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Surface wrinkling of mucosa induced by volumetric growth: Theory, simulation and experiment

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ABSTRACT

Mechanics of living tissues focusing on the relationships between growth, morphology and function is not only of theoretical interest but can also be useful for diagnosis of certain diseases. In this paper, we model the surface wrinkling morphology of mucosa, the moist tissue that commonly lines organs and cavities throughout the body, induced by either physiological or pathological volumetric growth. A theoretical framework of finite deformation is adopted to analyze the deformation of a cylindrical cavity covered by mucosal and submucosal layers. It is shown that compressive residual stresses induced by the confined growth of mucosa can destabilize the tissue into various surface wrinkling patterns. A linear stability analysis of the critical condition and characteristic buckling patterns indicates that the wrinkling mode is sensitive to the thicknesses of the mucosal and submucosal layers, as well as the properties of the tissues. The thinner the mucosal layer and the lower its elastic modulus, the shorter the buckling wavelength. A series of finite element simulations are performed to validate the theoretical predictions and to study local wrinkling or non-uniform patterns associated with inhomogeneous growth. Our postbuckling analysis shows that the surface pattern may evolve towards a period-doubling morphology due to continuous growth of mucosa or submucosa beyond the critical state. Finally, the theoretical predictions and numerical simulations are compared to experimental observations.

1. Introduction

Growth or, conversely, resorption of living biological tissues often involves complicated biochemical and biophysical processes at different length and time scales. Growth, which manifests itself in the increase of body mass, is crucial for the normal development of tissues and at the same time can be subject to various pathological disorders. Generally, to fulfill different biological functions, tissue growth may take place in three typical forms, namely, tip growth, surface growth, and volumetric growth (Ben Amar and Goriely, 2005). In tip growth, which happens in, for instance, root hairs, fungal hyphae and pollen tubes, cells typically form a slender structure capped by a prolate dome where expansion occurs (Heath, 1990; Goriely and Tabor, 2003; Dumais et al., 2006). Surface growth is often adopted by organisms such as seashells and hornshells, where mass tends to accrete on an existing surface (Skalak et al., 1997; Garikipati, 2009; Ganghoffer, 2010). In contrast, volumetric growth in the bulk of a tissue is responsible for the development of most soft tissues, e.g. arteries,

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airways, heart, muscles, and solid tumors (Taber, 1995; Ambrosi and Mollica, 2002; Humphrey, 2003; Cowin, 2004; Dunlop et al., 2010; Goriely and Vandiver, 2010; Dervaux and Ben Amar, 2011; Moulton and Goriely, 2011).

Considerable effort has been directed toward developing theoretical models for the volumetric growth of soft tissues. Most existing models fall into three classes, diffusion models (Brú et al., 2003; Anderson et al., 2006), elastic models (Rodriguez et al., 1994; Epstein and Maugin, 2000; Lubarda and Hoger, 2002; Ben Amar and Goriely, 2005; Goriely and Ben Amar, 2005; Dervaux et al., 2009), and mixture models (Humphrey and Rajagopal, 2002; Garikipati et al., 2004; Klisch et al., 2005; Ambrosi et al., 2010). In the present paper, an elastic model will be adopted to study, at a macroscopic scale, the mechanical behaviors of soft tissues under volumetric growth. The model is based on multiplicative decomposition of deformation gradient, which is formally analogous to the well-known decomposition of elastic and plastic deformation gradient tensors (Lee, 1969). Following Rodriguez et al. (1994), the deformation gradient is decomposed into the product of a growth tensor describing the addition of materials and an elastic deformation tensor to ensure local compatibility and integrity of the tissue. The elastic deformation gives rise to residual stresses, which is believed to play a significant role in the morphological evolution of tissues and their growth (Fung, 1990; Skalak et al., 1996; Holzapfel et al., 2000; Humphrey 2003). In the past, the strategy of multiplicative decomposition of deformation gradient has been adopted in various growth models of biological tissues such as arteries (Taber and Humphrey, 2001), heart (Taber and Perucchio, 2000), muscles (Taber, 1998), and solid tumors (Tracqui, 2009), and finite element methods have been developed to analyze the volumetric growth usually described by an internal variable (Kuhl et al., 2003; Rodríguez et al., 2007; Alastrué et al., 2008; Ramasubramanian and Taber, 2008; Kroon et al., 2009; Göktepe et al., 2010).

The present paper is aimed to investigate the mechanical behaviors of mucosa, a class of common but physiologically important soft tissue lining organs and cavities throughout the body, including esophagus, pulmonary airway, eustachian tube, gastrointestinal tract, and many other animal lumens. These organs normally consist of a muscular, a submucosal, and a mucosal layer. The muscular layer is usually much stiffer than the submucosal layer. The submucosal layer consists of loose connective tissue on the luminal side of the muscle. The mucosal layer includes the lamina propria or subepithelial collagen layer, the basement membrane, and the epithelium. The ratio between the elastic moduli of mucosa and submucosa can vary in a broad range: e.g. 1–50 (Wiggs et al., 1997; Yang et al., 2007) or 1–314 (Hrousis et al., 2002). The modulus of the combined mucosa–submucosa layer is in the range 3–24 kPa for the pulmonary airway of rabbits (Wang et al., 2000) and about 0.5 kPa for porcine esophagus (Yang et al., 2007). Fig. 1a illustrates a typical ring cut from a bovine esophagus, where the muscular layer is seen to occupy the outermost region. Some other organs (e.g., pulmonary airway in Fig. 1b) also share a similar layered structure. Due to the constraint from the muscular layer, volumetric growth in the mucosal layer (physiological or pathological) would lead to increasing mucosal thickness, accumulation of compressive residual stresses, and inhomogeneous deformation in the form of surface wrinkling. Experiments have confirmed the existence of compressive residual stresses in normal esophageal mucosa (Lu and Gregersen, 2001; Yang et al., 2007). It can be expected that, as the compressive residual stress exceeds a critical value, the tissue would buckle into some regular or irregular morphology. This problem is somewhat similar to growth-induced buckling of plant leaves (Dervaux and Ben Amar, 2008; Liang and Mahadevan, 2009).

Surface wrinkling in the mucosae of esophagus and pulmonary airway have been widely observed in experiments (Stiennon, 1995; Seow et al., 2000; Yang et al., 2007; Noble et al., 2010). On one hand, surface wrinkling is believed to play a significant physiological role in healthy biological tissues. However, pathological mucosal folding and phenotypic characteristics are sometimes associated with diseases such as inflammation, edema, lymphoma, asthma, and enterogastritis. Abnormal growth and alteration of wrinkling patterns in mucosa are important clinical signs and symptoms of diseases (Stiennon, 1995; Wiggs et al., 1997; Hogg, 1997). For instance, clinical observations found that asthmatic airways exhibit folds deeper than normal (Huber and Koessler, 1922). In view of its clinical relevance and significance,

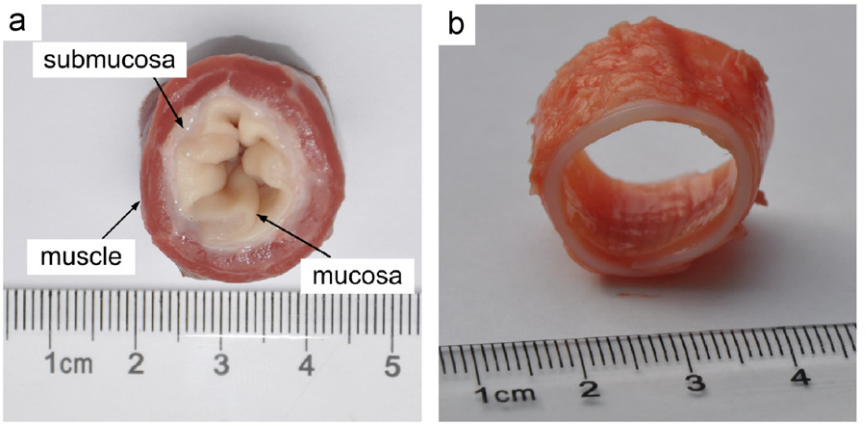

Fig. 1. Photographs of (a) a bovine esophagus and (b) a porcine airway.