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A generic approach towards finite growth with examples of athlete's heart, cardiac dilation, and cardiac wall thickening

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ABSTRACT

The objective of this work is to establish a generic continuum-based computational concept for finite growth of living biological tissues. The underlying idea is the introduction of an incompatible growth configuration which naturally introduces a multiplicative decomposition of the deformation gradient into an elastic and a growth part. The two major challenges of finite growth are the kinematic characterization of the growth tensor and the identification of mechanical driving forces for its evolution. Motivated by morphological changes in cell geometry, we illustrate a micromechanically motivated ansatz for the growth tensor for cardiac tissue that can capture both strain-driven ventricular dilation and stress-driven wall thickening. Guided by clinical observations, we explore three distinct pathophysiological cases: athlete's heart, cardiac dilation, and cardiac wall thickening. We demonstrate the computational solution of finite growth within a fully implicit incremental iterative Newton–Raphson based finite element solution scheme. The features of the proposed approach are illustrated and compared for the three different growth pathologies in terms of a generic bi-ventricular heart model.

1. Motivation

Unlike engineering materials, living biological tissues are known to grow and adaptively change their form and function in response to environmental changes. Almost a century ago, it was recognized that the physical laws of mechanics could provide a natural framework to characterize relations between form and function of growing biological structures (Thompson, 1917). Since the classical framework of continuum thermodynamics has originally been developed for non-living materials, however, we have now come to realize that the traditional kinematic equations, the balance equations, and the constitutive equations have to be reconsidered in the presence of growth (Cowin and Hegedus, 1976; Hsu, 1968; Humphrey and Rajagopal, 2002; Kuhl and Steinmann, 2003a, 2003b; Skalak, 1981). Deviations from the classical theory strongly depend on the particular type of biological adaptation (Cowin, 2004; Taber, 1995). We commonly distinguish

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between density growth common to hard tissues such as bone (Carter and Hayes, 1977; Cowin and Hegedus, 1976; Kuhl et al., 2003; Kuhl and Steinmann, 2003c), tip growth common to plants (Dumais et al., 2006), surface growth common to sea shells or horns (Skalak et al., 1997; Thompson, 1917), volume growth common to soft tissues such as arteries or tumors (Ambrosi and Mollica, 2002; Rodriguez et al., 1994; Taber and Humphrey, 2001), and remodeling common to the development of soft collageneous tissues (Ciarletta and Ben Amar, 2009; Himpel et al., 2008; Kuhl et al., 2005; Kuhl and Holzapfel, 2007; Menzel, 2005).

In this manuscript, we shall focus exclusively on volume growth which has experienced its breakthrough in continuum modeling with the introduction of an incompatible growth configuration and the corresponding multiplicative decomposition of the deformation gradient into an elastic and a growth part (Rodriguez et al., 1994), a concept that was originally developed for finite strain plasticity (Lee, 1969). Today, there seems to be a general agreement that the concept of an incompatible growth configuration is a suitable and effective approach towards finite growth, and a tremendous amount of research has been devoted to establish continuum theories of finite growth within the last decade (Ambrosi et al., 2008, under review; Ben Amar and Goriely, 2005; Chen and Hoger, 2000; Epstein and Maugin, 2000; Goriely and Ben Amar, 2007; Imatani and Maugin, 2002; Lubarda and Hoger, 2002). The theory of finite growth has been successfully applied to characterize growth of tendon (Garikipati et al., 2004), tumors (Ambrosi and Mollica, 2002), cartilage (Klisch et al., 2003), vascular tissue (Humphrey, 2002, 2008; Kuhl et al., 2007; Taber and Humphrey, 2001), and, most recently, cardiac tissue (Kroon et al., 2009; Göktepe et al., 2010a). While initial efforts have mainly been theoretical in nature (Ambrosi and Mollica, 2002; Garikipati, 2009; Humphrey, 2002; Taber and Humphrey, 2001), we can clearly observe a trend towards analyzing inhomogeneous finite growth based on computational modeling (Alastrue et al., 2009; Alford and Taber, 2008; Figueroa et al., 2009; Himpel et al., 2005; Kroon et al., 2009), usually by introducing the growth tensor as an internal variable within a finite element framework. Despite tremendous research aiming to provide a better understanding of the mechanics of growth, two fundamental questions still remain unanswered: How do we define an appropriate kinematic characterization of the growth tensor? And how do we identify mechanical driving forces for growth?

The main idea of this manuscript is to closely tie the definition of the macroscopic growth tensor and the forces driving its evolution to microstructural observations. Since the cellular microstructure can vary considerably for different types of tissue, we focus on one particular model system, the human heart, and tie its growth characterization to morphological changes in its key characteristic cell type, the cardiomyocyte. Although cardiomyocytes comprise only one-fourth of the total number of cells in the heart, they account for more than 90% of the volume of the cardiac muscle (Kumar et al., 2005). The functional contractile unit of the cardiomyocyte is the sarcomere, a $1.6-2.2\,\mu m$ long parallel arrangement of thick filaments of myosin that slide along thin filaments of actin. About 50 sarcomeres in series make up a myofibril and about 50–100 myofibrils in parallel make up a cardiomyocyte. Healthy cardiomyocytes have a cylindrical shape with a diameter of $10-25\,\mu m$ and a length of $100\,\mu m$ (Opie, 2003), consisting of approximately 5000 sarcomere units. Unlike most other cell types in the human body, functional adult cardiomyocytes cannot perform cell division (hyperplasia) such that the total number of cells, about 6 billion at birth, cannot increase. However, cardiomyocytes can grow in size (hypertrophy), and they do so by the deposition of new sarcomere units. The muscle fibers of cardiomyocytes are arranged in transmural layers or sheets which are organized helically around the heart. Fig. 1 illustrates the orthotropic architecture of the mycoardium in terms of the fiber directions $\boldsymbol{f}_0$ and sheet plane vectors $\boldsymbol{s}_0$.

We hypothesize that macrostructural maladaptive cardiac growth can be traced to the intrinsic microstructural architecture of the cardiomyocyte itself. Two classical examples are eccentric and concentric hypertrophy (Libby et al., 2007; Opie, 2003). In response to chronic volume overload, an increased diastolic wall stress leads to the addition of sarcomeres in series, resulting in a relative increase in cardiomyocyte length, associated with eccentric hypertrophy and ventricular dilation. In response to chronic pressure overload, however, an increased systolic wall stress leads to the

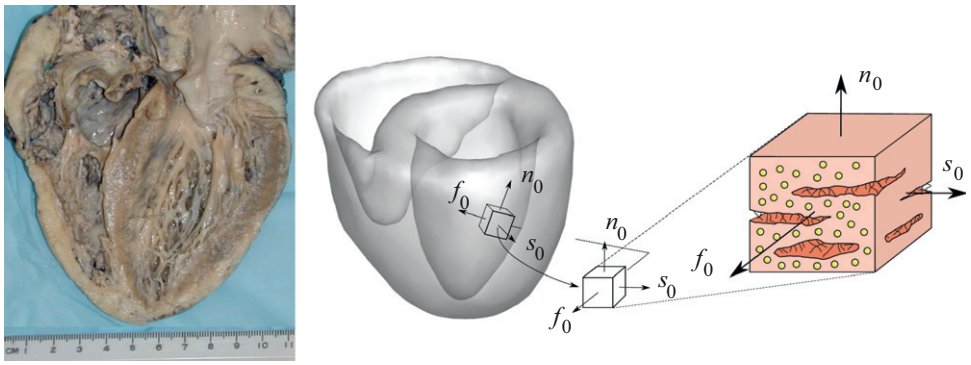

Fig. 1. Normal healthy heart, courtesy of Chengpei Xu (left). Microstructural architecture of the heart (right). The orthogonal unit vectors $\boldsymbol{f}_0$ and $\boldsymbol{s}_0$ designate the muscle fiber direction and the sheet plane vector in the undeformed configuration. The orthogonal vector $\boldsymbol{n}_0$ completes the local coordinate system, where the constitutive response of the heart is typically viewed as orthotropic.