LIVING SHELL-LIKE STRUCTURES

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A decade ago, the so-called Kröner-Lee decomposition—primarily introduced to discern between elastic and (visco-)plastic strains—was given a broader scope and a deeper interpretation than the original ones, as describing the interplay between the actual and the relaxed configuration of each body element. The main intended application was to growth mechanics of soft living tissues. In 2002, a novel (tensorial) balance law governing the time evolution of the relaxed configuration was devised, and endowed with a proper constitutive theory, thus establishing the foundations of a dynamical theory of material remodelling.

Material remodelling does not describe explicitly the chemistry or whatever else is acting behind the changes in material structure. However, it does account explicitly for the power expended by the biochemical control system, which is of the essence for modelling the mechanics of living tissue. Material remodelling discriminates active from passive remodelling, while treating both on the same footing. Thus it provides mechanistic models of living materials without conceiving of them as inert materials engineered with magic constitutive recipes. The present study develops a toy model of saccular aneurysms, focussing on the two-way coupling between growth and stress.

Keywords: Material remodelling; Growth mechanics; Growing spherical shells;

Soft tissue; Saccular aneurysms.

1. Introduction

Soft shell-like structures are ubiquitous in living organisms, ranging from organelles and cell membranes to lymph and blood vessels, the alimentary canal and respiratory ducts, the urinary tract, and the uterus. The passive mechanical response of these structures—a key feature of their physiological and pathological functioning—is highly diversified and rather subtle. However, a much more elusive issue is their ability to grow and remodel, in a way which is both biochemically controlled and strongly coupled with the prevailing mechanical conditions. While the characterization of the passive mechanical response of soft tissue is progressing at a reasonably fast pace nowadays, we find that growth mechanics is definitely the weakest link in the modelling chain. For this reason, we focus on the two-way coupling between growth and stress, which we study using the apparatus of the theory of material remodelling, set forth in Ref. 1 and further developed, expounded and applied in Refs. 2–6.

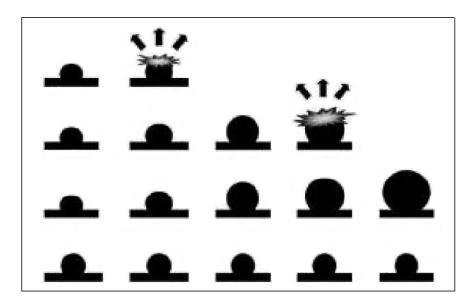
In Sec. 2 we introduce the model of a pressurized vessel which may undergo large deformations—both *passive* (visco-elastic) and *active* (accretive)—while keeping a spherically symmetric shape. Since we regard this as a drastically simplified model of saccular aneurysms, a short introductory section on real aneurysms is in order. Section 1.1 draws mostly from Refs. 7–10.

1.1. Saccular aneurysms

According to Yonekura,⁹ saccular aneurysms can be classified into four types (see Fig. 1 (top)):

- (1) the aneurysm ruptures within a time span as short as several days to several months after formation:
- (2) the aneurysm builds up slowly for a few years after formation and ruptures in this process;
- (3) the aneurysm keeps growing slowly for many years without rupturing;
- (4) the aneurysm grows up to a certain size (probably under 5 mm in diameter) and thereafter remains unchanged.

Fig. 1 (bottom) reproduces the cartoon where Humphrey⁷ has summarized the somewhat unpredictable evolution—either ill-fated or well-behaved—of a saccular aneurysm.



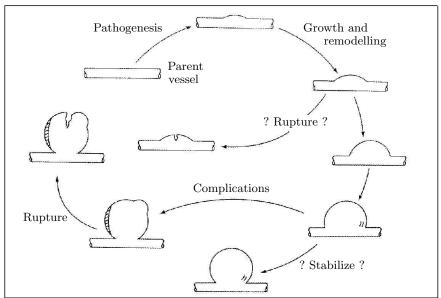


Fig. 1. Evolution paths of saccular aneurysms: (top) Process of growth and rupture: each row pictures one type of development (see text); each column corresponds to an aneurysm's lifetime: days to months for the 2nd, years for the 4th, decades for the 5th (schematics reproduced from Ref. 9); (bottom) Cartoon reproduced from Ref. 7.

Histological analyses provide limited information on the underlying mechanobiological processes. Here is an excerpt from Frösen *et al.*:⁸

The cellular mechanisms of degeneration and repair preceding rupture of the saccular cerebral artery aneurysm wall need to be elucidated for rational design of growth factor or drug-releasing endovascular devices. [...] Before rupture, the wall of saccular cerebral artery aneurysms undergoes morphological changes associated with remodelling of the aneurysm wall. Some of these changes, like SMC [smooth muscle cell] proliferation and macrophage infiltration, likely reflect ongoing repair attempts that could be enhanced with pharmacological therapy. [...] The morphological changes that result from the MH [myointimal hyperplasia] and matrix destruction are collectively referred to as remodelling of the vascular wall. Although MH is an adaptation mechanism of arteries to hemodynamic stress, in SAH [subarachnoid hemorrhage] patients, for undefined reasons, vascular wall remodelling [is] insufficient to prevent SCAA [saccular cerebral artery aneurysm] rupture.

To sum up, wall remodelling is generally believed¹⁰ to be stress driven. When the arterial wall is unduly stressed, some repair mechanisms get triggered. Their working, however, is still poorly understood.

2. Mathematical Model

In order to concentrate on growth mechanics, we strive to minimize all accessory difficulties, by tailoring an exceedingly simplified model of a saccular aneurysm. Our toy model consists in a highly deformable three-dimensional pressure vessel, constrained in such a way as to undergo only spherical symmetrical motions. Such a strong hypothesis curtails all technical difficulties related to finite kinematics and the allied dynamical issues; tensor algebra and analysis get elementary—though nontrivial, because of curvature and topology—, and a transparent treatment in components is made available by the exceptional existence of natural coordinates, provided by a spherical coordinate system. These features allow us to paraphrase the theory of material remodelling in terms perhaps more digestible than those in Refs. 1–6. However, the reader should be aware that simplicity is not synonymous with clarity, since in a highly simplified setting distinct general concepts may easily collapse into a single quantity and become confused. Warnings will be issued lest the naïve reader be caught in the most treacherous traps.

2.1. Geometry & kinematics

To a priori satisfy the above mentioned symmetry constraint, we conceive of a paragon shape \mathscr{D} of the vessel \mathscr{B} consisting in the (open) difference of two balls centred at $x_o \in \mathscr{E}$, the three-dimensional Euclidean ambient space. Let ξ_-, ξ_+ be the radii of the two balls, with $\xi_- < \xi_+$. From now on, we shall identify each body-point \boldsymbol{b} in \mathscr{B} and on its boundary $\partial \mathscr{B}$ with the place $\boldsymbol{\kappa}(\boldsymbol{b})$ it has in the assumed paragon configuration $\boldsymbol{\kappa} : \overline{\mathscr{B}} \leftrightarrow \overline{\mathscr{D}}$. In turn, each place $\boldsymbol{x} \in \mathscr{D}$ will be identified with the triple of its spherical coordinates $(\hat{\xi}(\boldsymbol{x}), \hat{\vartheta}(\boldsymbol{x}), \widehat{\varphi}(\boldsymbol{x}))$, where $\hat{\xi}(\boldsymbol{x}) = \|\boldsymbol{x} - \boldsymbol{x}_o\|$ is the radius of \boldsymbol{x} and $\hat{\vartheta}(\boldsymbol{x}), \widehat{\varphi}(\boldsymbol{x})$ are coordinates of its projection on the unit sphere. (Since all fields of interest will depend only on radius and time, there is no need to detail $\widehat{\vartheta}$ and $\widehat{\varphi}$.)

All (gross) placement of $\mathcal B$ will be described through the corresponding transplacement

$$p: \mathscr{D} \to \mathscr{E} \mathbf{x} \mapsto \mathbf{x}_{o} + \rho(\widehat{\xi}(\mathbf{x})) \, \mathbf{e}_{r}(\widehat{\vartheta}(\mathbf{x}), \widehat{\varphi}(\mathbf{x})),$$
 (1)

where $e_r(\vartheta, \varphi)$ is the outward unit normal to the sphere at (ϑ, φ) . Therefore, the (smooth) placements of \mathscr{B} compatible with the symmetry constraint are ultimately parameterized by the set of (smooth) real-valued, monotonically increasing maps

$$\rho: [\xi_-, \xi_+] \to \mathbb{R} \,, \tag{2}$$

which provide the actual radius $\rho(\xi)$ as a function of the paragon radius ξ . Henceforth, we will abridge notations by assuming that, whenever a place $\mathbf{x} \in \mathcal{D}$ is intended unambiguously, the triple $(\xi, \vartheta, \varphi)$ stands for $(\widehat{\xi}(\mathbf{x}), \widehat{\vartheta}(\mathbf{x}), \widehat{\varphi}(\mathbf{x}))$.

All spherically symmetric vector fields $\boldsymbol{v}: \mathcal{D} \to \mathsf{V}\mathscr{E}$ (with $\mathsf{V}\mathscr{E}$ the translation space of \mathscr{E}) admit the following parameterization, in terms of a scalar field $v: [\xi_-, \xi_+] \to \mathbb{R}$, which provides the *radial* component of \boldsymbol{v} (its only strict component):

$$\mathbf{v}(\mathbf{x}) = v(\xi) \, \mathbf{e}_{\mathsf{r}}(\vartheta, \varphi) \,. \tag{3}$$

Similarly, spherically symmetric tensor fields $\mathbf{L}: \mathscr{D} \to \mathsf{V}\mathscr{E} \otimes \mathsf{V}\mathscr{E}$ are linear combinations of the two fields of *orthogonal projectors*

$$\mathbf{P}_{\mathsf{r}}(\mathbf{x}) := \mathbf{e}_{\mathsf{r}}(\vartheta, \varphi) \otimes \mathbf{e}_{\mathsf{r}}(\vartheta, \varphi), \qquad \mathbf{P}_{\mathsf{h}}(\mathbf{x}) := \mathbf{I} - \mathbf{P}_{\mathsf{r}}(\mathbf{x})$$
 (4)

which depend only on (ϑ, φ) , weighted with scalar fields that depend only on ξ , representing the *radial* and *hoop* components of **L**, respectively:

$$\mathbf{L}(\mathbf{x}) = \mathbf{L}_{\mathsf{r}}(\xi) \, \mathbf{P}_{\mathsf{r}}(\vartheta, \varphi) + \mathbf{L}_{\mathsf{h}}(\xi) \, \mathbf{P}_{\mathsf{h}}(\vartheta, \varphi) \,, \tag{5}$$

In particular, the gradient of the transplacement (1) reads:

$$\nabla \mathbf{p}|_{\boldsymbol{x}} = \rho'(\xi) \, \mathbf{P}_{\mathsf{r}}(\vartheta, \varphi) + \frac{\rho(\xi)}{\xi} \, \mathbf{P}_{\mathsf{h}}(\vartheta, \varphi) \,, \tag{6}$$

where ρ' denotes the derivative of the radius-to-radius map (2). Of course, both components of $\nabla \mathbf{p}$ depend on the *single* scalar field ρ .

In order to distinguish growth from passive deformation, we postulate that, at each time $\tau \in \mathcal{T}$ (the *time line*, identified with the real line), there exists a dynamically distinguished tensor field $\mathbb{P}(\tau)$ —smoothly depending on time—which we call *prototypal transplant* or, briefly, *prototype*. The assignment of a gross placement and a prototype to each time defines a *refined motion* (\mathbf{p}, \mathbb{P}). The idea to refine the gross motion in this way dates back to Kröner¹¹ and Lee,¹² who introduced the notion of an "intermediate" configuration in the sixties, to distinguish between elastic and visco-plastic strains. Much later Rodriguez, Hoger and McCulloch imported that notion into biomechanics, reinterpreting it as the "zero-stress reference state" of a growing body element, to quote verbatim from their 1994 paper.¹³ Since there is no reason why the tensor field $\mathbb{P}(\tau)$ should be the gradient of any (gross) placement,^a it has *two* independent component:

$$\mathbb{P}(\boldsymbol{x},\tau) = \alpha_{\mathsf{r}}(\boldsymbol{\xi},\tau) \, \mathbf{P}_{\mathsf{r}}(\boldsymbol{\vartheta},\varphi) + \alpha_{\mathsf{h}}(\boldsymbol{\xi},\tau) \, \mathbf{P}_{\mathsf{h}}(\boldsymbol{\vartheta},\varphi) \,. \tag{7}$$

The warp \mathbf{F} , defined by the Kröner-Lee decomposition

$$\mathbf{F} := (\nabla \mathsf{p}) \, \mathbb{P}^{-1} = \, \lambda_{\mathsf{r}} \, \mathbf{P}_{\mathsf{r}} + \lambda_{\mathsf{h}} \mathbf{P}_{\mathsf{h}} \,, \tag{8}$$

gauges how the actual transplant of body elements, characterized by ∇p , differs from the prototypal transplant \mathbb{P} . Since all spherically symmetric tensor fields are symmetric-valued (orthogonal projectors are symmetric), \mathbf{F} coincides with the *stretch* \mathbf{U} , and its radial and hoop components are the fields of *principal stretches*. From Eqs. (6)–(8), one readily obtains:

$$\lambda_{\mathsf{r}}(\xi,\tau) = \frac{\rho'(\xi,\tau)}{\alpha_{\mathsf{r}}(\xi,\tau)} \,, \qquad \lambda_{\mathsf{h}}(\xi,\tau) = \frac{\rho(\xi,\tau)}{\xi\alpha_{\mathsf{h}}(\xi,\tau)} \,. \tag{9}$$

The *velocity* realized along the refined motion (p, \mathbb{P}) is, by definition, the pair consisting of the *gross velocity* \dot{p} and the *growth velocity* $\dot{\mathbb{P}} \mathbb{P}^{-1}$:

$$\dot{\mathbf{p}}(\boldsymbol{x},\tau) = \dot{\rho}(\boldsymbol{\xi},\tau) \, \boldsymbol{e}_{\mathsf{r}}(\vartheta,\varphi) ,
\dot{\mathbf{P}} \, \mathbb{P}^{-1}(\boldsymbol{x},\tau) = \frac{\dot{\alpha}_{\mathsf{r}}(\boldsymbol{\xi},\tau)}{\alpha_{\mathsf{r}}(\boldsymbol{\xi},\tau)} \, \mathbf{P}_{\mathsf{r}}(\vartheta,\varphi) + \frac{\dot{\alpha}_{\mathsf{h}}(\boldsymbol{\xi},\tau)}{\alpha_{\mathsf{h}}(\boldsymbol{\xi},\tau)} \, \mathbf{P}_{\mathsf{h}}(\vartheta,\varphi) ,$$
(10)

 $[\]overline{}^{a}$ Beware that spherical symmetry blots out the distinction between local and global obstructions to compatibility.

where a superposed dot denotes time differentiation. The linear space of instantaneous test velocities \mathfrak{T} , comprising all smooth fields $\boldsymbol{x} \mapsto (\boldsymbol{v}, \mathbb{V})$, with \boldsymbol{v} vector-valued and \mathbb{V} tensor-valued, will play a central role in Sec. 2.2.

2.2. Dynamics: brute and accretive forces; balance principle

The basic balance structure of a mechanical theory is encoded in the way in which forces expend *working* on a general test velocity. Because of the compound structure of test velocities, force splits here additively into a brute force, dual to \mathbf{v} , and an accretive force, dual to \mathbb{V} . To be specific, we postulate that the working expended on (\mathbf{v}, \mathbb{V}) is given by

$$\int_{\mathscr{D}} \left(\mathbb{A}^{\mathbf{i}} \cdot \mathbb{V} - \mathbf{S} \cdot \nabla \boldsymbol{v} \right) + \int_{\mathscr{D}} \mathbb{A}^{\mathbf{o}} \cdot \mathbb{V} + \int_{\partial \mathscr{D}} \boldsymbol{t}_{\partial \mathscr{D}} \cdot \boldsymbol{v} , \qquad (11)$$

where the integrals are taken with respect to the bulk volume and surface area of body elements in their paragon configuration—to be called paragon volume and paragon area, for short. The distinction between the inner working, given by the first bulk integral in Eq. (11), and the outer working, given by the remaining sum, is not germane to balance and was brought forward to this section just to save space. It will be discussed in Sec. 2.4. The inner and outer accretive couples per unit paragon volume \mathbb{A}^i , \mathbb{A}^o and the (brute) Piola stress \mathbf{S} —also a specific couple—take values in $V\mathscr{E} \otimes V\mathscr{E}$; the (brute) boundary-force per unit paragon area $\mathbf{t}_{\partial\mathscr{D}}$ take values in $V\mathscr{E}$. Because of spherical symmetry, Eq. (11) boils down to the one-dimensional representation:

$$\int_{\xi_{-}}^{\xi_{+}} \left(A_{\mathsf{r}} V_{\mathsf{r}} + 2 A_{\mathsf{h}} V_{\mathsf{h}} - S_{\mathsf{r}} v' - 2 S_{\mathsf{h}} v/\xi \right) 4 \pi \xi^{2} d\xi + \left(4 \pi \xi^{2} t v \right) \Big|_{\xi_{\mp}}, \quad (12)$$

with the obvious meaning of the components S_r, S_h of S and t of $t_{\partial D}$, and making use of the position:

$$\mathbb{A} := \mathbb{A}^{i} + \mathbb{A}^{o} = A_{r} P_{r} + A_{h} P_{h}. \tag{13}$$

Balance laws are provided by the balance principle stating that, at each time, the working expended on any test velocity should be zero. Via standard localization arguments, this yields the local statements of balance:

$$2(S_{r}(\xi) - S_{h}(\xi)) + \xi S'_{r}(\xi) = 0$$

$$A_{r}(\xi) = A_{h}(\xi) = 0$$

$$\mp S_{r}(\xi_{\pm}) = t_{\pm}.$$

$$(\xi_{-} < \xi < \xi_{+}), \qquad (14)$$

2.3. Energetics

To parametrize the state of the body, an additional energetic descriptor is needed. We postulate the existence of a real-valued *free energy* measure, such that the energy available to any part \mathscr{P} of \mathscr{D} is given by

$$\Psi(\mathscr{P}) = \int_{\mathscr{P}} J\psi \,, \tag{15}$$

where the density ψ is the free energy per unit prototypal volume and

$$J := \det(\mathbb{P}) = \alpha_{\mathsf{r}} \, \alpha_{\mathsf{h}}^2 > 0 \,, \tag{16}$$

so that $J\psi$ is the free energy per unit paragon volume, the integral in Eq. (15) being taken with respect to the paragon volume. Within the present symmetry-restricted theory, only spherically symmetric subsets of \mathscr{D} are to be considered as body-parts.

2.4. Constitutive issues

The *inner* force represents the interactions among the degrees of freedom resolved by the theory, *i.e.*, described by the refined motion (p, \mathbb{P}) ; the *outer force*, on the contrary, represents the interactions between these d.o.f.'s and those whose evolution is *not* described by (p, \mathbb{P}) . In the present theory of the biomechanics of growth, the outer accretive couple \mathbb{A}^o plays a primary role, representing the mechanical effects of the biochemical control system, finely distributed in the bulk of \mathscr{B} . Ignoring the chemical d.o.f.'s—as we do—does not allow us to neglect their feedback on mechanics.

The constitutive theory of inner forces rests on two main pillars, altogether independent of balance: the principle of material indifference to change in observer, and the dissipation principle. In the present context, the first of these principles is idle, since only the trivial action of the group of changes in observer is compatible with spherical symmetry.

2.4.1. Dissipation principle

We call power expended along a refined motion at any given time the opposite of the working expended by the inner force constitutively related to that motion on the velocity realized along the motion at the given time. Hence, the power expended measures the working done by a putative outer force balanced with the constitutively determined inner force. The dissipation principle we enforce requires that the power dissipated—defined as the difference between the power expended along a refined motion and the time

derivative of the free energy along that motion—should be non-negative, for all body-parts, at all times. This localizes into:

$$\mathbf{S} \cdot (\nabla \dot{\mathbf{p}}) - \mathbb{A}^{\mathbf{i}} \cdot (\dot{\mathbb{P}} \mathbb{P}^{-1}) - (J \, \psi) \geq 0. \tag{17}$$

2.4.2. Free energy and inner force

We posit that the value of the free energy $\psi(\boldsymbol{x},\tau)$ depends solely on the value of the warp $\mathbf{F}(\boldsymbol{x},\tau)$: there exists a map ϕ such that

$$\psi(\boldsymbol{x},\tau) = \phi\left(\lambda_{\mathsf{r}}(\xi,\tau), \lambda_{\mathsf{h}}(\xi,\tau); \xi\right). \tag{18}$$

The requirement that inequality (17) be satisfied along all refined motions is fulfilled if and only if for each ξ (which will be dropped from now on) the constitutive mappings for the (brute) stress **S** and the inner accretive couple \mathbb{A}^{i} satisfy the following equalities:^b

$$S_{r} = J\phi_{,r}/\alpha_{r} + \overset{\dagger}{S}_{r}, \qquad S_{h} = J\phi_{,h}/\alpha_{h} + \overset{\dagger}{S}_{h},$$

$$A_{r}^{i} = J\left[S_{r}\alpha_{r}\lambda_{r}/J - \phi\right] + \overset{\dagger}{A}_{r}, \qquad A_{h}^{i} = J\left[S_{h}\alpha_{h}\lambda_{h}/J - \phi\right] + \overset{\dagger}{A}_{h}, \qquad (19)$$

where the extra-energetic components $(\overset{+}{S}_r,\overset{+}{S}_h)$ and $(\overset{+}{A}_r,\overset{+}{A}_h)$ make the reduced dissipation inequality identically satisfied:

$$\stackrel{+}{\mathbf{S}_{\mathsf{r}}} \alpha_{\mathsf{r}} \dot{\lambda}_{\mathsf{r}} + 2 \stackrel{+}{\mathbf{S}_{\mathsf{h}}} \alpha_{\mathsf{h}} \dot{\lambda}_{\mathsf{h}} - \stackrel{+}{\mathbf{A}_{\mathsf{r}}} \dot{\alpha}_{\mathsf{r}} / \alpha_{\mathsf{r}} - 2 \stackrel{+}{\mathbf{A}_{\mathsf{h}}} \dot{\alpha}_{\mathsf{h}} / \alpha_{\mathsf{h}} \ge 0. \tag{20}$$

In Eqs. (19) $\phi_{,r}$ and $\phi_{,h}$ are shorthands for the derivatives of ϕ with respect to the radial and hoop stretches, λ_r and λ_h , respectively.

We regard all dissipative mechanisms extraneous to growth to be negligible, assuming the extra-energetic brute stress to be null: $\overset{+}{\mathbf{S}}_{r} = \overset{+}{\mathbf{S}}_{h} = 0$. Then, we make inequality (20) satisfied in the most facile—though scarcely warranted—way, letting each component of the extra-energetic accretive couple be simply proportional to the homonymous component of the growth velocity through a prescribed *negative* scalar factor:

$$\dot{\mathbf{A}}_{\mathsf{r}}^{\dagger} = -JD_{\mathsf{r}} \, \dot{\alpha}_{\mathsf{r}} / \alpha_{\mathsf{r}} \,, \qquad \dot{\mathbf{A}}_{\mathsf{h}}^{\dagger} = -JD_{\mathsf{h}} \, \dot{\alpha}_{\mathsf{h}} / \alpha_{\mathsf{h}} \,, \tag{21}$$

the radial and the hoop reluctance to growth (per unit prototypal volume) being positive: $D_{\sf r}>0$, $D_{\sf h}>0$.

^bNotice that the two bracketed quantities in Eqs. (19) are just the radial and hoop components of the *Eshelby tensor* $\mathbb{E} := (J^{-1}\mathbf{S}\mathbb{P}^{\top})\mathbf{F}^{\top} - \phi \mathbf{I}$ in disguise.

2.4.3. Characterizing the passive mechanical response of soft tissue: incompressible elasticity

Soft tissue—as all of soft matter—may be considered *elastically* incompressible (beware: growth may well change volume!):

$$\det \mathbf{F} = \lambda_{\mathsf{r}} \, \lambda_{\mathsf{h}}^2 = 1 \quad \Longleftrightarrow \quad \lambda_{\mathsf{r}} = 1/\lambda_{\mathsf{h}}^2 \,. \tag{22}$$

The incompressibility constraint (22) is maintained by a *reactive* inner force, which is requested to expend null working on all *divergence-free* test velocity. The ensuing set of reactions is parameterized by a scalar field $\overset{\bowtie}{\pi}$:

$$\overset{\bowtie}{\mathbf{S}} = J \overset{\bowtie}{\pi} \left(\frac{1}{\alpha_{\mathsf{r}} \lambda_{\mathsf{r}}} \mathbf{P}_{\mathsf{r}} + \frac{1}{\alpha_{\mathsf{h}} \lambda_{\mathsf{h}}} \mathbf{P}_{\mathsf{h}} \right), \qquad \overset{\bowtie}{\mathbb{A}} = J \overset{\bowtie}{\pi} \mathbf{I}.$$
 (23)

The active component of the inner force stems from the free-energy density (18) restricted to the constraint manifold:

$$\widetilde{\phi}: \lambda \mapsto \phi(1/\lambda^2, \lambda).$$
 (24)

Finally, collecting the active and reactive components, we get:

$$S_{r} = \frac{J}{\alpha_{r} \lambda_{r}} \left(\stackrel{\bowtie}{\pi} - (\lambda_{h}/3) \, \widetilde{\phi}' \right), \qquad S_{h} = \frac{J}{\alpha_{h} \lambda_{h}} \left(\stackrel{\bowtie}{\pi} + (\lambda_{h}/6) \, \widetilde{\phi}' \right),$$

$$A_{r}^{i} = J \left(T_{r} - \widetilde{\phi} - D_{r} \, \dot{\alpha}_{r} / \alpha_{r} \right), \qquad A_{h}^{i} = J \left(T_{h} - \widetilde{\phi} - D_{h} \, \dot{\alpha}_{h} / \alpha_{h} \right),$$

$$(25)$$

where $T_r = J^{-1}S_r \alpha_r \lambda_r$ and $T_h = J^{-1}S_h \alpha_h \lambda_h$ are the radial and hoop components of the *Cauchy stress* $\mathbf{T} = (J \det(\mathbf{F}))^{-1} \mathbf{S} \mathbb{P}^{\top} \mathbf{F}^{\top}$.

The constitutive function ϕ may be reasonably specified as follows:⁷

$$\widetilde{\phi}(\lambda) = (c/\delta) \exp((\Gamma/2) (\lambda^2 - 1)^2),$$
 (26)

where the moduli c and Γ may be identified—at least in principle—by performing biaxial traction tests on membrane samples, whose relaxed thickness is δ . According to Kyriacou and Humphrey,¹⁴ and Haslach and Humphrey,¹⁵ the best fit to the experimental findings of Scott et al.¹⁶ on an eurysmal tissue is given by $c = 0.88 \,\mathrm{N/m}$ and $\Gamma = 12.99$.

^cThe parameter $\overset{\bowtie}{\pi}$ is to be interpreted as (the opposite of) a *pressure*, since the reactive Cauchy stress $\overset{\bowtie}{\mathbf{T}} = (J \det(\mathbf{F}))^{-1} \overset{\bowtie}{\mathbf{S}} \mathbb{P}^{\top} \mathbf{F}^{\top}$ equals $\overset{\bowtie}{\pi} \mathbf{I}$.

2.4.4. Characterizing the active mechanical response of living tissue: constitutive recipes for the outer accretive couple

In the intended application, the brute boundary-force $t_{\partial \mathscr{D}}$ represents essentially the intramural blood pressure. To a first approximation, it may be assigned a constant value (10 KPa).^d The key assumption is the one concerning the outer accretive couple $\mathbb{A}^{\mathfrak{o}}$, whose constitutive prescription should hopefully short-circuit the complex—and ill-understood—sensing/actuating mechanobiological functions that control vascular wall remodelling.

We put forward a preliminary, crude proposal, along lines akin to those of Ref. 10. We posit a homeostatic *target value* T_h^{\odot} of the hoop component of the Cauchy stress and prescribe the outer accretive couple $\mathbb{A}^{\mathfrak{o}}$ as follows:

$$A_{r}^{o} = J\left(G_{r}\left(T_{h} - T_{h}^{\odot}\right) - T_{r} + \widetilde{\phi}\right),$$

$$A_{h}^{o} = J\left(G_{h}\left(T_{h}^{\odot} - T_{h}\right) - T_{h} + \widetilde{\phi}\right),$$
(27)

where G_r , G_h are positive *control gains*. Under this hypothesis, the evolution law for the prototypal transplant \mathbb{P} takes the form:

$$\dot{\alpha}_{r}/\alpha_{r} = (G_{r}/D_{r})(T_{h} - T_{h}^{\odot}),$$

$$\dot{\alpha}_{h}/\alpha_{h} = (G_{h}/D_{h})(T_{h}^{\odot} - T_{h}).$$
(28)

Notice that $\dot{\alpha}_r \geq 0$ while $\dot{\alpha}_h \leq 0$ when $T_h \geq T_h^{\odot}$.

3. Concluding remarks

We are presently attempting to fathom the computational depths of this model, numerically elusive despite its modest complexity. We defer therefore the presentation of numerical results to a later moment. In the meantime, a modicum of self-criticism is in order. Of course, the extreme geometrical and kinematical limitations of the present model need to be removed, if we want to develop a versatile mechanical theory of growing shells. However, its weakest point is elsewhere. In our opinion, a major conceptual improvement would be in distinguishing between different remodelling mechanisms. In the case at hand, at least three such mechanisms come to mind: passive viscous slipping between cells and various components of the extracellular matrix; active recovery due to cell adhesion and contractility; cell proliferation and collagen production. We are presently striving to formalize them separately, in order to include them individually into our model.

 $^{^{}m d}$ The brute bulk-force, playing a negligible role, has been neglected altogether.

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