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Homeostatic strain for pre-stressed arteries

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Abstract. Modelling the artery as an incompressible, isotropic tube, it is shown that a consequence of accounting for residual stress by using the opening angle method is that there exists a finite internal pressure for which the deformation is homogeneous. A simple formula linking this pressure to the strain-energy function, the residual strain and the thickness of the artery is presented. This pressure is assumed to be the mean blood pressure and it is proposed that the growth and remodelling processes of arterial tissue act so as to ensure that this homeostatic strain is achieved at mean blood pressure. Some consequences of this homogeneity of strain at a finite pressure are explored.

Keywords: mathematical modelling; arterial tissue; homeostatic strain.

1. Introduction

The review article of Rachev and Greenwald [1] contains an excellent summary of the evolution of the idea that tubular structures, and in particular, arteries, in mammals are residually strained and, as a consequence of this strain, residually stressed. It is now widely accepted that mathematical models of arteries should incorporate some measure of this residual strain in order to accurately and reliably predict the response of arteries to mechanical forces. A common method of achieving this goal is due to Chuong and Fung [2] who modelled the artery as a sector of a cylinder that is first closed perfectly and then axially stretched to form the artery. This method, usually called the *opening angle method*, has the advantage of an elegant mathematical formulation and the prospect of an experimental determination of the residual strain (see Rachev and Greenwald [1] for details). This is the method preferred here. Another method adopts a more general approach to the modeling of residual strain (see, for example, Ogden and Schulze-Bauer [3]). In that approach, the residual stress is assumed to be dependent on the radial coordinate only. The equations of equilibrium and a further ad hoc assumption (that of constant circumferential stress [3]) are then used to determine the residual stress explicitly. A more recent innovation by Cardamone et al. [4] is to model residual strain using a constrained mixture model of the arterial wall.

The purpose of the evolution of residual strain in arteries is an open question. Chuong and Fung [2] propose that residual strains exist so as to reduce transmural stress gradients. An alternative hypothesis is offered by Takamizawa and Hayashi [5] who, instead of homogenizing the stress, suggest that the purpose of residual strain is to homogenize the circumferential *strain*. Both approaches can be considered applications of the *Principle of Homeostatis*, which recognises the self-regulatory nature of physiological systems. The first precise formulation of this idea is due to Claude Bernard [6], who asserted that all 'vital mechanisms' preserve 'constant the conditions of life in the internal environment'. Bernard's insight was developed most notably by Cannon [7]. Both authors were concerned exclusively with the self-regulatory nature of the fluid matrix of the body, termed homeostasis by Cannon. However Cannon himself recognised that this concept of self-regulation to maintain constancy in the fluid matrix had the potential to be extended to 'other materials and environmental states, whose homeostasis is essentially important for optimal activity of the organisms'. This homeostatic idea has been adapted to the biomechanics of the arterial wall. For example in Liu and Fung [8], the concept that the opening angle is linked to the homeostatic stress distribution at normal blood pressure is established, and the effect of a change of the opening angle on the homeostatic stress is investigated experimentally. The homeostatic principle will also be applied here.

Here we focus on the effect of residual strain on elastic arteries only. For a review of the biomechanics of such arteries, using the aorta as an archetypal example, see Kassab [9], where the application of the homeostatic principle is a central theme. Despite the wide application of the opening angle method to such arteries, an interesting consequence of its adoption seems to have been overlooked. It is shown here that when one inflates a residually pre-strained cylinder, there exists a finite pressure at which the strain is *homogeneous*. It seems reasonable to hypothesize that this pressure is the mean blood pressure. Thus it is our contention here that the growth and remodelling of arterial tissue, which cause the residual strain, are used by the body to ensure

that the arterial wall strain is homogeneous at mean blood pressure. Of course, this is pure speculation on our part and it has to be verified by experiment, but this (theoretical) occurrence of homogeneous strain at a finite pressure in a residually strained artery is surely significant. We are encouraged in this view by the simplicity of the mathematical analysis.

Contributory factors in this analysis are the assumptions of material *homogeneity* and *isotropy* for the artery. Although at variance with the histology of arterial walls, these assumptions are widely used in the biomechanics literature (see, for example, Huang et al. [10]). One justification for these assumptions is that the inherent complexity of anisotropic, inhomogeneous models could reduce the appreciation of a new feature that is being introduced to the modeling of arterial tissue. An anisotropic version of this paper is currently being prepared and the initial indications are that the essential features of the model being discussed here carry over in a relatively straightforward manner to the anisotropic regime. The more fundamental assumption of hyperelasticity made here is justified on the basis that only elastic arteries are being considered.

The simple relation between blood pressure and residual strain obtained here can be used as a test for the validity of proposed constitutive models: a simple substitution of a proposed strain-energy function with typical values assumed for the residual strain should yield a value for the blood pressure close to 16 kPa. This is illustrated with an example strain-energy function from the literature. Perhaps a more interesting application is as a constitutive constraint, with one of the models parameters *determined* from this relation. This could be particularly useful, of course, for a parameter that is difficult to determine experimentally.

2. Problem formulation

Let $(\mathrm{R}, \Theta, \mathrm{Z})$ denote the cylindrical coordinates of the sector of an incompressible cylindrical tube defined by

$$R_1 \le R \le R_2, \; -(2\pi - \alpha)/2 \le \Theta \le (2\pi - \alpha)/2, \; 0 \le Z \le L. \tag{2.1}$$

This sector is assumed unstressed in the *reference configuration* for what follows. Assume now that this annular sector is bent into an annular cylinder (a tube), with the plane faces $\Theta = \pm(2\pi - \alpha)/2$ joined perfectly together, accompanied by a uniform axial stretch of amount $\lambda_z (\ge 1)$. In the literature, this cylinder with zero stress applied to the curved surfaces is called the *unloaded state*. Assume then that this cylinder is subjected to a quasi-static uniform internal pressure per unit deformed area, P_1, modelling the blood pressure, and a uniform external pressure, P_2, modelling the effect of the restraining external soft tissue. This configuration is usually called the *loaded state.*

Let $(\mathrm{r}, \theta, \mathrm{z})$ denote the cylindrical coordinates of a typical particle in a deformed configuration. Assume that the deformation from the sector into a cylinder can be modelled as

$$r = \hat{r}(R),\ \theta = k\Theta,\ z = \lambda_z Z, \tag{2.2}$$

Where the constant *k,*

$$k = \frac{2\pi}{2\pi - \alpha},\ k \geq 1, \tag{2.3}$$

is a measure of the *opening angle* of the sector.

The incompressibility constraint then yields the following form of the radial deformation field:

$$r^2 = \frac{R^2 - R_1^2}{k\,\lambda_z} + r_1^2, \tag{2.4}$$

where r_1 denotes the location of the deformed inner curved. We will assume that both k and λ_z are specified, as well as the dimensions of the undeformed sector (2.1). Let $x \equiv r^2/R^2$ and $x_i \equiv r^2(R_i)/R_i^2$, i = 1, 2. Then

$$x_2 = \frac{\gamma + k\lambda_z x_1}{k\lambda_z(\gamma + 1)},\ \gamma \equiv \frac{R_2^2}{R_1^2} - 1, \tag{2.5}$$

and

$$x - \frac{1}{k\lambda_z} = \frac{R_1^2}{R^2}\left(x_1 - \frac{1}{k\lambda_z}\right). \tag{2.6}$$

The corresponding deformation gradient tensor, **F**, is given by

$$\mathbf{F} = \mathrm{diag}(\lambda_1, \lambda_2, \lambda_3) = \mathrm{diag}\left(\frac{R}{k\lambda_z r}, \frac{kr}{R}, \lambda_z\right), \tag{2.7}$$

where λ_i, i = 1, 2, 3, are the principal stretches.

Only homogeneous, isotropic, non-linearly elastic materials are considered here. For such materials the corresponding principal Cauchy stresses are given by

$$T_{rr} = -q + \frac{R}{k\lambda_z r}\frac{\partial W}{\partial \lambda_1},\ T_{\theta\theta} = -q + \frac{kr}{R}\frac{\partial W}{\partial \lambda_2},\ T_{zz} = -q + \lambda_z \frac{\partial W}{\partial \lambda_3}, \tag{2.8}$$

where q is a Lagrange multiplier due to the incompressibility constraint, and the strain energy density $W = W(\lambda_1, \lambda_2, \lambda_3)$ is a symmetric function of the principal stretches. Then it follows that

$$T_{\theta\theta} - T_{rr} = \frac{kr}{R}\frac{\partial W}{\partial \lambda_2} - \frac{R}{k\lambda_z r}\frac{\partial W}{\partial \lambda_1} = 2x\hat{W}'(x), \tag{2.8}$$

where $\hat{W}(x) \equiv W(\lambda_1(x), \lambda_2(x), \lambda_z) \in C^2(0,\infty)$ and the prime notation denotes differentiation. By choosing q to be a function of r only, we can satisfy two of the equations of equilibrium identically. The remaining radial equation

$$dT_{rr}/dr + (T_{rr} - T_{\theta\theta})/r = 0, \tag{2.9}$$

must be solved subject to the boundary conditions

$$T_{rr}(r_1) = -P_1,\ T_{rr}(r_2) = -P_2, \tag{2.10}$$

where P_1 and P_2 are the respective inner and outer constant hydrostatic pressures applied on the faces of the tube.

Integrating (2.9) using the identity

$$\frac{dx}{dr} = \frac{2r}{R^2}(1 - k\lambda_z x), \tag{2.11}$$

then yields

$$P(x_1) = \int_{r_1}^{r_2}\left(\frac{kr}{R}\frac{\partial W}{\partial \lambda_2} - \frac{R}{k\lambda_z r}\frac{\partial W}{\partial \lambda_1}\right)\frac{dr}{r} = \int_{x_1}^{x_2}\frac{\hat{W}'(x)}{1 - k\lambda_z x}dx, \tag{2.12}$$

where $P \equiv P_1 - P_2$ is assumed positive in order to model the usual pressure boundary conditions of an internal pressure with a stress-free external boundary. Henceforth, only this interpretation of the pressure difference is used and P can therefore be referred to as the (internal) pressure. This equation, together with $(2.5)_1$, determines the location of the deformed inner radius for given values of P. The pressure P can be regarded as a function of $x_1(>0)$.

The corresponding stress distribution is given by

$$T_{rr} = \int\frac{\hat{W}'(x)}{1 - k\lambda_z x}dx + \alpha, T_{\theta\theta} = T_{rr} + 2x\hat{W}'(x), T_{zz} = T_{rr} + \lambda_3\frac{\partial W}{\partial \lambda_3} - \lambda_1\frac{\partial W}{\partial \lambda_1}. \tag{2.13}$$

The ordering of x_1, x_2 in (2.12) is important. Trivially it follows from (2.5) that

$$\begin{aligned} &x_2 > x_1 \text{ when } x_1 < (1/k\lambda_z);\\ &x_2 = x_1 \text{ when } x_1 = 1/(k\lambda_z);\\ &x_2 < x_1 \text{ when } x_1 > 1/(k\lambda_z). \end{aligned} \tag{2.14}$$

This raises the question as to whether (2.12) is well-defined when $x_1 = 1/(k\lambda_z)$. It is now shown that not only is (2.12) well-defined when $x_1 = 1/(k\lambda_z)$, but also that it is continuous there. First note that

$$\frac{dP}{dx_1} = \frac{1}{1 - k\lambda_z x_1}\left(W'(x_2) - W'(x_1)\right). \tag{2.15}$$

This shows that P is therefore differentiable at $x_1 = 1/(k\lambda_z)$, and therefore continuous, since it follows from L'Hospital's Rule that

$$\frac{dP}{dx_1}\left(1/(k\lambda_z)\right) = \frac{\gamma}{k\lambda_z(\gamma+1)} W''\left(1/(k\lambda_z)\right). \tag{2.16}$$

3. Convexity

In addition to the differentiability assumption made previously, it is further assumed that $\hat{W}(x)$ is a strictly convex function, i.e., $\hat{W}''(x) > 0$. The necessity of this assumption to ensure physically realistic behaviour of arterial tissue in response to mechanical forces is discussed in Holzapfel et al. [11].

The first consequence of convexity is that P is a monotonically increasing function of x_1. This is immediate from consideration of (2.15), (2.16).

Isotropy has been assumed here and, without loss of generality, the strain-energy function can be written as $W = \tilde{W}(I_1, I_2)$, where I_1, I_2 are the usual invariants of the Cauchy-Green strain tensor defined in terms of the principal stretches as follows:

$$I_1 = \lambda_1^2 + \lambda_2^2 + \lambda_3^2,\ I_2 = \lambda_1^2\lambda_2^2 + \lambda_1^2\lambda_3^2 + \lambda_2^2\lambda_3^2. \tag{3.1}$$

For the deformation field (2.2), (2.4) these invariants therefore have the form

$$\begin{aligned} I_1(x) &= \left(\frac{R}{k\lambda_z r}\right)^2 + \left(\frac{kr}{R}\right)^2 + \lambda_z^2 = \frac{1}{k^2\lambda_z^2 x} + k^2 x + \lambda_z^2, \\ I_2(x) &= \frac{1}{\lambda_z^2} + \left(\frac{R}{kr}\right)^2 + \left(\frac{k\lambda_z r}{R}\right)^2 = \frac{1}{k^2 x} + k^2\lambda_z^2 x + \lambda_z^{-2}. \end{aligned} \tag{3.2}$$

The function $\hat{W}'(x)$, occurring in the integrand of (2.12), can therefore be written as

$$\frac{d\hat{W}}{dx} = \frac{k^4\lambda_z^2 x^2 - 1}{k^2 x^2}\left(\frac{1}{\lambda_z^2}\frac{\partial\tilde{W}}{\partial I_1} + \frac{\partial\tilde{W}}{\partial I_2}\right). \tag{3.3}$$

An immediate conclusion is that for all isotropic materials,

$$\hat{W}'(x) = 0 \Leftrightarrow x = 1/(k^2\lambda_z). \tag{3.4}$$

Convexity then ensures that the unique *minimum* of the strain energy density occurs at $x = x_m = 1/(k^2\lambda_z)$. Since from (3.2)

$$I_1\left(1/(k^2\lambda_z)\right) = \frac{2}{\lambda_z} + \lambda_z^2,\ I_2\left(1/(k^2\lambda_z)\right) = 2\lambda_z + \frac{1}{\lambda_z^2}, \tag{3.5}$$

this minimum value of the strain-energy is *independent* of the measure of the opening angle *k*. For isotropy then, there is the interesting possibility of a radial surface of minimum potential energy, defined by $x = x_m = 1/(k^2\lambda_z)$, occurring within the current configuration.

Equation (2.13) yields

$$\frac{dT_{rr}}{dx} = \frac{\hat{W}'(x)}{1 - k\lambda_z x}, \tag{3.6}$$

and consequently the radial stress also has a unique extremum, a minimum, at $x = 1/(k^2\lambda_z)$. The corresponding relation for the hoop stress is also derivable from (2.13) and has the form

$$\frac{dT_{\theta\theta}}{dx} = \frac{\hat{W}'(x)}{1 - k\lambda_z x} + 2\hat{W}'(x) + 2x\hat{W}''(x). \tag{3.7}$$

Thus the hoop stress is increasing at $x = 1/(k^2\lambda_z)$; determination of its singular points depends on the form of the strain-energy function. When $x = 1/k^2\lambda_z$, it follows from $(2.13)_2$ that $T_{rr} = T_{\theta\theta}$ and from (2.7) that $\lambda_1 = \lambda_2$, so that both stresses and strains are equal there. The corresponding derivatives with respect to the radial variable *r* can be easily obtained from these using (2.11).

Another trivial consequence of convexity is that, using (3.3),

$$\begin{aligned} \hat{W}'(x) < 0, 0 < x < x_m, \\ \hat{W}'(x) > 0, x > x_m, \end{aligned} \tag{3.8}$$

if one further assumes that the following empirical inequalities hold:

$$\partial\widetilde{W}/\partial I_1 > 0, \partial\widetilde{W}/\partial I_2 \geq 0. \tag{3.9}$$

Finally, it is noted that convexity in $\hat{W}$ holds for many of the common isotropic strain-energy functions used in the modelling of arterial tissue including the Mooney-Rivlin model,

$$\widetilde{W}_{MH} = C(I_1 - 3) + D(I_2 - 3),\ C > 0,\ D \geq 0, \tag{3.10}$$

and the Fung model

$$\widetilde{W}_F = \frac{\mu}{2b}\left\{\exp b\left(I_1 - 3\right) - 1\right\},\ \mu > 0,\ b > 0. \tag{3.11}$$

For example, $\tilde{W}''_{MR}(x) = \left(C + D\lambda_z^2\right)\Big/\left(k^2\lambda_z^2 x^3\right)$, which is clearly positive. A similar, but more complicated, second derivative can be found for the Fung model that is also clearly positive.

4. The homogeneous deformation state

The value $x_1 = 1/(k\lambda_z)$ was discussed in Section 2 as being the only possible singular value of x_1 in the definition of the pressure difference given in (2.12); it was shown that the pressure is in fact continuous there. The value $x_1 = 1/(k\lambda_z)$ *does* however have a characteristic that distinguishes it from all other values: it follows from (2.6) that when $x_1 = 1/k\lambda_z$ the deformation is *homogeneous* of the form

$$r = R\Big/\sqrt{k\lambda_z},\ \theta = k\Theta,\ z = \lambda_z Z. \tag{4.1}$$

The equations of equilibrium then yield

$$-q = \frac{2}{k\lambda_z}\hat{W}'\left(\frac{1}{k\lambda_z}\right)\ln r + \alpha,\ \alpha = \text{constant}. \tag{4.2}$$

The corresponding radial stress is therefore given by

$$T_{rr} = \frac{2}{k\lambda_z}\hat{W}'\left(\frac{1}{k\lambda_z}\right)\ln r + \frac{1}{\sqrt{k\lambda_z}}\frac{\partial W}{\partial\lambda_1}\left(\frac{1}{\sqrt{k\lambda_z}}, \sqrt{\frac{k}{\lambda_z}}, \lambda_z\right) + \alpha. \tag{4.3}$$

Satisfying the boundary conditions yields

$$P_h \equiv P(\Omega) = 2\Omega\hat{W}'(\Omega)\ln\left(r_2/r_1\right),\ \Omega \equiv 1/(k\lambda_z). \tag{4.4}$$

This is the internal pressure at which the deformation within the cylindrical tube is homogeneous and therefore the pressure at which the strain, using any well-defined measure of this quantity, with respect to the reference configuration, is constant. It is immediate from (3.8) that $P_h > 0$. If it is assumed that the exterior pressure is identically zero, then P_h is simply the blood pressure. The key assumption here is that the blood pressure determined by (4.4) is the *mean blood pressure*. Note also that for homogeneous strain, since (4.1) now holds,

$$r_2/r_1 = R_2/R_1, \tag{4.5}$$

and thus there is no need to determine r_2/r_1 *in vivo* if opening angle data is available.

Residual stresses are the result of the remodelling and growth of arterial tissue and seem to depend primarily on intramural elastin (Cardamone et al. [4]). The key idea here is the suggestion that one important role of this complex process of growth and remodelling is to attempt to maintain the artery in a state of homogeneous strain at mean blood pressure. This is a specialisation of the uniform strain hypothesis of Takamizawa and Hiyashi [5] who proposed that 'the artery undergoes a uniform circumferential strain throughout the wall in the physiological loading state'; a specialisation because it is suggested here that *the full strain field is homogeneous* and not just the circumferential component. This theory of homogeneous strain at mean blood pressure is now assumed to hold, even in the pathological case of hypertension. This hypothesis is not new: Fung and Liu [12] proposed that the increase in opening angle and accompanying residual strain serves to maintain a uniform stress and strain gradients despite the hypertension. The increase in residual strain in blood vessels in response to hypertension has been well documented (see the review in Fung [13]). Thus, even though the residual stress in a hypertensive artery causes the mean blood pressure to be elevated, the hypothesis here is that it still tries to maintain homogenous strain even at this elevated level. This results in damage to the overall cardiovascular system. Using some engineering systems terminology, this is an example of 'suboptimisation', where a subsystem is optimised to the detriment of the overall system.

The opening angle method, together with an axial pre-stretch, is used here. The novelty is that an especially simple relation is obtained between the mean blood pressure and the residual stress that result in homogeneous strain. This relation relates the easily observable blood pressure to both the relatively easily observed thickness of the arterial wall and the residual stress, which is impossible to determine *in vivo*. Consequently this relation could be inverted to obtain the *in vivo* residual stress state, provided, of course, the corresponding strain-energy function is known.

5. The stress distribution at homeostatic pressure

Constant strain is accompanied by stress fields that are *slowly* varying functions of the radial coordinate since it is immediate from the analysis of the last section that both the radial and hoop stresses depend on the radial coordinate only through the natural logarithm. Specifically, the radial stress has the form

$$T_{rr} = 2\Omega\hat{W}'(\Omega)\ln(r/r_1) - P\,, \tag{5.1}$$

whilst the hoop stress is given by

$$T_{\theta\theta} = T_{rr} + 2\Omega\hat{W}'(\Omega) = 2\Omega\hat{W}'(\Omega)\left[1 + \ln(r/r_1)\right] - P\,. \tag{5.2}$$

The values $T^i_{\theta\theta}$ and $T^o_{\theta\theta}$ of the hoop stress at the inner and outer walls are therefore given respectively by

$$T^i_{\theta\theta} = P\left(\frac{1}{\ln(r_2/r_1)} - 1\right),\ T^o_{\theta\theta} = \frac{P}{\ln(r_2/r_1)}. \tag{5.3}$$

At homeostatic strain then, the hoop stress gradient is essentially the same as that for the radial stress given that the difference in the hoop stresses at the walls is simply P. The outer hoop stress is always tensile. There is a critical arterial thickness for the hoop stress, $r_2/r_1 = e = 2.72$. For this value, the inner and outer hoop stresses are 0 and P respectively and it follows from (4.4) and $(5.2)_1$ that then, $T_{\theta\theta} = T_{rr} + P$ everywhere. For thicknesses less than this critical value, the hoop stress is tensile and for thicknesses greater than this critical value, the inner hoop stress is compressive.

6. The homogenising pressure

Without loss of generality, it can be assumed the strain-energy function can be written as $W = \tilde{W}(I_1, I_2)$, where I_1, I_2 are the usual invariants of the Cauchy-Green strain tensor. At constant strain then, from (4.4),

$$P_h = 2\lambda_z \frac{k^2 - 1}{k}\left(\frac{1}{\lambda_z^2}\frac{\partial \tilde{W}}{\partial I_1} + \frac{\partial \tilde{W}}{\partial I_2}\right)\ln(r_2/r_1), \tag{6.1}$$

where

$$I_1 = \frac{1}{k\lambda_z} + \frac{k}{\lambda_z} + \lambda_z^2,\ I_2 = \frac{\lambda_z}{k} + k\lambda_z + \lambda_z^{-2}. \tag{6.2}$$

Intuition suggests that as the residual stress and thickness of the artery increase due to growth and remodelling, the mean blood pressure, at which the strain is homogeneous, should also increase. Indeed this is one suggested cause of hypertension. If the thickness parameter, γ_c, is defined by

$$\gamma_c \equiv (r_2/r_1)^2 - 1, \tag{6.3}$$

then it is immediate from (6.1) that $\partial P_h/\partial \gamma_c > 0$, in agreement with intuition.

It is immediate also from (6.1) that

$$\frac{\partial P_h}{\partial k} = 2\lambda_z \ln(r_2/r_1)\left[\frac{k^2+1}{k^2}\left(\frac{1}{\lambda_z^2}\frac{\partial \tilde{W}}{\partial I_1} + \frac{\partial \tilde{W}}{\partial I_2}\right) + \frac{k^2-1}{k}\frac{\partial}{\partial k}\left(\frac{1}{\lambda_z^2}\frac{\partial \tilde{W}}{\partial I_1} + \frac{\partial \tilde{W}}{\partial I_2}\right)\right], \tag{6.4}$$

where

$$\frac{\partial}{\partial k}\left(\frac{1}{\lambda_z^2}\frac{\partial \tilde{W}}{\partial I_1} + \frac{\partial \tilde{W}}{\partial I_2}\right) = \frac{\partial^2 \tilde{W}}{\partial I_1^2}\frac{k^2-1}{k^2\lambda_z^3} + 2\frac{\partial^2 \tilde{W}}{\partial I_1 \partial I_2}\frac{k^2-1}{k^2\lambda_z} + \frac{\partial^2 \tilde{W}}{\partial I_2^2}\frac{\lambda_z(k^2-1)}{k^2}. \tag{6.5}$$

Therefore, if in addition to the usual empirical inequalities (3.9), one further assumes that

$$\frac{\partial^2 \tilde{W}}{\partial I_1^2} \geq 0, \ \frac{\partial^2 \tilde{W}}{\partial I_1 \partial I_2} \geq 0, \ \frac{\partial^2 \tilde{W}}{\partial I_2^2} \geq 0, \tag{6.6}$$

then one can conclude from (6.4), (6.5) that $\partial P_h / \partial k > 0$, again in agreement with intuition. It is easy to check that for the special strain-energy functions (3.9)-(3.11) introduced earlier, the inequalities (6.6) are indeed satisfied.

Similarly,

$$\frac{\partial P_h}{\partial \lambda_z} = 2\frac{k^2-1}{k}\ln(r_2/r_1)\left[-\frac{1}{\lambda_z^2}\frac{\partial \tilde{W}}{\partial I_1} + \frac{\partial \tilde{W}}{\partial I_2} + \frac{1}{\lambda_z}\frac{\partial}{\partial \lambda_z}\left(\frac{\partial \tilde{W}}{\partial I_1}\right) + \lambda_z \frac{\partial}{\partial \lambda_z}\left(\frac{\partial \tilde{W}}{\partial I_2}\right)\right], \tag{6.7}$$

where

$$\frac{1}{\lambda_z}\frac{\partial}{\partial \lambda_z}\left(\frac{\partial \tilde{W}}{\partial I_1}\right) + \lambda_z \frac{\partial}{\partial \lambda_z}\left(\frac{\partial \tilde{W}}{\partial I_2}\right) = \frac{\partial^2 \tilde{W}}{\partial I_1^2}\frac{2k\lambda_z^3 - 1 - k^2}{k\lambda_z^3} + 2\frac{\partial^2 \tilde{W}}{\partial I_1 \partial I_2}\frac{\lambda_z^6 - 1}{\lambda_z^4} + \frac{\partial^2 \tilde{W}}{\partial I_2^2}\frac{\lambda_z^3(1+k) - 2k}{k\lambda_z^2}. \tag{6.8}$$

Determination of the sign of this derivative is not as straightforward as the previous cases: the sign depends on the specific form of the strain-energy function. Interestingly for the neo-Hookean strain energy function, $\tilde{W} = c(I_1 - 3)$, $c > 0$, the pressure is a *decreasing* function of the axial pre-stretch. Some sample strain-energy functions that have been used previously to model arterial tissue will be considered next.

7. Exponential strain-energy function

One possible use of the analysis presented here is as a check of the plausibility of constitutive models for arteries. Substitution of typical opening angles, axial pre-stretches and arterial dimensions into (4.4) for a specific material should yield a pressure that is physiologically possible.

The problem with this approach is to choose values of the model variables that are indeed 'typical'. This is complicated by the fact that for each of three variables concerned, there are significant variations both between species, between locations in the vascular system, and between studies. Here we use human aortic data. In what follows, the thickness parameter is fixed and the value used is obtained from Li [14] who gives a human aorta diameter of 25 mm and a wall thickness of 2 mm. Assuming that these data accurately reflect the dimensions of aorta at mean blood pressure yields $r_2 = 12.5$ mm, $r_1 = 10.5$ mm and consequently the pressure-residual strain relation (6.1) takes the form

$$P_h = 0.35\lambda_z \frac{k^2-1}{k}\left(\frac{1}{\lambda_z^2}\frac{\partial \tilde{W}}{\partial I_1} + \frac{\partial \tilde{W}}{\partial I_2}\right). \tag{7.1}$$

The axial pre-stretch is assumed to be uniform in the artery: Delfino et al. [19] estimate it to be $\lambda_z = 1.1$, as an average of measurements made *in situ* before excision of human carotids. Holzapfel et al. [11] qualify this value as the "physiological pre-stretch" for human carotids.

Delfino et al. [19] also present measurements of the opening angle with distance along the carotid artery, including along its bifurcations. They report an opening angle of 130^0 in the non-bifurcated part, which translates as the following value for the k opening angle parameter: $k = 1.38$.

A defining characteristic of arterial tissue is the strain-hardening exhibited even at small strains. The first model specifically introduced to capture this effect was by Fung [18] who used the exponential function to model the stress-strain data from the uniaxial testing of rabbit mesentery. A generalisation of this model that is widely used in the literature has the form given in (3.12). Delfino et al. [19] proposed an exponential strain-energy function to model the human carotid bifurcation with $\mu = 44.2$ kPa and $b = 8.35$. This model was subsequently analysed further by Holzapfel et al. [11]. The homogenising pressure for the exponential strain-energy function (3.12) is easily obtained from (7.1) and is given by

$$P_h = 0.174\mu \frac{k^2-1}{k\lambda_z}\exp\left(b\left[\frac{1}{k\lambda_z} + \frac{k}{\lambda_z} + \lambda_z^2 - 3\right]\right). \tag{7.2}$$

Plots of the homogenising pressures for different residual strains for the Delfino et al. [19] constants are given below:

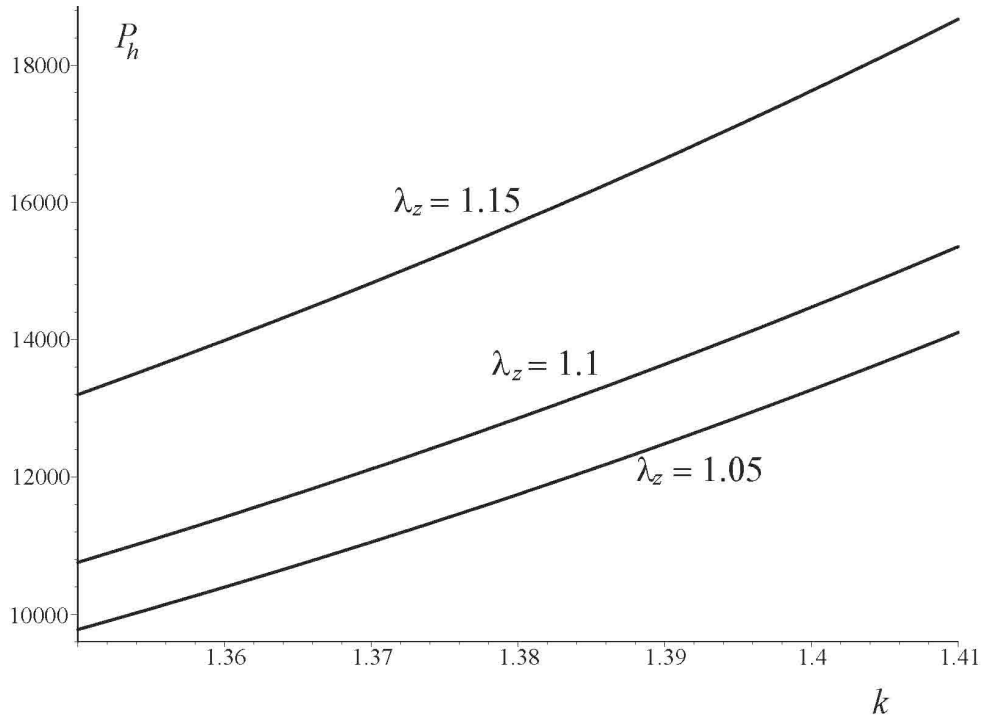

Figure 2. Plots of blood pressure for small axial pre-stretches

For the axial pre-stretches plotted above, it is easily seen that the Delfino et al. [19] model is compatible with (4.4), i.e., yielding predicted blood pressures of the order of 16 kPa.

Another related application of the relation (4.4) could be the actual *determination* of crucial model parameters, especially those parameters difficult to determine experimentally or those dependent on non-linear optimisation techniques for their determination, with resulting problems of non-uniqueness (see, for example, Ogden et al. [20] for an excellent treatment of the difficulties associated with determining model parameters from experimental data using such techniques). For the exponential model, the crucial parameter is the strain-hardening parameter, *b*. Inverting (7.2) yields

$$b = \frac{k\lambda_z}{1 + k^2 + k\lambda_z^3 - 3k\lambda_z} \ln\left(\frac{P_h k\lambda_z}{0.175\mu\left(k^2 - 1\right)}\right). \tag{7.3}$$

Assuming that (4.4) holds and the residual strains are known, this then *determines b*. For residual strains in the ranges $1.2 \le k, \lambda_z \le 1.6$ and using the original $\mu = 44$ kPa, yields the following possible values for *b*:

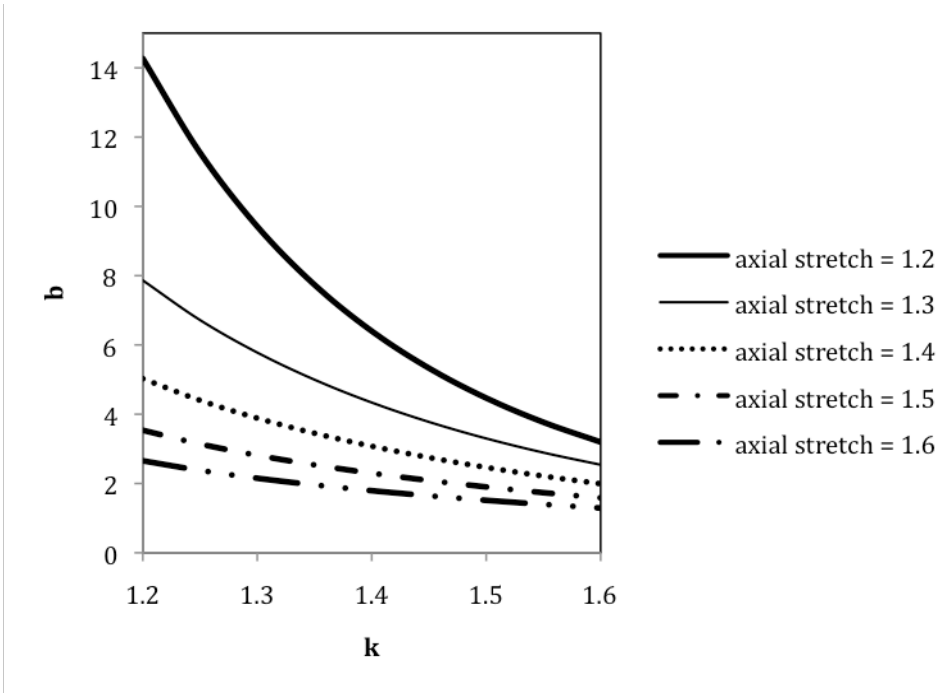

Figure 3. Determination of b

Increasing residual stress decreases the strain-hardening parameter *b*, in agreement with intuition. As noted earlier, the Delfino et al. [19] parameter of 8.35 is only possible for small residual strain.

9. Prof. Liu's data ??????

10. Conclusions

It is shown that there exists a finite internal pressure at which the strain is homogeneous for pre-stressed, incompressible, isotropic cylinders. Modelling elastic arteries in this way, the obvious assumption to make is that this pressure is the mean blood pressure. It is shown that this assumption is broadly compatible with representative existing models of arterial response to mechanical forces.

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