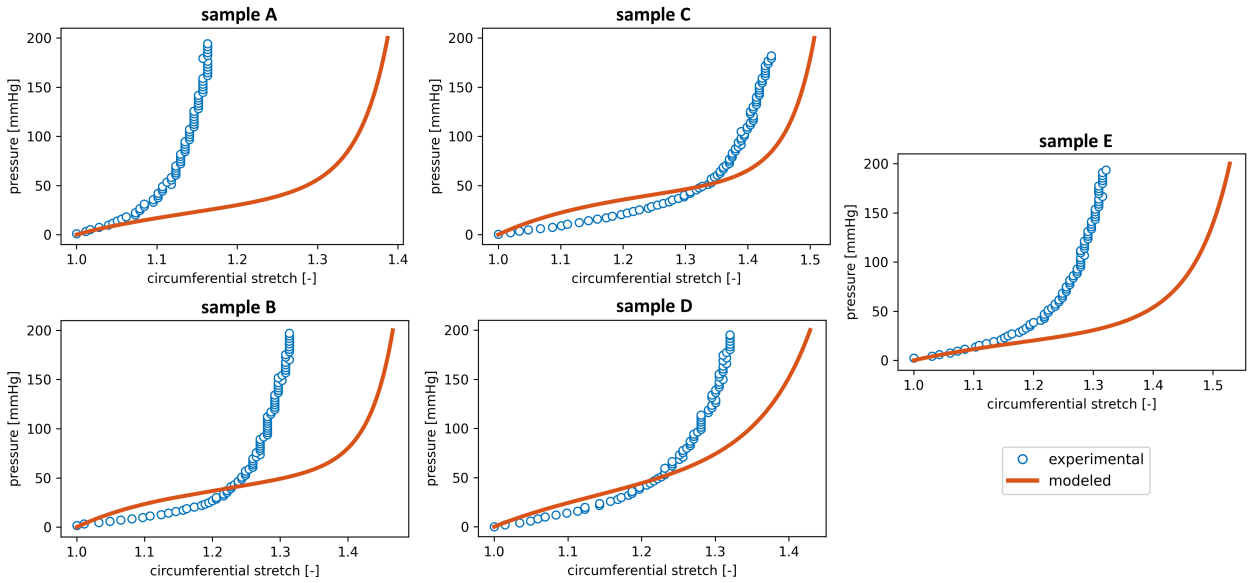

Figure B: **Modeled and Experimental Relative Pressure–Diameter Behavior.** Comparison of modeled and experimental pressure–circumferential stretch (P–λ_{circ}) relationships for the five carotid artery specimens (A–E).

sample	tubes [mm]			rings [mm]				[°]	[-]	[-]	[-]
	L	D_o	$d_o^{P=0}$	R_i^{open}	R_o^{open}	R_o^{clos}	R_i^{clos}	β	$g_{circ,i}$	$g_{circ,o}$	g_{ax}
A	36	5.36	4.84	1.95	3.10	2.58	1.85	44	1.08	0.95	0.98
B	52	5.49	4.99	2.40	3.15	2.45	1.83	77	0.97	0.99	1.04
C	54	6.18	5.59	2.60	3.15	2.63	2.08	42	0.90	0.94	1.17
D	30	6.04	5.47	2.85	3.70	2.80	2.00	94	0.95	1.02	1.02
E	49	4.82	4.42	3.30	3.90	2.53	1.85	131	0.88	1.02	1.11

Table B: **Dimensional Measurements and Prestretch Variables.** Tube dimensions and ring measurements for samples A to E. L represents the harvested axial length of the tubes. D_o highlights the mounted and unpressurized outer diameters, while $d_o^{P=0}$ describes the measured unpressurized outer diameters after applying the axial stretch λ_{ax}. R_i^{open} and R_o^{open} are the inner and outer radii of the ring in the open configuration, while R_i^{clos} and R_o^{clos} are the corresponding radii in the closed configuration. β is the opening angle in degrees, $g_{circ,i}$ and $g_{circ,o}$ are the resulting inner and outer circumferential prestretches respectively, and g_{ax} is the optimized axial prestretch.

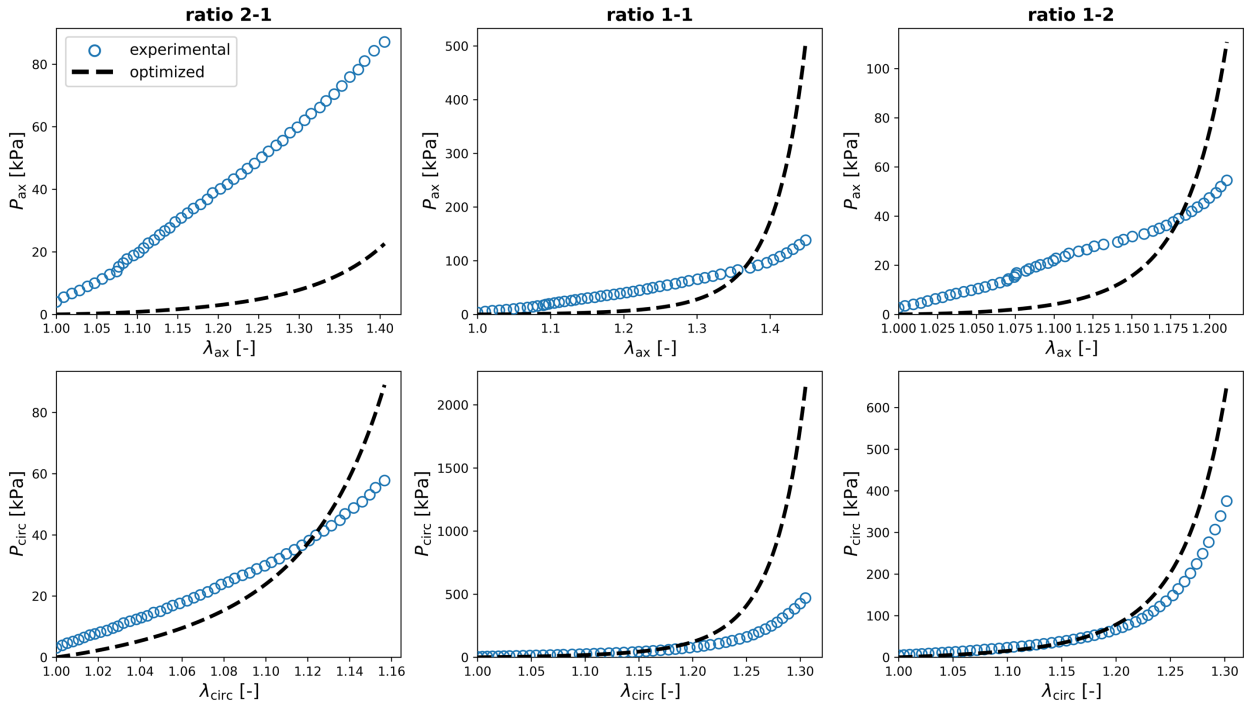

Figure C: **Experimental and Virtual Planar-Biaxial Stress–Stretch Curves.** Axial and circumferential first Piola-Kirchhoff stresses (P_{ax} and P_{circ}) plotted for biaxial sample B under three loading protocols with stretch ratios of 2:1, 1:1, and 1:2 in the axial and circumferential directions (λ_{ax} and λ_{circ}). Experimental stress–stretch data are shown alongside the the virtual stress responses computed using the optimized material parameters of the GOH constitutive model. These model parameters were obtained by, interdependently from the planar-biaxial data, fitting the GOH model directly to the pressure–diameter extension-inflation experimental data, see Section 3.3.1 and Fig. 7a.

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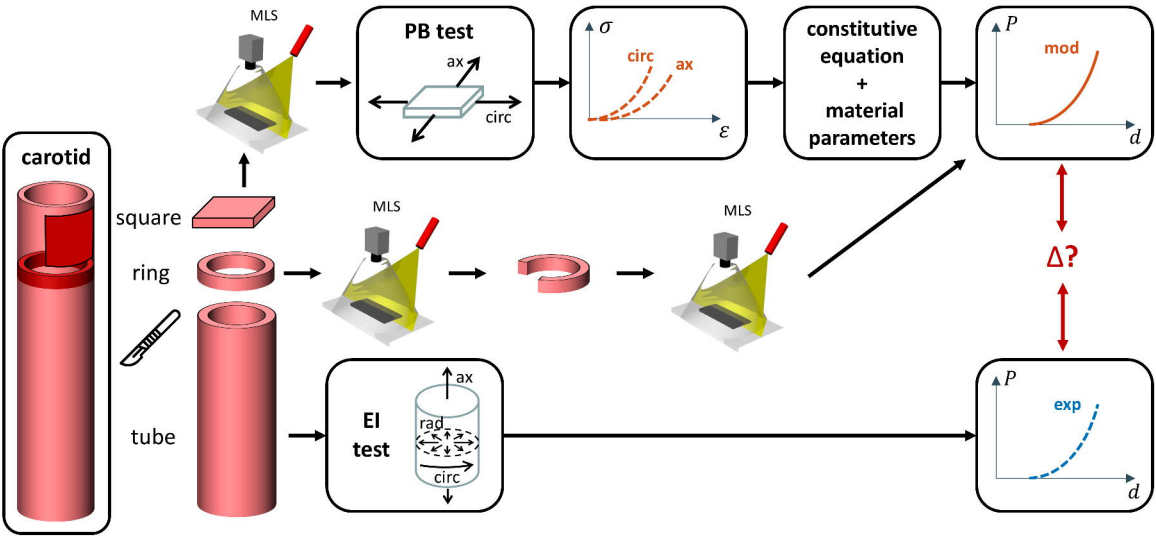
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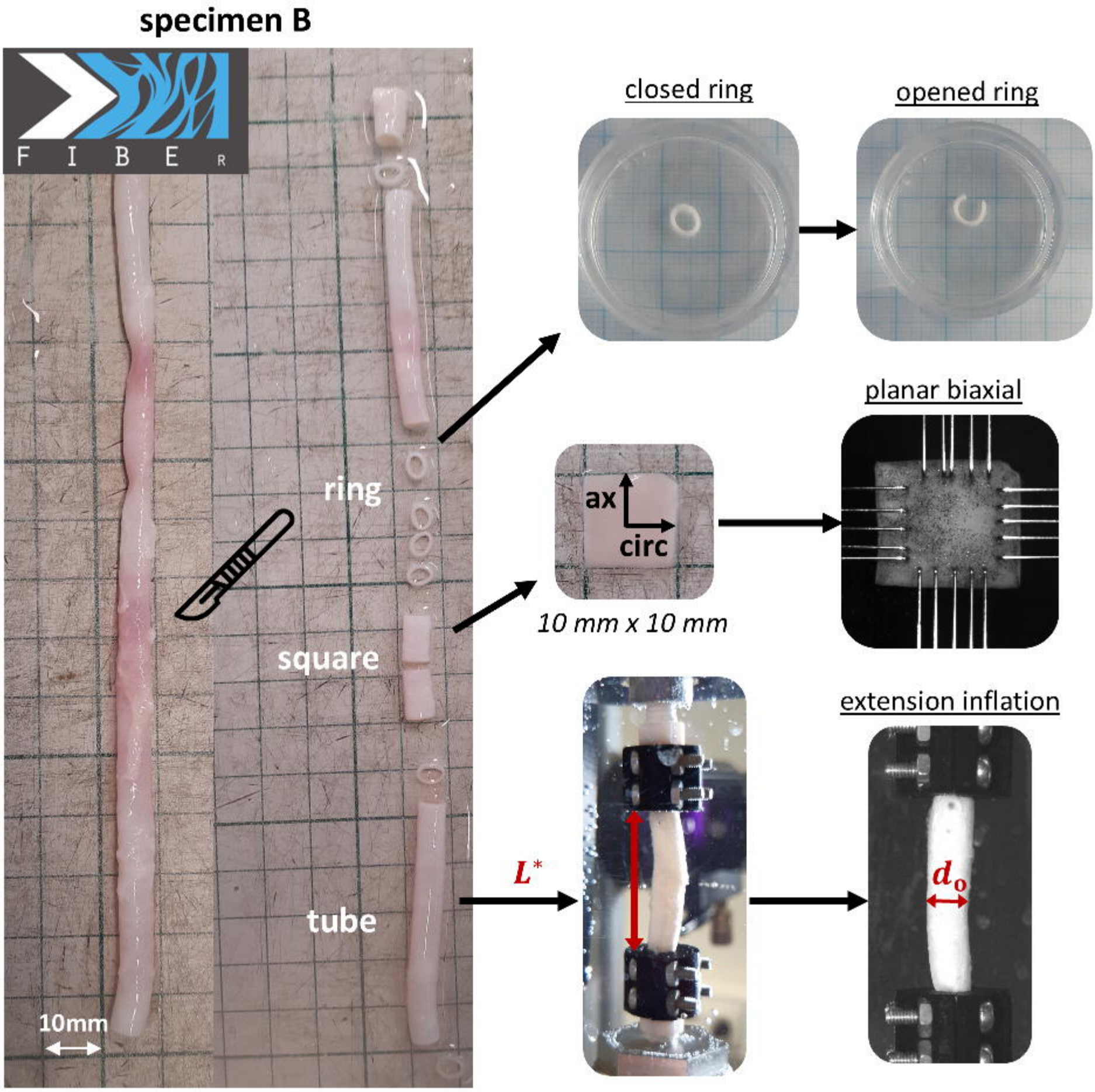
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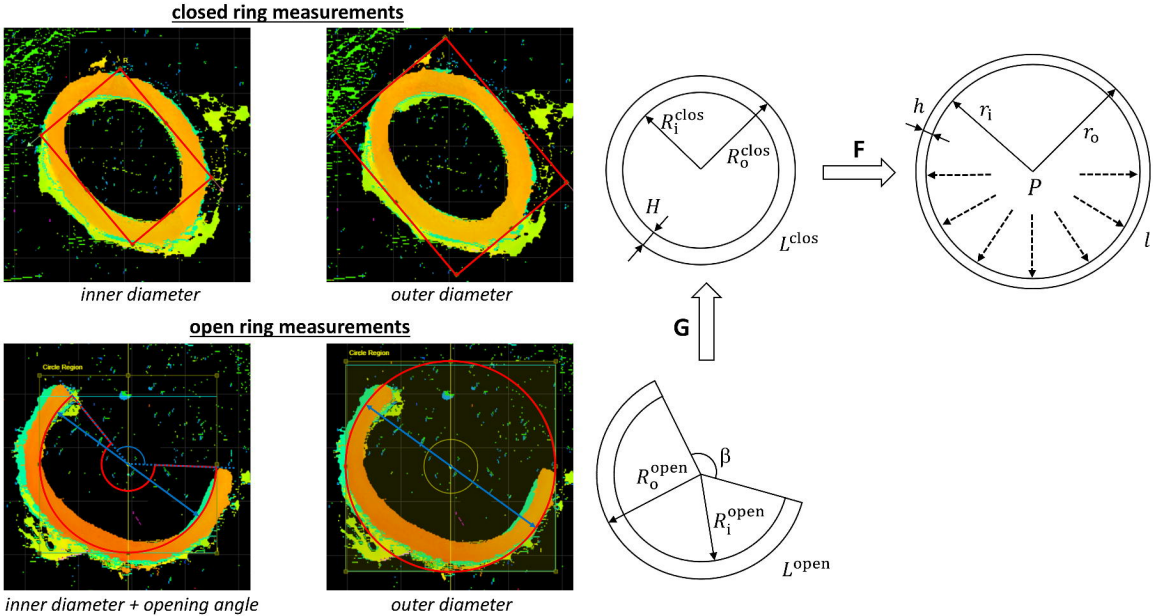
closed ring measurements
inner diameter
outer diameter
open ring measurements
Circle Region
Circle Region
inner diameter + opening angle
outer diameter
R_i^{clos}
R_o^{clos}
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L^{clos}
F
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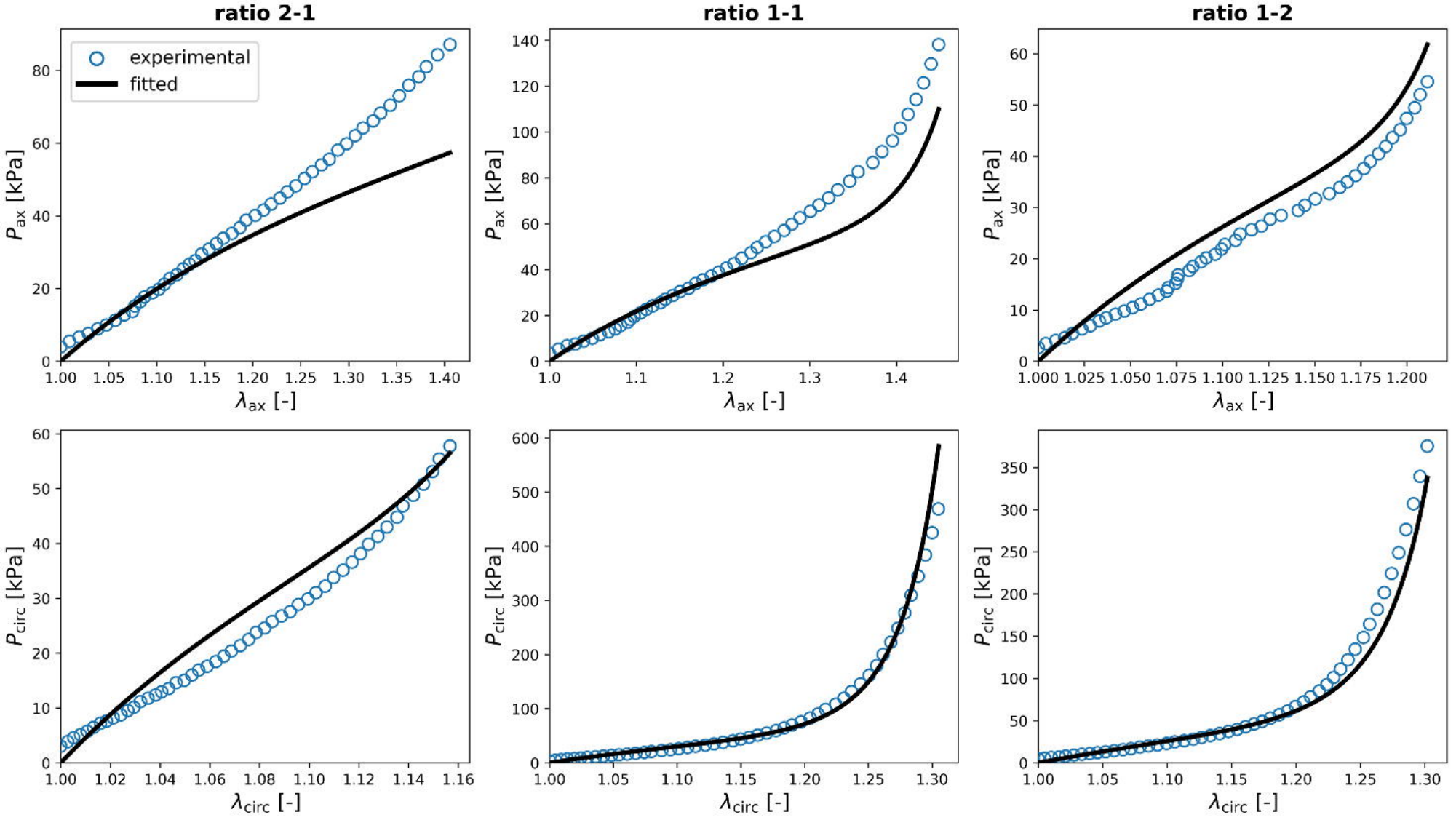
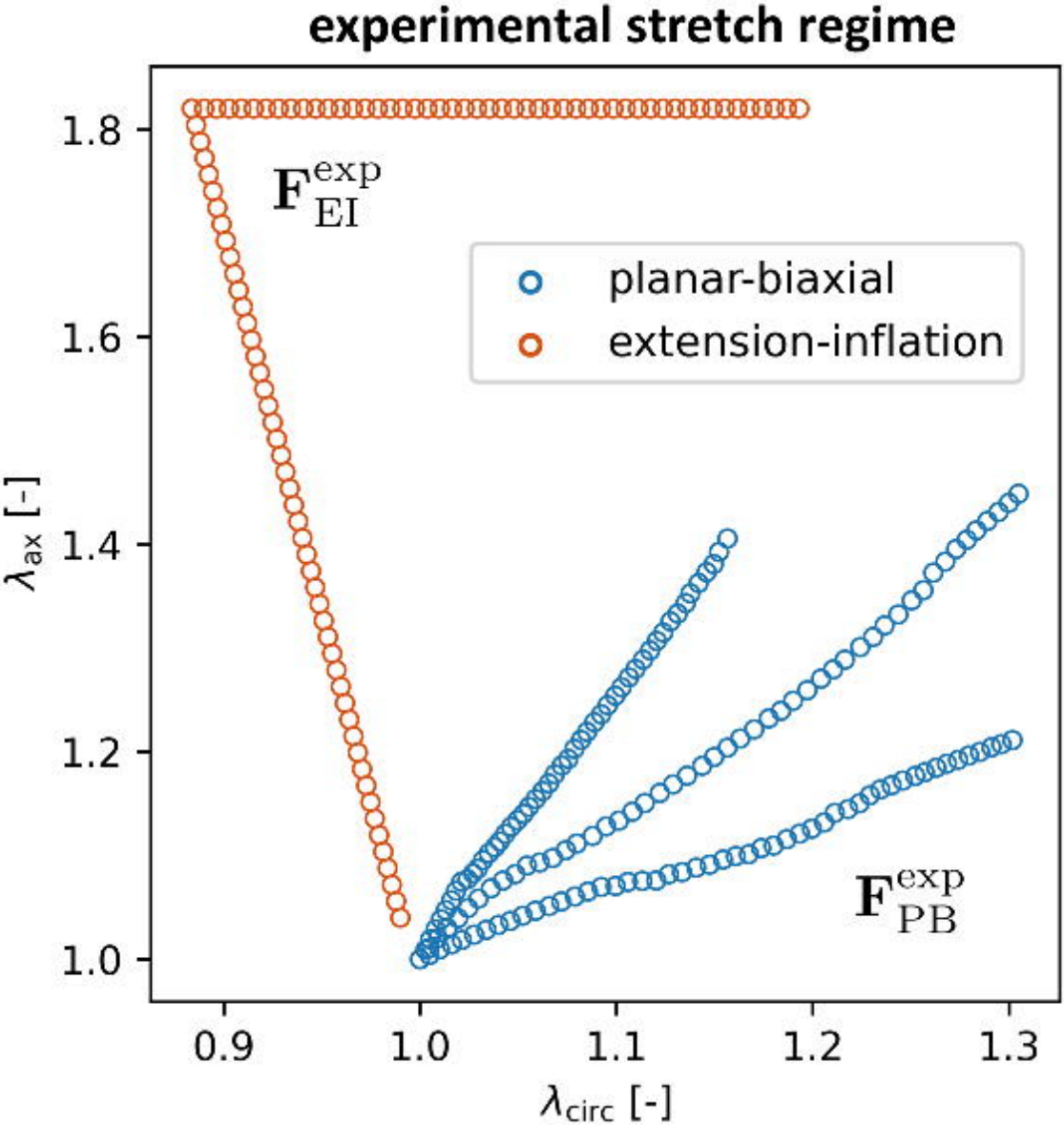
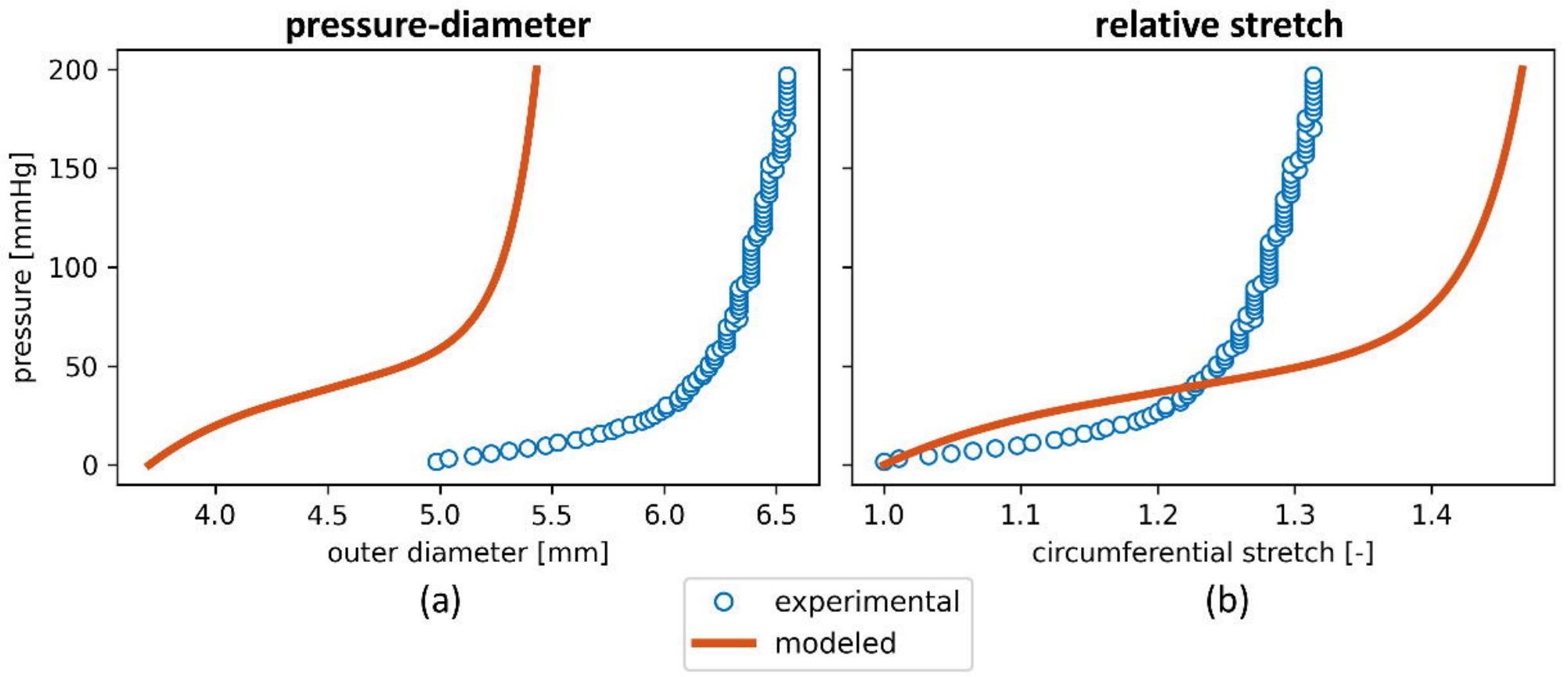
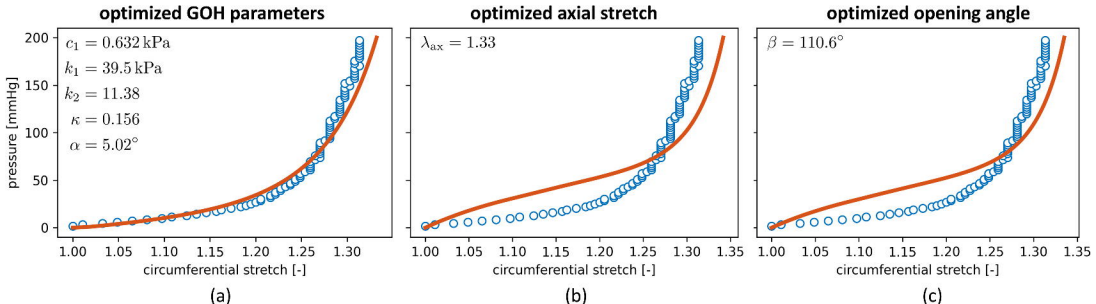
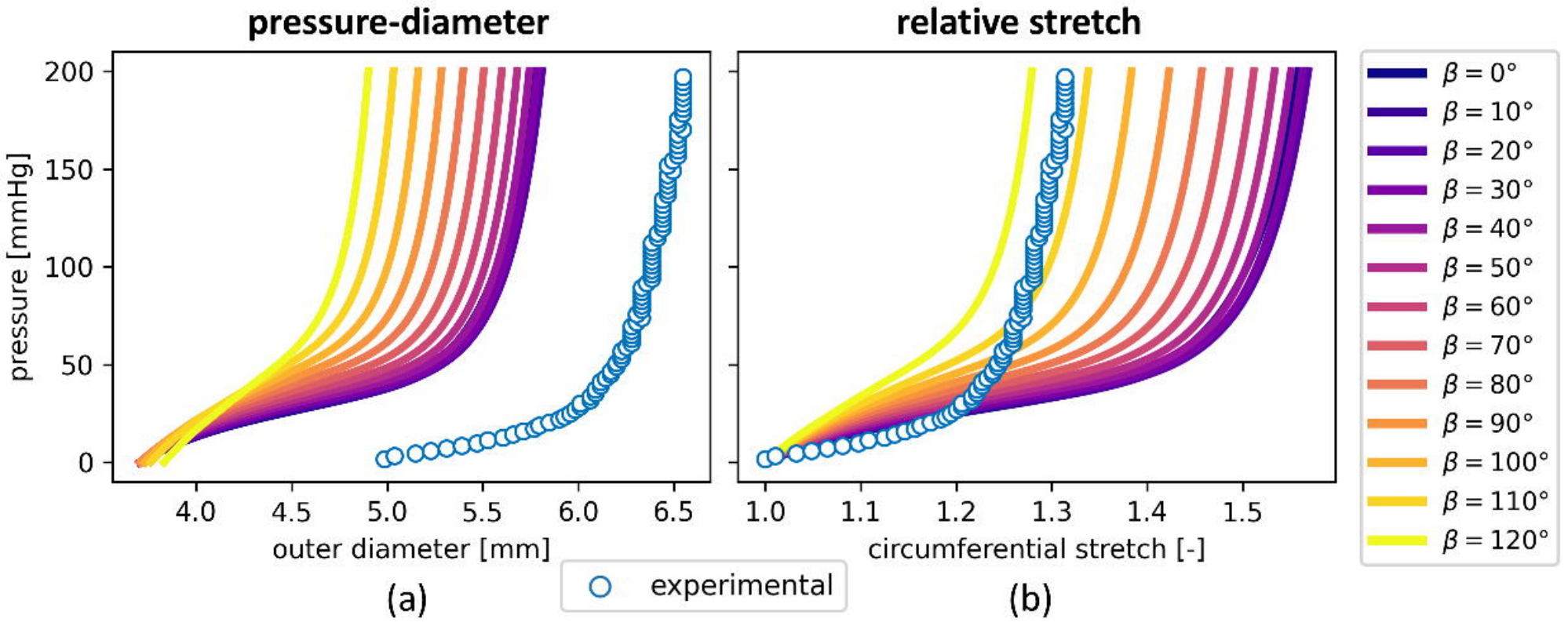
h
r_i
r_o
P
l
R_o^{open}
β
R_i^{open}
L^{open}

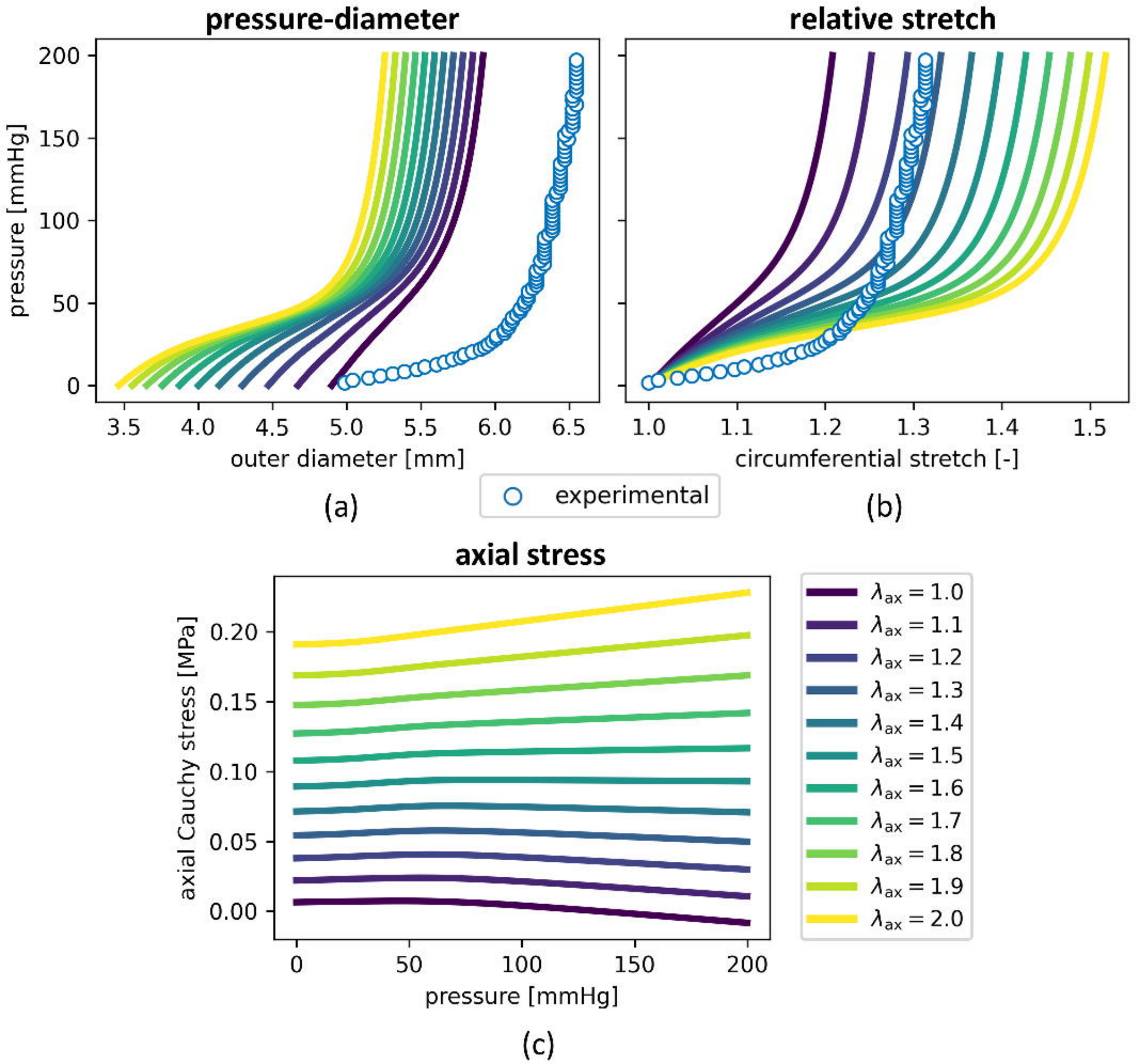

ratio 2-1
ratio 1-1
ratio 1-2
experimental
fitted
P_{ax} [kPa]
λ_{ax} [-]
P_{circ} [kPa]
λ_{circ} [-]

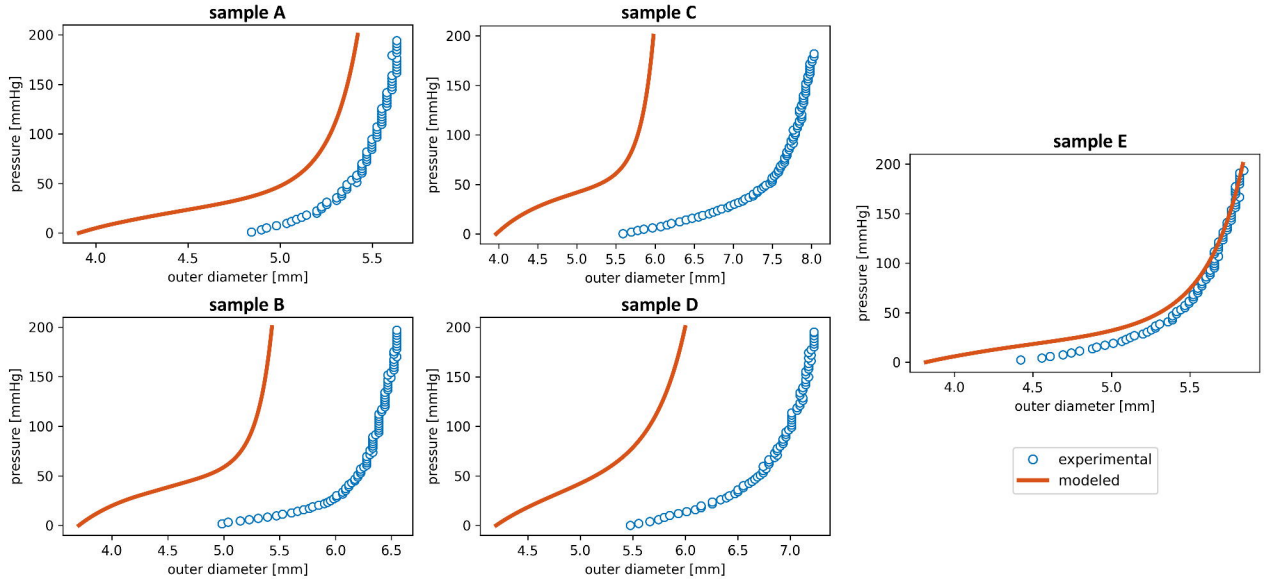

experimental stretch regime
$\mathbf{F}_{\mathrm{EI}}^{\mathrm{exp}}$
$\mathbf{F}_{\mathrm{PB}}^{\mathrm{exp}}$
planar-biaxial
extension-inflation
1.8
1.6
1.4
1.2
1.0
λ_{ax} [-]
0.9
1.0
1.1
1.2
1.3
λ_{circ} [-]

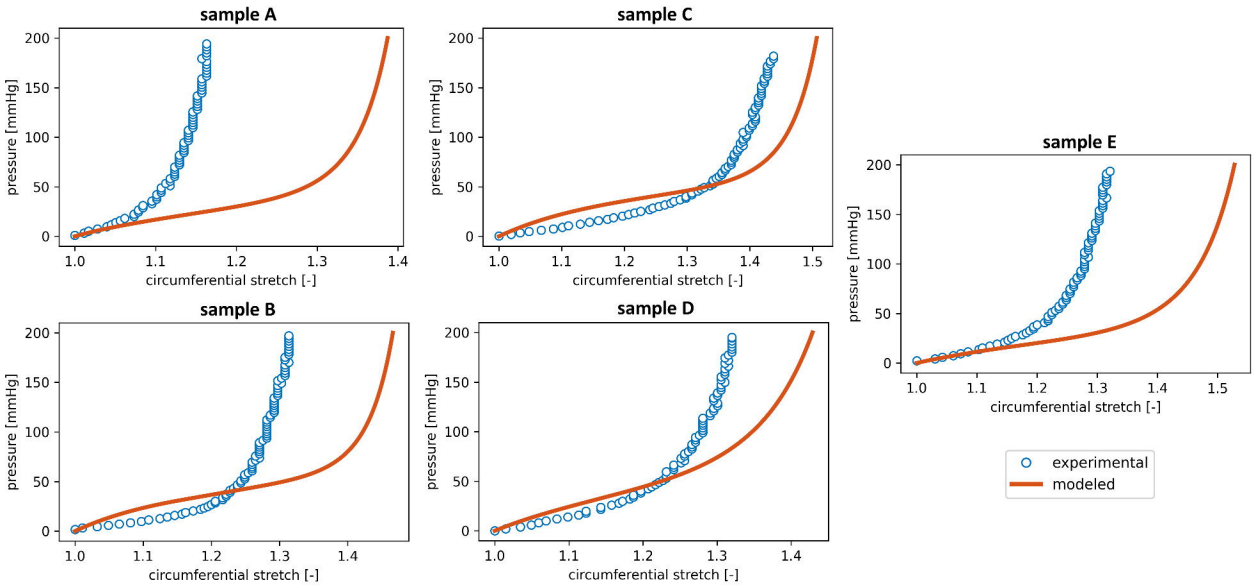

pressure-diameter
relative stretch
pressure [mmHg]
200
150
100
50
0
4.0
4.5
5.0
5.5
6.0
6.5
outer diameter [mm]
1.0
1.1
1.2
1.3
1.4
circumferential stretch [-]
(a)
(b)
experimental
modeled

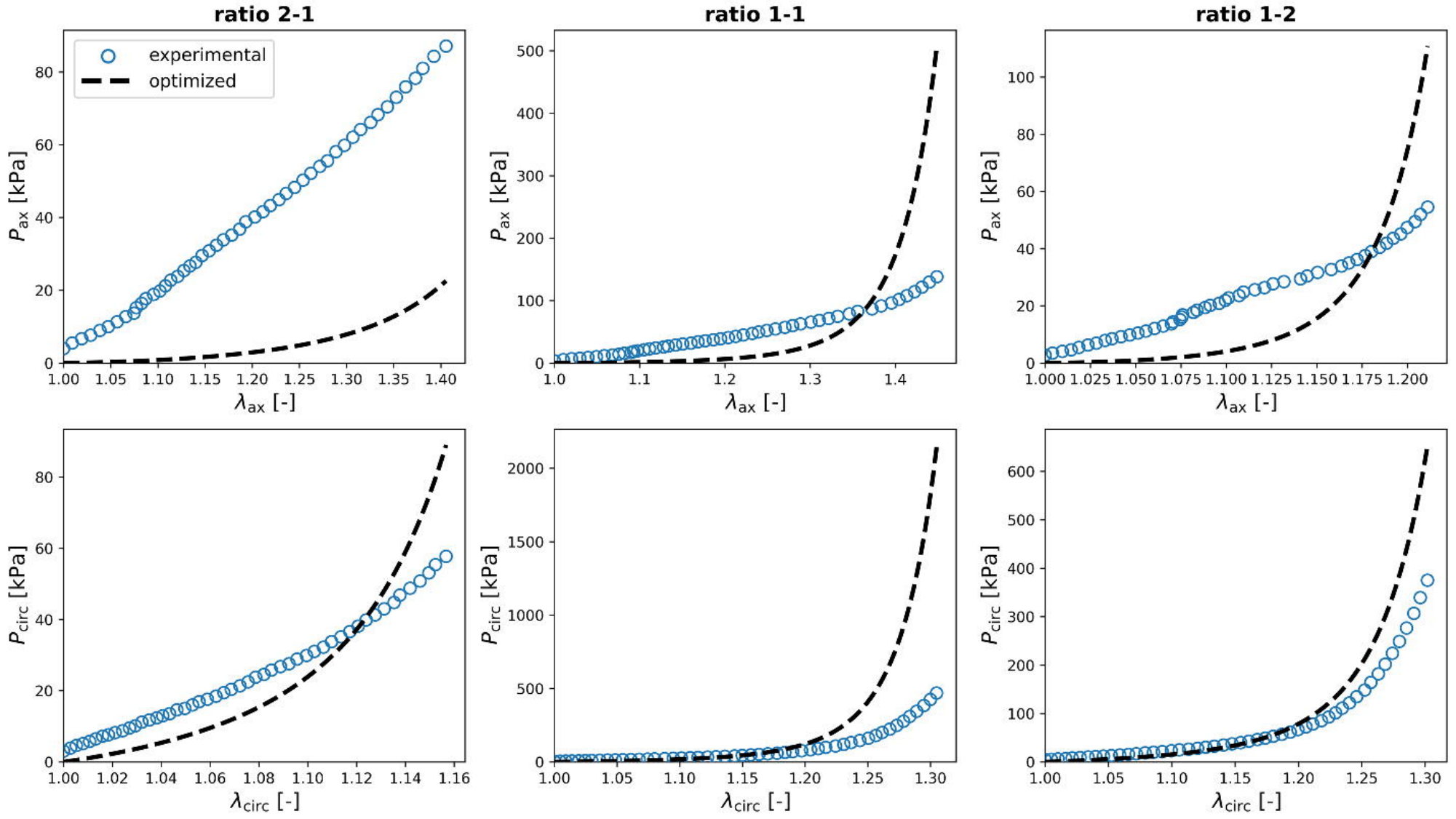

optimized GOH parameters
$c_1 = 0.632\,\mathrm{kPa}$
$k_1 = 39.5\,\mathrm{kPa}$
$k_2 = 11.38$
$\kappa = 0.156$
$\alpha = 5.02°$
pressure [mmHg]
circumferential stretch [-]
(a)
optimized axial stretch
$\lambda_{ax} = 1.33$
circumferential stretch [-]
(b)
optimized opening angle
$\beta = 110.6°$
circumferential stretch [-]
(c)


pressure-diameter
relative stretch
pressure [mmHg]
200
150
100
50
0
4.0
4.5
5.0
5.5
6.0
6.5
outer diameter [mm]
1.0
1.1
1.2
1.3
1.4
1.5
circumferential stretch [-]
β = 0°
β = 10°
β = 20°
β = 30°
β = 40°
β = 50°
β = 60°
β = 70°
β = 80°
β = 90°
β = 100°
β = 110°
β = 120°
experimental
(a)
(b)


pressure-diameter
relative stretch
pressure [mmHg]
outer diameter [mm]
circumferential stretch [-]
experimental
(a)
(b)
axial stress
axial Cauchy stress [MPa]
pressure [mmHg]
$\lambda_{ax} = 1.0$
$\lambda_{ax} = 1.1$
$\lambda_{ax} = 1.2$
$\lambda_{ax} = 1.3$
$\lambda_{ax} = 1.4$
$\lambda_{ax} = 1.5$
$\lambda_{ax} = 1.6$
$\lambda_{ax} = 1.7$
$\lambda_{ax} = 1.8$
$\lambda_{ax} = 1.9$
$\lambda_{ax} = 2.0$
(c)


sample A
sample B
sample C
sample D
sample E
pressure [mmHg]
outer diameter [mm]
experimental
modeled


sample A
sample B
sample C
sample D
sample E
pressure [mmHg]
circumferential stretch [-]
experimental
modeled


ratio 2-1
ratio 1-1
ratio 1-2
experimental
optimized
P_{ax} [kPa]
λ_{ax} [-]
P_{circ} [kPa]
λ_{circ} [-]