1 Introduction

Cerebral aneurysms are estimated to be prevalent in 1–5% of the adult population. Although most cerebral aneurysms remain asymptomatic, they may rupture, resulting in subarachnoid hemorrhage, which has a very high associated mortality (45% die within 30 days). Of those that survive, an estimated 30% will face moderate to severe disability [1]. Consequently, if an aneurysm is detected, clinical intervention may be deemed appropriate. However, the procedure is not without risk to the patient; interventional repair of an unruptured aneurysm has related mortality and morbidity rates of <2.5% and <6%, respectively [2]. Hence it would be beneficial to be able to distinguish those aneurysms most at risk of rupture. This would assist clinical diagnostic procedures and avoid the undesirable consequences of an unnecessary operation. Moreover, even if the elective repair was without risk, given the large number of the population affected by cerebral aneurysms, there would be significant financial cost to treat all cases. The ultimate ambition of computational models of aneurysm development is to aid clinical diagnosis on a patient-specific basis. However, due to the significant biological complexity coupled with limited histological information, such models are still in their relative infancy. Current research focuses on simulating the evolution of an aneurysm with an aim to yield insight into the growth and remodeling (G&R) processes that give rise to an aneurysm’s inception, enlargement, stabilization, and rupture.

Autopsies of human aneurysms reveal that the walls are characterized by disrupted internal elastic laminae, a thinned media and reduced smooth muscle cells [3]. Kondo et al. [4] used an animal model to induce cerebral aneurysms in rats and examined aneurysms at nonbranching points. These authors concluded that cerebral aneurysms at nonbranching sites and saccular aneurysms at branching sites can occur under the same etiologic conditions. The site of origin is strongly related to hemodynamic stress. In fact, it is postulated that high wall shear stress (WSS) is related to the initiation of cerebral aneurysm formation [5–8]. It is also suggested that high spatial gradients of the WSS may lead to destructive remodeling [3,9]. However, while high WSS is associated with the inception of a cerebral aneurysm, low WSS is thought to give rise to its continued enlargement [10].

Most previous models for aneurysm evolution (see, for example, Refs. [11–17]) have not considered the influence of the local hemodynamic environment on the G&R of the tissue. Chatziprodromou et al. [18] recognized the importance of the hemodynamic environment. They illustrated how the WSS evolves with a conceptual aneurysm evolution model; however, in their study, the G&R is prescribed and a simple linear mechanical model of the arterial wall is adopted. Feng et al. [19,20] appeared to be the first to explicitly model the coupling between the evolution of the cerebral aneurysm and the hemodynamic environment; i.e., they proposed that the modulus of the artery is reduced if the WSS is above a critical threshold. However, they modeled the artery as a linearly elastic material obeying Hooke’s law; realistic microstructural models of the arterial wall are required to gain more insight into the adaptive G&R of the arterial wall during aneurysm formation.

We adapt here the constitutive model of Holzapfel et al. [21] to incorporate microstructural aspects of the tissue and the abdominal aortic aneurysm evolution model developed in Ref. [11] to simulate saccular cerebral aneurysm development. The aneurysm evolution model is implemented into a novel computational...
framework that enables tissue G&R to be explicitly coupled to the local hemodynamic environment. In the present study we explore hypotheses coupling degradation of elastious constituents to deviations of WSS and spatial WSS gradients (WSSGs) from normotensive levels.

2 Methodology

2.1 Nonlinear Elasticity. A geometric nonlinear membrane theory (e.g., see Refs. [22,23]) is adopted to model the steady deformation of the arterial wall. The internal carotid artery is treated as a thin cylinder of undeformed radius \( R \), length \( L_1 \), and thickness \( H \) relating to the undeformed reference configuration \( \Omega_0 \). The thickness of the media and adventitia are denoted \( H_9258 \) and \( H_9251 \), respectively. It is subject to a physiological axial prestretch \( \lambda_2 \) and a constant systolic pressure \( p \) equal to 16 kPa, which causes a circumferential stretch of \( \lambda_0 \). The initial loaded configuration \( \Omega'_0 \) is thus a cylindrical tube of length \( L = \lambda_2 L_1 \), radius \( r = \lambda_0 R \), and thickness \( h = H/(\lambda_2 \lambda_0) \); see Fig. 1.

A body-fitted coordinate system is used to describe the membrane with Lagrangian coordinates \( \theta_a \) (\( a=1,2,3 \)) parallel to the midplane and the \( \theta_3 \) coordinate perpendicular to it. The midplane is positioned at \( \theta_3=0 \); the upper and lower surfaces of the membrane have coordinates \( \theta_3=\pm H/2 \). The principal of stationary potential energy is the governing equation for the steady deformation of the arterial wall. It requires that the first variation of the total potential energy vanishes \([24]\), i.e.,

\[
\delta \Pi_{\text{int}} - \delta \Pi_{\text{ext}} = 0
\]

where \( \delta \Pi_{\text{int}} \) represents the variation of the internal potential energy stored in the arterial wall, while \( \delta \Pi_{\text{ext}} \) is variation of the external potential energy caused by the normal pressure that acts on the artery. The WSS is four orders of magnitude lower than the external potential energy caused by the normal pressure, i.e., \(-2.5 \text{ Pa} \), as opposed to a systolic pressure of 16 kPa; hence its contribution to the virtual work is negligible. Consequently, the governing equation is

\[
\int_V \delta \Pi dV = \int_s \rho (\mathbf{\hat{a}}_i \cdot \delta \mathbf{s}) ds = 0
\]

where \( \delta \mathbf{s} = \delta (\mathbf{X} + \mathbf{u}) = \delta u_i \mathbf{A}_i, \quad ds = |\mathbf{a}_1 \times \mathbf{a}_2| d\theta_1 d\theta_2, \quad \mathbf{a}_i = (\mathbf{a}_i \times \mathbf{a}_j)/|\mathbf{a}_1 \times \mathbf{a}_2|, \) and \( \Psi \) is the strain-energy function (SEF). Here, we make the approximation that the area elements of the upper and lower surfaces are equal to that of the midplane. The assumption that the strain field in the aneurysm tissue is uniform through the thickness of the arterial wall, i.e., the strain field of the off-midplane is equal to that of the midplane, implies that the SEFs are independent of \( \theta_3 \). This enables an immediate integration yielding

\[
\int_0^\pi \int_0^{L_1} \{ \delta H_9258 \Psi_{\mathbf{a}_1} + H_9251 \Psi_{\mathbf{A}_1} \} - \rho (\mathbf{a}_1 \times \mathbf{a}_2) \cdot \delta u_i \mathbf{A}_i d\theta_1 d\theta_2 = 0
\]

Appropriate functional forms for the spatially and temporally heterogeneous strain-energy functions for the media \( \Psi_{\mathbf{a}_1} \) and the adventitia \( \Psi_{\mathbf{A}_1} \) must be specified. Details of the numerical formulation to solve Eq. (11) can be found in Ref. [11].
2.2 Collagen Remodeling. A developed aneurysm typically is a thin collagenous membrane. Models of aneurysm development must address the degradation of the elastinous constituents and the adaptive G&R of the collagen fabric. In general, the mechanical response of the elastinous constituents is always defined with respect to the same reference configuration. However, given that collagen fibers are continually being produced and degraded, the natural reference configuration of the collagenous constituents evolves. Watton et al. [11] proposed a framework that captures the gross effect of fiber deposition and degradation in altered configurations by evolving the natural configuration in which the collagen fabric begins to be recruited to load bearing. We briefly overview the key concepts of the framework to address the remodeling of the collagen. For a detailed account the interested reader is referred to Refs. [11,13,25], which consider models of abdominal aortic aneurysm development and Refs. [16,17] for cerebral aneurysm development. To gain a conceptual understanding it is sufficient to visualize the uniaxial stretching of a strip of an arterial tissue with the collagen fibers arranged parallel to the direction of the stretch.

2.2.1 Recruitment Stretch $\lambda_R$. It is assumed that the gross mechanical response of a population of collagen fibrils of varying undulation can be represented by a nonlinear function of stretch, which is defined relative to the onset of recruitment of the fibrils to load bearing. To simplify the material representation, we visualize a hypothetical fiber, hereon referred to simply as fiber, whose mechanical response represents the gross mechanical response of the population of fibrils as they are recruited to load bearing.

The stretch in the fiber is defined with respect to the reference configuration in which it is recruited to load bearing, denoted $\Omega_R$, while the stretch in the elastic is always defined with respect to the initial (unloaded) reference configuration $\Omega_0$. Let us consider a strip of tissue with collagen fibers aligned along its length, then collagen fibers are recruited to load bearing when the unstrained tissue is stretched by a factor $\lambda_R$ and their stretch is defined with respect to this recruitment configuration. A simple relationship between the elastic stretch $\lambda$ and the collagen stretch $\lambda^C$ exists, i.e.,

$$\lambda^C = \frac{\lambda}{\lambda_R} \quad (12)$$

The significance of relationship (12) is that the recruitment stretch $\lambda_R$ can remodel to maintain the stretch in the collagen to an equilibrium value while the stretch in the elastic increases as the aneurysm dilates.

2.2.2 Attachment Stretch $\lambda^A_R$. Collagen fibers are in a continual state of deposition and degradation [26]. We assume that collagen fibers always attach in a constant state of stretch, i.e., $\lambda^A_R > 1$, independent of the current configuration of the tissue

2.2.3 Collagen Remodeling Via the Recruitment Stretch. Remodeling of the recruitment stretch is subtle and it is helpful to visualize what is occurring on the scale of the collagen fibers. Figure 2 illustrates the effects of fiber deposition and degradation for a tissue that is stretched and held at fixed length while remodeling occurs. Note that the figure depicts hypothetical collagen fibers, each of which represents the mechanical response for a population of collagen fibrils of varying undulation. The figure illustrates that the microstructural changes in the tissue, which arise as a result of the physiological turnover of collagen fibrils, can be captured by remodeling the recruitment stretch $\lambda_R$. It is important to appreciate that the time for the tissue to remodel from state 4 to state 5 (see Fig. 2) is dependent on the turnover rate of the collagen fibers. Equivalently, the rate at which the recruitment stretch remodels is related to the turnover rate of the fibers.

2.3 Strain-Energy Functions for Heterogeneous Aneurysmal Tissue. The arterial wall is modeled as two layers. The inner layer models the mechanical response of the media (and intima), with contributions from the elastinous constituents (ground substance, elastin fibers, and passive smooth muscle cells) and a double helical pitch of collagen fibers. The outer layer models the mechanical response of the adventitia, which is considered to have a small elastinous contribution and a double helical pitch of collagen fibers. The mechanical response of each layer is modeled as the sum of a neo-Hookean SEF and a highly nonlinear SEF, which represents the mechanical response of the collagen [21]. Recent experiments by Gundiah et al. [27] and theoretical analysis [28] support the suitability of the neo-Hookean SEF to explicitly represent the mechanical behavior of elastinous constituents. The constitutive model is adapted to incorporate microstructural aspects of the tissue: a degradation function for the elastinous constituents, and microstructural recruitment stretch and concentration variables for the collagen fibers. Four fields of recruitment stretches are required to characterize the recruitment to load bearing of the positively and negatively wound collagen fibers throughout the medial and adventitial layers of the artery. This enables the remodeling of the collagenous fabric to be simulated. Similarly, four fields of fiber concentration variables are required. These define the ratio of the mass density of the collagen fibers at time $t$ to the mass density at time $t=0$ and enable the growth/atrophy of the collagenous fabric to be simulated.

The elastinous contributions in the medial and adventitial layers are multiplied by a normalized spatially and temporally dependent function, say, $m^E(\theta_1, \theta_2,t)$. This is employed to prescribe the degradation of the elastinous constituents, where $m^E(\theta_1, \theta_2,t)=1$. A field of spatially and temporally dependent fiber recruitment stretches $\lambda_R^j(\theta_1, \theta_2,t)$ and (normalized) fiber concentration $m^j(\theta_1, \theta_2,t)$ variables are defined throughout the midplane of the arterial wall, where the subindex $j$ stands for the media $M$ or the adventitia $A$. The SEFs are thus

$$\Psi^M = m^E \Psi^M \left( E_{11} + E_{22} + E_{33} \right)$$

$$+ \sum_{p=2}^\infty m^E_{p} \Psi^E_{p} \left( A^E \left( \frac{E_{11} + E_{22} + E_{33}}{E_{p}} \right)^2 - 1 \right)$$

(13)

for $X_3 \in [-H/2, (H+2H_M)/2]$, and

$$\Psi^A = m^E \Psi^A \left( E_{11} + E_{22} + E_{33} \right)$$

$$+ \sum_{p=2}^\infty m^A_{p} \Psi^A \left( A^C \left( \frac{E_{11} + E_{22} + E_{33}}{E_{p}} \right)^2 - 1 \right)$$

(14)

for $X_3 \in [(H+2H_A)/2, H/2]$. The GL strains in the collagen fibers are denoted by $E_{ij}^C(\theta_1, \theta_2,t)$. The fibers are orientated at an angle of $\gamma_j$ to the azimuthal axis, where $p$ denotes the pitch of $\gamma_j$ relative to the azimuthal axis in the unloaded reference configuration $\Omega_0$. The material parameters for the elastinous constituent are denoted by $K_j^E$, while $K_j^A$ and $A^j$ are parameters that relate to the collagen fabric. The GL strains $E_{ij}^C$ of the collagen fibers are a function of the GL strains of the elastin resolved in the directions of the collagen fibers, denoted $E_{ij}^R$. Thus,

$$E_{ij}^C = \frac{E_{ij}^R}{1 + 2E_{ij}^R}$$

(15)

where $E_{ij}^R = \sigma_{ij}^R / \lambda^R_j$, $\lambda^R_j(\theta_1, \theta_2,t)$ are the recruitment stretches, and

$$E_{ij}^R = E_{11} \sin^2 \gamma_j + E_{22} \cos^2 \gamma_j$$

$+ 2E_{12} \sin \gamma_j \cos \gamma_j$.

2.3.1 Value for Attachment Stretch and Initial Values for Recruitment Stretches. The initial values for the recruitment stretches and a value for the attachment stretch must be defined. Given that the model of the artery initially has a cylindrical geometry the magnitudes of the recruitment stretches are spatially uniform...
Fig. 2 Attachment of collagen fibers in altered configurations: (1) \( \Omega_0 \) is the unloaded reference configuration of the tissue in which the fibers have a characteristic waviness and the stretch \( \lambda \) of the elastin is 1; (2) \( \Omega_0^s \) is the initial recruitment configuration of the collagen fibers. The fibers have straightened out (\( \lambda_\theta = 1 \)) and begin to bear load; (3) \( \Omega_1^s \) is the initial loaded configuration such that the stretch in the collagen fibers is the equilibrium value, i.e., at systolic pressure the stretch of the fibers is \( \lambda_0^s \). Thereby, the tissue is in homeostasis, although the fibers are in a continual state of degradation and deposition, new fibers will attach with identical levels of stretch to those that decay. Thus, no changes occur to the mechanical properties of the tissue; (4) suppose the tissue is stretched further and, for the purposes of this example, held at fixed length. The stretch of the tissue is then \( \lambda = \lambda_\theta \lambda_0^s \), where \( \lambda_\theta > \lambda_0^s \). The collagen fabric is no longer in material equilibrium: Subsequent fiber deposition and degradation will result in a change in the configuration of the collagenous tissue. New fibers attach to the tissue so that at the new systolic configuration their stretch is \( \lambda_0^s \). The old fibers decay, and the distribution of collagen fibers changes. The naturally occurring turnover of the fibers will proceed to restore stretch in all the fibers to equilibrium levels; (5) all of the old fibers have decayed and have been replaced with new fibers of stretch \( \lambda_0^s \). The artery reaches a new equilibrium configuration \( \Omega_1^s \); (6) \( \Omega_1^n \) is the new recruitment configuration of the collagen fibers following remodeling of the tissue; (7) if the tissue is contracted back to the reference configuration \( \Omega_0 \), the crimp of the collagen will have increased. Equivalently, the factor the tissue must be stretched for the collagen to be recruited has increased. Hence, the effects of deposition and degradation in altered configurations can be captured by remodeling the recruitment stretch. Note that the time for the tissue to remodel from state (4) to state (5) is dependent on the turnover rate of the collagen fibers, i.e., the half-life. Equivalently, the rate at which the recruitment stretch remodels is dependent on the turnover rate of the fibers.

throughout the membrane. However, the values for the recruitment stretches in the media and adventitia differ due to the different orientations of the fibers in each of these layers.

The value for the attachment stretch \( \lambda_0^m \) is defined to be the stretch in the collagen fiber at systole at \( t=0 \). For the healthy artery, the collagen fiber does not bear significant load until the upper end of physiological pressures. To determine a suitable value for \( \lambda_0^m \) we assume that the medial collagen fibers (with predominant azimuthal orientation) are recruited to load bearing at diastole, i.e., when the circumferential stretch is \( \lambda_0^D = \lambda_0^D \), where \( \lambda_0^D \) denotes the cyclic variation in the circumferential stretch from diastolic to systolic pressure. This implies initial values \( \lambda_0^m = \lambda_0^D \) for the medial recruitment stretches (\( \lambda_0^M \) and \( \lambda_0^R \)) of

\[
\lambda_0^m = \lambda_0^D = \lambda_0^m |_{t=0} = \lambda_0^m |_{t=0} = (\lambda^D/\lambda^D)^2 \cos^2 \gamma_M + (\lambda^D/\lambda^D)^2 \sin^2 \gamma_M)
\]

Consequently, the attachment stretch, which is defined to be equivalent to the stretch of the medial collagen fibers at systole at \( t=0 \), i.e., \( \lambda_0^M |_{t=0} = \lambda_0^M |_{t=0} \), can be deduced to be

\[
\lambda_0^M = \lambda_0^M |_{t=0} = \lambda_0^M |_{t=0} = \frac{\sqrt{\lambda_0^D \cos^2 \gamma_M + \lambda_0^D \sin^2 \gamma_M}}{\lambda_0^D |_{t=0}}
\]

Finally, the initial values of the adventitial recruitment stretches are determined so that the stretch of the adventitial collagen fibers at systole at \( t=0 \) equals the attachment stretch, i.e.,

\[
\lambda_0^A = \lambda_0^A |_{t=0} = \frac{\sqrt{\lambda_0^D \cos^2 \gamma_A + \lambda_0^D \sin^2 \gamma_A}}{\lambda_0^A |_{t=0}}
\]

where \( \gamma_M \) and \( \gamma_A \) denote fiber orientations of the medial and adventitial collagen fibers relative to the azimuthal axis in the unloaded configuration.

2.4 Geometry, Physiological Data, and Material Parameters. The basilar and internal carotid arteries have diameters in the range 3–5 mm [14]. Monson et al. [29] reported the wall thickness of an unloaded middle cerebral artery to be ap-
proximately 1/5 of the thickness of the outer radius and that the average in vivo axial stretch of fresh human cerebral blood vessels to be 1.31 [30]. The unloaded geometry of our artery model has a radius $R$ of 1.6 mm and the wall thickness $H$ is 0.375 mm. In the systolic configuration, the artery has a radius $r_S$ of 2 mm, an axial prestretch $\lambda_A$ of 1.3, and a circumferential stretch of 1.25. The relative radius change during the cardiac cycle for the carotid artery decreases with age: approximately 13% in young adults (aged 15 years) to 5% in the elderly (aged 70 years). A 10% pulsation is representative of males/females aged 30 years [31]. We assume a 10% pulsation, which implies a diastolic radius $r_D$ of 1.82 mm. The deformed domain length $L$ is chosen to be eight times the systolic radius, i.e., 16 mm.

We choose a systolic pressure $p$ of 16 kPa (i.e., 120 mm Hg); this is consistent for subjects in the supine position [31]. We assume that the elastic constituents bear 80% of the load at systole. For our model of the human internal carotid artery fiber orientations are chosen to be $\gamma_M=30$ deg and $\gamma_A=60$ deg; these are consistent with the fiber orientations for the carotid artery of a rabbit [21]; however, we note that these may not be representative given that orientations are age, species, and vessel dependent.

The assumption that the medial collagen fibers begin to be recruited to load bearing in the diastolic configuration implies that the initial values of the recruitment stretches (see Eq. (16)) are $\lambda_{KM}^R = \lambda_{AM}^R = 1.18$. This implies that the attachment stretch $\lambda_{KM}^C$, which is defined to be the stretch of the medial collagen fibers in the systolic configuration at $t=0$, has magnitude of $\lambda_{KM}^C = 1.07$ (see Eq. (17)) and consequently the GL attachment strain is $E_{at} = ((\lambda_{KM}^C)^2 - 1)/2 = 0.07307$. Lasty, assuming that the stretch of the adventitial collagen fibers is equal to the attachment stretch in the initial systolic configuration implies initial values for the adventitial recruitment stretches (see Eq. (18)) of $\lambda_{AM}^R = \lambda_{AM}^C = 1.20$.

We assume that the media occupy 2/3 of the thickness of the arterial wall (media: $H_M=0.25$ mm; adventitia: $H_A=0.125$ mm), and that the ratio of the medial and adventitial collagen material parameters for the rabbit carotid artery is true for the human carotid artery; i.e., we specify $K_{KM}^C = K_{AM}^C/4$. Furthermore, we assume that the elastic response of the adventitia is an order of magnitude weaker than that of the media, i.e., $K_{KM}^E = K_{AM}^E/10$. The remaining three independent material parameters, namely, $K_{KM}^E$, $K_{AM}^E$, and $A^C$, are determined so that the SEFs adequately model the mechanical behavior of the artery; see Ref. [13] for details. The material parameters for the media and the adventitia, as well as all other values that serve the basis for our subsequent computation, are summarized in Table 1.

The pressure-diameter relationship for our model is shown in Fig. 3. Note that the collagen becomes the dominant load bearer as the pressure is increased above the systolic value. For our model of the internal carotid artery, the systolic (diastolic) axial and azimuthal Cauchy stresses are 135.96 kPa (117.4 kPa) and 138.7 kPa (95.1 kPa), respectively. The axial force is 0.24 N at diastole and 0.22 N at systole.

### 2.5 Hemodynamic Analysis

Here we briefly describe the methodological approach to analyze the hemodynamics. The geometry of the aneurysm is exported as a triangulated surface (STL format) from an in-house finite element code that solves the equilibrium deformation field of the membrane to the meshing suite ANSYS ICEM. To achieve fully developed flow in the region where the aneurysm develops, extensions are attached to the computational domain (see Fig. 4).

An unstructured tetrahedral mesh with prism layers lining the membrane boundary is generated in a scripted-automated manner for the fluid domain (see Fig. 5). This approach enhances grid quality close to the boundary and is the starting point for the creation of an unstructured tetrahedral mesh throughout the remaining volume domain. After meshing, appropriate boundary conditions are applied and the flow (steady Navier–Stokes equations) is solved by ANSYS CFX (ANSYS Inc., Canonsburg, PA), which solves the incompressible Navier–Stokes equations using a finite volume formulation [32,33]. The solver is based on a coupled approach (i.e., velocities and pressure are cast and solved as a single system) and a fully implicit time discretization, where

![Fig. 3 Pressure-diameter relationship for the model of the internal carotid artery. Relative radius change is 10% between systole and diastole (diastolic radius is 1.82 mm) and the onset of load bearing of the collagen begins in the initial diastolic configuration. Note that at systolic pressure the material parameters are determined such that the elastic constituents bear 80% of the load (input data for the model are provided in Table 1).](image-url)

<table>
<thead>
<tr>
<th>Table 1 Geometry, physiological data, and material parameters used for modeling the human internal carotid artery</th>
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<td><strong>Radius</strong></td>
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<td>At diastole</td>
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<td><strong>Wall thickness</strong></td>
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<td>Media</td>
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<td>Adventitia</td>
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<td><strong>Fiber orientation</strong></td>
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<td><strong>Recruitment stretch</strong></td>
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<td><strong>Material parameter</strong></td>
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<td>Elastin (adventitia)</td>
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<td>Collagen (media)</td>
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<tr>
<td>Collagen (adventitia)</td>
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<tr>
<td>Exponential constant for collagen</td>
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needed. An algebraic multigrid variant is used for convergence acceleration [34].

Blood is modeled as a Newtonian fluid with constant density $\rho = 1069$ kg m$^{-3}$ [18,35] and constant viscosity $\eta = 0.0035$ Pa s. Measurements for the flow velocity and volume for the internal carotid artery have been reported by Albayrak et al. [36]. We take the average (left and right combined) values for females (40–59 years) as the inlet condition, i.e., a systolic flow rate of 400 ml min$^{-1}$. The Reynolds number is $Re = 648$ (based on bulk velocity and diameter) and the flow is treated as laminar. Given that there is no detailed knowledge about the specific inlet velocity patterns, we prescribe a Poiseuille inlet flow profile for fully developed flow. A constant pressure of 16 kPa is prescribed at the outlet boundary. At the arterial wall a no slip condition is applied for a rigid wall. The WSSG is calculated as $[\nabla \tau]_i$, where $r$ is the magnitude of the WSS vector. High values of $[\nabla \tau]_i$ indicate regions with high spatial changes in the wall shear stress magnitude; these are typically regions of flow detachment and stagnation points [3].

### 3 Growth and Remodeling

#### 3.1 Elastin Degradation

In our model the geometry is initially cylindrical. Consequently, the initial spatial distributions of the WSS and the WSSG are uniform throughout the domain. To alter the hemodynamic environment, we generate a small outpouching of the arterial domain, i.e., simulate the inception of an aneurysm. To achieve this, a localized degradation of the elastin to deviations of the WSS/WSSG from homeostatic values.

We then explicitly link subsequent degradation of the WSS and the WSSG are uniform throughout the domain. To alter the hemodynamic environment, we generate a small outpouching of the arterial domain, i.e., simulate the inception of an aneurysm. To achieve this, a localized degradation of the elastin to deviations of the WSS/WSSG from homeostatic values.

We take the average (left and right combined) values for females (40–59 years) as the inlet condition, i.e., a systolic flow rate of 400 ml min$^{-1}$. The Reynolds number is $Re = 648$ (based on bulk velocity and diameter) and the flow is treated as laminar. Given that there is no detailed knowledge about the specific inlet velocity patterns, we prescribe a Poiseuille inlet flow profile for fully developed flow. A constant pressure of 16 kPa is prescribed at the outlet boundary. At the arterial wall a no slip condition is applied for a rigid wall. The WSSG is calculated as $[\nabla \tau]_i$, where $r$ is the magnitude of the WSS vector. High values of $[\nabla \tau]_i$ indicate regions with high spatial changes in the wall shear stress magnitude; these are typically regions of flow detachment and stagnation points [3].

| Fig. 4 Vessel geometry with developed aneurysm. The central section illustrated in the figure is the deformable region where the proposed wall model is used. Note that to achieve fully developed flow in the region where the aneurysm develops, extensions are attached to the computational domain. |

| Fig. 5 Computational mesh for the fluid domain |

| Fig. 6 The elastinous constituents are prescribed to degrade in a circular patch in the center of a domain in the unloaded reference configuration $\Omega_0$. The degradation within the inner circular patch of radius $R_i^E$ is prescribed. The degradation in the outer circular annulus, with outer radius $R_o^E$, is linearly interpolated using radial splines between the values on the inner annulus and the values on the outer annulus where no degradation occurs. Throughout the remaining domain no degradation of the elastinous constituents occurs. |

#### 3.2 Collagen Adaption

The adaptive response of the collagen fabric has two key features. Remodeling the reference configurations of the fibers simulates the effect of fiber deposition and degradation in altered configurations. The growth/atrophy of the collagen fabric is simulated by evolving the fiber concentration. Increases (decreases) in the fiber concentration simulates fibroblasts upregulating (downregulating) collagen synthesis and downregulating (upregulating) enzymes that degrade the collagenous matrix.

#### 3.2.1 Remodeling the Recruitment Configuration of Collagen

The turnover of collagen and the consequence of fibers attaching...
in a fixed state of stretch \( \lambda_{0c} \) are simulated by proposing remodeling equations that act to maintain the GL strain in the collagen fibers to an equilibrium value \( E^c_{eq} \) (equivalently the stretch of the collagen fibers to \( \lambda_{eq} \)). This is achieved by remodelling the reference configuration \( \Omega^r \) of the collagen fibers throughout the arterial domain, i.e., remodeling the recruitment stretches. Linear differential equations are proposed for the remodeling of the recruitment stretches according to

\[
\frac{d \lambda_{0c}}{dt} = \alpha \left( E^c_{eq} - E^c_{eq} \right) / E^c_{eq} \tag{21}
\]

with \( E^c_{eq} = ((\lambda_{eq}^2 - 1)/2, \) and the remodeling parameter \( \alpha (\alpha_H^c) > 0 \) is numerically determined so that it corresponds to a prescribed half-life \( \alpha_H^c \) (months) of the collagen fibers. This is achieved as follows: The internal carotid artery is modeled using the physiologically determined set of material parameters, as described. It is initially subject to physiological axial and systolic circumferential stretches and the stretch of the collagen fabric is initially equal to the attachment stretch throughout the artery. The circumferential stretch is then instantaneously increased. The stretches of the collagen increase, and, for the purposes of the analysis, the artery is held in this altered configuration while the collagen remodeling to restore its strain. Two remodeling mechanisms are considered for restoring strain.

(i) A half-life model [26], which models two populations of collagen fibers, i.e., fibers being deposited in the altered configuration with stretch equal to the attachment stretch and the decay of the stretched fibers.

(ii) Remodeling via the recruitment stretch using differential equation (21).

The two remodeling mechanisms are compared to give a value for \( \alpha \) associated with the turnover rate of the collagen fibers (for further details, see Ref. [25]). Collagen in the healthy arterial wall typically has a half-life of 60 days; however, turnover rates may increase to 15 days in hypertensive conditions [37]. Rates are typically regarded to be increased in ayeural tissue [38]; consequently we adopt a half-life of 1 month, which corresponds to \( \alpha = 0.6 \) years \(^{-1} \) for this model.

3.2.2 Growth/Atrophy of the Collagen Fabric. Fibroblasts adhere to the extracellular matrix (ECM) via specialized cell surface receptors, in particular, integrins [39]. The integrins physically link the ECM to the cytoskeleton of the fibroblast. They transduce mechanical signals to the fibroblast interior [40]. Evidence suggests that the integrins act as stretch sensors [41] and enable the fibroblasts to sense changes in the mechanical strains applied to them. In response to increased stretch, they attempt to reduce their stretch and reach a new equilibrium by restructuring their cytoskeleton and ECM contacts; i.e., fibroblasts reconfigure their natural reference configuration (see Fig. 1 in Ref. [41], which illustrates possible responses of fibroblasts on elastic substrates to stretch and relaxation). To simplify the mathematical analysis, we assume that the local reference configuration of the fibroblast cell is identical to that of the collagen fabric it is maintaining. Hence the GL strain of the fibroblast cell, say, \( E^F_p \), is assumed to be equal to the GL strain of the collagen, i.e., \( E^F_p = E_{eq}^c \).

Fibroblasts deposit collagen fibers and secrete proteases to degrade the collagenous material. We assume that the rate of change in the concentration of the collagenous constituents is dependent on the concentration of fibroblasts, say, \( m^F_p \), in the arterial wall; where \( m^F_p \) denotes the ratio of the number density of the fibroblast cells at time \( t \) to the number density at time \( t=0 \). Furthermore, we assume that the concentration of fibroblasts in the arterial tissue is proportional to the concentration (equivalently mass) of collagenous constituents, i.e., \( m^F_p = \xi_p m^c_p \); \( \xi_0 > 0 \). These assumptions imply that the rate of evolution of the collagen fiber concentration \( m^F_p \) can be expressed in terms of the current fiber concentration

\[
\frac{dm^c_p}{dt} = m^F_p \frac{dE^c_p}{dt} \quad \text{and} \quad m^F_p \frac{dE^c_p}{dt} = m^F_p \xi_p \left( E^c_p - E^c_{eq} \right) \tag{22}
\]

where \( E^c_p = E^c_{eq} \) the collagen fabric is in homeostasis; i.e., the secretion of ECM is balanced by the degradation and there is no change in concentration. Hence if \( E^c_p = E^c_{eq} \), it is required that \( E^c_p = E^c_{eq} \). The exact functional form of \( \xi_p \) is unknown. However, if the substrate is stretched, a net positive force acts on the cell, and signaling to the nucleus results in an upregulation of ECM protein expression and a downregulation of collagen expression. Conversely, relaxation of the substrate can trigger different signals resulting in a reversed pattern of protein expression [41], i.e., downregulation of ECM protein expression and upregulation of collagen expression. Although we do not explicitly model protein synthesis and enzymatic degradation, the net result is to stimulate increases/decreases in the ECM. The simplest functional form for \( \xi_p \) that satisfies these requirements is linear, i.e., \( \xi_p = ?(E^c_p - E^c_{eq}) / E^c_{eq} \), and hence we propose the following evolution equation for the collagen fiber concentration:

\[
\frac{dm^c_p}{dt} = \beta m^c_p \left( E^c_p - E^c_{eq} \right) / E^c_{eq} \tag{23}
\]

where \( \beta \) is a phenomenological growth parameter that relates to the rate at which the fibroblasts increase or decrease the mass of the collagenous constituents in response to deviations of stretch from normotensive levels. For the analysis in this paper we consider \( \beta = 0.5, 0.75, 1.0 \).

To simplify the presentation of the results, we define the average fiber concentration \( m^c \) of the medial and adventitial layers, where

\[
m^c = \frac{1}{H M} \left( \frac{m^c_{M} + m^c_{M}}{2} \right) - \frac{1}{H A} \left( \frac{m^c_{A} + m^c_{A}}{2} \right) \tag{24}
\]

3.3 Modeling the Influence of Hemodynamics on Growth and Remodeling. Recall that a small initial dilatation is generated by prescribing a degradation of elastin in a localized region of the tissue. The artery is then allowed to stabilize until it achieves a new homeostasis. The altered geometry alters the hemodynamics in the vicinity of the outpouching. This generates an altered hemodynamic environment in which subsequent degradation of elastin can be linked to deviations of the WSS or the WSSG from homeostatic values.

We suppose that there is a maximum value, say, \( D_{max} \), that the elastinous constituents can degrade per year. For example, \( D_{max} = 0.75 \) means that at most 75% of the existing elastinous constituents are degraded per year. The concentration of elastin \( m^E \) is updated for each time-step as follows:

\[
m^E(\theta_0, \theta_2, t + \Delta t) = m^E(\theta_1, \theta_2, t) \left[ 1 - F_D(\tau, \nabla \tau) \right] (1 - D_{max}) \tag{25}
\]
In a computational fluid dynamics (CFD) study of 20 middle cerebral artery aneurysms, Shojima et al. [10] observed the average magnitude of the WSS at peak systole in the aneurysm region (1.64 ± 1.16 Pa) to be significantly lower than in the healthy vessel region (3.64 ± 1.25 Pa). The authors hypothesized that a (systolic) WSS of approximately 2 Pa is necessary for maintaining the structure of the arterial vessels and a (systolic) WSS lower than 1.5 Pa will lead to apoptosis of the endothelial cells. Based on these data we assume $\tau_{\text{crit}} = 2$ Pa and $\tau_{X} = 0.5$ Pa. The related functional form is illustrated in Fig. 7.

3.3.2 High WSSG. High spatial WSSGs play an important mechanistic link between hemodynamics and vessel wall pathology [9], which is demonstrated by the recent study of Meng et al. [3]. These authors surgically created new branch points in the carotid vasculature of six female adult dogs. In vivo angiographic imaging and CFD simulations revealed the detailed hemodynamic micro-environment, which was then spatially correlated with histologic features showing specific tissue responses. Degenerative remodeling was observed in regions subject to high WSSs and high spatial WSSGs. They hypothesized that such a hemodynamic environment induces matrix metalloproteinase production by endothelial cells and smooth muscle cells, which leads to the type of destructive remodeling that is observed in cerebral aneurysms. Although it is suggested that a combination of high WSSGs and high WSSs leads to degenerative remodeling of the tissue, here we only consider the influence of WSSGs. We define the degradation function $F_D$ that describes the relation between local WSSGs and local degradation of elastin according to

$$F_D(\tau(\theta_1, \theta_2, t)) =\begin{cases} 0, & |\nabla \tau| \leq |\nabla \tau|_{1\text{crit}} \\ \left(\frac{|\nabla \tau - |\nabla \tau|_{1\text{crit}}|}{|\nabla \tau|_{X} - |\nabla \tau|_{1\text{crit}}\right)^2, & |\nabla \tau|_{1\text{crit}} < |\nabla \tau| \leq |\nabla \tau|_{X} \\ 1, & |\nabla \tau| > |\nabla \tau|_{X}\end{cases} \quad (27)$$

We assume $|\nabla \tau|_{1\text{crit}} = 500$ Pa m$^{-1}$ for the onset of elastin degradation and a maximum degradation at $|\nabla \tau|_{X} = 2000$ Pa m$^{-1}$. These values are guided by the initial values of the WSSG in the region of the outpouching of the artery in the computational simulation; i.e., $|\nabla \tau|$ needs to be within the range of values observed for the small outpouching otherwise no degradation of the tissue will occur in the computational simulation. The related functional form is illustrated in Fig. 8.

4 Summary of the Model

Equations (13) and (14) are the (spatially and temporally) anisotropic SEFs for the medial and adventitial layers of the aneurysmal tissue. These functions model the independent reference configurations for the elastin and collagen at each point throughout the membrane. The variation of the total potential energy (9) governs the equilibrium displacement field, and is solved by the finite element method.

The aneurysm develops as the elastin degrades and the collagen fabric adapts to restore its stretch to the homeostatic value, i.e., to the attachment stretch. As the aneurysm develops, volume meshes of the computational domain are generated and the steady hemodynamics are solved automatically. Initially, an elastin degradation is prescribed (see Eq. (19)) and the artery adapts, via collagen G&R, to a new homeostasis. The recruitment configuration of the collagen fibers evolves according to Eq. (21); this simulates remodeling, i.e., the effect of fiber deposition and degradation in altered configurations under the assumption that the fibers attach
to the extracellular matrix in a fixed state of stretch, i.e., the attachment stretch $\lambda^E_0$. The fiber concentrations evolve according to Eq. (23), which simulates fibroblasts responding to increases and decreases in stretch from normotensive levels and adapting the mass of the collagenous constituents. The small change in the geometry alters the spatial distributions of the WSSs and the WSSGs acting on the endothelial layer of the artery. Subsequent elastin degradation is no longer prescribed: Loss of elastin is now explicitly coupled to deviations of the WSS (see Eq. (26)) or WSSG (see Eq. (27)) from homeostatic values. As the elastin degrades, the stretch in the collagen fabric increases to compensate for the loss of load bearing by the elastinous constituents. The collagen fabric continues to evolve according to Eqs. (21) and (23).

5 Numerical Results

Figure 9 illustrates the geometry of the arterial domain at $t=5$ following the development of a small outpouching of the wall. In addition, the prescribed distribution of elastin concentration $m^E$ is also provided. Note that at $t=0$ the artery had cylindrical geometry. Between $t=0$ and $t=4$, the elastin was prescribed to degrade to 50% of its original amount in a small patch in the center of the domain, and for $4 \leq t \leq 5$ no degradation of elastin occurred; this was to enable the collagen to adapt so that the artery achieves a new homeostasis; i.e., the collagen recruitment configuration and fiber concentration evolve until a new equilibrium for the collagen fabric is obtained.

The purpose of enabling the artery to achieve a new homeostasis is so that subsequent degradation of elastin and enlargement of the aneurysm can be attributed solely to the effects of the local hemodynamics. To demonstrate that a new homeostasis is achieved we inspect the GL strains in the elastin and collagen and the collagen fiber concentration at $t=4$ and $t=5$. Figure 10 illustrates the spatial distribution of the GL strains $E_{11}$ and $E_{22}$ in the elastin at $t=4$ and $t=5$. It can be seen that there is a negligible change in the magnitude of the elastin strains as the aneurysm stabilizes. Note that the strains of the elastin are identical in this model in the medial and adventitial layers due to the membrane assumption that the strain field is uniform through the thickness of the arterial wall. However, the collagen fibers have different orientations in the media and adventitia and thus the strain fields are not identical in each layer.
Fig. 11 Green–Lagrange strains of the collagen fibers $E_{M}^{c}$ in the media at $t$ = 4 and $t$ = 5 (a) and (c). At $t$ = 4 the collagen strains are slightly elevated; however, at $t$ = 5, they have restored to homeostatic levels throughout the domain. Average fiber concentration $m^{c}$ in the medial and adventitial layers at $t$ = 4 and $t$ = 5 (b) and (d). The concentration increases to compensate for the loss of elastin and the artery achieves a new homeostasis.

Figures 11(a) and 11(c) show the GL strains $E_{M}^{c}$ of the collagen fibers in the media, while Figs. 11(b) and 11(d) show the average fiber concentration $m^{c}$ (see Eq. (24)) between $t$ = 4 and $t$ = 5, respectively. It can be seen that the collagen fiber strains are restored to equilibrium levels at $t$ = 5, i.e., to the attachment stretch, throughout the artery as the tissue stabilizes. The fiber concentration increases to compensate for the loss of elastin. The stretch of the collagen fabric decreases as the concentration increases. Note that the fiber concentration increases by a factor of approximately 2, which is consistent with the fact that half of the elastin has degraded and the geometry has changed negligibly (see theoretical analysis in Ref. [16]). Figure 12 illustrates the spatial distribution of the magnitudes of the WSS and the WSSG at $t$ = 5: The WSS within the small outpouching has decreased and distal to this region there is elevated WSS; the WSSG has elevated levels in the distal and proximal necks.

We now suppose that the elastin degradation is coupled to the local hemodynamics. We consider the degradation linked to altered levels of WSS; i.e., if the WSS is below a critical magnitude the elastin will degrade. Subsequently, the small outpouching evolves into a large aneurysm. Figure 13 illustrates the evolution of the spatial distribution of WSS, i.e., $τ$, and elastin concentration $m^{E}$, respectively, for $t$ = 6, 7, and 8 years; recall $m^{E}$ defines the concentration of the elastinous constituents in both the medial and adventitial layers. As can be seen the WSS is predominately low within the aneurysm region and that a maximum of the WSS develops downstream of the aneurysm. As the aneurysm enlarges, a local maximum of the WSS is additionally observed within the distal neck region. The evolution of the WSS distribution gives rise to an aneurysm with an asymmetric geometry. The concentration of elastin degrades progressively within the aneurysm region due to the persistently low level of WSS. An asymmetry in the elastin concentration $m^{E}$ develops due to the elevated WSS at the distal neck region.

Figure 14 illustrates axial profiles of the evolution of the radius, WSS, elastin concentration $m^{E}$, and WSSG for $t$ = 5, 6, 7, and 8 years, respectively. It can be seen that a region of high WSS is developed and maintained distal to the aneurysm and regions of high WSSG develop in the proximal and distal necks. As the aneurysm enlarges, the WSS within the dome region decreases. Consequently, the elastin concentration $m^{E}$ progressively decreases within this region. Figure 15 illustrates the evolution of the elastin GL strains $E_{11}^{E}$ and $E_{22}^{E}$ and the collagen GL strains in the media $E_{M}^{c}$ and the adventitia $E_{A}^{c}$ for $t$ = 5, 6, 7, and 8 years, respectively. Note that the elastin strains, which are defined with respect to the unloaded configuration $Ω_{0}$ of the artery, increase significantly, whereas the collagen fibers strains remain relatively low as their recruitment configuration remodels to simulate the effect of fiber deposition and degradation in altered configurations. Figure 16 illustrates the evolution of the average fiber concentration $m^{c}$ (in the medial and adventitia) for $t$ = 5, 6, 7, and 8 years. In this example, the growth rate parameter $β$ is relatively small so that the qualitative behavior of the enlargement of the aneurysms can be analyzed. Consequently, significant increases in $m^{c}$ are not observed and the fiber strains increase to maintain...
Fig. 14 Axial profiles of the evolution of the (a) radius, (b) elastin concentration $m^E$, (c) WSS, and (d) WSSG for $t=5, 6, 7, $ and $8$ years. Degradation of elastin is linked to the level of WSS.

Fig. 15 Evolution of the Green–Lagrange strains (a) $E_{11}$ and (b) $E_{22}$ in the elastin (left) and the Green–Lagrange strain in the collagen in the media (c) $E_{CM}$ and the adventitia (d) $E_{CA}$, for $t=5, 6, 7, $ and $8$ years. Even though the aneurysm is subject to large deformation the collagen strains increase only slightly due to remodeling of the configuration at which they are recruited to load bearing.
mechanical equilibrium to compensate for the loss of the elastin. Increasing the value of $\beta$ would increase $\dot{m}^C$ and reduce the rate of enlargement of the aneurysm.

Figure 17 illustrates the evolution of the aneurysm when the elastin degradation is linked to WSSG. At $t=5$ it can be seen that there is an elevated WSSG of approximately 2000 Pa m$^{-1}$ proximal to the outpouching and 3000 Pa m$^{-1}$ distal to the outpouching. Recall the WSSG degradation scheme prescribes that onset of elastin degradation is modeled if the WSSG exceeds 500 Pa m$^{-1}$ and that maximum degradation occurs if it exceeds 2000 Pa m$^{-1}$. Thus the initial hemodynamic environment degenerates elastin within the proximal and distal neck regions of the small outpouching of the artery. Consequently, an aneurysm forms and propagates upstream and downstream. Notably though due to the greater WSSG at the distal end, the aneurysm propagates downstream faster and the aneurysm develops an asymmetric geometry. As the aneurysm enlarges, the WSSG within the dome decreases below critical levels required for degradation of the elastin; consequently regions in the dome do not continue to degrade. Note that the proximal peak of the WSSG remains approximately constant as the aneurysm evolves; however, the distal peak continues to increase; for example, at $t=8$, it is equal to 10,000 Pa m$^{-1}$.

6 Discussion

We have developed a computational framework to explore the coupling between the G&R of arterial tissue and the hemodynamic environment. The approach is based on a realistic micro-structural model of the arterial wall, and explicitly accounts for degradation of elastin, remodeling the recruitment configuration of the collagen fibers, and increases/decreases in the mass of the collagenous constituents. We explored two hypotheses: The degradation of the elastinous constituents was explicitly linked to either low WSS or high WSSGs. The model enables the qualitative behavior of the evolution of the aneurysm to be explored under such hypotheses.

The low WSS hypothesis leads to almost complete degradation of elastin within the aneurysm dome. This is to be expected as the aneurysm enlarges, a region of slow recirculating flow develops and the WSS within this region is low, i.e., below 1 Pa, and hence elastin continues to be degraded. However, the aneurysm neck continues to enlarge upstream and downstream, slightly faster upstream due to an asymmetry in the WSS distribution. As the aneurysm enlarges at the distal neck there is a secondary peak within the dome of the actual aneurysm, and hence degradation in the distal neck region is ultimately halted. This is not the case at the proximal end where low levels of WSS are observed right into the neck of the aneurysm.

The high WSSG hypothesis leads to aneurysms that propagate upstream and downstream. Due to the fact that the WSS is low...
and relatively uniform within the aneurysm dome the WSSG is negligible within the dome region. Consequently, the elastin constituents do not continue to progressively degrade within the aneurysm when using the high WSSG hypothesis alone. The low WSS hypothesis is necessary to completely degrade the elastin constituents within this region. One limitation of both hypotheses is that neither yielded an aneurysm with a well-defined neck. Given that the neck region of the aneurysm is likely to experience a complex hemodynamic environment, for example, high WSS, high spatial WSSG, and high oscillatory shear index, this raises the question of whether this environment actually gives rise to a protective nonleterious response within this region of the tissue. Although such complex hemodynamics may be associated with degradation of the tissue, most people do not develop aneurysms (there is a natural healthy adaption of the artery without the development of an aneurysm). Hence, we hypothesize that the complex hemodynamic environment of the neck may give rise to a healthy protective response and prevent further degradation of the tissue within this region. This may lead to an aneurysm with a well-defined neck while the dome region continues to remodel and evolve due to the low levels of WSS.

Sluijer et al. [42] observed that flow induced remodeling causes a net increase in collagen turnover with no net increase in collagen mass. Increased turnover rates were observed for both increased and decreased WSSs from current normotensive values and remained elevated until the WSS was restored via remodeling. It is thought that flow is directed to suboptimal remodeling. To incorporate such remodeling, i.e., by relating the remodeling rate parameter α to deviations of the WSS from normotensive values. This would act to increase the rate of remodeling of the reference configuration of the collagen in certain regions of the aneurysm.

Mimata et al. [43] examined 15 cerebral aneurysm walls and compared with control vessels. They stained for Type III collagen in both the luminal and the abluminal layers. In situ hybridization showed that the signals for collagen Type III mRNA on fibroblastic and smooth muscle cells were higher in the aneurysmal walls than the control arteries, suggesting upregulation of Type III collagen transcription in the cerebral aneurysmal wall. They suggested that fibroblasts and smooth muscle cells in the aneurysmal wall may step up the synthesis of Type III collagen to strengthen the aneurysmal wall. Ultimately, the aneurysm predominately consists of a collagenous tissue maintained by fibroblasts. Although for most unruptured aneurysms, the inner surface of the aneurysm sac is completely covered with normally shaped, regularly orientated endothelial cells, it is unclear what role they may play in the maintenance of the collagenous tissue. However, the fibroblasts do need nutrients. Given that the cerebral arteries have no vaso-vasorum such nutrients must presumably be obtained from the bloodstream. Although, the role of the WSS and the WSSGs on the functionality of the fibroblasts in a developed aneurysm is unclear, we hypothesize that recirculating flow with long particle resident times may create a suboptimum environment for the fibroblasts ultimately leading to faulty maintenance of the ECM and the development of secondary blebs on the dome.

7 Conclusions
We have developed a computational framework to explore the coupling between the growth and remodeling of arterial tissues and the hemodynamic environment. The model utilizes a realistic microstructural model of the arterial wall, which explicitly relates degradation of the elastinous constituents to the deviations of the hemodynamic environment from normotensive levels. Although further sophistication is required to explicitly represent the walls and the complex signaling pathways within the arterial wall, we conclude that our model provides the basis to further explore the etiology of aneurysmal disease.

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References


