Micromechanical Model of a Collagen-Based Tendon Surrogate

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Introduction. Collagen in tendons and ligaments is organized hierarchically into fibrils at the nanoscale, fibers at the microscale and fascicles at the mesoscale. Force transfer across scales is complex and poorly understood, and macroscale strains are not always representative of microscale strains [1]. Since innervation, vascularization, damage and mechanotransduction occur at the microscale, understanding the multiscale interactions in these tissues is high relevant to the function of normal and injured connective tissues. There is very little experimental data on the multiscale mechanics of connective tissues, and virtually no results that include simultaneous measurements at different scales. Further, it is virtually impossible to study the influence of different structural features of native connective tissues parametrically, since the parameters cannot be isolated or varied in a controlled manner. This research developed a collagen-based surrogate material and used the surrogate in combination with computational micromechanical models to isolate and study the mechanisms of force transfer between scales [2].

Methods. Physical surrogates were created from dense (~25% collage/wt), extruded collagen fibers embedded within a collagen gel matrix (~0.5% collagen /wt). Surrogates served as physical models to emulate features of ligament and tendon tissue, including a nanoscale organization of collagen fibrils and a mesoscale organization of aligned collagen fibers coupled via an interfiber matrix, in a controlled and reproducible manner. Two different colors of fluorescent beads were embedded in the fibers and gel matrix (Fig. 1, left). 3D micromechanical FE models of the surrogates were constructed. Constitutive models and material coefficients were based on experimental material characterization of isolated gel and fiber samples. Micromechanical FE models were subjected to uniaxial strain, and the macroscale and microscale stress and 2D strain were determined. FEBio was used for all analysis (http://www.febio.org). To validate the FE models, the physical surrogates were subjected to tensile loading in a custom testing apparatus on an inverted confocal microscope. Confocal images were acquired at 6 strain increments at both 2.5X and 10X, while force was measured simultaneously. Texture correlation was used to measure strain at the macroscale, strain within the fibers and strain in the inter-fiber matrix at the microscale.

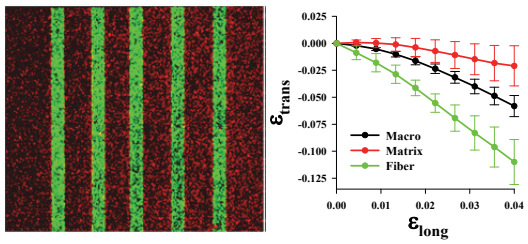

Fig. 1: Left - dual channel 4X image of surrogate. Right - the macroscopic transverse strain (black line) was not representative of the microscopic fiber strain (green line). Error bars = standard deviation.

Results. The microscopic 2D strains were inhomogeneous, and the macroscopic 2D strain was not representative of the microscopic 2D strain (Fig. 1, right). The transverse strain in the fibers greatly exceeded the macroscopic transverse strain, while the transverse matrix strain was significantly less than the macroscopic strain. The macroscopically measured Poisson's ratio was 1.72±0.26.

The micromechanical FE model was able to simultaneously predict the macroscopic stress-strain behavior and the 2D macroscale and microscale strains (Fig. 2). The predicted macroscopic stress and macroscopic transverse strain closely matched the experimentally measured values (NRMSE=0.015 and 0.085, respectively). The predicted microscopic transverse fiber strain was closely matched by the experimentally measured values (NRMSE=0.018), while predictions for the microscopic transverse matrix strain were reasonable but not as accurate (NRMSE=0.190). When simulations were performed using coefficients that varied by a single standard deviation, all of the predictions were closely bounded by this uncertainty (Fig. 2, dashed lines).

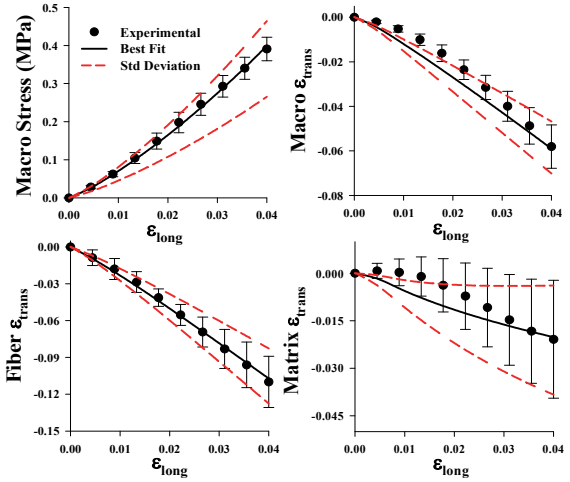

Fig. 2: FE predictions agreed with experimental data. Stress-strain (upper left), macroscopic strain (upper right), fiber strain (lower left) and matrix strain (lower right). Black points = experimental data. Solid black line = FE predictions. Dashed red lines are FE predictions obtained using coefficients plus or minus one standard deviation.

Discussion. The results of this study indicate that the continuum assumption is not valid for describing the macroscale behavior of the physical surrogates. The micromechanical model was able to accurately predict the strains at both physical levels, demonstrating the utility of this approach for the study of fibrous biological composites. The use of physical surrogate materials provides a means for developing and validating more complex and physiologically relevant micromechanical and multiscale mechanical models. In addition to its contribution in the field of multiscale ligament and tendon mechanics, the results of this study have relevance to tissue engineering, where computational modeling is poised to help develop future generations of tissue scaffolds.

References. [1] Screen, et al., Proc Inst Mech Eng [H], 218(2), 2004. [2] Reese, et al., Proc ASME Summer Bioengineering Conf., 2012.

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