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The influence of external free energy and homeostasis on growth and shape change

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ABSTRACT

Mechanical forces are essential for the proper growth and biomechanical remodeling of several biological tissues. However, the relationship between mechanical forces and changes in tissue volume and shape is only beginning to be revealed in experiments. Theoretical contributions have provided an appropriate framework to interpret growth and remodeling in terms of mechanical loading. We present a volumetric growth model that shares features of these previous models. We focus on three key parameters for predicting tissue growth: (1) the characterization of the homeostatic reference state in which no growth occurs, (2) the mechanical energy of newly created tissue, and (3) the effect of shear forces on growth and inelastic shape change. To facilitate this analysis, we decompose the deformation gradient into a product of the inelastic growth and elastic deformations. We then place the evolution equation for the growth deformation in a thermodynamic context. Homeostasis, incoming free energy, and shear forces each directly affect the evolution of the tissue. We demonstrate this using numerical examples.

1. Introduction

Embryonic development is characterized by rapid transitions in tissue size, shape, and function. Examples of this include the folding of the heart tube into four chambers (Manner, 2000) and the elongation and condensation of the atrioventricular valve leaflets (Kruithof et al., 2007; Buskohl et al., 2012a). Experimental studies have demonstrated that abnormal mechanical loading in the early heart can generate defects. As examples, the ligation of the left atrium of a chick embryo results in reduced blood flow and a decrease in left ventricle volume (Sedmera et al., 1999), and obstruction of blood flow in a zebrafish embryo generates enlarged atrias and impaired valves (Hove et al., 2003). Even in less mechanically robust environments, such as neural tube formation (Nerurkar et al., 2006) or torsion of the early cardiac tube (Xu et al., 2010), residual stresses exist that are essential for proper formation. These examples illustrate the need for mathematical frameworks in which to connect mechanical loading with changes in tissue size, shape, and function during development.

Such development may be divided into three categories: mass addition (growth), material property change (remodeling), and shape change ("morphogenesis") (Taber, 1995). Growth involves extra-cellular matrix production, cell proliferation, and cell enlargement. In these processes, mass is converted and redistributed by the cells. Sources of mass include soluble factors, such as those present in the blood stream or cell culture media, or assembled protein structures, such as

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glycoaminoglycan or collagen networks from neighboring tissues. Growing systems are generally modeled as open, at least with respect to mass, because the origin of the incoming mass is external to the mechanical element(s) being modeled (Lubarda and Hoger, 2002; Epstein and Maugin, 2000; Ganghoffer, 2010). Remodeling involves changes in material properties, such as stiffness, material symmetry, constituent volume fractions, and/or chemical reactivity. Remodeling, growth, and shape change often occur simultaneously. We do not consider remodeling here, but instead focus on growth and shape change using a single-constituent model.

Embryogenesis is the dynamic process in which embryonic tissues form, change shape, and mature into functional organs. Kinematic descriptions of morphogenesis as a mapping of material points have been considered in research on plant growth (Richards and Kavanagh, 1943; Silk and Erickson, 1979). In the context of bone remodeling, Cowin and Buskirk (1979) introduced a mechanically driven, small strain, surface growth model that related the normal velocity of the bone surface to the difference in current and referential strain experienced by the tissue. Skalak et al. (1982) applied the concept of growth as velocity field to finite strain problems, and considered both volumetric and surface additions. Rodriguez et al. (1994) extended this work with a multiplicative decomposition of the deformation gradient into inelastic and elastic components, borrowing ideas from metal plasticity (Lee, 1969). In their approach, tissue growth and shape change occur through the evolution of a local stress-free configuration. Other approaches include mixture theory (Gleason and Humphrey, 2005), poroelastic modeling (Cowin and Cardoso, 2012), and multi-scale models connecting molecular and continuum level processes (Hayenga et al., 2011). Another important area of growth mechanics is growth-induced bifurcation behavior deriving from shape and material instabilities (Amar and Goriely, 2005; Goriely and Amar, 2005). However, these aspects are not within the scope of our study.

The determination of the appropriate form of evolution equations for growth and shape change has been the focus of much research (Epstein and Maugin, 2000; Lubarda and Hoger, 2002; DiCarlo and Quiligotti, 2002; Ambrosi and Guana, 2007; Ganghoffer, 2010). With limited experimental data available, this research has employed thermodynamic arguments based on the entropy inequality or a dissipation principle to motivate appropriate forms. Regardless of the means used to satisfy the inequality, such as the assumption of maximal dissipation (Rajagopal and Srinivasa, 2000; Fusi et al., 2006) or the introduction of quadratic dissipative parts, it is necessary to consider the influence of mass addition on the thermodynamics. For example, does new mass enter with mechanical energy density equal to that at the material point, with no mechanical energy (stress-free), or with some intermediate, constituent-specific energy? External sources of energy or entropy associated with the incoming mass are sometimes neglected (DiCarlo and Quiligotti, 2002; Garikipati et al., 2005). In this paper, we evaluate how these different assumptions influence the evolution.

Various assumptions have also been made regarding the mechanical stimuli for growth and shape change, including strain (Cowin and Buskirk, 1979; Hart, 1990), stress (Fung, 1990; Rodriguez et al., 1994), and strain energy (Harrigan and Hamilton, 1992). Experimental evidence suggests that certain plants and embryos maintain a target, or homeostatic, stress state (Beloussov, 1998; Beloussov and Grabovsky, 2006). At the homeostatic stress state, growth and shape change do not occur. Evidence for a homeostatic stress is seen in arteries, where the artery wall develops a residual stress to equalize, as much as possible, the stress under physiological loading (Chuong and Fung, 1986). We assume the existence of a homeostatic stress state and incorporate it into the evolution equations through an expression for the balance of biochemical forces (DiCarlo and Quiligotti, 2002; DiCarlo, 2005).

Shear forces are a significant part of the mechanical environment in certain instances of development. In particular, blood flow through the primitive heart generates significant wall shear stress on the valve and vascular structures (Hove et al., 2003; Biechler et al., 2010; Yalcin et al., 2011). Experiments suggest that these shear forces are important for activating biochemical cascades within the cell that drive the production and rearrangement of extra-cellular matrix proteins, cellular proliferation, cell contraction, and other mechanically relevant processes (Groenendijk et al., 2005). While previous growth models have the capacity to evolve in shear (Ambrosi and Guana, 2007; Ramasubramanian and Taber, 2008), examples of growth and shape change under shear loading are limited. We present some simple numerical examples to demonstrate the shearing behavior of the growth model.

2. Theory/calculations

2.1. Kinematics

We consider a stress-free body in the initial configuration at time $t=0$. The body undergoes a deformation from the initial to current configuration defined by the mapping $\boldsymbol{x}=\boldsymbol{x}(\boldsymbol{X},t)$. The deformation gradient of this mapping, defined as $\boldsymbol{F}=\delta\boldsymbol{x}/\delta\boldsymbol{X}$, may include elastic deformation due to mechanical loading and inelastic deformation due to growth. To distinguish between these contributions, we decompose $\boldsymbol{F}$ into the product of its elastic, $\boldsymbol{f}$, and inelastic, $\mathcal{F}$, parts

$$\boldsymbol{F}=\boldsymbol{f}\mathcal{F}. \tag{1}$$

This multiplicative decomposition was first applied to growth mechanics by Rodriguez et al. (1994), and is employed as a means to mathematically access the inelastic deformation. With the deformation decomposed, we may define the evolution of the inelastic deformation using the deformation rate tensor:

$$\mathcal{L}=\dot{\mathcal{F}}\mathcal{F}^{-1}, \tag{2}$$