Theoretical Analyses of Electrospun Scaffolds and Engineered Tissues

We have recently employed electrospinning for the engineering of fiber-reinforced soft tissues such as the knee meniscus [1-2] and the annulus fibrosus of the intervertebral disc [3-5]. To improve our understanding of electrospun scaffolds, we have developed constitutive relations to elucidate how microscopic form relates to macroscopic function of static and dynamic electrospun nanofibrous scaffolds and the evolving function of growing engineered tissues. Constitutive approaches range from linear homogenization models to describe the interplay between fiber alignment and tensile properties (**Fig. 1**) to hyperelastic models to describe the time-varying properties of composite multi-polymer scaffolds where the constituents possess varying degradation rates (**Fig. 2**) [6]. Finally, we have developed and applied novel constitutive models to describe the evolving behavior of engineered tissues, using material parameters as metrics of functional growth (**Fig. 3**) [7]. Because of the inherent nonlinearity of many tissues of interest, nonlinear models that characterize the full stress-strain response (not simply the linear region modulus) are compulsory for meaningful comparisons in function between engineered and native tissues.

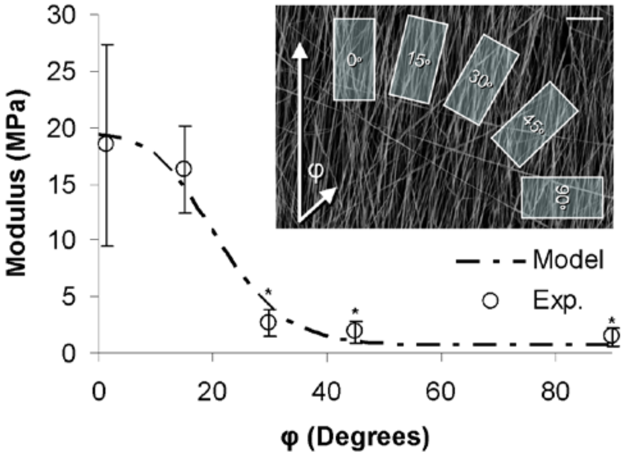

Figure 1. A linear homogenization model successfully captures the dependence of linear region modulus on the angle of fiber alignment in uniaxial tensile tests of aligned electrospun poly-(ε-caprolactone) scaffolds [4].

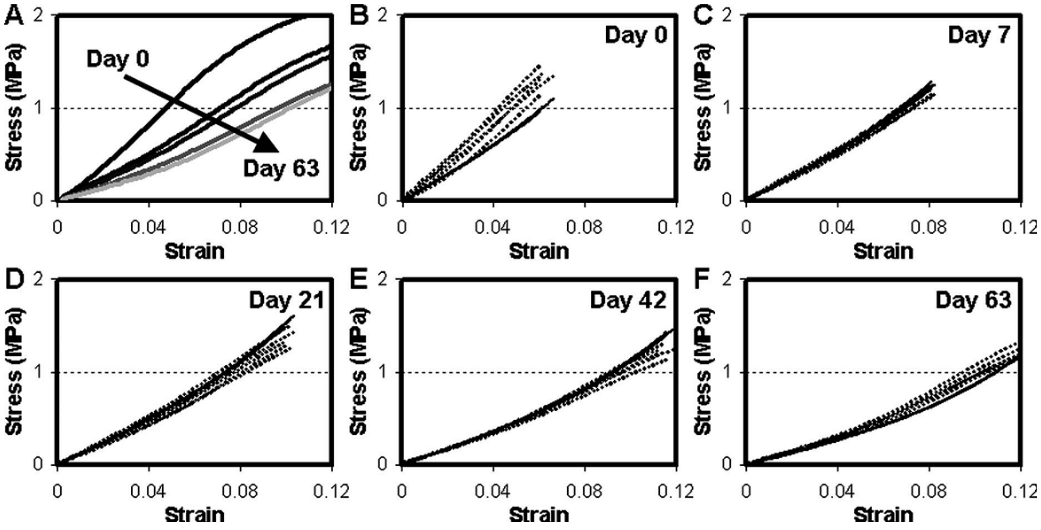

Figure 2. A constrained mixture model *predicts* the mechanical response of composite nanofibrous scaffolds over the course of component degradation [6]. Due to the combination of fiber populations with distinct stress-strain profiles and degradation rates, incubation over 63 days results in changes in both the profile and magnitude of composite tensile response (A). By applying hyperelastic models to single-polymer data sets to obtain polymer-specific material properties, a constrained mixture approach allows incorporation of these values into a composite model that successfully predicts (solid lines) the experimentally measured stress-strain behavior (dotted lines) over the entire time-course of degradation (B-F).

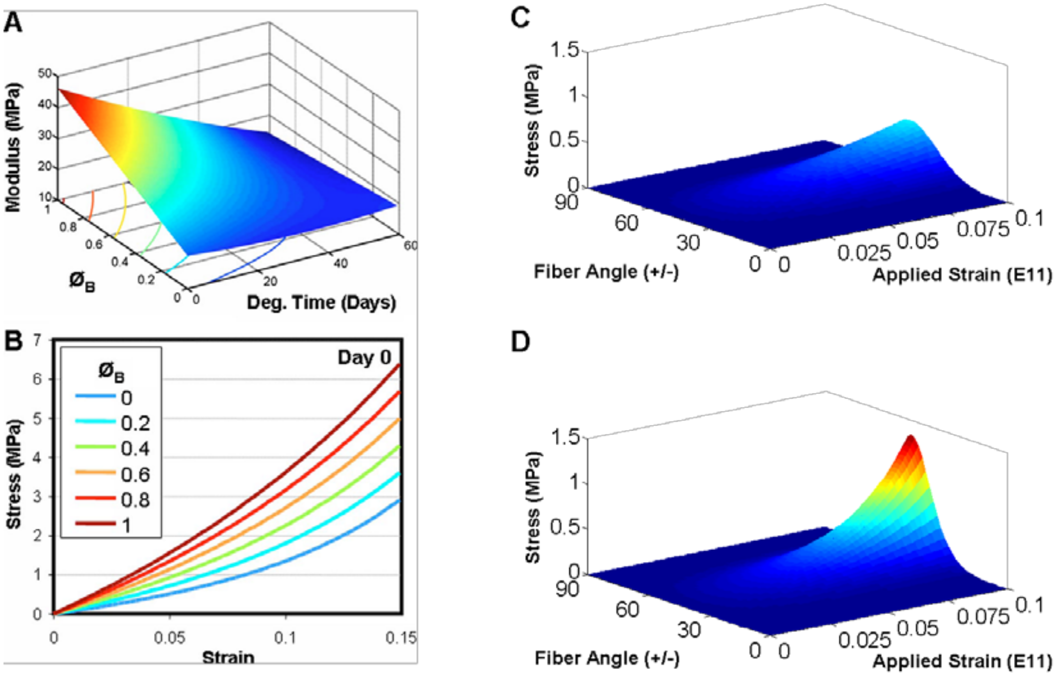

Figure 3. Model predictions guide the design and analysis of scaffolds and engineered fiber-reinforced soft tissues. Using a constrained mixture model (see Fig. 2), it is possible to simulate a

wide range of responses (A, B). Analyses of this type instruct the design of application-specific scaffolds by indicating the time-varying composite response that can be obtained from various combinations of constituents [6]. Similarly, for engineered tissues constitutive models indicate the functional consequences of extracellular matrix deposition [5]. For instance, we have recently developed a novel hyperelastic model to describe the role of inter-lamellar shearing in reinforcing the tensile response of biologic laminates [7], demonstrating that with ECM deposition, the stress contribution from this unique reinforcement mechanism increases considerably from 2 weeks (C) to 10 weeks (D) of culture.

Recent Publications:

1. Baker BM, Mauck RL. “Alignment Enhances the Maturation of Nanofiber-Based Engineered Meniscus Constructs,” 2007, Biomaterials, 28(11):1967-77.
2. Baker BM, Nathan AS, Huffman GR, Mauck RL. “Tissue Engineering with Meniscus Cells Derived from Surgical Debris,” 2009, Osteoarthritis and Cartilage, 17(3):336-45.
3. Nerurkar NL, Baker BM, Sen S, Wible EW, Elliott DM, Mauck RL. “Nanofibrous biologic laminates replicate the form and function of the annulus fibrosus,” 2009, Nature Materials, 8(12): 986-92.
4. Nerurkar NL, Elliott DM, Mauck RL. “Mechanics of oriented electrospun nanofibrous scaffolds for annulus fibrosus tissue engineering,” 2007, Journal of Orthopaedic Research, 25(8):1018-28.
5. Nerurkar NL, Mauck RL, Elliott DM. “ISSLS prize winner: integrating theoretical and experimental methods for functional tissue engineering of the annulus fibrosus,” 2008, Spine, 33(25):2691-701.
6. Baker BM, Nerurkar NL, Burdick JA, Elliott DM, Mauck RL. “Fabrication and modeling of dynamic multi-polymer nanofibrous scaffolds,” 2009, Journal of Biomechanical Engineering, 131(10): 101012.
7. Nerurkar NL, Mauck RL, Elliott DM. “Modeling inter-lamellar interactions in engineered nanofibrous biologic laminates for annulus fibrosus tissue engineering,”2010, Proceedings of the ASME 2010 Summer Bioengineering Conference, Naples, FL, June 16 – 19.

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Project Personnel:
Brendon Baker
Nandan Nerurkar