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Research Paper

From single fiber to macro-level mechanics: A structural finite-element model for elastomeric fibrous biomaterials

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ABSTRACT

In the present work, we demonstrate that the mesoscopic in-plane mechanical behavior of membrane elastomeric scaffolds can be simulated by replication of actual quantified fibrous geometries. Elastomeric electrospun polyurethane (ES-PEUU) scaffolds, with and without particulate inclusions, were utilized. Simulations were developed from experimentally-derived fiber network geometries, based on a range of scaffold isotropic and anisotropic behaviors. These were chosen to evaluate the effects on macro-mechanics based on measurable geometric parameters such as fiber intersections, connectivity, orientation, and diameter. Simulations were conducted with only the fiber material model parameters adjusted to match the macro-level mechanical test data. Fiber model validation was performed at the microscopic level by individual fiber mechanical tests using AFM. Results demonstrated very good agreement to the experimental data, and revealed the formation of extended preferential fiber orientations spanning the entire model space. We speculate that these emergent structures may be responsible for the tissue-like macroscale behaviors observed in electrospun scaffolds. To conclude, the modeling approach has implications for (1) gaining insight on the intricate relationship between fabrication variables, structure, and mechanics to manufacture more functional devices/materials, (2) elucidating the effects of cell or particulate inclusions on global construct mechanics, and (3) fabricating better performing tissue surrogates that could recapitulate native tissue mechanics.

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1. Introduction

Fibrous biomaterials are ubiquitous and have important function in numerous biomedical applications which motivates the development of more advanced modeling strategies for these materials. Research efforts on this front engage a very broad spectrum of both basic and applied approaches: non-woven and woven 3D meshes (Moutos et al., 2007), cell compacted collagen gels (Aghvami et al., 2013; Sander et al., 2009; Stylianopoulos and Barocas, 2007), electrospun polyurethane scaffolds (Nerurkar et al., 2009; Stylianopoulos et al., 2008), collagen-agarose gels and fibers networks (Chandran and Barocas, 2006; Lake et al., 2012) engineered heart valves (Argento et al., 2012), decellularized tissue (D'Amore et al., 2010), arterial walls tissue (Stylianopoulos and Barocas 2007), skeletal muscle tissue (Breuls et al., 2002), actin networks (Huisman et al., 2007; Gardel et al., 2004). Historically, the term "tissue engineering" was attributed in 1988 to Y.C. Fung (Woo and Seguchi, 1989). The term underscored the importance of "the application of principles and methods of engineering and life sciences toward a *fundamental understanding of structure–function* relationships in normal and pathologic mammalian tissues and the development of biological substitutes to restore, maintain, or improve tissue function." Thus, it is imperative that fundamental structure–function relations of the fibrous biomaterials be established to guide the reproduction of native tissue equivalent behaviors if they are to emulate the native tissue counterparts successfully (Butler et al., 2000).

From these considerations, the connection of the structure and function of fibrous biomaterials have been conducted in a variety of studies. For example, multi-layered fibrous materials have been designed to replicate the annulus fibrous (Nerurkar et al., 2009), native cartilage (Moutos et al., 2007), and cardiac tissue anisotropy (Engelmayr et al., 2008). As related to cell-matrix biology, substrate stiffness is known to play a key role in directing stem cell lineage specification (Engler et al., 2006), and as well as responding to the stiffness and deformation of their substrate (Stella et al., 2008; Discher et al., 2005). It was also noted (Boerboom et al., 2008) that the macroscopic strain of the extracellular matrix (ECM) during engineered cardiovascular tissue growth induced modifications in gene expression and protein synthesis similar to those produced by modulating local deformations (Thomas et al., 2002). Matrix structure and mechanics were determined to be relevant factors in the etiology and pathological remodeling of cancer development (Huang and Ingber, 2005) as well as in atherogenesis (Nerem, 1992).

In structural deterministic approaches, the constituent microstructure is typically modeled by reproducing the material geometry at the fiber level using idealized fiber networks that are stochastically generated. The mechanics can be solved at its original micro-meso scales (Ostoja-Starzewski and Wang, 1989; Shahsavari and Picu, 2013; Wu and Dzenis, 2005), or can be coupled to the macroscopic scale through a multi-scale technique such as volume averaging or homogenization (Stylianopoulos and Barocas, 2007; Stylianopoulos et al., 2008). These models have shown predictive capacity potential at multiple length scales.

At the macroscopic scale (≥ 1 mm), a large number of models (Aghvami et al., 2013; Sander et al., 2009; Stylianopoulos and Barocas, 2007; Stylianopoulos et al., 2008; Chandran and Barocas, 2006; Lake et al., 2012; Argento et al., 2012; Stylianopoulos and Barocas, 2007; Breuls et al., 2002; Wu and Dzenis 2005; Liu et al., 2013; Onck et al., 2005; Wang and Sastry 2000; Wang et al., 2000) have been implemented to predict the uniaxial mechanical response and relate it to the biomaterial microscopic architecture (e.g., overall fiber orientation). Such structural deterministic models have had fundamental implications for (1) gaining insight on the intricate relationship between fabrication variables, structure, and mechanics to manufacture more functional devices/materials (Stella et al., 2010; Mauck et al., 2009), (2) elucidating the effects of cell or particulate inclusions on global construct mechanics (Amoroso et al., 2011), and (3) fabricating better performing tissue surrogates (Moutos et al., 2007; Nerurkar et al., 2009; Engelmayr et al., 2008) that could recapitulate native tissue mechanics both in terms of in-plane behavior (e.g., non-linearity, anisotropy and elastic moduli (Sacks, 2000)) and of out-of-plane behavior (e.g., bending stiffness (Amoroso et al., 2012)). At smaller scales (mesoscopic scale with a characteristic length of $\sim 100\,\mu$m), various model predictions (Aghvami et al., 2013; Sander et al., 2009; Stylianopoulos and Barocas 2007; Argento et al., 2012; Breuls et al., 2002; Ostoja-Starzewski and Wang, 1989; Liu et al., 2013) can estimate fibers network kinematics and mechanics (Stella et al., 2010) and elucidate the effects of macroscopic deformations and micro-architecture on cells/inclusions. For example, the global-local strain transfer at focal adhesion complexes (Stella et al., 2008). Going smaller (microscopic scale $\sim 1\,\mu$m), structural deterministic models (Gardel et al., 2004; Holzapfel and Ogden, 2011; Holzapfel and Ogden, 2013) are used to describe single fiber mechanics (Gu et al., 2005), or determine intrinsic material mechanical properties (e.g., elastic and shear moduli, Poisson ratio) (Mauck et al., 2009; Gu et al., 2005).

Yet, current structural deterministic models utilize idealized fiber geometries and generally lack experimental validation at the various length scales (Bashur et al., 2006). The lack of fiber-level geometric realism can be a limiting factor in model fidelity and utility. For example, current models can assist material fabrication by indentifying which fiber network geometries can reproduce specific macro level mechanics (Nerurkar et al., 2009; Engelmayr et al., 2008). However, specific changes in structure cannot be utilized to predict nor to elicit a desired level of local strain on embedded inclusions at the mesoscopic scale (Stella et al., 2008, 2010). There is thus a need to extend present approaches in modeling fibrous scaffolds starting from the level of the fiber and proceeding up to macro-level stress-strain responses.

The purpose of the present work is to explore the potential benefits of incorporation of actual measured fiber geometry into a structural finite element model for elastomeric fibrous scaffolds. We utilized both isotropic and anisotropic electrospun polyurethane (ES-PEUU) scaffolds, both with and without particulate inclusions, to explore a wide range of architectures. We also utilized electrospun polyethylene terephthalate (Dacron), a relatively stiff material, for further