Elastic properties of anisotropic vascular membranes examined by inverse analysis

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An inverse method for estimating the distributions of the nonlinear elastic properties of inhomogeneous and anisotropic vascular membranes such as cerebral aneurysms is proposed. The material description of the membrane is based on a versatile structural model able to represent multiple collagen layers and the passive response of the vascular wall. Each individual layer is assumed to behave transversely isotropic following exponential stiffening with increasing loading. The model includes four parameters to be explainable physically: two initial stiffnesses of the collagen fabric, a parameter related to the nonlinearity of the collagen fabric, angle between the principal directions of the collagen fabric and a reference coordinate system. For this finite deformation problem a finite element framework for membranous structures considering pressure boundary loading is outlined, i.e. the principle of virtual work, its linearisation and the related spatial discretisation. The estimation procedure consists of the following three steps: (i) in vivo or in vitro approaches record the mechanical responses of membranous structures whose properties are to be determined; (ii) define a corresponding finite element model; (iii) minimise an error function (regarding the unknown parameters) that quantifies the deviation of the numerical prediction from the recorded data. To achieve a robust parameter estimation, an element partition method is employed. The outcome of the procedure is affected by the number of nodes defined on the membrane surface and the number of load steps. In a numerical example, the proposed procedure is assessed by reestablishing given reference distributions in a reference membrane. The deviations of the estimated material parameter distributions from the related reference fields are within just a few percent. In most of the investigated cases the standard deviation for the resulting maximum principal stress was even below 1%, which is accurate enough for rupture risk assessment of vascular membranes.

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1. Introduction

In structural analyses, it is desirable to have comprehensive information about the mechanical response of materials to be investigated. Material data may be obtained from uniaxial, biaxial or triaxial tests including shear tests. For materials undergoing finite deformations planar biaxial testing of rectangular sheets, combined extension and torsion of cylindrical solids, and combined inflation, extension and torsion of cylindrical tubes are examples of convenient tests. However, there are many situations in which one has little or no control of the geometry and the mechanical response of the material of interest, or the applied loads. This pertains, in particular, to tests on soft biological tissues such as cardiovascular tissues whose geometries and material composition and behaviour are basically dictated by nature. For such cases, inverse analysis may be employed to determine the material parameters. Inverse problems can be found in several topics of engineering mechanics. Roughly speaking, inverse problems deal with the determination of (bio)mechanical systems – with unknown material properties, geometry, sources or boundary conditions – from the responses to given excitations on their boundary. Several studies have, for example, been devoted to the determination of the reference configuration of a loaded structure \cite{8,22,25}. The present study, however, deals with the estimation of material properties, which is a kind of system identification \cite{1}. For this type of study, a set of material parameters is determined on the basis of structural analyses, where the reference state, the deformed state, and the applied boundary conditions are known. For this type of analysis, several schemes have been proposed, see for example, \cite{16,2,3,6,21}.

The theoretical determination of the material behaviour is usually performed in two steps; first, a mathematical model is built to capture the physics of the material in question, and second the coefficients of this model are estimated by use of an inverse analysis. This second step usually involves the minimisation of an error function, which in some way quantifies the agreement between experimental data and the response of the theoretical material...
model [other names used for this function are, for example, objective function [21], loss function [1], cost function [3]]. However, engineering problems tend to be nonlinear (in terms of geometry, material and/or boundary conditions), and there is no general theory available that guarantees the uniqueness of the solution of a nonlinear identification problem. The solution obtained may depend on the initial values of the parameters, and several parameter sets may provide the same value of the error function.

Many biological and engineering structures can be characterised as membranous, implying that their geometry can be characterised as a thin sheet and their mechanical behaviour is essentially governed by the stiffness and strength in the two in-plane dimensions. This pertains, for example, to some types of soft biological tissue such as cerebral aneurysms which can be expected to be both anisotropic and inhomogeneous [4,18,19]. In the context of biomechanics, the study [20] employs the inverse finite element (FE) method to show that the material behaviour of neo-Hookean membranes can be determined, and the study [15] presents a method to determine the viscoelastic material properties of soft tissues by inverse analysis under in vivo conditions. Inhomogeneity is addressed in [26] by using a sub-domain method and considering a local region of the membrane which is assumed to be fairly homogeneous. Boundary and inner displacements are used to identify the material properties for the local region. The same issue is addressed in [17] by estimating the distribution of the elastic modulus in atherosclerotic tissues, and by lumping the material into a few regions which are taken to exhibit a homogeneous and isotropic elastic behaviour locally.

The present study aims at estimating the distributions of the nonlinear elastic properties of inhomogeneous and anisotropic (vascular) membranes using the inverse analysis. We allow a continuous variation of the initial stiffnesses of the collagen fabric and the material principal directions over the membrane surface. Such an approach has several applications, for example, in cardiovascular biomechanics, where material properties of thin soft biological tissues need to be estimated. The proposed approach is versatile, and may be employed in other areas as well where the elastic properties of membranous structures need to be determined. Thus, in order to characterise this type of material, distributions of the elastic properties need to be estimated. From a numerical point of view, this is a complicating factor since it requires the estimation of a large number of unknown parameters, which tend to make inverse problems ill-conditioned.

The proposed method involves the following main steps:

- **Experiments** are performed on the membrane whose material characteristics are to be determined. This task can be done, for example, by planar biaxial tests of a membranous specimen, by inflation–extension tests of a tube-like specimen, or by inflation tests of a flat specimen clamped along its boundary. A number of points, defining nodal points, are marked on the membrane surface. The position of the nodes and the membrane wall thickness at the nodal points are measured in the load-free configuration. The specimen is then loaded to different load levels. The nodal displacements from the FE analysis are evaluated at different load levels. The nodal displacements from the FE analysis (denoted by superscript 'fem') and from the experiments (denoted by superscript 'exp') are used to establish a representative deformation measure (denoted by $\kappa$) that enables comparison between FE predictions and experiments in a convenient way. This error function is then minimised with respect to the vector $\mathbf{q}$. Since each element has its own set of parameters, the size of $\mathbf{q}$ increases rapidly with the density of nodal points defined on the membrane surface. The vector $\mathbf{q}$ that minimises $f_{\text{err}}$ is the outcome of the inverse analysis and the required estimate of the material parameters.

The paper is organised as follows: in Section 2, we propose a versatile constitutive model that enables the modelling of nonlinear elastic, inhomogeneous and anisotropic vascular membranes. The constitutive model includes the material and structural parameters, the distributions of which are to be estimated. In Section 3, we provide the finite element framework required to analyse pressurised membranous structures undergoing large deformations. In particular, the principle of virtual work, its linearisation and the related spatial discretisation is provided. In Section 4, we give a thorough description of the estimation procedure, which is followed by a simple numerical example in Section 5, with the aim to assess the applicability of the estimation procedure. Finally, Section 6 contains a discussion and some concluding remarks.

## 2. Constitutive model

In this section, we propose a constitutive model for vascular membranes such as cerebral aneurysms. The model is versatile enough for the application to other types of nonlinear elastic, inhomogeneous and anisotropic membranes. We assume that the membrane can be modelled as a hyperelastic solid and we assume that the constitutive response is governed by a strain-energy function $\Psi$ (defined per unit reference volume). The vascular membrane is modelled as a laminate, consisting of $n$ discrete and distinct layers (plies) of nonlinear elastic collagen fibres. Within a layer (ply) with index $i$, fibres are perfectly aligned in a direction, say $\phi_i$, defined with respect to a 2D in-plane reference coordinate system. The fibre angles $\phi_i$ are defined according to

$$
\phi_i = \frac{i - 1}{n}, \quad 1 \leq i \leq n,
$$

where the fibre orientations are thus uniformly distributed over the whole azimuthal range [7]; see Fig. 1a, and $n \geq 2$ provides the even number of tissue layers.
In addition, assume that the in-plane principal directions $1$ and $2$ of the vascular membrane are associated with fibre orientations $\phi_i$ and $\phi_i+\pi/2$, respectively, and that the fibre stiffnesses $k_i > 0$ of the different layers are defined by the two given stiffnesses $k_i$ and $k_{i+2i+1}$ according to

$$
k_i = k_1 + \frac{k_{i+2} - k_i}{n/2}, \quad 2 \leq i \leq n/2,
$$

$$
k_i = k_{n/2+i} + \frac{k_i - k_{i+2}}{n/2}, \quad n/2+2 \leq i \leq n.
$$

(3)

see Fig. 1b for $n = 8$. The orientation of the principal coordinate system $\vec{z}_i - \vec{z}_j$ of the fabric with respect to the local 2D reference coordinate system $\vec{z}_1 - \vec{z}_2$ is defined by an angle $\beta$ (Fig. 1a), which is a structural parameter.

Similar to [12], the strain-energy for the passive material (no activation of smooth muscle cells) is now taken to be

$$\Psi = \sum_{i=1}^{n} \frac{k_i}{8a} \left\{ \exp[\alpha(C : A(\phi_i, \beta) - 1)^2] - 1 \right\}, \quad C : A(\phi_i, \beta) > 1. \tag{4}$$

where $a > 0$ is a material parameter describing the nonlinearity the collagen fibres exhibit, $C$ is the 2D right Cauchy–Green tensor, and $A(\phi_i, \beta)$ is a structural tensor, defined as $A = \mathbf{M} \otimes \mathbf{M}$ with components $[\mathbf{M}] = \begin{pmatrix} \cos(\phi_i + \beta) & \sin(\phi_i + \beta) \end{pmatrix}$. Here, we do not incorporate the active state (smooth muscle contraction) in the form of the strain-energy function.

The second Piola–Kirkhoff stress tensor is then obtained as $\mathbf{S} = 2\Psi/\mathbf{C}$, and the related Cauchy stress tensor as $\sigma = J^{-1} \mathbf{F} \mathbf{S} \mathbf{F}^T$, with the deformation gradient $\mathbf{F}$ and the volume ratio $J = \det \mathbf{F} = \det \mathbf{C}^{1/2} > 0$. [10]. We assume incompressibility, implying $J \equiv 1$. In index notation, the material stiffness tensor $C$ is given as $(C)_{\gamma \delta \rho \sigma} = 2\psi S_{\gamma \delta \rho \sigma} / \partial C_{\gamma \delta \rho \sigma}$ where the indices $\alpha, \beta, \gamma, \delta$ pertain to $\vec{z}_1 - \vec{z}_2$ (Fig. 1a). The components of a corresponding stiffness tensor $(C')_{\alpha \beta \gamma \delta}$ can be obtained for any rotated system $\vec{z}_1 - \vec{z}_2'$.

The initial stiffness of the fabric in the principal directions $(\vec{z}_1', \vec{z}_2')$ are denoted by $E_1$ and $E_2$, respectively, and are defined as

$$E_1 = (C')_{1111}[c-4], \quad E_2 = (C')_{2222}[c-4].$$

(5)

where $\mathbf{I}$ is the identity tensor. Hence, for a given set of parameters $E_1$ and $E_2$, the stiffness coefficients $k_1, \ldots, k_n$ are uniquely defined and thus, for a material point in the vascular membrane, the nonlinear elastic, inhomogeneous and anisotropic behaviour of a vascular membrane is defined by the entities $E_1, E_2, a, \beta$.

### 3. Finite element framework

The aim of this section is to derive the principle of virtual work and its linearisation for a vascular membrane. In addition, the spatial discretisation of the continuous problem is provided, in particular the element residua, and the element stiffness matrix.

#### 3.1. Principle of virtual work in material description

The membrane formulation utilised here is based on formulations previously presented, [9,14,11,10]. The formulation (and notation) has been modified to suit the purposes of the present work. A brief outline is provided, for a more detailed description, however, we refer to the above references.

Material points on the vascular membrane are labelled by two (convected) surface coordinates. Greek indices are used to denote the quantities measured within the membrane metric and commas denote partial derivatives with respect to the reference (undeformed) membrane geometry. The position vector $\mathbf{X}$ in the reference configuration $\Omega_0$ and the position vector $\mathbf{x}$ in the current configuration $\Omega$ are given as

$$\mathbf{X} = \mathbf{x}_i \mathbf{e}_i, \quad \mathbf{x} = \mathbf{x}_i \mathbf{e}_i,$$

(6)

respectively, where the set $\mathbf{e}_i, i = 1, 2, 3$, are right-handed basis vectors characterising a fixed Cartesian coordinate system. The components of the vectors $\mathbf{X}$ and $\mathbf{x}$ are referred to this system, and we label $\mathbf{X}_i$ and $\mathbf{x}_i$ as the referential and current coordinates, respectively. The displacement vector $\mathbf{u}$ in the spatial description is given as

$$\mathbf{u} = \mathbf{x} - \mathbf{x}(\mathbf{X}) = \mathbf{u}_i \mathbf{e}_i,$$

(7)

where $\mathbf{u}_i$ are the spatial coordinates of $\mathbf{u}$. Membrane strains may be defined as the components $E_{a\beta}$ of the symmetric Green–Lagrange strain tensor $\mathbf{E}$ according to

$$E_{a\beta} = \frac{1}{2}(C_{a\beta} - C_{\beta a}), \quad C_{a\beta} = \mathbf{x}_a \cdot \mathbf{x}_\beta, \quad G_{a\beta} = \mathbf{X}_a \cdot \mathbf{X}_\beta,$$

(8)

where $G_{a\beta}$ denote the metric coefficients of the undeformed membrane and $C_{a\beta}$ denote the components of the symmetric right Cauchy–Green tensor $\mathbf{C}$. The related membrane stresses are represented as the components $S_{a\beta}$ of the second Piola–Kirkhoff stress tensor $\mathbf{S}$ according to

$$S_{a\beta} = \frac{1}{2} \frac{\partial \Psi}{\partial C_{a\beta}}.$$

(9)

where $\Psi$ is the strain-energy function provided in Eq. (4).

The principle of virtual work in material description for the vascular membrane may be written as [10]

$$\int_{\Omega_0} \mathbf{S} : \delta \mathbf{E} \, d\Omega = \int_{\Omega_0} \mathbf{n} \cdot \delta \mathbf{u} \, d\Omega,$$

(10)

where the two dots denote a double contraction of the tensors $\mathbf{S}$ and $\delta \mathbf{E}$, and $H$ is the thickness of the vascular membrane in the reference...
configuration and $\partial \Omega_p$ is the portion of the boundary surface on which the normal pressure $p$ is assumed to be constant, is applied. The surface elements in the reference and current configurations are denoted by $dS$ and $ds$, respectively. The (first) variation of a quantity ($\cdot$) is denoted by $\delta(\cdot)$ (in mechanics $\delta u$ and $\delta E$ are also known as the virtual displacement field and the virtual Green–Lagrange strain tensor, respectively). The unit exterior vector normal $n$ to the boundary surface $\partial \Omega_p$ and the relation between the surface elements $ds$ and $dS$, are, respectively,

$$n = \frac{x_1 \times x_2}{|x_1 \times x_2|}, \quad ds = \frac{x_1 \times x_2}{|x_1 \times x_2|} \cdot dS,$$

(11)

while the components of $\delta E$, i.e. the virtual membrane strains $\delta E_{\text{ne}}$, required for (10) are

$$\delta E_{\text{ne}} = \frac{1}{2} (\delta u_1 \cdot x_2 + \delta u_2 \cdot x_1) .$$

(12)

With Eq. (11) the principle of virtual work (10) may be written in the form

$$\mathcal{F}(u, \delta u) = \int_{\Omega_p} \left( S : \delta \mathbf{E} H - p \frac{x_1 \times x_2}{|x_1 \times x_2|}, \cdot \delta u \right) \, dS = 0,$$

(13)

where $\mathcal{F}$ is a smooth and nonlinear function of the displacement vector $u$ and the virtual displacement vector $\delta u$ (test function). Eq. (13) is the weak form of the equilibrium equation with respect to the material configuration.

Since we employ an incremental/iterative solution technique of Newton’s type we need to linearise the nonlinear function $\mathcal{F}$. The linear change in $\mathcal{F}$ due to $\partial \mathbf{u}$ at $u$ is the directional derivative of $\mathcal{F}$ at $u$ (fixed) in the direction of the incremental displacement field $\partial \mathbf{u}$, i.e.,

$$\Delta \mathcal{F}(u, \partial \mathbf{u}) = \frac{d}{d\partial \mathbf{u}} \mathcal{F}(u + \varepsilon \partial \mathbf{u})|_{\varepsilon=0},$$

(14)

where $\Delta(\cdot)$ denotes the linearisation operator similar to $\delta(\cdot)$ so that $\Delta \mathcal{F}(u, \partial \mathbf{u})$ is the linearisation of $\mathcal{F}$ at $u$. Thus, the linearisation procedure of (13) yields

$$\Delta \mathcal{F}(u, \partial \mathbf{u}) = \int_{\Omega_p} \left( S : \Delta \mathbf{E} + \Delta S : \delta \mathbf{E} \right) H - p \left. \frac{\partial u_1 \times x_2 + \partial u_2 \times x_1}{|x_1 \times x_2|} \cdot \delta u \right| \, dS,$$

(15)

where $\Delta \mathbf{E}$ denotes the linearisation of the virtual Green–Lagrange strain tensor $\delta E$, with the components

$$\Delta E_{\text{ne}} = \frac{1}{2} \left( \partial u_1 \cdot x_2 + \partial u_2 \cdot x_1 \right).$$

(16)

In order to specify the linearisation $\Delta S$ of the second Piola–Kirchhoff stress tensor $S$ in Eq. (15), we use the chain rule to obtain

$$\Delta S(E(u)) = C(u) : \Delta \mathbf{E}(u),$$

(17)

where $C$ is the material stiffness tensor as defined in the previous section, and $\Delta \mathbf{E}$ denotes the linearisation of the Green–Lagrange strain tensor $\mathbf{E}$. Note that the components of $\Delta \mathbf{E}$ are simply obtained by replacing $\delta$ with the operator $\Delta$ in (12).

The first term in the linearised principle of virtual work (15) results from the current state of stress and represents the geometrical (initial) stress contribution to the linearisation, while the second term represents the material contribution. The third term in (15) results from the deformation dependent pressure boundary loading which leads, in addition, to a non-symmetric (tangent) stiffness matrix upon discretisation.

3.2. Finite element representation for the vascular membrane

In this section, we outline the spatial discretisation of the continuous membrane problem presented above. The element residua, and the material, geometrical and pressure contributions to the element stiffness are provided.

We subdivide the membrane surface into $n_e$ finite elements with domain $\Omega_e$, where the subscript $e$ is an index (running between 1 and $n_e$) referring to a typical finite element. We use isoparametric elements and interpolate the reference geometry $X$, the displacement vector $u$ and the membrane thickness $H$ according to

$$X = \sum_{i=1}^{n_e} N_i X_i, \quad u = \sum_{i=1}^{n_e} N_i u_i, \quad H = \sum_{i=1}^{n_e} N_i H_i,$$

(18)

where $N_i$ are the standard (polynomial) interpolation functions, and $i$ is an index running between 1 and the total number of element nodes denoted by $n_{\text{node}}$ (4 or 9). The nodal values of $X, u, H$ within $\Omega_e$ are represented by $X_i, u_i, H_i$, respectively, where

$$X = [x_1 \, x_2 \, x_3]^T, \quad u = [u_1 \, u_2 \, u_3]^T,$$

(19)

are 3 × 1 column matrices representing $X$ and $u$, respectively. The variation $\delta u$ is the analogue of Eq. (18), and with Eqs. (18) and (18b) the position vector of the current configuration is given by

$$\mathbf{X} = \mathbf{X}_0 + \delta \mathbf{u}.$$

Following the standard concept of the finite element method, we introduce the matrix $\mathbf{B}$, which is the gradient operator associated with the $i$th node so that the following matrix expressions

$$\mathbf{E} = \sum_{i=1}^{n_{\text{node}}} \mathbf{B}_i u_i, \quad \delta \mathbf{E} = \sum_{i=1}^{n_{\text{node}}} \mathbf{B}_i \delta u_i, \quad \mathbf{B}_i = \begin{bmatrix} N_{i1} x_1^2 + N_{i2} x_1 x_2 + N_{i3} x_2^2 \\ N_{i2} x_1 x_2 + N_{i3} x_2^2 \\ N_{i3} x_2^2 \end{bmatrix},$$

(20)

hold. The 3 × 1 column matrix $\mathbf{E} = [E_{11} E_{12} E_{13}]^T$ represents the (2D) Green–Lagrange strain tensor $\mathbf{E}$ (a similar column matrix holds for $\delta \mathbf{E}$). The stationarity condition (13) may then be given in the following matrix form

$$\sum_{i=1}^{n_{\text{node}}} \delta u_i^T \left( \mathbf{B}^T \mathbf{S} H - p \frac{x_1 \times x_2}{|x_1 \times x_2|} N_i \right) \, d\Omega_e = 0,$$

(21)

where the 3 × 1 column matrix $\mathbf{S} = [S_{11} S_{12} S_{13}]^T$ is obtained through the discretisation of the constitutive model, as expressed in Section 2.

On the basis of Section 3.1, the stiffness matrix $\mathbf{K}_e$ for an element may be expressed in the form

$$\mathbf{K}_e = \mathbf{K}_{e}^{\text{mat}} + \mathbf{K}_e^{\text{geo}} + \mathbf{K}_e^{\text{pre}}, \quad 1 \leq j \leq n_{\text{node}},$$

(22)

where the indices $i$ and $j$ pertain to the nodes of a finite element. In (22) the $3 \times 3$ sub-stiffness matrices $\mathbf{K}_e$ consist of material, geometrical and pressure contributions, i.e. $\mathbf{K}_{e}^{\text{mat}}, \mathbf{K}_e^{\text{geo}}, \mathbf{K}_e^{\text{pre}}$, respectively. They are according to

$$\mathbf{K}_e^{\text{mat}} = \int_{\Omega_e} \mathbf{B}_i^T \mathbf{C}_b \mathbf{B}_i \, d\Omega_e, \quad \mathbf{K}_e^{\text{geo}} = \mathbf{g}_b \mathbf{I}, \quad \mathbf{K}_e^{\text{pre}} = \int_{\Omega_e} \mathbf{P}_b \, d\Omega_e,$$

(23)

where $\mathbf{I}$ denotes the $3 \times 3$ unit matrix. The matrix $\mathbf{C}_b$ and the scalars $\mathbf{g}_b$ have the forms

$$\mathbf{C}_b = \begin{bmatrix} \frac{\partial S_{11}}{\partial E_{11}} & \frac{\partial S_{11}}{\partial E_{12}} & \frac{\partial S_{11}}{\partial E_{13}} \\ \frac{\partial S_{12}}{\partial E_{11}} & \frac{\partial S_{12}}{\partial E_{12}} & \frac{\partial S_{12}}{\partial E_{13}} \\ \frac{\partial S_{13}}{\partial E_{11}} & \frac{\partial S_{13}}{\partial E_{12}} & \frac{\partial S_{13}}{\partial E_{13}} \end{bmatrix}, \quad \mathbf{g}_b = \int_{\Omega_e} N_i S_{\text{ne}} N_j H \, d\Omega_e,$$

(24)

where $\mathbf{C}$ represents the elasticity tensor $C$ in a material setting. In addition, we have introduced the skew-symmetric matrix $\mathbf{P}_b$ which is the contribution from the external loads, i.e. [27].

1 Characters indicated by underlines denote interpolated quantities. In addition, for vectors and tensors they represent the related matrix. For example, $\mathbf{u}$ is the matrix representation of vector $u$.\]
where \( p_0^T = \langle x_0, N_{12} - x_0, N_{11} \rangle N_{0}, n = 1, 2, 3, \) and \( x_0 \) denote here the components of the matrix \( X \).

The interpolation functions \( N_i \) are expressed in natural coordinates, say \( \xi \) and \( \eta \). However, in Eqs. (20), (24), and (25) the derivatives of the interpolation functions \( N_{x}, x = 1, 2, \) with respect to the surface coordinates need to be established. The tangent plane of the membrane surface may be characterised by the two tangent vectors

\[
G_i = \frac{\partial X}{\partial \xi}, \quad G_\eta = \frac{\partial X}{\partial \eta},
\]

(26)

With these vectors a local orthonormal Euclidean frame \( a_1, a_2, a_3 \) can then be constructed as

\[
a_1 = \frac{G_x \times G_\eta}{|G_x \times G_\eta|}, \quad a_2 = \frac{G_y \times G_\xi}{|G_y \times G_\xi|}, \quad a_3 = a_1 \times a_2,
\]

(27)

where \( a_1, a_2 \) define the local 2D reference coordinate system \( \xi_1 - \xi_2 \) introduced in Section 2. Derivatives of \( N_i \) with respect to the surface coordinates may then be computed according to

\[
\begin{bmatrix}
N_{1,i} \\
N_{2,j}
\end{bmatrix} = \begin{bmatrix}
G_x \cdot a_1, G_y \cdot a_2 \\
G_x \cdot a_1, G_y \cdot a_2
\end{bmatrix}^{-1} \begin{bmatrix}
N_{1,i} \\
N_{2,j}
\end{bmatrix},
\]

(28)

The map from the area element \( d\Omega \) to \( d\xi \, d\eta \), as required in Eqs. (20) and (23), is according to \( d\Omega = |G_x \times G_\eta| \, d\xi \, d\eta \). When we evaluate Eqs. (21)-(25) we use standard Gaussian integration. A (consistent) linearisation of the nonlinear condition (21) and the assembling of the contributions of all \( n_e \) finite elements lead to a system of algebraic equations. We may write these equations in the typical form

\[
\mathbf{K} \Delta \mathbf{U} = \mathbf{f}_{\text{ex}} - \mathbf{f}_{\text{int}},
\]

where \( \mathbf{K} \) denotes the global stiffness matrix, \( \mathbf{f}_{\text{ex}} \) and \( \mathbf{f}_{\text{int}} \) are the global residuum assembled using standard procedures, while \( i \) and \( i - 1 \) denote the iteration steps associated with a global Newton iteration. The external forces, i.e., the deformation dependent pressure acting on the von Neumann boundary, and the internal forces are summarised in the \( 3 \times n_e \times 1 \) column matrices \( \mathbf{f}_{\text{ex}} \) and \( \mathbf{f}_{\text{int}} \), respectively, where \( n_e \) denotes the total number of nodal points on the membrane surface.

4. Estimation procedure

This section aims at establishing a procedure for the estimation of the mechanical properties of nonlinear elastic, inhomogeneous and anisotropic vascular membranes. In Section 2, we proposed a constitutive model with four parameters. Now we make the assumption that the two parameters \( E_1, E_2 \) (initial stiffnesses) and the angle \( \beta \) vary continuously over the membrane surface, whereas the fourth parameter \( a \) is taken to be constant over the membrane. The assumption \( a = \text{constant} \) means that all fibres in the vascular membrane are taken to have the same mechanical properties. The goal is now the determination of these parameter distributions on the basis of given experimental data.

As mentioned in Section 1, different experimental approaches could serve as a basis for this type of inverse analysis. The experimental method to be adopted here is the inflation of a membranous tissue specimen, clamped along its boundary. The specimen is exposed to a pressure boundary loading \( p \). On the membrane surface, a set of nodal points \( n_\text{g} \) are defined, as can be seen in the principle sketch of Fig. 2. The initial geometry of the specimen is a regular rectangle which lies in the plane spanned by the coordinates \( X_1, X_2, \) where \( X_3 \) is the coordinate orthogonal to the plane. It is worth noting that any initial geometry is possible as long as it can be properly clamped along the boundary. We assume that the initial geometry of the vascular membrane is known in terms of nodal coordinates and thickness at the nodal points. The specimen is exposed to \( n_\text{g} \) different load levels, and the displacements of the nodal points are recorded at different levels of pressure boundary loading. The coordinates \( X_1, X_2, X_3 \) pertain to a rectangular reference coordinate system.

4.1. Error function and minimisation procedure

In order to determine the material parameters, an error function, say \( f_{\text{err}} \), is defined according to

\[
f_{\text{err}} = \sqrt{\frac{1}{3n_{\text{g}}^3} \sum_{i=1}^{n_e} \sum_{k=1}^{n_\text{g}} \sum_{j=1}^{3} \left( C_{ijkl}^{\text{fem}} - C_{ijkl}^{\text{exp}} \right)^2},
\]

(29)

where the entities \( C_{ijkl}^{\text{fem}} \) and \( C_{ijkl}^{\text{exp}} \) denote the components of the (2D) right Cauchy–Green tensor obtained by the finite element method (indicated by superscript ‘fem’), and from experiments (indicated by superscript ‘exp’), respectively. The quantities \( C_{ijkl}^{\text{fem}} \) result naturally from the finite element analysis. It is assumed that in the tested specimen the displacement field can be approximated by the use of the same shape functions as in the finite element analysis. Hence, the quantities \( C_{ijkl}^{\text{fem}} \) can then be computed by means of the (experimental) nodal displacements. In Eq. (29), the index \( i \) is related to the three independent components of the right Cauchy–Green tensor (two normal and one shear component), the index \( j \) pertains to the number of Gauss points \( n_\text{g} \) in the elements, the index \( k \) pertains to the summation over all elements, and the index \( l \) to the summation over all load levels considered.

The vector \( \mathbf{q} \) contains all material and structural parameters to be estimated, which in matrix notation reads

\[
[\mathbf{q}] = [E_{1,1}, \ldots, E_{1,n}, E_{2,1}, \ldots, E_{2,n}, \beta_{1}, \ldots, \beta_{n}]^T.
\]

(30)
The error function $f_{err}$ is now minimised with respect to the parameters in $\mathbf{q}$. In the minimisation of $f_{err}$, a steepest descent method is employed [24], which consists of the following steps:

- While $\Delta f_{err}/f_{err} >$ tolerance do
- Calculate the direction $\mathbf{n} = -\partial f_{err}(\mathbf{q})/\partial \mathbf{q}$ of the steepest descent
- Find the value $\mathbf{q}^*$ that minimises the function $f_{err}(\mathbf{q} + \mathbf{n})$
- Calculate the change of $f_{err}$ as $\Delta f_{err} = f_{err}(\mathbf{q}) - f_{err}(\mathbf{q} + \mathbf{n})$
- Update the parameter vector according to $\mathbf{q} = \mathbf{q} + \mathbf{q}^*$
- End

This procedure is repeated until the relative change $\Delta f_{err}/f_{err}$ is less than a predefined tolerance.

However, as the present problem is formulated, the number of unknown parameters to be estimated will, in general, be large. In order to attain a robust parameter estimation procedure, an element partition method is employed. For the specimen in Fig. 2, for example, the problem is divided into four partition levels ($n_p = 4$, where $n_p$ denotes the number of partition levels), and the element structure is divided into four element group refinements, as illustrated in Fig. 3. In partition 1, for example, all elements are included in one large group. In the next partitions the element structure is divided into smaller and smaller element (sub)groups, while in partition 4 the element groups correspond to single elements, and no further refinement is possible.

We now consider $n_{eg}$ element groups within a partition, i.e. in Fig. 3 $n_{eg} = 1, 4, 16, 64$ relating to the partition levels 1–4, respectively. We then define a modified material parameter vector $\mathbf{q}_{eg}$, which in matrix notation reads

$$\mathbf{q}_{eg} = \begin{bmatrix} E_{1,1}, \ldots, E_{1,n_{eg}} E_{2,1}, \ldots, E_{2,n_{eg}}, \beta_{1,1}, \ldots, \beta_{1,n_{eg}} \end{bmatrix}^T,$$

where the subscript ‘eg’ stands for ‘element group’. The data in $\mathbf{q}_{eg}$ is used for all elements within the group ‘eg’. It is now straightforward to distribute the three parameters $E_1, E_2, \alpha$ within the different elements in a group. The angle $\beta$, however, is defined with respect to the (local) reference coordinate system $\zeta_1 - \zeta_2$ (compare with Fig. 1a), and since each point on the vascular membrane is related to a specific local coordinate system, the administration of $\beta$ requires some further consideration.

In Eq. (31), the $\beta$ values are indicated by the additional superscript $\ast$, indicating that the values are not the ones actually assigned to the individual elements. Each material point on the vascular membrane may be characterised by the three basis vectors $\mathbf{a}_1, \mathbf{a}_2, \mathbf{a}_3$, where $\mathbf{a}_1$ and $\mathbf{a}_2$ define the (local) reference coordinate system $\zeta_1 - \zeta_2$, see Figs. 1a and 4. Furthermore, the principal coordinate system $\zeta_1 - \zeta_2$ may be characterised by the two corresponding vectors $\mathbf{a}_1$ and $\mathbf{a}_2$ ($\mathbf{a}_3 = \mathbf{a}_1$), and $\beta$ is then defined as the (rotation) angle between the two coordinate systems according to Fig. 4. When using the element partition method, additional local coordinate systems have to be defined for each element group. The values $\beta$, pertaining to the different element groups, are defined with respect to these new coordinate systems. These values are then transformed to the local (element) coordinate systems within the groups. The transformation from the group level to the element level is now further addressed.
We define the local coordinate system of a (sub)group of elements by the vectors $a_1^s$, $a_2^s$, $a_3^s$, see Fig. 4. We assume that a vector $a_1^s$ characterises the first principal direction in the element group coordinate system, and $\beta$ is the angle between $a_1^s$ and $a_2^s$. This vector $a_1^s$ is projected onto the membrane plane (spanned by $a_1$ and $a_2$) according to

$$a_1^l = a_1^s - (a_1^s \cdot a_3) a_3.$$  \hspace{1cm} (32)

Hence, the angle between $a_1$ and $a_3$ defines $\beta$ in the local (element) coordinate system. It should be noted that this strategy only works if the curvature of the membrane is moderate. If this is not the case, more sophisticated mapping strategies need to be employed.

The parameter estimation procedure outlined above is now repeated for each partition (loop over all partitions) and the parameter vector $q$ is simply replaced by $q_{est}$. For the first partition, the four parameters $E_1$, $E_2$, $\beta$, $a$ are estimated, pertaining to all elements. When the relative change of the error function is less than a predefined tolerance, the parameter estimation is refined by switching to partition 2. The four parameters from partition 1 serve then as initial values for the estimations within partition 2. For the second partition, $4 \cdot 3 + 1 = 13$ parameters are estimated, pertaining to four element groups, and so forth. This procedure turns out to be more robust than the original one in which all material parameters are estimated within one step. Thus, for the specific example considered (Fig. 2), the numbers of parameters to be estimated are 4, 13, 49, 193 for the four different partitions, respectively. For the final partition $q_{est} = q$. Once the loops over the last partition have been completed the parameters have been estimated.

5. Numerical example

Here we provide a numerical example for the assessment of the estimation procedure, as proposed in Section 4.

5.1. Input data

We consider a plane and quadratic vascular membrane, which is clamped along its boundary as illustrated in Fig. 5. The membrane coincides with the $X_1 - X_2$ plane and has a side length of $s = 2.0$ cm and a constant initial thickness of $H = 200$ μm. The membrane is taken to consist of $n = 8$ layers of collagen fibres and is exposed up to $n_0 = 8$ load levels ($p_1, \ldots, p_i, \ldots, p_{n_0}$), which are linearly distributed according to

$$p_i = \frac{p_{\text{max}}}{n_0} i \leq n_0,$$  \hspace{1cm} (33)

where $p_{\text{max}} = 150$ kPa is the maximum pressure applied.

Instead of comparing with experimental results, we use here solutions from a ‘reference’ membrane. The material parameters $E_1$, $E_2$ (in MPa) and $a$, and the geometric parameter $\beta$ of the reference membrane are defined by the following distributions

$$E_1 = 10 + \frac{s}{3} X_1 + X_2, \quad E_2 = 10 + \frac{s}{3} X_1 + X_2, \quad \beta = \frac{\pi}{4} \frac{X_1 + X_2}{s}, \quad a = 10.$$  \hspace{1cm} (34)

As the reference finite element solutions are generated, the material properties of the elements of the reference membrane are defined by the coordinates of the element centroid together with the expressions in (34). Hence, the parameters are constant within an element in the reference solution as well, and the reference mesh is the same as the finite element mesh used for the estimation. Thus, the proposed estimation procedure is tested to see if it is able to reestablish the reference distribution of the parameters as defined above.

According to Fig. 2, the membrane is divided into a uniform mesh of finite elements, and solutions for the meshes with different levels of element refinement are evaluated. The number of partition levels $n_{ll}$ is chosen to be four or five so that the total number of elements for each partition is according to $n_e = 2^{2(n_{ll} - 1)}$, i.e. 64 and 256. For the membrane elements, $n_{gp} = 4$ Gauss points are used and the same material properties are taken to apply for all Gauss points within an element. For the minimisation of the error function $f_{\text{err}}$, the estimation procedure switched to a new element partition level when a relative difference between consecutive values of $f_{\text{err}}$ was below a tolerance of $\Delta f_{\text{err}}/f_{\text{err}} = 0.001$. The estimation procedure and the finite element framework from Section 3 together with this numerical example was implemented in MATLAB; the computations were performed on a standard PC.

5.2. Deviation measures

In order to quantify the deviation between the estimated distributions (denoted by the superscript ‘est’) and the reference distribution of the parameters (denoted by the superscript ‘ref’), we introduce useful deviation measures, i.e.

$$\Delta E_1 = \left( \frac{1}{n_e} \sum_{k=1}^{n_e} \left( E_{\text{est}}^{(k)} - E_{\text{ref}}^{(k)} \right)^2 \right)^{1/2},$$

$$\Delta E_2 = \left( \frac{1}{n_e} \sum_{k=1}^{n_e} \left( E_{\text{est}}^{(k)} - E_{\text{ref}}^{(k)} \right)^2 \right)^{1/2},$$

$$\Delta \beta = \left( \frac{1}{n_e} \sum_{k=1}^{n_e} (\beta_{\text{est}}^{(k)} - \beta_{\text{ref}}^{(k)})^2 \right)^{1/2},$$

$$\Delta a = \left( \frac{(a_{\text{est}} - a_{\text{ref}})^2}{a_{\text{ref}}} \right).$$  \hspace{1cm} (35)

In some situations the estimation of the elastic and structural properties is not the final aim. The resulting stresses in the structure is often of interest. Therefore, in addition, we introduce $\Delta \sigma$, which denotes a deviation measure of the resulting maximum principal Cauchy stress $\sigma$ according to

$$\Delta \sigma = \left( \frac{1}{n_{ll} n_q n_0} \sum_{j=1}^{n_0} \sum_{k=1}^{n_{ll}} \sum_{l=1}^{n_q} \left( \sigma_{\text{est}}^{(jk)} - \sigma_{\text{ref}}^{(jk)} \right)^2 \right)^{1/2}. $$  \hspace{1cm} (36)
The entities in (35) and (36) may be seen as the standard deviation of the relative error of the estimates, denoted by overlines.

5.3. Results

The initial parameter values were chosen to be constant distributions according to $E_1 = E_2 = 15$ MPa, $\beta = \pi/2$ and $\alpha = 20$. Different initial values were explored (i.e. different constant distributions), but the final estimations were essentially the same. Hence, the computation seems to be rather insensitive to the choice of initial parameters. For some initial value combinations it turned out that the final result of the angle $\beta$ relates to the principal coordinate $z_2$ rather than to $z_1$. This implies that the estimates of the parameters $E_1$ and $E_2$ had switched when compared with the reference values $E_1$ and $E_2$. However, this effect did not influence the general outcome of the analysis.

Fig. 6 shows the evolution of the error function $f_{\text{err}}$ in relation to the number of iterations elapsed during the minimisation procedure. The regions pertaining to the different partition levels are bounded by dashed lines and indicated as P1–P5. As can be seen for each partition, the error function decreases to and stabilises at a plateau level. The minimisation procedure switches from P1 to P2 after the relative change of $f_{\text{err}}$ was below the given tolerance, and the error function again decreases until a new plateau level is reached. This pattern is repeated until the estimated parameters have stabilised for the last partition level. From Fig. 6 it is clear that the successive partition levels enable the determination of the reference distribution of parameters to be estimated.

In Fig. 7, the evolution of the deviation measures, as introduced in (35), are displayed for the same example. All deviation measures decrease significantly during the first three partition levels, and after these they continue to decrease, but at a lower rate. The final values of the deviation measures are $\Delta E_1 = 0.0257$, $\Delta E_2 = 0.0184$, $\Delta \beta = 0.0957$, $\Delta \alpha = 0.00177$. Obviously, the material parameter $\alpha$ is the easiest to estimate since $\alpha$ is constant over the membrane and only a single value needs to be estimated. The estimates of the distributions of the two stiffnesses $E_1$ and $E_2$ are also satisfying, with a deviation from the reference values of only a few percent. The distribution of $\beta$ appears to be the most difficult distribution to estimate. The standard deviation for $\beta$ is about 0.10 rad, which is equal to about 5.7°. The difference between the estimated and the reference principal directions is further illustrated in Fig. 8.

The finite element mesh is shown in addition to the estimated orientations of the principal direction 1, that is along the coordinate $z_1$, indicated as lines within the elements. For the sake of clarity, we show results for a coarser mesh ($n_\Phi = 4$ with $n_\Theta = 2$), but the resulting value of $\Delta \beta$ at that partition level is approximately the same as for $n_\Phi = 5$ (compare with Fig. 7). In some finite elements the estimated orientations do not show good agreement with the reference orientations. As can be seen in Fig. 8, the general tendency is that the estimation procedure succeeds well in estimating the orientations of the principal
axes. We compare now the estimated membrane stress with the reference stress, and we do this in terms of the maximum principal Cauchy stress $\sigma$. The evolution of the deviation measure $\Delta\sigma$ with the number of iterations is shown in Fig. 9. As with the other deviation entities, $\Delta\sigma$ decreases rapidly during the first three partition levels. It then continues to decrease, and at the end of the analysis $\Delta\sigma$ has a value of 0.0189. It should be noted, that even though there might be notable deviations in the estimations of the collagen fibre angle $\beta$, the deviation in the estimated maximum stress is very low. This is an important finding, because in many situations the final goal of an inverse analysis is the computation of the stresses in the material.

The number of elements $n_e$ used in the finite element mesh and the number of load levels $n_l$ affect the estimation procedure. In general, a finer mesh leads to a more complex problem since more material parameters have to be estimated. Table 1 lists some estimation data resulting from different analyses. We start by comparing the first two data rows, pertaining to estimations for $n_l = 4$, but different numbers of partition levels ($n_p = 4$ and 5). As is to be expected, the estimation with five partition levels requires more iterations to be completed when compared with $n_p = 4$. For $n_p = 5$, one additional partition level needs to be evaluated, and more material parameters are to be estimated, which, in general, leads to a slower convergence rate. It is worth noting, however, that for the three variables $E_1$, $E_2$ and $\beta$, the deviation measures are actually larger for $n_p = 4$, in spite of the fact that the FE mesh is coarser in this case, which means that less material parameters need to be estimated. For the two other parameters $\sigma$ and $\epsilon$, the trend is just the opposite. For $n_p = 3$, the FE mesh consists of only 16 elements, which was considered to be too crude to yield meaningful results, and for $n_p > 5$, the computational time became unmanageable for a standard PC.

Table 1 also compares estimation data for cases with different number of load levels ($n_l$), but the same number of partition levels ($n_p = 4$). Concerning the number of iterations required to pass the tolerance criterion, there is no consistent trend. The solution with $n_l = 2$ required most iterations, and the solution with $n_l = 4$ required the least. The case for $n_l = 8$ had the largest number of evaluation points. We would have expected to obtain a faster convergence rate than for $n_l = 4$, but this was not the case. Also in terms of the final value of the error function, the case with $n_l = 4$ gives the best result. When comparing the deviation measures for the cases $n_l = 2, 4, 8$, the solution for $n_l = 4$ again gives the best results, except for the variable $\Delta\beta$, where $n_l = 8$ gives the smallest deviation.

6. Discussion

In the present paper, a procedure for estimating the material and structural properties of nonlinear elastic, inhomogeneous and anisotropic vascular membranes in their passive states has been proposed. The pursued procedure of inverse analysis has been used in many previous works to determine parameters pertaining to the material behaviour of isotropic and/or homogeneous structures [2,20,5,28,13,22,23]. A severe limitation with these approaches is, however, that there are many structures to which they cannot be applied reliably, in particular to biological structures since they are both anisotropic and inhomogeneous. A few studies have addressed the issue of inhomogeneity [15,26,17]. The parameter estimation procedure proposed here has particular applications in cardiovascular biomechanics, where, for example, stresses in vascular walls such as cerebral aneurysm walls need to be estimated in order to facilitate the assessment of aneurysm rupture risk.

In Section 1, we introduced the parameter $k$ as a representative measure of deformation used to quantify the deviation between the measured experiment data and the FE analysis predictions. An obvious choice for $k$ is the set of nodal displacements obtained from experiments and from computational analyses. The advantage with this choice is that no extra treatment of the data and no further assumptions are required since the displacements are a natural outcome of both experiments and computations. However, in the proposed method, we have used the 2D right Cauchy–Green tensor as a deviation measure. A drawback with this choice is that additional assumptions are needed (we have to approximate the displacement field in the test specimen by use of shape functions) and additional computations are required (we have to determine the components of the right Cauchy–Green tensor from the nodal displacements); but we are estimating parameters that are related to the elements rather than the nodes, we wanted to work with a measure that pertains to the elements...
that is as sensitive as possible to changes in the material properties in an element. These considerations motivated us to use the right Cauchy–Green tensor.

An important feature of the proposed approach is the element partition strategy, which gives the estimation procedure its robustness. In addition, it also makes the procedure insensitive to initial values of the material parameters, at least when the estimation procedure was assessed with the reference distribution as employed in the numerical example of Section 5. The reason for the insensitivity is that in the first phase only four material parameters — taken to pertain to the whole membrane — are estimated. The total error function is then minimised with respect to only four parameters. Since the outcome of this first estimation phase is rather insensitive to initial values, the method as a whole will be insensitive as well since the estimated values from the first phase serve as initial values for the preceding phases. We wanted to emphasise here that we are not claiming uniqueness on behalf of the finally obtained parameter estimations; we only claim that the estimation method as such appears to be fairly insensitive with regard to initial values. This does not, however, necessarily imply that estimations of more complex membranous vascular tissues (in terms of structure and material parameter fields) will also be independent of the initial values.

The estimation procedure was assessed by the use of a reference distribution for the two initial stiffnesses $E_1$, $E_2$, the collagen fibre angle $\beta$ and the material parameter $a$ describing the nonlinearity of the collagen fibres exhibit (it was taken to be constant over the membrane). The proposed procedure was able to reestablish the reference distributions of these parameters in a satisfying way. Measures were defined to quantify the deviation of the estimated from the reference values. Standard deviations for the estimated material and structural parameters of just a few percent were obtained. This is a good result, especially by considering the fact that the standard deviation for the resulting maximum principal stress was below 1% in most of the investigated cases.

The use of a constant value of $a$ rests on the assumption that all fibres in the membrane essentially have the same mechanical properties and that any variation in $a$ may be sufficiently compensated for by adjusting $E_1$ and $E_2$. In fibre-reinforced tissues, the progressive stiffening of collagen fibres during stretching is a very important feature of the mechanical behaviour of vascular walls. The parameter $a$ that accounts for this stiffening is, therefore, of pivotal importance when modelling these tissues. We have performed some preliminary studies using a varying field $a = a(x_1, x_2)$, and one initial observation is that the convergence rate in the estimation procedure decreases. Since the analyses for a constant $a$ are already very time-consuming we have not explored reference fields with varying $a = a(x_1, x_2)$ any further.

When assessing the proposed inverse method, it has been assumed that the data obtained from experiments — applied pressure levels, imposed boundary conditions, initial geometry, nodal displacements, etc. — are accurate. In a real experimental situation all of these factors will be associated with some amount of error, which may, in principle, affect the robustness and accuracy of the proposed inverse method. This pertains above all to the measurements of nodal displacements, where some kind of image analysis technique has to be utilised. The element partition method introduced here does seem to render the estimation method very robust, and a limited amount of error in the input data should not jeopardise the robustness of the method. A systematic sensitivity analysis with regard to possible errors in these input data is, however, beyond the scope of the present paper.

The influence of the number of load levels on the parameter predictions was also investigated. In general, the more load levels that are used the more data are available when determining the unknown parameters, and the less ill-conditioned the problem is as a whole. We would have expected that by an increase of the number of load levels $n_L$ a better convergence rate and more accurate estimations of the parameters would have been obtained. In general, this will be the scenario, but we were not able to reproduce this pattern in our results. When using $n_L = 2, 4, 8$, we did not see any consistent pattern of decreasing number of iterations required or increasing accuracy in estimations.

The relatively high computational time was a problem in the present inverse analysis. The posed problem is ill-conditioned, and the convergence rate is relatively low. For the used predefined tolerance, it took between 500 and 1000 iterations before the results were below that tolerance. The use of more complex structures would require even lower tolerances with more iterations. Above all, the computational time increases rapidly with the number of nodes and elements defined in the problem. In the numerical example provided here we have used a maximum number of $n_L = 256$ finite elements, but for challenging clinically relevant analyses, a significantly larger number of elements is required, which does not necessarily cause any serious problems. The estimation procedure may to a large extent be parallelised. The two most time-consuming steps in the estimation procedure are the computation of the gradient vector $\mathbf{n}$ and the minimisation of the error function $r_{err}$ in the direction of $\mathbf{q} = \lambda \mathbf{n}$. The computation of the gradient vector can easily be parallelised. The minimising procedure is more difficult to parallelise since consecutive values of $\lambda$ depend on the previous results; but also this procedure can be improved by using parallel computations. An increase in mesh size also increases the number of unknown material parameters to be estimated, and this might prove to be a more serious problem than the computational time. By increasing the number of elements with a factor of 4, the deviation between estimates and reference fields did not increase.

In summary, we established an inverse methodology for estimating the material properties of nonlinear elastic, inhomogeneous and anisotropic vascular membranes. In particular, we proposed a versatile constitutive model for vascular membranes, which includes four material and structural parameters whose distributions are to be estimated. The estimation procedure consists of the following main steps: (i) perform (inflation) experiments on a vascular membrane whose properties are to be determined; (ii) define a corresponding FE model; (iii) minimise an error function with respect to the material parameters, which quantifies the deviation between experimental data and FE predictions. In a simple numerical example, we used the proposed procedure to reestablish the given reference distributions. The standard deviations of the estimated parameters (as compared to the reference field) were within just a few percent, which is a satisfying result for several applications in cardiovascular biomechanics.

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**Table 1**

Estimation data for cases with different values of $n_L$, $n_0$ and $n_0$, i.e. partition, number of elements and load levels, respectively

<table>
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<tr>
<th>$n_L$</th>
<th>$n_0$</th>
<th>$n_0$</th>
<th>Iteration</th>
<th>$r_{err}$</th>
<th>$\Delta C_1$</th>
<th>$\Delta C_2$</th>
<th>$\Delta C_0$</th>
<th>$\Delta C_0$</th>
<th>$\Delta q$</th>
<th>$\Delta q$</th>
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<td>642</td>
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