Estimation of the distributions of anisotropic, elastic properties and wall stresses of saccular cerebral aneurysms by inverse analysis

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A new method is proposed for estimating the elastic properties of the inhomogeneous and anisotropic structure of saccular cerebral aneurysms by inverse analysis. The aneurysm is modelled as a membrane and the constitutive response of each individual layer of the passive tissue is characterized by a transversely isotropic strain energy function of exponential type. The collagen fibres in the aneurysm wall are assumed to govern the mechanical response. Four parameters characterize the constitutive behaviour of the tissue: two initial stiffnesses of the collagen fabric in the two in-plane principal directions, one parameter describing the degree of nonlinearity that the collagen fibres exhibit and the other structural parameter, i.e. the angle which defines the orientation of the collagen fibres. The parameter describing the fibre nonlinearity is assumed to be constant, while all others are assumed to vary continuously over the aneurysm surface. Two model aneurysms, with the same initial geometry, boundary and loading conditions, constitutive behaviour and finite-element discretization, are defined: a ‘reference model’ with known distributions of material and structural properties and an ‘estimation model’ whose properties are to be estimated. An error function is defined quantifying the deviations between the deformations from the reference and the estimation models. The error function is minimized with respect to the unknown parameters in the estimation model, and in this way the reference parameter distributions are re-established. In order to achieve a robust parameter estimation, a novel element partition method is employed. The accordance between the estimated and the reference distributions is satisfactory. The deviations of the maximum stress distributions between the two models are below 1%. Consequently, the wall stresses in the cerebral aneurysm estimated by inverse analysis are accurate enough to facilitate the assessment of the risk of aneurysm rupture.

Keywords: inverse analysis; cerebral aneurysm; membrane; constitutive modelling; inhomogeneous; anisotropic
1. Introduction

Aneurysms are abnormal dilatations of the vascular wall which may rupture and cause a major and, in many cases, lethal bleeding. They are especially prevalent in the thoracic artery, the abdominal aorta and the arterial circle of Willis at the base of the brain. In the cerebral vasculature, the saccular type of aneurysm dominates and is mainly found in the branching regions of the circle of Willis (Austin et al. 1993; MacDonald et al. 2000; Canham et al. 2006). The saccular cerebral aneurysm tends to form a sac-like expansion of the parent artery. Cerebral aneurysms are often very thin (Canham & Ferguson 1985; Abruzzo et al. 1998) and may, therefore, be modelled as a membrane (Kyriacou & Humphrey 1996; Kroon & Holzapfel 2007, in press). A rupture risk assessment of existing aneurysms is frequently performed on the basis of their size and morphology, but criteria based on the mechanical fields in the aneurysm wall (such as stress and strain) may potentially contribute to a more reliable prediction of the rupture risk. In order to obtain reliable predictions of the mechanical behaviour of aneurysm walls, suitable constitutive models are needed and the related material (and structural) parameters need to be determined.

In many situations, the determination of material parameters is difficult or even impossible to perform. Hence, in several cases, an inverse analysis is an alternative way for obtaining material (and structural) parameters. Roughly speaking, the 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 boundaries (e.g. Kavanagh & Clough 1971; Berzi et al. 1994; Cailletaud & Pilvin 1994; Govindjee & Mihalic 1996; Delalleau et al. 2006; Lei & Szeri 2006; Lu et al. 2007; Rajagopal et al. 2007). Often, inverse analysis is a convenient approach for use within the field of biomechanics and biomedical engineering, where one has little (or no) control of the geometry and/or the material properties in question. Cartilage and intervertebral discs, for example, are two collagenous soft tissues that have been examined by inverse analysis (Laible et al. 1994; Cohen et al. 1998; Soulhat et al. 1999; Huang et al. 2003), and aneurysmal arterial tissue has also been analysed by the use of inverse methods (Lu et al. 2007, in press). In addition, Kyriacou et al. (1997) show that the material behaviour of neo-Hookean membranes can be characterized by employing the inverse finite-element (FE) method. However, soft biological tissues are inhomogeneous. Kauer et al. (2002) present an interesting method for determining the viscoelastic material properties of soft tissues by inverse analysis under in vivo conditions. Seshaiyer & Humphrey (2003) address the issue of inhomogeneity using a subdomain method. They estimate the material properties of soft biological membranes by considering a local region that is assumed to be fairly homogeneous. Boundary displacements and inner displacements are used to identify material properties for this local region. Khalil et al. (2006) address the same issue by estimating the elastic modulus in atherosclerotic vascular tissue. They lump the material into a few regions which are assumed to exhibit a homogeneous and isotropic elastic behaviour locally, but they use different elastic moduli for different regions; but to the authors’ knowledge, an inverse analysis has never been used to determine the distribution of anisotropic properties inherent in biological tissues.
In the present paper, we propose a method for estimating the elastic properties of inhomogeneous and anisotropic membranous structures by inverse analysis. In particular, we focus on the application of this method to a saccular cerebral aneurysm. We use a reference FE solution of the aneurysm exposed to internal pressure that we obtain with a (given) reference distribution of the material and structural parameters. The task of the estimation method is then to re-establish this reference distribution.

This paper is organized as follows. In §2 we define the problem to be solved; in particular, the geometry, the boundary and loading conditions and the constitutive and FE models of a saccular cerebral aneurysm are provided. In §3 an outline of the parameter estimation procedure is given with a specific focus on the definition of an error function, the related minimization procedure and on the deviation measures to be used. Section 4 provides specific data for the aneurysm to be analysed and presents the numerical results, while §5 contains a discussion of the proposed approach and summarizes the findings.

2. Problem formulation

Two model aneurysms are defined, subsequently designated as ‘reference model’ and ‘estimation model’. Both models are based on the same initial geometry, boundary conditions, constitutive behaviour and FE discretization. For the reference model the distributions of the material and structural parameters are given, while for the estimation model the parameters are to be estimated. In §2a we define the geometry and boundary conditions of the model aneurysms; in §2b we briefly describe the constitutive model employed; while in §2c we present the FE model.

(a) Geometry and boundary conditions

The initial geometry of the model aneurysm is illustrated in figure 1. We introduce a (global) Cartesian coordinate system which we assume to be right-handed and characterized by the set $e_1$, $e_2$ and $e_3$ of basis vectors. The components of a vector $X = X_A e_A$, $A = 1, 2, 3$, are referred to these axes, and we label $X_A$ as the referential coordinates. The (initial) geometry of the aneurysm is modelled as a membranous spherical cap. The cap is defined as a part of a sphere with radius $R_0$ that has been cut off at $X_3 = 0$. The central point of the spherical cap is located at a distance $Z_0$ ($Z_0 < R_0$) above the $X_1–X_2$ plane. We introduce two curvilinear coordinates, $S \in [0, S_0]$ and $\theta \in [0, 2\pi]$, where $S$ is assumed to be 0 at the fundus of the aneurysm and $S_0 = R_0 [\pi - \arccos (Z_0 / R_0)]$ at the neck, while $\theta$ is an angular coordinate defined in the $X_1–X_2$ plane, as shown in figure 1. In addition, we introduce a (local) two-dimensional coordinate system with the coordinates $\zeta_1$ and $\zeta_2$, where $\zeta_1$ is oriented in the circumferential direction, always parallel to the $X_1–X_2$ plane, and $\zeta_2$ is parallel to the curvilinear coordinate $S$. The aneurysm is assumed to have a constant initial wall thickness $H_0$.

The aneurysm is clamped along its neck and exposed to an internal inflation pressure $p$. This implies that $t_n = -p$ on the inner surface of the aneurysm, where $t_n$ is the normal component of the traction vector $t$. Finally, we introduce a displacement vector $u$, which is represented uniquely by $u = u_a e_a$, $a = 1, 2, 3$, where the three real numbers $u_a$ are the components of $u$. At $S = S_0$ we describe the boundary conditions $u_1 = u_2 = u_3 = 0$. 

Constitutive model

We assume that the mechanical behaviour of the aneurysm wall is governed by the collagen fabric (Canham et al. 1991; Austin et al. 1993; Abruzzo et al. 1998), and that the constitutive response is characterized by the use of a strain energy function, subsequently denoted as $\Psi$. We model the aneurysm wall as a laminate, consisting of $n$ discrete and distinct layers (plies) of collagen fibres. Within a layer with index $i$, the collagen fibres are perfectly aligned in the direction characterized by the angle $\phi_i$, defined with respect to a two-dimensional in-plane reference coordinate system. The collagen fibre angles $\phi_i$ are defined according to

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

where the value $n \geq 2$ provides the even number of tissue layers. Thus, the fibre orientations are uniformly distributed over the whole azimuthal range (figure 2a). We also assume that the in-plane principal directions 1 and 2 of the membrane are associated with fibre orientations $\phi_1$ and $\phi_{n/2 + 1}$, respectively, and that the fibre stiffnesses $k_i$ of the different layers are defined by the two given stiffnesses $k_1$ and $k_{n/2 + 1}$ (associated with the directions $\phi_1$ and $\phi_{n/2 + 1}$, respectively) according to (figure 2b)

$$
\begin{align*}
    k_i &= k_1 + \frac{k_{n/2 + 1} - k_1}{n/2} (i - 1), \quad 2 \leq i \leq n/2, \\
    k_i &= k_{n/2 + 1} + \frac{k_1 - k_{n/2 + 1}}{n/2} (i - n/2 - 1), \quad n/2 + 2 \leq i \leq n,
\end{align*}
$$

Figure 1. Initial geometry of the model for a saccular cerebral aneurysm ($Z_0 < R_0$).

(b) Constitutive model

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\end{align*}
$$

Figure 1. Initial geometry of the model for a saccular cerebral aneurysm ($Z_0 < R_0$).
for \( n = 8 \). The orientation of the principal coordinate system \( z_0^1 - z_0^2 \) of the collagen fabric with respect to \( z_1^1 - z_2^2 \) is defined by an angle \( \beta \), as shown in figure 2a.

The strain energy function \( \Psi \) for the collagenous soft tissue is assumed to be

\[
\Psi = \sum_{i=1}^{n} \frac{k_i}{8a} \{ \exp[a(I_{4i} - 1)^2] - 1 \}, \quad I_{4i} = C : A(\phi_i, \beta),
\]

which is a similar function to the one proposed by Holzapfel et al. (2000). In equation (2.3) the index \( i \) denotes layer-specific entities, \( A(\phi_i, \beta) \) is a structure tensor, defined as \( A = M \otimes M \) with components \( [M] = [\cos(\phi_i + \beta) \ \sin(\phi_i + \beta) \ \ 0]^T \), \( C \) is the right Cauchy–Green tensor and \( k_i \geq 0 \) are non-negative layer-specific material parameters. The exponent \( a > 0 \) describes the degree of nonlinearity that the collagen fibres exhibit. Finally, we require that \( I_{4i} > 1 \).

The second Piola–Kirchhoff stress tensor is obtained as \( S = 2\partial \Psi / \partial C \), and the symmetric Cauchy stress tensor as \( \sigma = J^{-1} FSF^T \), where \( F \) is the deformation gradient, and \( J = \det F = (\det C)^{1/2} > 0 \) is the Jacobian determinant (Holzapfel 2000); note that we assume incompressibility, implying \( J = 1 \). In index notation, the elasticity tensor in the material description \( \hat{C} = 2\partial S / \partial C \) takes the form

\[
(C)_{\alpha\beta\gamma\delta} = 2 \frac{\partial S_{\alpha\delta}}{\partial C_{\gamma\delta}},
\]

where the indices \( \alpha, \beta, \gamma \) and \( \delta \) pertain to the reference coordinate system \( \zeta_1^1 - \zeta_2^2 \), as shown in figure 2a. The components of a corresponding stiffness tensor \( (C')_{\alpha\beta\gamma\delta} \) can be obtained for a (rotated) principal coordinate system \( \epsilon_1^1 - \epsilon_2^2 \).

The initial stiffnesses of the collagen fabric in the two principal directions \( \epsilon_1^1 \) and \( \epsilon_2^2 \), which we subsequently label as \( E_1 \) and \( E_2 \), respectively, are defined as \( E_1 = (C')_{1111} I \) and \( E_2 = (C')_{2222} I \), where \( I \) is the identity tensor. For a given set of parameters \( E_1 \) and \( E_2 \), the stiffness coefficients \( k_1, \ldots, k_n \) are uniquely defined. Thus, for a material point in the aneurysm the anisotropic, nonlinearly elastic behaviour is defined by the entities \( E_1, E_2, a \) and \( \beta \).
Now, we make the assumption that the parameters $E_1$, $E_2$ and $\beta$ vary continuously over the aneurysmal surface, whereas $a$ is assumed to have a constant value. The distributions of the material and structural parameters for the reference model and the estimation model may then be written in terms of the curvilinear coordinates as

$$E_1 = E_1(S, \theta), \quad E_2 = E_2(S, \theta), \quad \beta = \beta(S, \theta), \quad a = \text{const.} \quad (2.5)$$

In order to be able to handle $\beta$ in an appropriate way within a computational framework, the three-dimensional aneurysm surface is mapped to a two-dimensional circular plane surface with radius $S_0$ by the mapping $X(S, \theta) \mapsto \Phi(X(S, \theta))$, $X \in \mathbb{R}^3$ and $\Phi(X) \in \mathbb{R}^2$, where $X$ is the position vector in the reference configuration and

$$[\Phi(X(S, \theta))] = [S \cos \theta \quad S \sin \theta]^T \quad (2.6)$$

are the components of the vector function $\Phi$ (figure 3). The mappings of the coordinates $S$, $\theta$, $\zeta_1$ and $\zeta_2$ are also illustrated in figure 3.

(c) **Finite-element model**

The aneurysm surface is divided into an FE structure using four-node membrane elements. It is assumed that the material behaviour is constant within each element. In the directions of $\theta$ and $S$, 24 and 12 membrane elements are used, respectively. The resulting FE model is shown in figure 4. Note that collapsed elements are used at the fundus.
3. Parameter estimation method

(a) Outline of the estimation method

The parameter estimation method involves three steps.

Experimental testing is needed for those specimens whose material characteristics are to be determined. *In vitro* inflation tests, for example, on cerebral aneurysms can be performed by marking a number of points on the membrane surface by certain markers defining nodal points in space. The positions of the nodal points and the membrane thicknesses at those points are then measured in the load-free configuration. Finally, the specimen is pressurized to different load levels, and the displacements of the nodal points are registered during inflation. Hence, the initial geometry, the boundary conditions, the applied loads and the three-dimensional deformation pattern are provided by experiments. A similar approach can be used for the *in vivo* situation where a specimen such as an aneurysm is deformed during a cardiac cycle, and imaging data are recorded and analysed during changes in loading so that the three-dimensional deformation pattern of the specimen may be identified. It is worth noting that the identification of the initial geometry, the boundary conditions and the applied loads is not a straightforward task for some *in vivo* situations.

An FE model of the tested specimen can then be generated from the given nodal points. It is suggested that the network of the points on the membrane surface serves as the FE structure. Hence, the initial geometry of the (tested) specimen used for the FE analysis is generated from the nodal positions and the membrane thicknesses at those nodes. We characterize the constitutive behaviour of the membrane by a function $\Psi = \Psi(q(X), \ldots)$, where $q$ is a vector containing all parameters of the constitutive model to be determined. In the
FE analysis, the material and structural parameters are assumed to be constant within an element, but are allowed to vary discretely between different elements. Since the initial geometry, the boundary conditions and the applied loads are known from the experiments, the displacements of the nodal points may be predicted through an FE analysis.

An error function \( f_{\text{err}} = f_{\text{err}}(q) \) is then defined with the aim of identifying the deviations between the experimental data and the FE predictions. In particular, the components of the right Cauchy–Green tensor are used in the error function \( f_{\text{err}} \) to be minimized with respect to \( q \). This minimization procedure establishes the required estimates of the material and structural parameters for all FE involved, which represent the outcome of the inverse analysis.

Since we have not performed experimental tests on cerebral aneurysms according to the above-described protocol, we use here an FE solution in terms of the three-dimensional deformation (and stress) patterns obtained with given initial geometry, boundary conditions, applied loads and distributions of material and structural parameters. This FE solution then serves as a reference. The task of the parameter estimation method is now to re-establish the reference distributions of the material and structural parameters. This is carried out by the minimization of an error function and the use of deviation measures to be described in the following.

(b) Definition of an error function and related minimization procedure

We define an error function \( f_{\text{err}} \) according to

\[
 f_{\text{err}} = \sqrt{\frac{1}{3 n_{\text{gp}} n_e n_{\text{II}}} \sum_{l=1}^{n_{\text{II}}} \sum_{k=1}^{n_e} \sum_{j=1}^{n_{\text{gp}}} \sum_{i=1}^{3} \left[ C_{i,j,k,l}^{\text{est}}(q) - C_{i,j,k,l}^{\text{ref}}(q_{\text{ref}}) \right]^2}, \quad (3.1)
\]

where \( n_{\text{II}}, n_e, n_{\text{gp}} \) denote the number of load levels, the total number of FEs (here \( 24 \times 12 = 288 \)) and the number of Gauss points, respectively. The entities \( C_{i,j,k,l}^{\text{est}} \) and \( C_{i,j,k,l}^{\text{ref}} \) denote the components of the right Cauchy–Green tensor obtained from the estimation FE model (indicated by superscript ‘est’) and from the reference FE model (indicated by superscript ‘ref’), respectively. The index \( i \) pertains to the three independent components of the in-plane right Cauchy–Green tensor (two normal components and one shear component), the index \( j \) pertains to the different Gauss points in the elements, the index \( k \) is related to the summation over all elements, and the index \( l \) to the summation over all considered load levels.

The vector \( q \) contains all material and structural parameters to be estimated with the estimation model, which, in matrix notation, reads

\[
 [q] = [E_{1,1}, \ldots, E_{1,n_e}, E_{2,1}, \ldots, E_{2,n_e}, \beta_1, \ldots, \beta_{n_e}, \alpha]^T. \quad (3.2)
\]

The vector \( q_{\text{ref}} \) contains the corresponding parameters for the reference model. The error function \( f_{\text{err}} \) now has to be minimized with respect to the parameters in \( q \), implying that \( q \rightarrow q_{\text{ref}} \).

In order to attain a robust parameter estimation method, an element partition is employed, meaning that the element structure is divided into subgroups. For the model aneurysm of figure 4 it is illustrated in figure 5, where five element
Figure 5. (a–e) The model aneurysm from figure 4 is partitioned into five levels of element refinements, denoted as P1–P5. The five levels with 1, 4, 24, 72 and 288 element subgroups are displayed in the mapped planes, as defined in equation (2.6). In P5, the subgroups consist of single elements and no further refinement is possible.
partitions are displayed in the mapped planes, as defined in equation (2.6). The partitions correspond to five levels of element subgroups. In partition 1 (figure 5a) all elements are included in one (large) group. In the next partitions, as shown in the figure 5b–d, the element structure is divided into 4, 24 and 72 element subgroups, respectively. In partition 5 (figure 5e), the subgroups consist of single elements, i.e. 288 subgroups, and no further refinement is possible.

We now consider \( n_{eg} \) to be the number of element groups within a partition and define the modified parameter vector \( \mathbf{q}_{eg} \), which, in matrix notation, reads

\[
[\mathbf{q}_{eg}] = \begin{bmatrix} E_{1,1}, \ldots, E_{1,n_{eg}} & E_{2,1}, \ldots, E_{2,n_{eg}} & \beta_{1}^{eg}, \ldots, \beta_{n_{eg}}^{eg} & a \end{bmatrix}^T. \tag{3.3}
\]

The data in \( q_{eg} \), pertaining to a specific element group, is used for all elements within that group. Note that the parameters \( E_1 \), \( E_2 \) and \( a \) can be distributed within the different elements in a group in a straightforward way. However, since \( \beta \) is defined in a local reference coordinate system and since each point on the aneurysm surface has its own local coordinate system, the administration of \( \beta \) requires some further treatment. The entities \( \beta_{1}^{eg}, \ldots, \beta_{n_{eg}}^{eg} \) in equation (3.3) denote element group values and are defined in the mapped plane \( \Phi_1-\Phi_2 \) as shown in figure 3. In the plane \( \Phi_1-\Phi_2 \), the angle \( \beta_{i}^{eg} \), for example, defines a vector with components \( \mathbf{a}_{eg} = [\cos \beta_{i}^{eg}, \sin \beta_{i}^{eg}]^T \). In the global coordinate system \( X_1-X_2-X_3 \), the directions of the coordinates \( \zeta_1 \) and \( \zeta_2 \) are defined by the vectors \( \mathbf{a}_1 \) and \( \mathbf{a}_2 \), respectively; however, in the mapped plane, the coordinates \( \zeta_1 \) and \( \zeta_2 \) are instead associated with the mapped vectors \( \mathbf{a}_1^\Phi = \mathbf{a}_1 \) and \( \mathbf{a}_2^\Phi = \mathbf{e}_3 \times \mathbf{a}_1 \), respectively. The vector \( \mathbf{a}_{eg} \), which defines the principal direction 1 in the mapped plane, is projected on the vectors \( \mathbf{a}_1 \) and \( \mathbf{a}_2 \), and through the relations \( \mathbf{a}_{eg} \cdot \mathbf{a}_1 = \cos \beta \) and \( \mathbf{a}_{eg} \cdot \mathbf{a}_2 = \sin \beta \) the element-specific value \( \beta \) can then be determined.

In the minimization of \( f_{err} \), a steepest descent method is employed (cf. Press et al. 1994). The method consists of the following steps.

— Loop over all partitions
  — While \( \Delta f_{err}/f_{err} > \text{tolerance} \) do
    — Calculate the direction \( \mathbf{n}_{eg} = -\partial f_{err}(\mathbf{q}_{eg})/\partial \mathbf{q}_{eg} \) of the steepest descent
    — Find the value \( \lambda^* \) that minimizes the function \( f_{err}(\mathbf{q}_{eg} + \lambda \mathbf{n}_{eg}) \)
    — Calculate the change of \( f_{err} \) as \( \Delta f_{err} = f_{err}(\mathbf{q}_{eg}) - f_{err}(\mathbf{q}_{eg} + \lambda^* \mathbf{n}_{eg}) \)
    — Update the parameter vector according to \( \mathbf{q}_{eg} \leftarrow \mathbf{q}_{eg} + \lambda^* \mathbf{n}_{eg} \)
  — End
— End

The inner loop is repeated for each partition until the relative change \( \Delta f_{err}/f_{err} \) is less than a prescribed tolerance. Then the routine switches to the next partition level. For the first partition, four parameters are estimated, pertaining to all elements. When the relative change of the error function is less than a predefined tolerance, the estimation is refined by switching to the next partition. The four material and structural parameters obtained with the first partition then serve as initial values for the estimation of the second partition. For this second partition, \( 4 \times 3 + 1 = 13 \) parameters are estimated, pertaining to four element groups, and henceforth. The number of parameters to be estimated is 4, 13, 73, 217 and 865 for the five different partitions, respectively. For the final
partition, where \( q_{\text{est}} = q \), and once the estimation loop is completed for this last partition, the material and structural parameters have been estimated, and the problem is solved.

\( \text{(c) Deviation measures} \)

In order to quantify the deviation between the distributions of the estimated and the reference parameters, we introduce the following variables that measure the related deviations:

\[
\begin{align*}
\Delta \bar{E}_1 &= \left( \frac{1}{n_{\text{gp}} n_e n_{\Pi}} \sum_{l=1}^{n_{\Pi}} \sum_{k=1}^{n_e} \sum_{j=1}^{n_{\text{gp}}}(E_{1,j,k,l}^{\text{est}} - E_{1,j,k,l}^{\text{ref}})^2 \right)^{1/2}, \\
\Delta \bar{E}_2 &= \left( \frac{1}{n_{\text{gp}} n_e n_{\Pi}} \sum_{l=1}^{n_{\Pi}} \sum_{k=1}^{n_e} \sum_{j=1}^{n_{\text{gp}}}(E_{2,j,k,l}^{\text{est}} - E_{2,j,k,l}^{\text{ref}})^2 \right)^{1/2}, \\
\Delta \bar{\beta} &= \left( \frac{1}{n_{\text{gp}} n_e n_{\Pi}} \sum_{l=1}^{n_{\Pi}} \sum_{k=1}^{n_e} \sum_{j=1}^{n_{\text{gp}}} (\beta_{j,k,l}^{\text{est}} - \beta_{j,k,l}^{\text{ref}})^2 \right)^{1/2}, \\
\Delta \bar{a} &= \left( \frac{a^{\text{est}} - a^{\text{ref}}}{a^{\text{ref}}} \right)^2.
\end{align*}
\]

(3.4)

In several situations, it is not an aim to estimate the material properties but rather the resulting stress in the structure. Therefore, we also introduce the entity \( \Delta \bar{\sigma} \), which denotes a deviation measure of the resulting maximum principal Cauchy stress \( \sigma \) according to

\[
\Delta \bar{\sigma} = \left( \frac{1}{n_{\text{gp}} n_e n_{\Pi}} \sum_{l=1}^{n_{\Pi}} \sum_{k=1}^{n_e} \sum_{j=1}^{n_{\text{gp}}} (\sigma_{j,k,l}^{\text{est}} - \sigma_{j,k,l}^{\text{ref}})^2 \right)^{1/2}.
\]

(3.5)

The entities in equations (3.4) and (3.5) may be interpreted as a kind of standard deviation of the relative error of the estimates, labelled by the overline.

The parameter estimation method was implemented in MATLAB.

4. Numerical example

(a) Specified data

A saccular cerebral aneurysm sac was defined with the initial geometry of \( R_0 = 8 \) mm, \( Z_0 = 6 \) mm and \( H_0 = 200 \) \( \mu \)m (Canham et al. 1996; Mimata et al. 1997; MacDonald et al. 2000). The aneurysm wall is assumed to consist of \( n = 8 \) layers of collagen fibres (Canham et al. 1999). The FE mesh had a total number of \( n_e = 288 \) elements (24 in the \( \theta \) direction and 12 in the \( S \) direction) and the corresponding node number was \( n_n = 289 \). The membrane elements had \( n_{\text{gp}} = 4 \) Gauss points and the same material properties were assumed to apply for all Gauss points within an element. The aneurysm was exposed to \( n_{\Pi} = 4 \)

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pressure load levels, and the load levels $p_1, ..., p_i, ..., p_{n_{II}}$ are linearly distributed according to $p_i = i p_{\text{max}} / n_{II}$, $1 \leq i \leq n_{II}$, where $p_{\text{max}} = 60 \text{ kPa}$ was the maximum pressure applied.

We defined the reference distributions of the material properties $E_1$, $E_2$ (in MPa) and $a$, and the geometric parameter $\beta$, all for the reference aneurysm model, according to

$$E_1 = 10 + 2 \frac{X_1 + X_2}{R_0}, \quad E_2 = \frac{7}{10} E_1, \quad \beta = \frac{\pi}{4} \frac{X_1 + X_2}{R_0}, \quad a = 1. \quad (4.1)$$

The functional forms in equation (4.1) have been chosen to reflect a physiologically reasonable level of anisotropy, but are otherwise arbitrary. The element properties were defined by the coordinates $X_1$ and $X_2$ of the element centroid, together with the expressions in equation (4.1). These reference values established the vector $\mathbf{q}^{\text{ref}}$.

When minimizing the error function $f_{\text{err}}$ with respect to $\mathbf{q}_{\text{eg}}$, the estimation routine was instructed to switch to a new element partition level when a relative difference between consecutive values of $f_{\text{err}}$ was below a tolerance of $\Delta f_{\text{err}} / f_{\text{err}} = 0.01$.

(b) Numerical results

The initial values of the parameters in the estimation model were chosen to be constant distributions with $E_1 = E_2 = 20 \text{ MPa}$, $\beta = 0$ and $a = 5$. Figure 6 shows the evolution of the error function $f_{\text{err}}$ versus the number of iterations elapsed during the minimization procedure. The regions pertaining to the different partition levels (P1–P5) are indicated by dashed lines. As shown, the error function $f_{\text{err}}$ decreases to and stabilizes at a minimum level for each partition. If $\Delta f_{\text{err}} / f_{\text{err}}$ is
smaller than a given tolerance of accuracy, then the minimization routine switches to the next partition. This pattern is repeated until the estimated material and structural parameters have stabilized for the last partition level. From figure 6 it is clear that the successive partition levels enable the determination of the reference values $E_1$, $E_2$, $b$ and $a$ for each FE. The partition 5 clearly requires the largest number of iterations before the predefined tolerance is achieved. The large number of parameters to be estimated in the last partition makes the minimization problem ill-conditioned and this causes the rather slow convergence rate, as observed in figure 6.

In figure 7, the evolutions of four variables that measure the deviations between the estimated and reference parameters are displayed. The four variables are as given in equation (3.4). As far as the two initial stiffnesses $\Delta E_1$ and $\Delta E_2$ of the collagen fabric are concerned, they increase during the first partition. This is somewhat peculiar, but since a single value of $E_1$ and $E_2$ is assumed to apply for the whole aneurysm, this effect is obviously present. For subsequent partitions, $\Delta E_1$ decreases monotonically, whereas $\Delta E_2$ displays a second peculiarity as it again increases during the final part of partition 2. The deviations of the two initial stiffnesses reach the values $\Delta E_1 = 0.047$ and $\Delta E_2 = 0.043$ (4.7 and 4.3%) at the end of the analysis.

The distribution of $\beta$ appears to be the most difficult to estimate. The deviation between the estimated and the reference directions is 0.12 rad (or 6.9°; figure 8). Here the FE mesh is displayed in the $\Phi_1$–$\Phi_2$ plane, and the estimated

Figure 7. (a–d) Evolutions of $\Delta E_1$, $\Delta E_2$, $\Delta \beta$ and $\Delta a$ that measure the deviations between estimated and reference values according to equation (3.4). The regions pertaining to the different partition levels are indicated by dashed lines.
and the reference directions after the final partition 5 are included as curves within the individual elements (the estimations are denoted by solid curves and the reference directions by dotted curves). In some elements the deviation between estimates and reference orientations is notable. The general tendency, though, is that the parameter estimation method succeeds well in re-establishing the reference orientations of the principal axes.

Returning to figure 7, we note that the variable $\frac{D}{C_{22}}$ decreases drastically during the first four partition levels. For the last partition, the value of $\frac{D}{C_{22}}$ starts to oscillate and it reaches a final value of 0.05 (5%). This oscillation indicates that the problem is ill-conditioned.

We now compare the estimated membrane stress with the reference stress, and we do this in terms of the maximum principal Cauchy stress $s$ according to equation (3.5). The evolution of the variable $\Delta \hat{a}$ is shown in figure 9. It decreases rapidly during the first four partition levels and $\Delta \hat{a}$ has a value of 0.0085 (0.85%) at the end of the analysis. It should be noted that even though there might be notable deviations in the estimations of the angle $\beta$ (and the remaining material parameters), the deviation measure in the estimated maximum principal Cauchy stress is very low. This is an important outcome, because in many situations the final goal of an inverse analysis is the estimation of the stress distribution in the material.

5. Discussion and summary

In the present paper, an inverse FE method has been proposed with the aim of estimating material and structural properties and wall stresses of saccular cerebral aneurysms. The approach of an inverse analysis has also been used in several previous works in order to determine parameters pertaining to the material behaviour of isotropic and/or homogeneous structures (Berzi et al. 1994; Kyriacou et al. 1997; Cohen et al. 1998; Soulhat et al. 1999; Huang et al. 2003; Lu et al. 2007, in press). A notable limitation with all these approaches is, however, that several materials are in fact both inhomogeneous and anisotropic. Soft biological tissue is an example of such a material. Within this context, some
papers have addressed the issue of inhomogeneity (Kauer et al. 2002; Seshaiyer & Humphrey 2003; Khalil et al. 2006), but to the authors’ knowledge, the inverse method proposed here is the first attempt to predict the distribution of anisotropic material properties.

In order to introduce material anisotropy in a convenient way, the tissue was modelled as a multilayered membrane, where the collagen fibres for each layer have a preferred direction and these different directions are uniformly distributed over the azimuthal range. Anisotropy was then introduced by assigning a different stiffness to different layers. The layer stiffness is assumed to vary linearly with the angular coordinate $\phi$ according to equation (2.2) (figure 2b). However, this linear dependence is not self-evident. For example, instead of the distribution in figure 2b, a smooth circular function could also be used. The influence of other possible forms of stiffness distributions has not been explored, but a moderate change of the functional type should not have any significant influence on the model behaviour.

The deviation measures for the two initial stiffnesses $\Delta E_1$ and $\Delta E_2$ of the collagen fabric in the two principal directions $\zeta_1$ and $\zeta_2$ and the exponent $\Delta \hat{a}$ characterizing the degree of nonlinearity that the collagen fibres exhibit were 4.7, 4.3 and 5%, respectively, whereas the deviation measure for the fibre angle $\beta$ was 6.9°. It is straightforward to further decrease the number of these deviations by lowering the tolerance $\Delta f_{err}/f_{err}$ below 0.01. For example, a tolerance value of 0.001 has provided the measures for $\Delta E_1$ and $\Delta E_2$ in the range of 2%. It is worth noting that these results do not depend on the choice of the initial parameter values in the estimation model. An important outcome of the analysis is that in spite of these deviations between estimated and reference properties, the deviation of the estimated maximum principal stress with respect to the reference stress was below 1%. This is accurate enough to be used, for example, in the rupture risk assessment of cerebral aneurysms.

Figure 9. Evolution of $\Delta \hat{\sigma}$ that measure the deviations between estimated and reference values of the maximum principal Cauchy stress according to equation (3.5). The regions pertaining to the different partition levels are indicated by dashed lines.
Since distributions of material and structural properties are to be estimated, the number of unknown parameters quickly increases with the number of FEs used for the structure to be analysed. In the proposed parameter estimation method, we therefore assumed that only the parameters $E_1$, $E_2$ and $\beta$ vary continuously over the aneurysm surface, whereas $a$ is assumed to be constant. The assumption for $a$ is probably valid, provided that all collagen fibres through the thickness of the aneurysm wall exhibit similar mechanical behaviours. However, aneurysmal walls are known to exhibit a higher rate of collagen turnover when compared with healthy arterial walls (Abdul-Hussien et al. 2007). As a consequence, newly produced collagen in aneurysmal walls tends to result in collagen fabrics with lower stiffnesses than for collagen in healthy arterial walls (Busuttil et al. 1980; Barnes 1985). Thus, the collagen fibres in an aneurysmal wall will not have the same mechanical stiffness, but it may be conjectured that this weakening can be compensated for by adjusting the local values $E_1$ and $E_2$, while maintaining a constant value of $a$. Another option, of course, is to allow $a$ to vary continuously as well. This has not been explored in the present study.

In an accompanying study, we investigate some numerical properties related to the proposed parameter estimation method, including the influence of the number of FEs and load levels on the estimation results. Preliminary results show that the required CPU time increases drastically, but the values of the deviation measures do not increase as the model size increases. Thus, the obtained results indicate that the proposed estimation model is robust and that further refinements of the FE mesh will basically not produce severe obstacles to the method.

In the present study, we applied pressures in the range from 0 to 60 kPa. This may be compared with the physiological systolic blood pressure for a human, which is approximately 16 kPa. From an estimation point of view, a large pressure range is preferable, since it better exposes the nonlinear behaviour of soft tissues than a narrow range does. Under in vitro conditions, this wide pressure range can be applied, but under in vivo conditions, the pressure range is defined by the diastolic and systolic pressures in the artery. Thus, the pressure range available is narrower under in vivo conditions. We have not examined the influence of a narrower pressure range on the estimation procedure, but it is conjectured that the convergence rate will be slower.

The inverse FE method presented here may serve as a vital basis for assessing the rupture risk of cerebral aneurysms. For the time being, this assessment is performed on the basis of the lesion size, which is a rather crude criterion. If accurate estimators of aneurysm wall stresses could be obtained in vivo, then this would most likely contribute to a more reliable assessment of the risk of rupture. A precursor for determining the stress fields would then be the estimation of the material and structural properties of the aneurysm wall, as suggested here. However, if the Cauchy stresses in the wall are to be estimated, then the wall thickness of the aneurysm dome has to be known. Under in vitro testing conditions, the distribution of the wall thickness can be obtained, but under in vivo conditions this turns out to be problematic. With currently existing technology, it is possible to establish the three-dimensional morphology of cerebral aneurysms in vivo (and thereby the surface geometry of the aneurysm), but in vivo measurements of the aneurysm wall thickness (which can vary regionally) are virtually unattainable by current diagnostic tools (Ma et al. 2007). Future
technical progress may, however, make this possible, and then it is straightforward to use the proposed estimation method for predicting the actual wall stresses in aneurysms under \textit{in vivo} conditions.

In summary, a method for estimating the material and structural properties and wall stresses of saccular cerebral aneurysms has been proposed. Four parameters have been introduced that characterize the constitutive behaviour of the collagenous soft tissue: two initial stiffnesses $E_1$ and $E_2$ of the collagen fabric in the in-plane principal directions $\zeta_1^1$ and $\zeta_2^1$ of the tissue, one angle $\beta$ that defines the orientation of the principal directions of the material with respect to a reference coordinate system, and the other parameter $a$ describing the degree of nonlinearity of the collagen fibres. With the chosen tolerance value, the estimated parameter distributions of $E_1$, $E_2$ and $a$ deviate from the reference distributions by approximately 4–5\%. The deviation in the angle $\beta$ is 6.9\%, while the estimated maximum principal Cauchy stress is very accurate, with a deviation of less than 1\%. For the proposed parameter estimation method the results obtained are promising. Provided that future diagnostic tools are able to measure the wall thickness of the cerebral aneurysm \textit{in vivo}, the proposed method may be used to estimate wall stresses in aneurysms under \textit{in vivo} conditions, which may facilitate the assessment of the risk of rupture of diagnosed cerebral aneurysms.

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