

LIVING SHELL-LIKE STRUCTURES (*continued*)

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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 remodeling. Material remodeling 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 modeling the mechanics of living tissue. Material remodeling discriminates active from passive remodeling, 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 remodeling; 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 modeling 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 remodeling, 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.

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

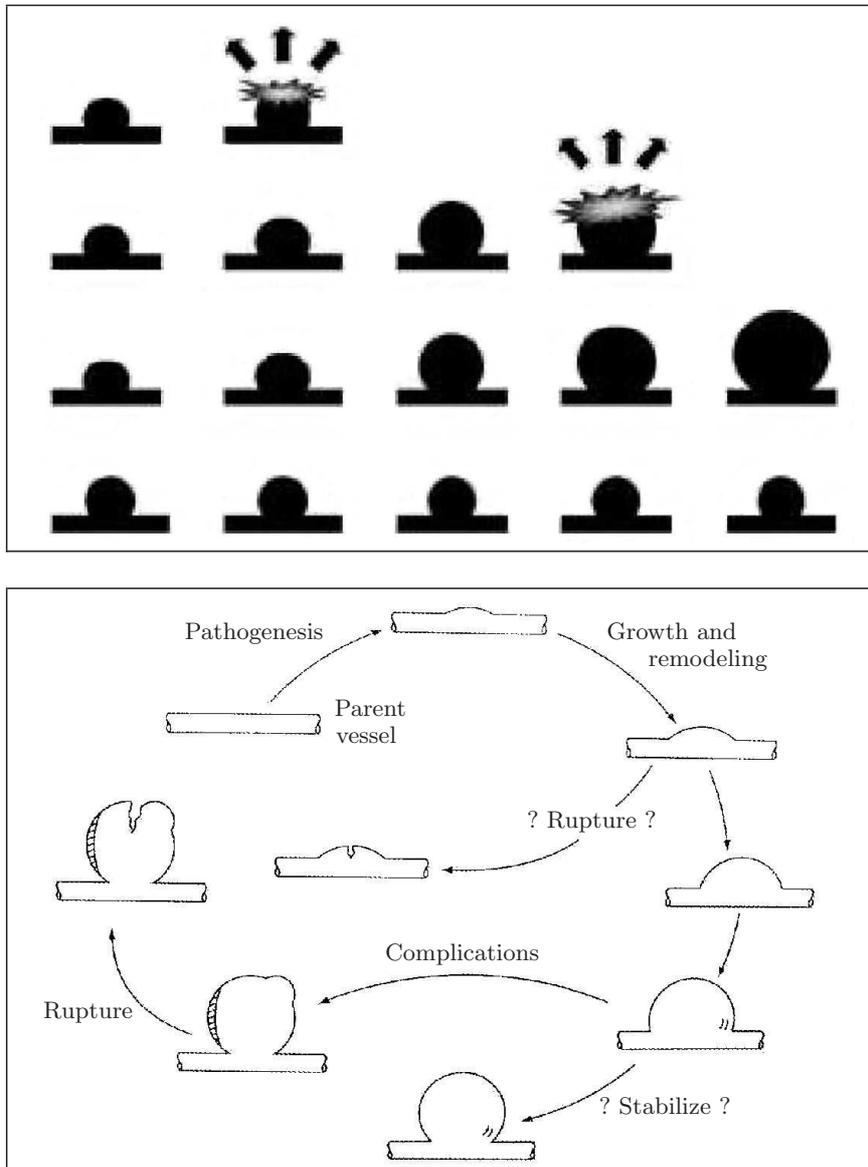


Fig. 1. Evolution paths of saccular aneurysms: (top) Process of growth and rupture: each row pictures one type of development (see text); each column corresponds to an aneurysm's lifetime: days to months for the 2nd, years for the 4th, decades for the 5th (schematics reproduced from Ref. 9); (bottom)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

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 remodeling 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 remodeling 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 remodeling [is] insufficient to prevent SCAA [saccular cerebral artery aneurysm] rupture.

To sum up, wall remodeling 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 remodeling 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* \mathcal{D} of the vessel \mathcal{B} consisting in the (open) difference of two balls centred at $\mathbf{x}_o \in \mathcal{E}$, 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 \mathbf{b} in \mathcal{B} and on its boundary $\partial\mathcal{B}$ with the place $\kappa(\mathbf{b})$ it has in the assumed *paragon configuration* $\kappa: \overline{\mathcal{B}} \leftrightarrow \overline{\mathcal{D}}$. In turn, each place $\mathbf{x} \in \mathcal{D}$ will be identified with the triple of its spherical coordinates $(\widehat{\xi}(\mathbf{x}), \widehat{\vartheta}(\mathbf{x}), \widehat{\phi}(\mathbf{x}))$, where $\widehat{\xi}(\mathbf{x}) = \|\mathbf{x} - \mathbf{x}_o\|$ is the radius of \mathbf{x} and $\widehat{\vartheta}(\mathbf{x}), \widehat{\phi}(\mathbf{x})$ 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 $\widehat{\phi}$.)

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

$$\begin{aligned} \mathbf{p}: \mathcal{D} &\rightarrow \mathcal{E} \\ \mathbf{x} &\mapsto \mathbf{x}_o + \rho(\widehat{\xi}(\mathbf{x})) \mathbf{e}_r(\widehat{\vartheta}(\mathbf{x}), \widehat{\phi}(\mathbf{x})), \end{aligned} \quad (1)$$

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

$$\rho: [\xi_-, \xi_+] \rightarrow \mathbb{R}, \quad (2)$$

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 $(\widehat{\xi}(\mathbf{x}), \widehat{\vartheta}(\mathbf{x}), \widehat{\phi}(\mathbf{x}))$.

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

$$\mathbf{v}(\mathbf{x}) = v(\xi) \mathbf{e}_r(\vartheta, \varphi). \quad (3)$$

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

$$\mathbf{P}_r(\mathbf{x}) := \mathbf{e}_r(\vartheta, \varphi) \otimes \mathbf{e}_r(\vartheta, \varphi), \quad \mathbf{P}_h(\mathbf{x}) := \mathbf{I} - \mathbf{P}_r(\mathbf{x}) \quad (4)$$

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

$$\mathbf{L}(\mathbf{x}) = L_r(\xi) \mathbf{P}_r(\vartheta, \varphi) + L_h(\xi) \mathbf{P}_h(\vartheta, \varphi), \quad (5)$$

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

$$\nabla \mathbf{p}|_{\mathbf{x}} = \rho'(\xi) \mathbf{P}_r(\vartheta, \varphi) + \frac{\rho(\xi)}{\xi} \mathbf{P}_h(\vartheta, \varphi), \quad (6)$$

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:

$$\mathbb{P}(\mathbf{x}, \tau) = \alpha_r(\xi, \tau) \mathbf{P}_r(\vartheta, \varphi) + \alpha_h(\xi, \tau) \mathbf{P}_h(\vartheta, \varphi). \quad (7)$$

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

$$\mathbf{F} := (\nabla \mathbf{p}) \mathbb{P}^{-1} = \lambda_r \mathbf{P}_r + \lambda_h \mathbf{P}_h, \quad (8)$$

gauges how the actual transplant of body elements, characterized by $\nabla \mathbf{p}$, 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:

$$\lambda_r(\xi, \tau) = \frac{\rho'(\xi, \tau)}{\alpha_r(\xi, \tau)}, \quad \lambda_h(\xi, \tau) = \frac{\rho(\xi, \tau)}{\xi \alpha_h(\xi, \tau)}. \quad (9)$$

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

$$\begin{aligned} \dot{\mathbf{p}}(\mathbf{x}, \tau) &= \dot{\rho}(\xi, \tau) \mathbf{e}_r(\vartheta, \varphi), \\ \dot{\mathbb{P}} \mathbb{P}^{-1}(\mathbf{x}, \tau) &= \frac{\dot{\alpha}_r(\xi, \tau)}{\alpha_r(\xi, \tau)} \mathbf{P}_r(\vartheta, \varphi) + \frac{\dot{\alpha}_h(\xi, \tau)}{\alpha_h(\xi, \tau)} \mathbf{P}_h(\vartheta, \varphi), \end{aligned} \quad (10)$$

^aBeware 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 $\mathbf{x} \mapsto (\mathbf{v}, \mathbb{V})$, with \mathbf{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

$$\int_{\mathcal{D}} (\mathbb{A}^i \cdot \mathbb{V} - \mathbf{S} \cdot \nabla \mathbf{v}) + \int_{\mathcal{D}} \mathbb{A}^o \cdot \mathbb{V} + \int_{\partial \mathcal{D}} \mathbf{t}_{\partial \mathcal{D}} \cdot \mathbf{v}, \quad (11)$$

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 $\mathbb{V}^{\mathcal{E}} \otimes \mathbb{V}^{\mathcal{E}}$; the (*brute*) *boundary-force* per unit paragon area $\mathbf{t}_{\partial \mathcal{D}}$ take values in $\mathbb{V}^{\mathcal{E}}$. Because of spherical symmetry, Eq. (11) boils down to the one-dimensional representation:

$$\int_{\xi_-}^{\xi_+} \left(A_r V_r + 2 A_h V_h - S_r v' - 2 S_h v/\xi \right) 4\pi \xi^2 d\xi + \left(4\pi \xi^2 t v \right) \Big|_{\xi_{\mp}}, \quad (12)$$

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

$$\mathbb{A} := \mathbb{A}^i + \mathbb{A}^o = A_r \mathbf{P}_r + A_h \mathbf{P}_h. \quad (13)$$

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:

$$\left. \begin{aligned} 2(S_r(\xi) - S_h(\xi)) + \xi S_r'(\xi) &= 0 \\ A_r(\xi) = A_h(\xi) &= 0 \end{aligned} \right\} (\xi_- < \xi < \xi_+), \quad (14)$$

$$\mp S_r(\xi_{\mp}) = t_{\mp}.$$

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 \mathcal{P} of \mathcal{D} is given by

$$\Psi(\mathcal{P}) = \int_{\mathcal{P}} J\psi, \quad (15)$$

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

$$J := \det(\mathbb{P}) = \alpha_r \alpha_h^2 > 0, \quad (16)$$

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 \mathcal{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 (\mathbf{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 (\mathbf{p}, \mathbb{P}) . In the present theory of the biomechanics of growth, the outer accretive couple \mathbb{A}° plays a primary role, representing the mechanical effects of the biochemical control system, finely distributed in the bulk of \mathcal{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:

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

2.4.2. Free energy and inner force

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

$$\psi(\mathbf{x}, \tau) = \phi(\lambda_r(\xi, \tau), \lambda_h(\xi, \tau); \xi). \quad (18)$$

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 \mathbf{S} and the inner accretive couple \mathbb{A}^i satisfy the following equalities:^b

$$\begin{aligned} \mathbf{S}_r &= J \phi_{,r} / \alpha_r + \overset{\dagger}{\mathbf{S}}_r, & \mathbf{S}_h &= J \phi_{,h} / (2\alpha_h) + \overset{\dagger}{\mathbf{S}}_h, \\ \mathbb{A}_r^i &= J [\mathbf{S}_r \alpha_r \lambda_r / J - \phi] + \overset{\dagger}{\mathbb{A}}_r, & \mathbb{A}_h^i &= J [\mathbf{S}_h \alpha_h \lambda_h / J - \phi] + \overset{\dagger}{\mathbb{A}}_h, \end{aligned} \quad (19)$$

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

$$\overset{\dagger}{\mathbf{S}}_r \alpha_r \dot{\lambda}_r + 2\overset{\dagger}{\mathbf{S}}_h \alpha_h \dot{\lambda}_h - \overset{\dagger}{\mathbb{A}}_r \dot{\alpha}_r / \alpha_r - 2\overset{\dagger}{\mathbb{A}}_h \dot{\alpha}_h / \alpha_h \geq 0. \quad (20)$$

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: $\overset{\dagger}{\mathbf{S}}_r = \overset{\dagger}{\mathbf{S}}_h = 0$. 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:

$$\overset{\dagger}{\mathbb{A}}_r = -J D_r \dot{\alpha}_r / \alpha_r, \quad \overset{\dagger}{\mathbb{A}}_h = -J D_h \dot{\alpha}_h / \alpha_h, \quad (21)$$

the radial and the hoop *reluctance to growth* (per unit *prototypal* volume) being positive: $D_r > 0$, $D_h > 0$.

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

$$\det \mathbf{F} = \lambda_r \lambda_h^2 = 1 \iff \lambda_r = 1/\lambda_h^2. \quad (22)$$

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 $\overset{\boxtimes}{\pi} :^c$

$$\overset{\boxtimes}{\mathbf{S}} = J \overset{\boxtimes}{\pi} \left(\frac{1}{\alpha_r \lambda_r} \mathbf{P}_r + \frac{1}{\alpha_h \lambda_h} \mathbf{P}_h \right), \quad \overset{\boxtimes}{\mathbf{A}} = J \overset{\boxtimes}{\pi} \mathbf{I}. \quad (23)$$

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

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

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

$$\begin{aligned} \mathbf{S}_r &= \frac{J}{\alpha_r \lambda_r} \left(\overset{\boxtimes}{\pi} - (\lambda_h/3) \tilde{\phi}' \right), & \mathbf{S}_h &= \frac{J}{\alpha_h \lambda_h} \left(\overset{\boxtimes}{\pi} + (\lambda_h/6) \tilde{\phi}' \right), \\ \mathbf{A}_r^i &= J \left(\mathbf{T}_r - \tilde{\phi} - D_r \dot{\alpha}_r / \alpha_r \right), & \mathbf{A}_h^i &= J \left(\mathbf{T}_h - \tilde{\phi} - D_h \dot{\alpha}_h / \alpha_h \right), \end{aligned} \quad (25)$$

where $\mathbf{T}_r = J^{-1} \mathbf{S}_r \alpha_r \lambda_r$ and $\mathbf{T}_h = J^{-1} \mathbf{S}_h \alpha_h \lambda_h$ 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 $\tilde{\phi}$ may be reasonably specified as follows:⁷

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

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 Humphrey¹⁴ and Haslach and Humphrey,¹⁵ the best fit to the experimental findings of Scott *et al.*¹⁶ on aneurysmal tissue is given by $c = 0.88$ N/m and $\Gamma = 12.99$.

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

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 $\mathbf{t}_{\partial\mathcal{P}}$ 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}° , whose constitutive prescription should hopefully short-circuit the complex—and ill-understood—sensing/actuating mechanobiological functions that control vascular wall remodeling.

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

$$\begin{aligned} A_r^\circ &= J \left(G_r (T_h - T_h^\circ) - T_r + \tilde{\phi} \right), \\ A_h^\circ &= J \left(G_h (T_h^\circ - T_h) - T_h + \tilde{\phi} \right), \end{aligned} \quad (27)$$

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

$$\begin{aligned} \dot{\alpha}_r / \alpha_r &= (G_r / D_r) (T_h - T_h^\circ), \\ \dot{\alpha}_h / \alpha_h &= (G_h / D_h) (T_h^\circ - T_h). \end{aligned} \quad (28)$$

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

3. 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 remodeling 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. In the next sections we are going to formalize them separately, in order to include them individually into our model.

^dThe brute bulk-force, playing a negligible role, has been neglected altogether.

4. Different remodeling mechanisms

In order to distinguish between different remodeling mechanisms, we assume that the *prototype* \mathbb{P} is the composition of different prototypes:^e

$$\mathbb{P} = \mathbb{P}_p \mathbb{P}_c \mathbb{P}_s \quad (29)$$

each of them describing separately *slipping*, *slipping recovery* and *proliferation*. Because of spherical symmetry we can define their components accordingly to (7). Thus the radial and hoop components of \mathbb{P} will be:

$$\alpha_r = \alpha_r^p \alpha_r^c \alpha_r^s, \quad \alpha_h = \alpha_h^p \alpha_h^c \alpha_h^s. \quad (30)$$

The *growth velocity* has now three terms:

$$\dot{\mathbb{P}} \mathbb{P}^{-1} = \dot{\mathbb{P}}_p \mathbb{P}_p^{-1} + \mathbb{P}_p \dot{\mathbb{P}}_c \mathbb{P}_c^{-1} \mathbb{P}_p^{-1} + \mathbb{P}_p \mathbb{P}_c \dot{\mathbb{P}}_s \mathbb{P}_s^{-1} \mathbb{P}_c^{-1} \mathbb{P}_p^{-1}. \quad (31)$$

Denoting them by $\mathbb{V}_p, \mathbb{V}_c, \mathbb{V}_s$, we postulate that the working expended on *test velocities* ($\mathbf{v}, \mathbb{V}_p, \mathbb{V}_c, \mathbb{V}_s$) is given by:

$$\begin{aligned} & \int_{\mathcal{D}} (\mathbb{A}_p^i \cdot \mathbb{V}_p + \mathbb{A}_c^i \cdot \mathbb{V}_c + \mathbb{A}_s^i \cdot \mathbb{V}_s - \mathbf{S} \cdot \nabla \mathbf{v}) \\ & + \int_{\mathcal{D}} (\mathbb{A}_p^o \cdot \mathbb{V}_p + \mathbb{A}_c^o \cdot \mathbb{V}_c + \mathbb{A}_s^o \cdot \mathbb{V}_s) + \int_{\partial \mathcal{D}} \mathbf{t}_{\partial \mathcal{D}} \cdot \mathbf{v}. \end{aligned} \quad (32)$$

4.1. Dissipation principle

We assume that only \mathbb{P}_p affects volume changes, while both \mathbb{P}_s and \mathbb{P}_c leave the volume unchanged separately. Hence:

$$J := \det(\mathbb{P}) = \det(\mathbb{P}_p); \quad \det(\mathbb{P}_s) = 1; \quad \det(\mathbb{P}_c) = 1, \quad (33)$$

and

$$\dot{J} = J \operatorname{tr}(\mathbb{V}_p); \quad \operatorname{tr}(\mathbb{V}_s) = 0; \quad \operatorname{tr}(\mathbb{V}_c) = 0. \quad (34)$$

The *dissipation principle* states now that along any motion:

$$\mathbf{S} \cdot \nabla \dot{\mathbf{p}} - (\mathbb{A}_p^i \cdot \mathbb{V}_p + \mathbb{A}_c^i \cdot \mathbb{V}_c + \mathbb{A}_s^i \cdot \mathbb{V}_s) - (J \dot{\psi}) \geq 0. \quad (35)$$

From the definition (8) of \mathbf{F} follows:

$$\begin{aligned} \mathbf{S} \cdot \nabla \dot{\mathbf{p}} &= \mathbf{S} \mathbb{P}^T \cdot \nabla \dot{\mathbf{p}} \mathbb{P}^{-1} = \mathbf{S} \mathbb{P}^T \cdot (\dot{\mathbf{F}} + \mathbf{F} \dot{\mathbb{P}} \mathbb{P}^{-1}) \\ &= \mathbf{S} \mathbb{P}^T \cdot (\dot{\mathbf{F}} + \mathbf{F} (\mathbb{V}_p + \mathbb{V}_c + \mathbb{V}_s)) \\ &= \mathbf{S} \mathbb{P}^T \cdot \dot{\mathbf{F}} + \mathbf{F}^T \mathbf{S} \mathbb{P}^T \cdot (\mathbb{V}_p + \mathbb{V}_c + \mathbb{V}_s). \end{aligned} \quad (36)$$

^eThe order of composition (29) should be irrelevant. Such requirement and its implications will not be discussed in general. It is trivially fulfilled here by spherical symmetry.

By substituting (36) into (35) we get:

$$\begin{aligned} & \mathbf{S} \mathbb{P}^\top \cdot \dot{\mathbf{F}} - J \dot{\psi} - (\mathbb{A}_p^i - (\mathbf{F}^\top \mathbf{S} \mathbb{P}^\top - J \phi \mathbf{I})) \cdot \mathbb{V}_p \\ & - (\mathbb{A}_c^i - \mathbf{F}^\top \mathbf{S} \mathbb{P}^\top) \cdot \mathbb{V}_c - (\mathbb{A}_s^i - \mathbf{F}^\top \mathbf{S} \mathbb{P}^\top) \cdot \mathbb{V}_s \geq 0. \end{aligned} \quad (37)$$

This inequality motivates the following decompositions. If we assume $\psi(\mathbf{x}, \tau) = \phi(\mathbf{F}(\mathbf{x}, \tau))$ we can decompose \mathbf{S} into the sum of an *energetic* part $\check{\mathbf{S}}$ and a *dissipative* part $\overset{+}{\mathbf{S}}$ such that:

$$\mathbf{S} = \check{\mathbf{S}} + \overset{+}{\mathbf{S}}, \quad J^{-1} \check{\mathbf{S}} \mathbb{P}^\top \cdot \dot{\mathbf{F}} = \dot{\phi}. \quad (38)$$

The inner accretive couples can be decomposed into:

$$\begin{aligned} \mathbb{A}_p^i &= (\mathbf{F}^\top \mathbf{S} \mathbb{P}^\top - J \phi \mathbf{I}) + \overset{+}{\mathbb{A}}_p^i, \\ \mathbb{A}_c^i &= \mathbf{F}^\top \mathbf{S} \mathbb{P}^\top + \overset{+}{\mathbb{A}}_c^i, \\ \mathbb{A}_s^i &= \mathbf{F}^\top \mathbf{S} \mathbb{P}^\top + \overset{+}{\mathbb{A}}_s^i, \end{aligned} \quad (39)$$

where both $\overset{+}{\mathbb{A}}_c^i$ and $\overset{+}{\mathbb{A}}_s^i$ are traceless tensors, because of the corresponding accretive velocities being isochoric.

Now we can rephrase the dissipation principle as follows: along any motion all the *extra-energetic* components make the *reduced dissipation inequality*:

$$\overset{+}{\mathbf{S}} \mathbb{P}^\top \cdot \dot{\mathbf{F}} - \overset{+}{\mathbb{A}}_p^i \cdot \mathbb{V}_p - \overset{+}{\mathbb{A}}_c^i \cdot \mathbb{V}_c - \overset{+}{\mathbb{A}}_s^i \cdot \mathbb{V}_s \geq 0 \quad (40)$$

identically satisfied. By using the Cauchy stress $\mathbf{T} = (J \det(\mathbf{F}))^{-1} \mathbf{S} \mathbb{P}^\top \mathbf{F}^\top$, expressions (39) turn into:

$$\begin{aligned} \overset{+}{\mathbb{A}}_p^i &= J (\mathbf{F}^\top \mathbf{T} \mathbf{F}^{-\top} - \phi \mathbf{I}) + \overset{+}{\mathbb{A}}_p^i, \\ \overset{+}{\mathbb{A}}_c^i &= J (\mathbf{F}^\top \mathbf{T} \mathbf{F}^{-\top}) + \overset{+}{\mathbb{A}}_c^i, \\ \overset{+}{\mathbb{A}}_s^i &= J (\mathbf{F}^\top \mathbf{T} \mathbf{F}^{-\top}) + \overset{+}{\mathbb{A}}_s^i. \end{aligned} \quad (41)$$

4.2. Remodeling balance laws

The remodeling balance laws provided by the balance principle corresponding to the working (32) are:

$$\begin{aligned} \mathbb{A}_p^i + \mathbb{A}_p^o &= 0, \\ \mathbb{A}_c^i + \mathbb{A}_c^o &= 0, \\ \mathbb{A}_s^i + \mathbb{A}_s^o &= 0. \end{aligned} \quad (42)$$

Substitution of (41) transforms them into:

$$\begin{aligned}
-\overset{+}{\mathbb{A}}_{\mathbf{p}}^{\mathbf{i}}/J &= (\mathbf{F}^{\top} \mathbf{T} \mathbf{F}^{-\top} - \phi \mathbf{I}) + \mathbb{A}_{\mathbf{p}}^{\circ}/J, \\
-\overset{+}{\mathbb{A}}_{\mathbf{c}}^{\mathbf{i}}/J &= (\mathbf{F}^{\top} \mathbf{T} \mathbf{F}^{-\top}) + \mathbb{A}_{\mathbf{c}}^{\circ}/J, \\
-\overset{+}{\mathbb{A}}_{\mathbf{s}}^{\mathbf{i}}/J &= (\mathbf{F}^{\top} \mathbf{T} \mathbf{F}^{-\top}) + \mathbb{A}_{\mathbf{s}}^{\circ}/J.
\end{aligned} \tag{43}$$

Because of the incompressibility constrain in (33) the spherical parts of $\mathbb{A}_{\mathbf{c}}^{\circ}$ and $\mathbb{A}_{\mathbf{s}}^{\circ}$ have to be considered *reactive*.

4.3. Evolution laws and control couples

Let us assume that there is only radial proliferation:

$$\begin{aligned}
\mathbb{P}_{\mathbf{p}} &= \alpha_r^{\mathbf{p}} \mathbf{P}_r + \mathbf{P}_h, \\
\mathbb{P}_{\mathbf{c}} &= \alpha_r^{\mathbf{c}} \mathbf{P}_r + \alpha_h^{\mathbf{c}} \mathbf{P}_h, \\
\mathbb{P}_{\mathbf{s}} &= \alpha_r^{\mathbf{s}} \mathbf{P}_r + \alpha_h^{\mathbf{s}} \mathbf{P}_h,
\end{aligned} \tag{44}$$

with

$$\begin{aligned}
\alpha_r^{\mathbf{c}} (\alpha_h^{\mathbf{c}})^2 &= 1, \\
\alpha_r^{\mathbf{s}} (\alpha_h^{\mathbf{s}})^2 &= 1.
\end{aligned} \tag{45}$$

From (30), the expressions for radial and hoop components are:

$$\begin{aligned}
\alpha_r &= \alpha_r^{\mathbf{p}} / (\alpha_h^{\mathbf{c}} \alpha_h^{\mathbf{s}})^2, \\
\alpha_h &= \alpha_h^{\mathbf{c}} \alpha_h^{\mathbf{s}}.
\end{aligned} \tag{46}$$

We assume the extra-energetic *brute* stress be null: $\overset{+}{\mathbf{S}} = 0$. Further we set:

$$\begin{aligned}
\overset{+}{\mathbb{A}}_{\mathbf{p}}^{\mathbf{i}} &= -J D_r^{\mathbf{p}} \dot{\alpha}_r^{\mathbf{p}} / \alpha_r^{\mathbf{p}} \mathbf{P}_r, \\
\overset{+}{\mathbb{A}}_{\mathbf{c}}^{\mathbf{i}} &= -J (D_r^{\mathbf{c}} \dot{\alpha}_r^{\mathbf{c}} / \alpha_r^{\mathbf{c}} \mathbf{P}_r + D_h^{\mathbf{c}} \dot{\alpha}_h^{\mathbf{c}} / \alpha_h^{\mathbf{c}} \mathbf{P}_h), \\
\overset{+}{\mathbb{A}}_{\mathbf{s}}^{\mathbf{i}} &= -J (D_r^{\mathbf{s}} \dot{\alpha}_r^{\mathbf{s}} / \alpha_r^{\mathbf{s}} \mathbf{P}_r + D_h^{\mathbf{s}} \dot{\alpha}_h^{\mathbf{s}} / \alpha_h^{\mathbf{s}} \mathbf{P}_h).
\end{aligned} \tag{47}$$

Because of assumptions (45):

$$\begin{aligned}
\dot{\alpha}_r^{\mathbf{c}} / \alpha_r^{\mathbf{c}} &= -2 \dot{\alpha}_h^{\mathbf{c}} / \alpha_h^{\mathbf{c}}, \\
\dot{\alpha}_r^{\mathbf{s}} / \alpha_r^{\mathbf{s}} &= -2 \dot{\alpha}_h^{\mathbf{s}} / \alpha_h^{\mathbf{s}}.
\end{aligned} \tag{48}$$

Hence the scalar form of the (reaction free) remodeling balance laws turns out to be:

$$\begin{aligned} D_r^p \dot{\alpha}_r^p / \alpha_r^p &= (T_r - \tilde{\phi}) + Q_r^p, \\ (2D_r^c + D_h^c) \dot{\alpha}_h^c / \alpha_h^c &= (T_h - T_r) + (Q_h^c - Q_r^c), \\ (2D_r^s + D_h^s) \dot{\alpha}_h^s / \alpha_h^s &= (T_h - T_r) + (Q_h^s - Q_r^s). \end{aligned} \quad (49)$$

where the components of \mathbb{A}_c^o/J are denoted by (Q_r^c, Q_h^c) and so on.

Setting $D^p := D_r^p$, $D^c := (2D_r^c + D_h^c)$, $D^s := (2D_r^s + D_h^s)$, $Q^p := Q_r^p$, $Q^c := (Q_h^c - Q_r^c)$, $Q^s := (Q_h^s - Q_r^s)$, we get:

$$\begin{aligned} D^p \dot{\alpha}_r^p / \alpha_r^p &= (T_r - \tilde{\phi}) + Q^p, \\ D^c \dot{\alpha}_h^c / \alpha_h^c &= (T_h - T_r) + Q^c, \\ D^s \dot{\alpha}_h^s / \alpha_h^s &= (T_h - T_r) + Q^s. \end{aligned} \quad (50)$$

If we further assume $Q^s = 0$ we get:

$$\begin{aligned} \dot{\alpha}_r^p / \alpha_r^p &= (T_r - \tilde{\phi}) / D^p + Q^p / D^p, \\ \dot{\alpha}_h^c / \alpha_h^c &= (T_h - T_r) / D^c + Q^c / D^c, \\ \dot{\alpha}_h^s / \alpha_h^s &= (T_h - T_r) / D^s. \end{aligned} \quad (51)$$

By using the relation between velocities derived from (48):

$$\begin{aligned} \dot{\alpha}_r / \alpha_r &= -2(\dot{\alpha}_h^c / \alpha_h^c + \dot{\alpha}_h^s / \alpha_h^s) + \dot{\alpha}_r^p / \alpha_r^p, \\ \dot{\alpha}_h / \alpha_h &= \dot{\alpha}_h^c / \alpha_h^c + \dot{\alpha}_h^s / \alpha_h^s, \end{aligned} \quad (52)$$

we obtain the relevant evolution laws:

$$\begin{aligned} \dot{\alpha}_r / \alpha_r &= -2((T_h - T_r)(1/D^c + 1/D^s) + Q^c/D^c) \\ &\quad + (T_r - \tilde{\phi})/D^p + Q^p/D^p, \end{aligned} \quad (53)$$

$$\dot{\alpha}_h / \alpha_h = (T_h - T_r)(1/D^c + 1/D^s) + Q^c/D^c.$$

Note that only these equations are coupled to the first balance equation in (14), while equations (51) need not even to be integrated separately. They just give the velocities of the three competing mechanisms.

We may use (51) to compute the expression for the power of the control force Q^c :

$$\varpi^c := Q^c \dot{\alpha}_h^c / \alpha_h^c = Q^c ((T_h - T_r)/D^c + Q^c/D^c). \quad (54)$$

We say that slipping and recovery mechanisms are *balanced* in a time interval centered at τ_0 if:

$$\begin{aligned} \alpha_r^c(\tau) \alpha_r^s(\tau) &= \alpha_r^c(\tau_0) \alpha_r^s(\tau_0), \\ \alpha_h^c(\tau) \alpha_h^s(\tau) &= \alpha_h^c(\tau_0) \alpha_h^s(\tau_0). \end{aligned} \quad (55)$$

As a consequence, in the same time interval:

$$\begin{aligned}\dot{\alpha}_r^s/\alpha_r^s &= -\dot{\alpha}_r^c/\alpha_r^c, \\ \dot{\alpha}_h^s/\alpha_h^s &= -\dot{\alpha}_h^c/\alpha_h^c.\end{aligned}\quad (56)$$

The condition for slipping and recovery mechanisms to be balanced is that Q^c be such that:

$$Q^c = -(1 + D^c/D^s)(T_h - T_r). \quad (57)$$

The corresponding expression for (54) is:

$$\varpi^c = (T_h - T_r)^2(1 + D^s/D^c)/D^c. \quad (58)$$

It is worth noting that when slipping and recovery are balanced then for the power dissipated we get:

$$\begin{aligned}-\mathbb{A}_c^+ \cdot \mathbb{V}_c - \mathbb{A}_s^+ \cdot \mathbb{V}_s &= 2D^c(\dot{\alpha}_h^c/\alpha_h^c)^2 + 2D^s(\dot{\alpha}_h^s/\alpha_h^s)^2 \\ &= 2(D^c + D^s)(\dot{\alpha}_h^s/\alpha_h^s)^2 = 2\varpi^c.\end{aligned}\quad (59)$$

5. Simulated natural histories

In order to figure out what kind of control could prevent an aneurysm from rupture, we can conjecture different ways it would respond to some perturbation during hypothetical histories.

Our goal is to find which control is able to make a homeostatic state stable and to compute the stability regions of the parameters.

We will consider also mechanisms leading the aneurysm to a new stable homeostatic state after a perturbation. The new state should hopefully be at the same hoop stress value.

Let us assume that an aneurysm, subjected to a constant intramural pressure, has reached a spherical shape in a homeostatic state with hoop and radial stress:

$$T_h^\diamond, \quad T_r^\diamond, \quad (60)$$

thanks to a full slipping recovery control force Q^c .

5.1. History A

- (1) Q^c is held fixed to the previous value for the rest of the time:

$$Q^c(t) = -(1 + D^c/D^s)(T_h^\diamond - T_r^\diamond), \quad (61)$$

simulating an inability of the slipping recovery mechanism to keep pace with a sudden perturbation;

- (2) the intramural pressure experiences a jump or an oscillation.

5.1.1. Remarks from numerical simulations

It looks as if the homeostatic state were *unstable*: however small the perturbation amplitude be, the system goes away from the homeostatic state.

5.2. History B

- (1) Q^c experiences a jump or an oscillation around the previous homeostatic value:

$$Q^c(t) = -(1 + D^c/D^s)(T_h^\circ - T_r^\circ)h(t), \quad (62)$$

simulating a temporary damage or malfunction of the slipping recovery mechanism;

- (2) the intramural pressure is held constant.

5.2.1. Remarks from numerical simulations

It looks as if the homeostatic state were *unstable*: however small the perturbation amplitude be, the system goes away from the homeostatic state.

5.3. History C

- (1) The intramural pressure experiences a jump or an oscillation;
 (2) Q^c is increased to a fraction of the value of a full slipping recovery control:

$$Q^c(t) = -(1 + D^c/D^s)((T_h^\circ - T_r^\circ) + g((T_h(t) - T_h^\circ) - (T_r(t) - T_r^\circ))), \quad (63)$$

which is meant to simulate an impaired recovery mechanism, not able to keep full pace with a sudden perturbation; if $g = 0$ then Q^c is held constant; if $g = 1$ then Q^c is a full slipping recovery control, synchronized with any perturbation.

Note that the expression for Q^c corresponding to the hoop control law in (27) would be instead:

$$Q^c(t) = -(1 + D^c/D^s)((T_h - T_r) + g(T_h(t) - T_h^\circ)), \quad (64)$$

subtly different from the previous one, not to mention the difference between T_h° , a uniform field, and T_h° , the homeostatic hoop stress field.

5.4. History D

- (1) Q^c is held fixed to the previous value for the rest of the time:

$$Q^c(t) = -(1 + D^c/D^s)(T_h^\circ - T_r^\circ); \quad (65)$$

- (2) the intramural pressure experiences a jump or an oscillation;
 (3) a radial proliferation mechanisms comes into action through a stress driven control law:

$$Q^p = G^p(T_h - T_h^\circ) - (T_r - \tilde{\phi}). \quad (66)$$

Note how the above expression looks like the radial control law in (27), apart from the difference between T_h° and T_h^\diamond .

6. Stability issues

Definition 6.1. A motion M is said to be Lyapunov stable if, given any $\epsilon > 0$ there exists a $\delta > 0$ such that if N is any motion which starts out at $t = 0$ inside a δ -ball centered at M , then it stays in an ϵ -ball centered at M for all time t .

In particular this means that an equilibrium point P will be Lyapunov stable if you can choose the initial conditions sufficiently close to P (inside a δ -ball) so as to be able to keep all the ensuing motions inside an arbitrarily small neighborhood of P (inside an ϵ -ball). A motion is said to be Lyapunov unstable if it is not Lyapunov stable.

Definition 6.2. If, in addition to being Lyapunov stable, all motions N which start out at $t = 0$ inside a δ -ball centered at M (for some δ) approach M asymptotically as $t \rightarrow \infty$, then M is said to be asymptotically Lyapunov stable.

Theorem 6.1. *Lyapunov's theorems:*

- (1) *An equilibrium point in a nonlinear system is asymptotically Lyapunov stable if all the eigenvalues of the linear variational equations have negative real parts.*
 (2) *An equilibrium point in a nonlinear system is Lyapunov unstable if there exists at least one eigenvalue of the linear variational equations which has a positive real part.*

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