homework II - first draft of final project

due 10/21/10, 11:00am, 420-040

Late homework can be dropped off in a box in front of Durand 217. Please mark clearly with date and time @drop off. We will take off 1/10 of points for each 24 hours late, every 12pm after due date. This homework will count 10% towards your final grade.

problem 1 - understanding

The manuscript *"The kinematics of biological growth"* by Krishna Garikipati reviews different aspects of modeling growth phenomena. Read the manuscript carefully.

1.1 Rewrite the first paragraph in your own words in view of what we have discussed in class (about 150 words). Focus on *the three fundamental elements of continuum mechanics*. Why do they change in the context of growth?

1.2 Discuss *the notion of incompatibility* in the context of growth (about 100 words). Focus on what incompatibility means mathematically and biologically. Discuss why $\boldsymbol{F}^{\mathrm{g}}$ is incompatible and why $\boldsymbol{F}$ is not. Use primarily equation (18) and the following text. You do not have to focus too much on section 3.1, since it is pretty theoretical and does not relate much to our formulation used in class.

1.3 What are the advantages and disadvantages of using *mixture theories*, e.g. the theory of porous media, to describe growth? Use 3.2, 4.1, and what we have discussed in class.

problem 2 - shaping your research project

2.1 Identify *three key references* for your work and at least *three additional references* that you consider relevant. In larger groups, you may identify overlapping key references and individual additional references with special focus. Create a bibliography and submit it with this homework.

2.2.a If you plan to write a scientific paper, identify a key *hypothesis*. The purpose of the hypothesis is to provide focus throughout the manuscript. A good hypothesis is objectively testable, non-trivial, and specific. For example, you could hypothesize that cardiac growth in athletes is reversible and vanishes gradually upon detraining. If you plan a finite element analysis, regional variations in density or volume growth are generally a good hypotheses.

2.2.b If you plan to write a review paper, it might be more difficult to keep focus. In one sentence, specify precisely which aspects of growth you want to review.

2.3 Identify a catchy *opening sentence*. This sentence is meant to catch the attention of the reader. If you plan on writing something disease related, this sentence should reflect the medical importance of your work. For example, this sentense can state the number of people affected, the health care cost involved, or the predicted growth of this disease. Provide a citation to back up your statement.

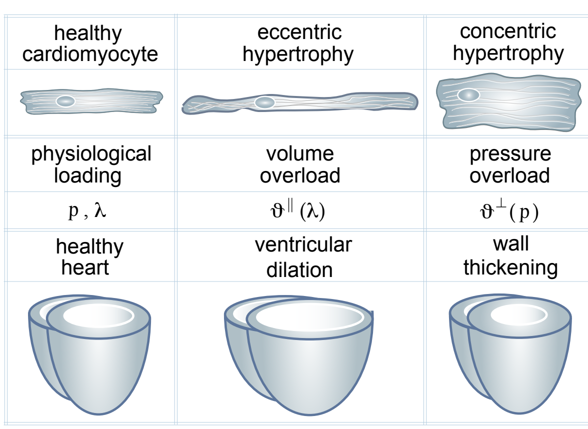
2.4 Summarize the *current knowledge* citing the literature you have listed in your bibliography file.

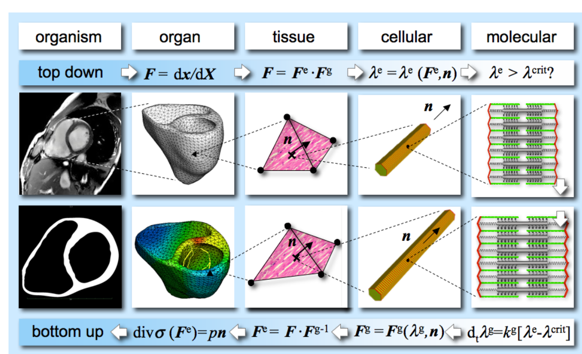
2.4.a If you plan to write a scientific paper, consider breaking the current knowledge section into two paragraphs, one on the biological nature and one mechanical modeling.

2.4.b If you plan to write a review paper, consider breaking the current knowledge section into two or three paragraphs for the individual aspects you plan to review and compare.

2.5 Sketch a *bulleted outline* for your project. This does not need to be your final layout, it is just meant to organize your ideas. Identify the sections and subsections of your paper.

2.6 Create a schematic drawing that summarizes your project. The figures below show two samples of schematic drawings. If you like, you can draft this drawing by hand first. Ultimately, this figure will go into the introduction of your paper, to give the reader a quick overview about your work.





Schematic of data transfer between organism, organ, tissue, cellular, and molecular levels. We test the hypothesis that the overstretch-induced serial addition of sarcomeres on the molecular level translates into cardiac dilation on the organ level.

Although these sub-problems seem to require just a few words, put some effort into structuring your work - this will definitely pay off in the end.

The Kinematics of Biological Growth

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The kinematic aspects of biological growth models are reviewed by paying attention to the handful of crucial ideas on which modern treatments rest. Both surface and volumetric growth are considered. A critical appraisal is presented of the geometric and physical features of the models. Links are made to the mathematical treatment of growth and evolving interface phenomena in other physical problems. Computational issues are pointed out wherever appropriate. [DOI: 10.1115/1.3090829]

1 Introduction

The mathematical theory of biological growth is currently in an adolescent stage. Progress has been made beyond the observation of geometric features—the "form" of D'Arcy Thompson's classic "On Growth and Form" [1]—so that most papers appearing today in the mechanics literature include treatments of balance laws and constitutive relations. A cursory reading of many papers cited in this review would suggest that of the three components of a continuum mechanical treatment, *kinematics*, *balance laws*, and *constitutive relations*, there is broad agreement only on balance laws (however, see Ref. [2]). Constitutive theory for growth remains virtually undeveloped. It is common to observe that the dissipation inequality places certain restrictions on growth rates [3,4] and to use these restrictions to examine some rate forms [5,6]. However, theoretical work relating the mechanical state and biochemistry of growth remains conspicuously underexplored (see Ref. [7], for evidence of some revival of interest in the field formulation of coupled mechano-chemistry). It also lies beyond the scope of this review.

On the kinematics of growth, a great deal has been written, and many important ideas are now settled. Nevertheless there remain areas in need of theoretical developments and computational algorithms, and there even are some outright disagreements on fundamental issues. This review seeks to reiterate what is now commonly accepted, highlight problems in need of further theoretical or algorithmic development, and air some of the controversies that persist regarding the kinematics of growth.

It is useful to begin by stating that the term "growth" is taken to refer to an increase in mass.[1] The closely-related phenomena of remodeling and morphogenesis have been consciously avoided. While the term "remodeling" suggests to some a change in microstructure at constant mass (as an idealization of homeostasis), there is a significant biological literature that labels as remodeling what this review treats as a consequence of growth. The issue has simply not been taken up in this review. "Morphogenesis," the change in form, is applicable at the global scale of the system, rather than the local kinematics that is focused on here. The interested reader is directed to the detailed overview provided by Taber [8] encompassing growth, remodeling, and morphogenesis.

This paper is organized by topics on growth kinematics. Section 2 discusses surface growth. Section 3 is on volumetric growth and residual stresses related to growth. Computational issues associated with known kinematic models are discussed in Sec. 4, and outstanding theoretical questions are highlighted in Sec. 5.

2 Surface Growth

2.1 Formulation Preliminaries. The analytical treatment of surface growth was laid out by Skalak and co-workers [9,10] in a pair of papers. The latter of these papers bears many references to the description of the forms of shells, antlers, horns, tusks, and teeth in Ref. [1]. The particular ingenuity of Skalak and co-workers lay in the analytical treatment that they provided to relate growth rates using the kinematic language of continuum mechanics to the final geometry of forms described by D'Arcy Thompson. They considered an initial growth surface Γ_0, which is a subset of the boundary of the region R_0. As growth takes place on Γ_0, the region R_0 moves as a rigid body (see Fig. 1). The instantaneous growth surface at the current time t is labeled Γ_t, and Γ_τ is the growth surface laid down at time $\tau \leq t$. The Cartesian coordinates of a material point $x_i, i=1,2,3$ are parametrized by convected curvilinear material coordinates $(\theta_1, \theta_2, \theta_3)$ and time.

$$x_i = \hat{x}_i(\theta_1, \theta_2, \theta_3, t) \tag{1}$$

where, for fixed $\theta_1, \theta_2, \theta_3$, Eq. (1) describes the curve traced through space by the material point for these values of θ_1, θ_2, and θ_3. This map is assumed to be invertible.

Two types of functional forms were chosen for surface growth. In the first form, the growth surface is represented by requiring that the θ_3 coordinate on the growth surface $\theta_3^{\Gamma_t}$ be a function of time only.

$$\theta_3^{\Gamma_t} = \hat{\theta}_3^{\Gamma_t}(x_1^{\Gamma_t}, x_2^{\Gamma_t}, x_3^{\Gamma_t}, t) = f_3(t) \tag{2}$$

The second form is suitable for an analytical description of seashells, horns, and teeth. For fixed (θ_1, θ_2) on the growth surface, the same surface cell produces growth by "extrusion." In this case, the positions $\boldsymbol{x}^{\Gamma_t}$ for fixed (θ_1, θ_2) can vary. Then, a curve through the body tracing the growth trajectory of all material points produced by the same cell is obtained by setting the following:

$$\theta_1 = \text{constt}_1, \quad \theta_2 = \text{constt}_2, \quad 0 \leq \theta_3 \leq f_3(t) \tag{3}$$

The velocity of a material point is

$$\boldsymbol{v}^m = \frac{\partial \hat{\boldsymbol{x}}}{\partial t} \tag{4}$$

but the velocity of the generating cell[2] is

$$\boldsymbol{v}^{\Gamma_t} = \left.\frac{\partial \hat{\boldsymbol{x}}}{\partial t}\right|_{\theta_1, \theta_2} = \left.\frac{\partial \hat{\boldsymbol{x}}}{\partial t}\right|_{\theta_1, \theta_2, \theta_3} + \frac{\partial \hat{\boldsymbol{x}}}{\partial \theta_3}\frac{df_3}{dt} \tag{5}$$

The authors defined the growth velocity to be the difference

$$\boldsymbol{v}^g = \boldsymbol{v}^m - \boldsymbol{v}^{\Gamma_t} \tag{6}$$

With this formulation, Skalak and co-workers demonstrated how judicious choices of the vector fields $\boldsymbol{v}^g$ and $\boldsymbol{v}^m$ could generate complex shapes of horns, tusks, and seashells. A crucial in-

[1]Loss of mass is referred to as "resorption."

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[2]These are the cells that produce the new mass.

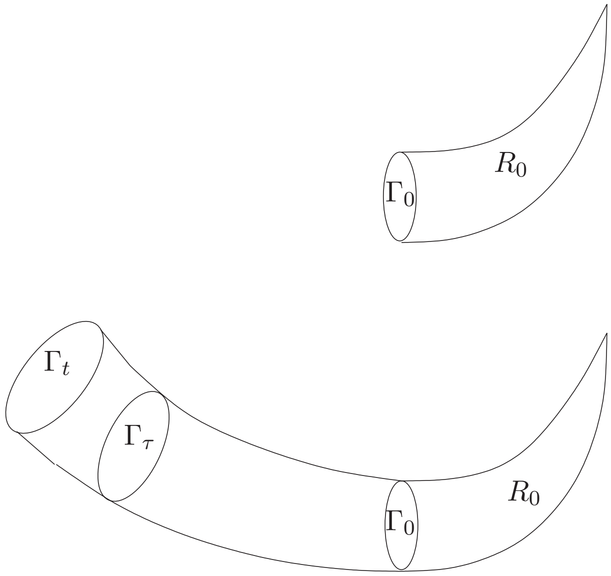

Fig. 1 The initial growth surface Γ_0 and the initial domain R_0, current growth surface Γ_t, and intermediate growth surfaces Γ_τ

sight that they exploited repeatedly was that $\boldsymbol{v}^g$ must include a component tangential to Γ_t if corners and curves in space are to be generated.

2.2 Relation to Classical Continuum Mechanics. In a recent paper Ateshian [7] considered surface and volumetric growth in light of the classical continuum mechanical treatment of motion as an invertible point-to-point map of a reference configuration. The author addressed the admissibility of the notion of a classical deformation gradient $\boldsymbol{F}(\boldsymbol{X},t)=\partial\boldsymbol{\varphi}(\boldsymbol{X},t)/\partial \boldsymbol{X}$, where $\boldsymbol{\varphi}(\boldsymbol{X},t)$ is the deformation map. In the case of surface growth, this notion runs into some difficulties since material points are continually being laid down on the growth surface Γ_t at the current time t but not all material points defining the body at t can be mapped back to a unique reference configuration by a single-valued function.

Ateshian noted that the reference configuration of a material point must remain fixed while the set of material points that makes up the body can change. With this condition he proposed that the reference configuration of a material point be chosen to be that at the instant of deposition via surface growth. The difference between material and surface growth velocities was written as

$$-(\boldsymbol{v}^m-\boldsymbol{v}^{\Gamma_t})\cdot\boldsymbol{n}=\frac{\bar{\rho}}{[\![\rho]\!]} \tag{7}$$

where $\boldsymbol{n}$ is the unit outward normal to the growth surface, $\bar{\rho}$ is the mass production rate per unit surface area, and $[\![\bullet]\!]=\bullet^{+}-\bullet^{-}$ is the jump operator with $\bullet^{\pm}$ being the limiting values of the relevant quantity at the growth surface when approached opposite to and in the direction of $\boldsymbol{n}$, respectively. Using this result the reference placement of a material point deposited on Γ_t at time t was written in terms of the reference placement of a material point that was on $\Gamma_{t-\Delta t}$ at $t-\Delta t$ (Fig. 2):

$$\boldsymbol{\varphi}(\boldsymbol{X}_{\Gamma_t},t)=\boldsymbol{\varphi}(\boldsymbol{X}_{\Gamma_{t-\Delta t}-\Delta t},t-\Delta t)+\boldsymbol{v}^m(\boldsymbol{X}_{\Gamma_{t-\Delta t}-\Delta t},t-\Delta t)\Delta t + \frac{\bar{\rho}}{[\![\rho]\!]}\boldsymbol{n}(\boldsymbol{X}_{\Gamma_{t-\Delta t}-\Delta t},t-\Delta t) \tag{8}$$

2.2.1 New Reference Configuration Due to Tangential Surface Growth Velocity. Equation (8) from Ref. [7] does not account for surface growth velocity that includes a tangential component—an important requirement, as demonstrated by Skalak et al. [10]. Ateshian's treatment is based on Ref. [11], a classical treatment of

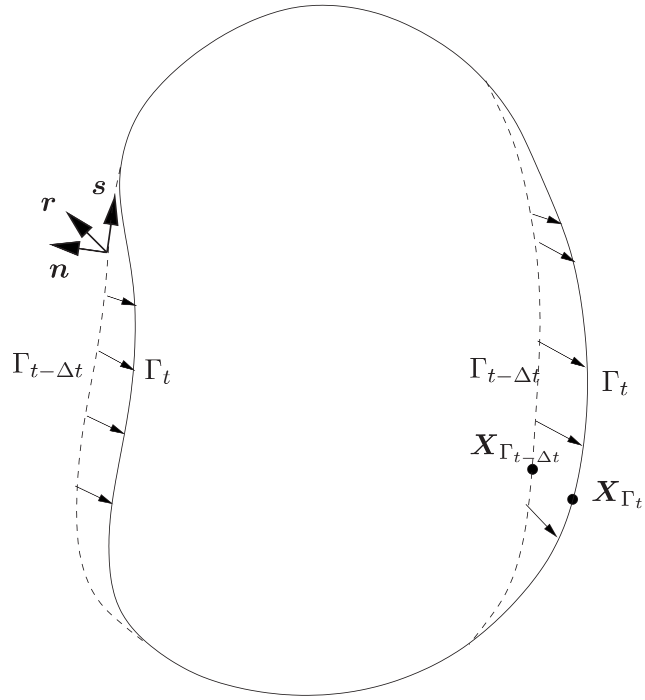

Fig. 2 Determination of the reference configuration of a material point at the instant of deposition on the surface Γ_t

transport equations on domains that could include evolving interfaces. For the purposes of surface growth it suffices to consider Reynolds' transport theorem for mass on the evolving current configuration, Ω_t, of a body with surface Γ_t. The classical result is

$$\frac{d}{dt}\int_{\Omega_t}\rho(\boldsymbol{x},t)dv=\int_{\Omega_t}\frac{\partial\rho(\boldsymbol{x},t)}{\partial t}dv+\int_{\Gamma_t}\rho(\boldsymbol{x},t)\boldsymbol{v}\cdot\boldsymbol{n}ds \tag{9}$$

Here, the surface Γ_t is itself evolving in time, and the surface integral on the right-hand side includes the effect of surface growth. The argument implicit in Ref. [11], and used commonly before and since then, is that only normal growth velocities contribute to surface growth because of the form of the integrand in the surface integral. However, if as shown in Fig. 3 the surface is nonsmooth, there is no unique normal. In this case the surface integral loses the interpretation of "normal," meaning *perpendicular* growth velocity, because multiple definitions of $\boldsymbol{n}$ are possible as shown. Consequently, any choice of $\boldsymbol{n}$ includes a component of surface growth velocity that is tangential to some subdomain of Γ_t. At the risk of loss of rigor, one may present a physical argument: When the surface is smooth, the tangential growth velocity deposits material on the boundary Γ_t at points that already lie on Γ_t. For this reason, the surface does not evolve. However, when the surface is nonsmooth a growth velocity that is tangential to one subdomain of Γ_t does deposit material that causes Γ_t to move perpendicular to itself over another subdomain, and the surface evolves. It is in these cases of nonsmooth surfaces that Skalak's treatment of tangential surface growth velocities applies.

In order to extend the result in Ref. [7] to account for tangential growth, one must proceed as follows. When surface growth includes perpendicular and tangential components, the relation between the velocity jump at Γ_t and surface mass deposition rate is

$$-(\boldsymbol{v}^m-\boldsymbol{v}^{\Gamma_t})\cdot\boldsymbol{n}=\frac{\bar{\rho}_n}{[\![\rho]\!]},\quad -(\boldsymbol{v}^m-\boldsymbol{v}^{\Gamma_t})\cdot\boldsymbol{s}=\frac{\bar{\rho}_s}{[\![\rho]\!]} \tag{10}$$

where $\boldsymbol{s}$ is the unit tangent to Γ_t defined so that the ordered triad $\{\boldsymbol{n},\boldsymbol{s},\boldsymbol{r}\}$ form a right-handed system as shown Fig. 2, and the vectors $\boldsymbol{v}^m-\boldsymbol{v}^{\Gamma_t}$, $\boldsymbol{n}$ and $\boldsymbol{s}$ are co-planar. The surface mass deposi-

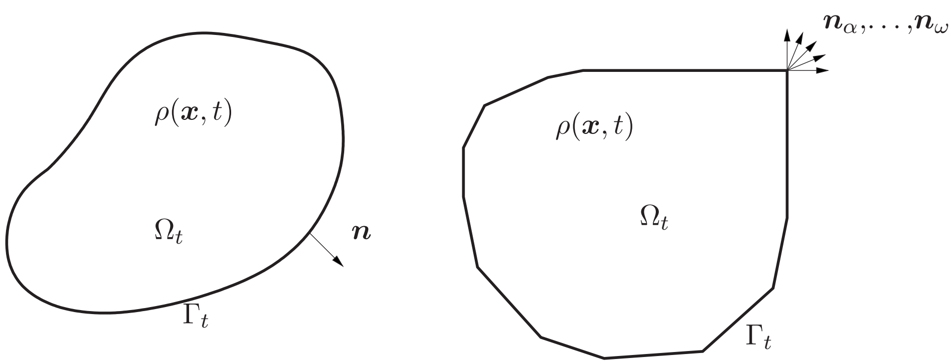

Fig. 3 Admissibility of tangential surface growth velocities on nonsmooth surfaces

tion rates in the perpendicular and tangential directions to Γ_t are $\bar{\rho}_n$ and $\bar{\rho}_s$, respectively.[3]

The above equation can be derived as follows. First write the velocity jump condition as

$$-[\![\rho(\boldsymbol{v}^m - \boldsymbol{v}^{\Gamma_t}) \cdot \mathbf{n}]\!] = \bar{\rho}_n, \quad -[\![\rho(\boldsymbol{v}^m - \boldsymbol{v}^{\Gamma_t}) \cdot \boldsymbol{s}]\!] = \bar{\rho}_s \tag{11}$$

Next, define the normal and tangential jumps of a vector $\boldsymbol{u}$, respectively, as

$$[\![\boldsymbol{u}\cdot\boldsymbol{n}]\!] = \boldsymbol{u}^+\cdot\boldsymbol{n}^+ + \boldsymbol{u}^-\cdot\boldsymbol{n}^-, \quad [\![\boldsymbol{u}\cdot\boldsymbol{s}]\!]\cdot\boldsymbol{s} = \boldsymbol{u}^+\cdot\boldsymbol{s}^+ + \boldsymbol{u}^-\cdot\boldsymbol{s}^- \tag{12}$$

where $\boldsymbol{n}^+ := \boldsymbol{n}$, $\boldsymbol{n}^- := -\boldsymbol{n}$, and the same notation holds for $\boldsymbol{s}^+$ and $\boldsymbol{s}^-$. Also define the jump of a scalar α as

$$[\![\alpha]\!] = \alpha^+ - \alpha^- \tag{13}$$

Finally, use Eqs. (11)–(13) with $\boldsymbol{u}=\boldsymbol{v}^m-\boldsymbol{v}^{\Gamma_t}$, $\alpha=\rho$, $[\![(\boldsymbol{v}^m-\boldsymbol{v}^{\Gamma_t})\cdot\boldsymbol{n}]\!]=0$, and $[\![(\boldsymbol{v}^m-\boldsymbol{v}^{\Gamma_t})\cdot\boldsymbol{s}]\!]=0$ to establish Eq. (10).

With this extension to arbitrary growth direction on Γ_t, Eq. (8) can be extended to

$$\varphi(X_{\Gamma_t},t) = \boldsymbol{\varphi}(\boldsymbol{X}_{\Gamma_{t-\Delta t}}, t-\Delta t) + \boldsymbol{v}^m(\boldsymbol{X}_{\Gamma_{t-\Delta t}}, t-\Delta t)\Delta t + \frac{\bar{\rho}_n}{[\![\rho]\!]_n}\boldsymbol{n} + \frac{\bar{\rho}_s}{[\![\rho]\!]_s}\boldsymbol{s} \tag{14}$$

Based on the reference configuration of newly-deposited material according to Eq. (8), Ateshian proceeded to consider the deformation gradient of a growing material for the cases of inherited strain, stress-free growth, and surface-adhered growth.

2.3 Other Mathematical Treatments of Surface Motion. Growth at an internal surface, or interface, is a common phenomenon in diffusing-reacting systems and has been treated with sophisticated mathematical methods in nonbiological fields. The mathematical treatment requires two components of which the first is a description of the evolving internal surface, which can be accomplished via either a sharp or diffuse interface theory. However, diffuse interface theories require a modification of the mass transport equation in order to incorporate the evolving growth surface by the introduction of a phase field parameter. The result is a fourth-order diffusion equation with the form of the classical Cahn–Hilliard equation [12]. This equation unveils a great beauty of patterns generated and has spawned a vast body of literature in material science and mathematics, but its modification of the transport equation while relevant to a wide range of problems is not appropriate to surface growth. Instead, attention will be directed here to the sharp interface theories that exploit the elegance of the level set formulation [13,14].

A scalar field $\psi(\boldsymbol{x},t)$ with the interpretation of a signed distance function is defined over the spatial domain Ω_t. Thus if Γ_t separates the subdomains Ω_{t_1} and Ω_{t_2}, and $\boldsymbol{x}_{\Gamma_t}\in\Gamma_t$ is a point on the growth surface, then

$$\psi(\boldsymbol{x},t) = \begin{cases} |\boldsymbol{x}-\boldsymbol{x}_{\Gamma_t}| & \boldsymbol{x}\in\Omega_{t_1} \\ -|\boldsymbol{x}-\boldsymbol{x}_{\Gamma_t}| & \boldsymbol{x}\in\Omega_{t_2} \end{cases} \tag{15}$$

The following Hamilton–Jacobi equation is obtained for the evolution of the zero level set $\psi=0$, which represents Γ_t:

$$\frac{\partial\psi}{\partial t} + \boldsymbol{v}^{\Gamma_t}\cdot\nabla\psi = 0 \tag{16}$$

with $\boldsymbol{v}^{\Gamma_t}$ being obtained from the physics that determines the growth velocity, such as Eq. (10). The level set formulation thus is a purely mathematical treatment for the evolution of Γ_t and can be appended to the standard treatment of continuum mechanics.

The second component required to complete the mathematical treatment of growth at an interface is the kinematics to accommodate the newly-formed or consumed material on one side of the interface. This is accomplished via a growth strain that mirrors the treatment of volumetric growth in Sec. 3. See Refs. [15,16] for computationally-focused discussions of growth problems in the thermal oxidation of silicon using these methods and Refs. [17,18] for further numerical advances in treatment of the level set equation.

3 Volumetric Growth

Volumetric growth occurs when mass is added or resorbed from points interior to the body. It is therefore governed by the equation of mass balance in a continuum treatment. Pointwise, such growth causes swelling or contraction that is, in general, anisotropic. An early treatment of the kinematics of volumetric growth driven by mass balance was provided by Hsu [19], who wrote the mass balance relation for an incompressible, growing body,

$$\rho \operatorname{div} \boldsymbol{v} = \tilde{\rho} \tag{17}$$

where $\tilde{\rho}$ is the volumetric mass source. However, Hsu considered an isotropic swelling or contraction of material driven by the density changes. This was followed by Rodriguez et al. [20] who modeled the residual stress due to nonuniform growth via a multiplicative decomposition of the deformation gradient $\boldsymbol{F}=\partial\boldsymbol{\varphi}/\partial\boldsymbol{X}$. Using an approach that was already well-established in finite strain plasticity [21] they wrote

$$\boldsymbol{F} = \boldsymbol{F}^e\boldsymbol{F}^g \tag{18}$$

where $\boldsymbol{F}^g$, sometimes called the growth tensor, is the tangent map induced by growth. Since $\tilde{\rho}$ is a field quantity, $\boldsymbol{F}^g$ evolves independently of $\boldsymbol{F}$. Furthermore, $\boldsymbol{F}^g$ is not compatible in the sense that it is not the gradient of a vector field. Compatibility of $\boldsymbol{F}$, however, is guaranteed by its definition. In this sense $\boldsymbol{F}^e$ is a

[3]While purely tangential growth, $\bar{\rho}_n=0$, $\bar{\rho}_s\neq 0$ is mathematically admissible; it does not appear that it is observed in Nature.

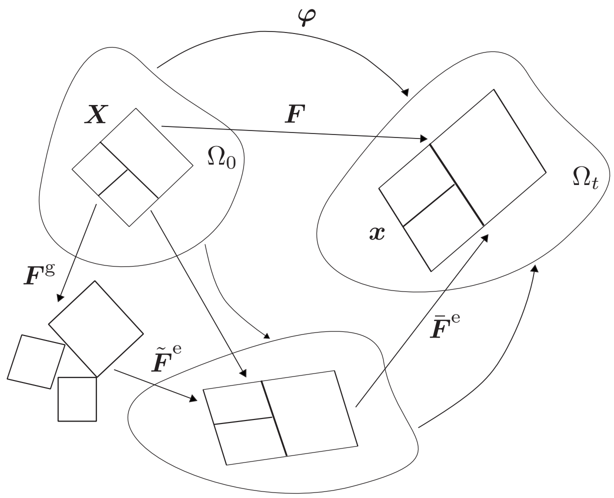

Fig. 4 The kinematics induced by the incompatible volumetric growth tensor F^g and its role in the multiplicative decomposition of the deformation gradient $F=\bar{F}^e\tilde{F}^e F^g$

"compatibility-restoring" field but is itself incompatible.

A hyperelastic biological material has a strain energy function $W(\boldsymbol{F}^e)$, and a corresponding first Piola–Kirchhoff stress $\boldsymbol{P} = \partial W / \partial \boldsymbol{F}^e$. In general, $\boldsymbol{F}^e$ itself admits a multiplicative split.

$$\boldsymbol{F}^e = \bar{\boldsymbol{F}}^e \tilde{\boldsymbol{F}}^e \tag{19}$$

where $\tilde{\boldsymbol{F}}^e$ alone restores a compatible tangent map $\tilde{\boldsymbol{F}}^e\boldsymbol{F}^g$, and $\bar{\boldsymbol{F}}^e$ is compatible by itself (Fig. 4). With these definitions, the body is under purely residual stress if $\bar{\boldsymbol{F}}^e = \boldsymbol{1}$ and $\tilde{\boldsymbol{F}}^e \neq \boldsymbol{1}$ while there are residual and external stress contributions if $\bar{\boldsymbol{F}}^e \neq \boldsymbol{1}$ and $\tilde{\boldsymbol{F}}^e \neq \boldsymbol{1}$.

Rodriguez et al. [20] considered problems in axially-symmetric and rectangular parallelepiped shaped domains, in which either $\boldsymbol{F}^g$ or the rate of the corresponding right stretch tensor $\dot{\boldsymbol{U}}^g$ were specified as functions of the stress. They analytically solved for the residual stress distribution in cases where $\boldsymbol{F}^g$ was specified, and for both $\boldsymbol{F}^g$ and the stress where $\dot{\boldsymbol{U}}^g$ was specified. This kinematics of volumetric growth has become a central feature of growth models [3–6,8,22–28].

3.1 Incompatibility of Growth. A detailed analytical treatment of the incompatibilities entailed by growth was presented by Skalak et al. [29]. While the authors did not use the elasto-growth decomposition adopted above, their treatment in the context of the infinitesimal theory is immediately applicable if the symmetric infinitesimal growth strain is denoted by $\boldsymbol{\varepsilon}^g$. Compatibility is ensured over a domain Ω_0 if

$$\oint_S (\varepsilon^g_{ij}(\boldsymbol{y}) + (x_k - y_k)(\varepsilon^g_{ij,k}(\boldsymbol{y}) - \varepsilon^g_{kj,i}(\boldsymbol{y})))dy_j = 0 \tag{20}$$

for all closed contours $S \subset \Omega_0$. Then, a compatible "growth displacement" field is obtained as the path integral

$$u^g_i(\boldsymbol{x};\boldsymbol{x}_0) = \int_{\boldsymbol{x}_0}^{\boldsymbol{x}} (\varepsilon^g_{ij}(\boldsymbol{y}) + (x_k - y_k)(\varepsilon^g_{ij,k}(\boldsymbol{y}) - \varepsilon^g_{kj,i}(\boldsymbol{y})))dy_j \tag{21}$$

as also discussed by Love [30] and Gurtin [31]. A different form of the compatibility condition is $\nabla \times \nabla \times \boldsymbol{\varepsilon}^g = \boldsymbol{0}$. Alternately, the incompatibility is

$$\boldsymbol{\eta}^g = \nabla \times \nabla \times \boldsymbol{\varepsilon}^g \tag{22}$$

and is related to the dislocation density tensor $\boldsymbol{\alpha}$ via the relation

$$\eta^g_{ij} = \tfrac{1}{2}(\varepsilon^g_{ipk}\alpha_{jk,p} + \varepsilon^g_{jpk}\alpha_{ik,p}) \tag{23}$$

as discussed widely in the classical theory of dislocations [32]. The treatment in this paper by Skalak et al. [29] makes direct connections with Volterra dislocations.

In the finite strain regime compatibility is obtained if, equivalent to Eq. (20), the following relation is satisfied:

$$\oint_S (\boldsymbol{F}^g - \boldsymbol{1})d\boldsymbol{X} = \boldsymbol{0} \tag{24}$$

A pointwise condition given by Blume [33] is

$$R^g_{ijkl} = 0$$

where with the right Cauchy–Green growth tensor $\boldsymbol{C}^g = \boldsymbol{F}^{gT}\boldsymbol{F}^g$ and the Cristoffel symbols

$$\Xi^g_{ijk} = \tfrac{1}{2}(C^g_{jk,i} + C^g_{ik,j} - C^g_{ij,k})$$

we have

$$R^g_{ijkl} = \Xi^g_{jli,k} - \Xi^g_{jki,l} + C^{g-1}_{pq}(\Xi^g_{jkp}\Xi^g_{ilq} - \Xi^g_{jlp}\Xi^g_{ikq})$$

By these ideas, the problem of compatibility of growth at finite strain makes connections with the differential geometric treatment of Kondo [34], Bilby et al. [35], and Kröner and Anthony [36]. The idea that growth tensors are incompatible and can generate residual stress has been used to explain the stressed state of soft biological tissues such as arteries [37,38], veins [39], ventricular myocardium [40], and trachea [41].

3.2 The Evolving Natural Configuration. Humphrey and Rajagopal [42] adopted a view of volumetric growth kinematics that is diametrically-opposed to the notion that residual stress is generated due to the incompatibility of growth. They did not view residual stress to be the consequence of incompatible growth in stress-free configurations. Instead, in the setting of the mixture theory, they interpreted the experimental literature (such as that of Fung and co-workers cited above) as pointing to fundamental growth processes in which the tissue's constituents, which are grown in stressed states that differ from one another, are spatially nonuniform and differ from the existing stress state of the same constituent in the tissue at the instant of deposition. They allowed that each sufficiently small neighborhood could have a different *natural configuration* $\boldsymbol{\kappa}_n$. If these neighborhoods all have the same natural configuration when the body is traction-free, then it will also be stress-free. If the natural configurations are different, then the traction-free body will have a residual stress unless the natural configurations are all obtained from their corresponding, possibly hypothetical, reference configurations via a tangent map that is a pure rotation tensor, including the isotropic tensor.

The authors argued that in addition to the stress state, the heterogeneity and anisotropy of deposition must be known. As an example they considered isotropic deposition of material on to a stress-free tissue state versus on a deformed—and therefore stressed—state. While the response of newly-deposited material will be isotropic in the first case, it will be anisotropic in the second. Nonhomogeneity of deformation and deposition further complicate the problem. They proposed, therefore, that the placement in the natural configuration be denoted by $\boldsymbol{X}_{\boldsymbol{\kappa}_n}$, and that the appropriate deformation gradient to consider is

$$\boldsymbol{F} = \frac{\partial \boldsymbol{x}}{\partial \boldsymbol{X}_{\boldsymbol{\kappa}_n(\tau)}} \tag{25}$$

where a material point has natural configuration $\boldsymbol{\kappa}_n(\tau)$, with τ indicating the instant of deposition of tissue constituents. This leads to the need to specify constitutive relations for the evolving natural configurations $\boldsymbol{\kappa}_n$—a complex task from experimental, theoretical, and computational standpoints.

3.3 Admissibility of an Elasto-Growth Decomposition to Represent Volumetric Growth. Ateshian [7] challenged the admissibility of the multiplicative decomposition $\boldsymbol{F}=\boldsymbol{F}^e\boldsymbol{F}^g$ to model volumetric growth. When the tissue is modeled as a biphasic mixture of solid and fluid, this decomposition would be applied to each phase. The author considered the limiting cases of (a) "cavitation" when the solid apparent density vanishes, $\rho^s \to 0$ at a point, and the tissue is entirely fluid at that point and (b) nucleation when the solid is formed at a point that previously contained only fluid. It was pointed out that cavitation corresponds to a singular $\boldsymbol{F}^{g^s}$ in the classical continuum framework, i.e., disappearance of matter, where the superscript s indicates "solid." For nucleation the difficulty is that $\boldsymbol{F}^{g^s}$ must be defined relative to a reference configuration that has $\rho^s=0$, and therefore is not even a solid material point. The author pointed out that nucleation can be modeled in the manner of surface growth described in the same paper [7] and outlined in Sec. 2.2. However, the difficulty associated with cavitation motivated the author to reject the use of the elasto-growth decomposition to model volumetric growth.

In weighing this criticism of the elasto-growth decomposition, the following fundamental aspects may be recalled. The kinematics of the classical continuum formulation is not meant to extend to cavitation—a restriction that is embedded in the requirement that $\det \boldsymbol{F}^s = \det \boldsymbol{F}^{e^s} \det \boldsymbol{F}^{g^s} > 0$. Clearly, this is violated by cavitation. Instead, the condition $\rho^s \to 0$ over a finite neighborhood (and it has to be a *finite* neighborhood since *continuum* mechanics requires that ρ^s be continuous) signals that a cavity of fluid has formed, bounded by a surface $\mathcal{S}_t$. This surface then advances further into the solid phase at subsequent time instants via surface resorption of the solid phase (see Sec. 2). The use of the decomposition $\boldsymbol{F}=\boldsymbol{F}^e\boldsymbol{F}^g$ is rigorously applicable only in the solid phase where $\rho^s > 0$.

4 Computational Issues

4.1 Homogeneity of Deformation Gradients. If the tissue is modeled as a multiphase material, mixture theory requires that individual balances of mass and momentum be written for each phase [43]. However, the momentum balance equations can be summed over the phases and an effective momentum balance equation can be written for the composite tissue [3]. The reduction in number of equations must be compensated by kinematic assumptions, of which the simplest possible is that the deformation gradient is homogeneous among the summed phases. Such an approach was also followed for the solid tissue components by Humphrey and Rajagopal [42].

In a recent paper Narayanan et al. [44] studied the effect of this strain homogenization assumption. Guided by elementary results in the theory of composite materials, they identified this kinematic assumption as leading to an upper bound on the modulus of the composite tissue. If applied to coupled computations of mass transport and mechanics of the biphasic fluid-solid tissue, this assumption has the unsavory feature of retarding numerical convergence of staggered solution schemes that are often used in conjunction with finite element methods. Narayanan et al. [44] found the slow convergence to be due to the strong fluid-solid coupling engendered by the strain homogenization. A small variation in deformation gradient during each pass of the staggered solution algorithm causes unequal variations in the fluid and solid hydrostatic stresses. If the fluid is modeled as incompressible (or nearly incompressible), its hydrostatic stress variation is much higher and causes large stresses in the composite tissue. As a result, convergence of the momentum balance equations is severely hampered. When compared against the convergence rate with a stress homogenization assumption, the number of passes for convergence to the same numerical tolerance is at least two orders of magnitude more if the strain homogenization assumption is used. This has implications for numerical stability: If unconverged solutions are used to advance the problem, it will eventually diverge.

4.2 Data Storage for Evolving Natural Configurations. As expressed by Eq. (25) drawn from Ref. [42] a material point has natural configuration $\boldsymbol{X}_{\boldsymbol{\kappa}_n(\tau)}$ if deposited at time τ. Consider the solid component with the current concentration $\rho^s(\boldsymbol{x},t)$. The mass balance equation gives

$$\rho^s(\boldsymbol{x},t) - \rho^s(\boldsymbol{x},0) = \int_0^t (\tilde{\rho}^s(\boldsymbol{x},\tau) - \mathrm{div}(\rho^s \boldsymbol{v}^s))d\tau \qquad (26)$$

The material contained in a neighborhood at $\boldsymbol{x}$ was deposited at different instants $\tau \in [0,t]$, and through the integrand on the right-hand side in Eq. (26), the deposited masses depend on the stress and other state variables at each time instant $\tau \in [0,t]$. The evolution equation for the natural configuration $\boldsymbol{\kappa}_n(t)$ therefore requires integration over the time interval $[0,t]$. It is determined by the entire history of states through which the neighborhood at $\boldsymbol{x}$ evolved. The general formulation is therefore data intensive. Simplifying hypotheses must be made for tractability (e.g., Ref. [45], where it was assumed that material is deposited with its stress or stretch lying in a certain range).

5 Outstanding Theoretical Questions

The state of the science of soft tissue mechanics has advanced to the point where constitutive relations for passive mechanical response have been studied in considerable depth. There are now many classes of constitutive models for hyperelastic, viscoelastic, and poroelastic response. At the risk of overlooking a number of relevant works the following list can be considered as representative: Refs. [46–53]. The reader is also encouraged to consult the number of excellent constitutive models presented in Ref. [54]. There remain areas for development related to the entropic versus energetic response, homogenization of response across phases, competition between viscoelastic and biphasic responses, and others. There have already been several important papers on these questions, and some of them are included in the list just above. These constitutive models are used in formulations of growth. However, on evolution equations for the kinematics of growth, much remains to be done.

5.1 Evolution of the Growth Tensor. When the formulation for volumetric growth (3) is adopted, the growth tensor evolves with the change in concentration. Consider the solid phase and its mass balance equation written in the reference configuration as

$$\frac{\partial \rho_0^s}{\partial t} = \tilde{\rho}_0^s \qquad (27)$$

where ρ_0^s is the concentration and $\tilde{\rho}_0^s$ is the volumetric mass production rate, both per unit reference volume. The volume change due to growth is

$$\det \boldsymbol{F}^{g^s} = \left(\frac{\rho_0^s}{\rho_{0_{\mathrm{ini}}}^s}\right)$$

where $\rho_{0_{\mathrm{ini}}}^s$ is the initial concentration. The full tensorial form of $\boldsymbol{F}^{g^s}$, however, remains to be specified. While, in its simplest mathematical form, growth is isotropic and $\boldsymbol{F}^{g^s} = (\rho_0^s/\rho_{0_{\mathrm{ini}}}^s)^{1/3}\mathbf{1}$, anisotropic growth is also common and is demonstrated by the oriented deposition of collagen by fibroblasts [55,56] in tendons and ligaments. Kinematic forms for $\boldsymbol{F}^{g^s}$, or more appropriately, for $\dot{\boldsymbol{F}}^{g^s}$, can then be specified on the basis of experiments. Stress-dependent growth laws were specified for the aorta by Taber and Eggers [57] and for the muscle by Taber [58]. In both cases growth rates $\dot{\boldsymbol{F}}^g$ were written as linear functions of the stress, with coefficients chosen to match experiments. A somewhat more theoretical approach stems from the preference for continuum constitutive laws that are, by construction, consistent with the second law of thermodynamics. When imposed à fortiori this reduces to the requirement that the scalar product ${\boldsymbol{F}^{e}}^{T}\boldsymbol{P}:\dot{\boldsymbol{F}}^{g}$ be non-negative. Here, $\boldsymbol{P}$ is the first Piola–Kirchhoff stress tensor. Ambrosi and Guana [6] used this approach to lay down an evolution law for $\dot{\boldsymbol{F}}^{g}$.

A weaker form of consistency with the second law was used by Garikipati et al. [3]. The sum of several terms including one of the form ${\boldsymbol{F}^{e}}^{T}\boldsymbol{P}:\dot{\boldsymbol{F}}^{g}$ was specified to be non-negative. With this approach it remains to choose forms for $\dot{\boldsymbol{F}}^{g}$ and à posteriori check whether the sum of the terms is in compliance with the second law. While allowing for more flexibility in the choice of constitutive relation, this approach has the drawback that noncompliance with the second law is more difficult to rectify.

It appears that there are opportunities to be mined in systematic studies that combine the thermodynamics of growth laws with experimental data on tensorial growth rates.

5.2 Evolution Laws for Natural Configurations. In addition to the data-intensive nature of computations with evolving natural configurations (Sec. 4.2), the specification of evolution equations remains in as undeveloped a state as for the growth tensor. Besides the paper by Gleason and Humphrey [45] cited above, there has been recent work in this direction by Kroon and Holzapfel [59] on the growth of saccular cerebral aneurysms. In their paper the prestretch of deposited collagen was included as a parameter. The response and stability of the aneurysm were studied as a function of the prestretch, which defines the natural configuration in which the collagen is deposited. Further studies are also needed in which such quantities that define the natural configuration are not fixed parameters but depend on the state variables.

5.3 Cell Growth. Much of the literature on the kinematics of biological growth is applicable to a cell. A reading of modern cell biology textbooks (such as the contemporary classic by Alberts et al. [56]) reveals the cell to be an ideal subject for application of the topics considered in this review. It has a well-defined boundary, the cell membrane, which evolves with growth, and undergoes complicated morphological changes during cell division. It can also be argued that nonkinematic aspects of the continuum treatment of growth also find direct—even literal—application to cell growth. However, that is a topic that is appropriately dealt with in a broader commentary on biological growth

6 Closing Remarks

While this review has focused on kinematics of growth, it is important to note that there remain many open issues with regard to constitutive relations, thermodynamics, and their bearing on computational algorithms. Problems of remodeling pose a separate set of theoretical issues for constitutive relations, thermodynamics, and even balance laws. Morphogenesis has received even lesser attention other than for some recent work by Ramasubramanian et al. [60]. A much more detailed review, or series of reviews, is needed to fully address the state of models for growth, remodeling, and morphogenesis. The aim of this review has been a narrow one: to revisit models for the kinematics of growth, some classical and some recent, with an attempt to place in perspective some papers that have appeared lately. In the process some contrasting views have been aired, such as on the use of growth tensors and the origins of residual stress. Progress has been highlighted in mathematics and numerical methods for which growth is but one application. Several open questions have been given prominence—particularly constitutive laws for the evolution of growth.

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