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Research Paper

Statistical model for the mechanical behavior of the tissue engineering non-woven fibrous matrices under large deformation

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ABSTRACT

The fibrous matrices are widely used as scaffolds for the regeneration of load-bearing tissues due to their structural and mechanical similarities with the fibrous components of the extracellular matrix. These scaffolds not only provide the appropriate microenvironment for the residing cells but also act as medium for the transmission of the mechanical stimuli, essential for the tissue regeneration, from macroscopic scale of the scaffolds to the microscopic scale of cells. The requirement of the mechanical loading for the tissue regeneration requires the fibrous scaffolds to be able to sustain the complex three-dimensional mechanical loading conditions. In order to gain insight into the mechanical behavior of the fibrous matrices under large amount of elongation as well as shear, a statistical model has been formulated to study the macroscopic mechanical behavior of the electrospun fibrous matrix and the transmission of the mechanical stimuli from scaffolds to the cells via the constituting fibers. The study establishes the load–deformation relationships for the fibrous matrices for different structural parameters. It also quantifies the changes in the fiber arrangement and tension generated in the fibers with the deformation of the matrix. The model reveals that the tension generated in the fibers on matrix deformation is not homogeneous and hence the cells located in different regions of the fibrous scaffold might experience different mechanical stimuli. The mechanical response of fibrous matrices was also found to be dependent on the aspect ratio of the matrix. Therefore, the model establishes a structure–mechanics interdependence of the fibrous matrices under large deformation, which can be utilized in identifying the appropriate structure and external mechanical loading conditions for the regeneration of load-bearing tissues.

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1. Introduction

The fibrous components of the extracellular matrix (ECM) are composed of fibers with large length to diameter ratio. They dictate the mechanical behavior of various load-bearing tissues under diverse loading conditions ((Kielty et al., 2002; Dunlop and Fratzl, 2010) and references therein). Along with providing the required mechanical strength, they also provide the residing cells with appropriate microenvironment for the transmission of mechanical stimuli and growth (Dunlop and Fratzl, 2010; Frantz et al., 2010). This dual role is achieved by the tissue specific structural arrangement of the fibers in the ECM (Murakumo et al., 1995; Eyre, 2002; Frantz et al., 2010). The fibrous components of the ECM have inspired the use of structurally and mechanically similar synthetic fibrous matrices as the tissue engineering scaffolds for the regeneration of load bearing tissues (Burger et al., 2006). These synthetic fibrous matrices are fabricated mostly by using a technique known as electrospinning, which has been shown to produce non-woven fibrous matrices for diverse ranging applications (reviewed in Burger et al. (2006)). It provides control over the orientation, alignment and diameter of the fibers, and thus produces non-woven matrices which are amenable to further modifications. The fabrication of the fibrous matrices, which can provide mechanically analogous microenvironment to the cells as that of the native tissue, requires an understanding of the mechanical behavior and characterization of synthetic fibrous materials as well as fibrous components of the ECM.

The prevalent method for the mechanical characterization of the non-woven electrospun fibrous matrices involves obtaining the relationship between the matrix elongation and load from the experiments or by computational means (Nerurkar et al., 2007; Kim, 2008). Although, these methodologies do provide the load-deformation or stress-strain relationships, *i.e.* the mechanical behavior at the macroscopic scale, they do not give any information about the tension generated in individual fibers on stretching and shearing of the matrix, *i.e.* mechanics at the microscopic scale. As the fate of the cells seeded on the scaffolds depends on the mechanical properties of the scaffolds (Engler et al., 2006), it is essential to characterize the mechanical nature of the fibrous matrices at the microscopic scales. An understanding of the tension present in the fibers will guide us towards the nature of the forces experienced by the cells present on the fibrous scaffold.

Along with the mechanical properties, the structural parameters of the fibers in the matrix (defined by the fiber diameter, curvature, orientation and alignment) also influence the behavior of the cells present in the matrix (Honda and Fujimi, 2010; Kim and Provenzano, 2012; Vogel and Sheetz, 2006). Moreover, the structure–mechanics relationship of the fibrous materials also needs to be established as the mechanical properties of the fibrous materials depend on the structural parameters of the fibers. Further, any deformation in the matrix changes the fiber arrangement in the matrix. Therefore, the analysis of the mechanical and structural characterization of the fibrous materials will not only provide an insight into their mechanical behavior, but will also equip us with guiding principles for the optimization of their fabrication processes.

The experimental studies performed with the tissue explants and cell seeded electrospun fibrous matrices have focused on obtaining the changes in the geometries of the cells and their nuclei under mechanical compression and stretching (Guilak et al., 1995; Stella et al., 2008, 2009; Han et al., 2013). These investigations have established that the strain transfer to the cells under mechanical loading is not uniform over the whole matrix and depends on the fiber arrangement around the cells. On the other hand, there have been extensive computational and modeling studies since the pioneering works of Lanir (1983)and Spencer (1972). These works have attempted to incorporate the structural fiber arrangement of the matrix in the formulated constitutive theory (Gasser et al., 2006; Federico and Gasser, 2010). Recently, the computational studies based on the finite element methods have also attempted to establish the structure–mechanics relationship for the fibrous materials (Breuls et al., 2002; Lacroix et al., 2006; Stylianopoulos and Barocas, 2007; Stops et al., 2008; Stylianopoulos et al., 2008; Argento et al., 2012). These studies generated the geometry for the simulation either from the imaging of the native tissues and electrospun fibrous matrices or computationally by using the random processes. These works highlighted the non-uniformity in the deformation field observed in experiments as well as inhomogeneous strain transfer to the cells. Influence of the fiber orientation and diameter on the mechanical behavior of the fibrous matrices was also predicted (Stylianopoulos et al., 2008).

In spite of extensive work on the mechanics of the tissue engineering fibrous matrices under compression and elongation, their behavior under shear deformation remains less explored. The few studies which have been performed in this direction have considered only the aligned fiber matrices (Gardiner and Weiss, 2001; Horgan and Murphy, 2010; Driscoll et al., 2011). These works have reported the inhomogeneity in the matrix strain as well as the effects of the fiber orientation, angle and sample aspect ratio under shear.

Fibrous matrices, used as tissue engineering scaffolds for the regeneration of load bearing tissues, have to experience large amount of mechanical loading which causes large deformations and might lead to their failure. Therefore, the information about the large deformation mechanics of fibrous matrices is essential for their design as scaffolds. Although load bearing tissues experience complex mechanical loading environments, the understanding of the mechanics of fibrous matrices under large deformations and their failure has also been limited to the matrix elongation (Hadi et al., 2012; Hadi and Barocas, 2013).

The present work provides a theoretical framework for determining the relationship between the mechanical behavior and structural properties of the non-woven fibrous matrices under large elongation as well as shear. By utilizing a statistical description for the fiber arrangement in the matrix, the model also explores the failure behavior of the matrices arising due to the breakage of the individual fibers at large strains. The effects of the arrangement of the fibers, defined by the fiber diameter, orientation, alignment and