In-silico Evaluation of Structure-Function Relationship in Biopolymer Networks

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Abstract

The fields of mechanobiology and biomechanics are advancing our understanding of the complex behavior of soft tissues across multiple scales. A current challenge is linking tissue microstructure to its functional role. While traditional methods like in-vitro studies and mechanical testing remain vital, the significance of computational techniques is growing. Early imaging methods were less sophisticated than current methods, leading to histology-inspired models (1) that primarily focused on dominant fiber directions and overlooked the complex 3D architecture of soft biological tissues. Recent advances in imaging and topology extraction workflows have revolutionized tissue microstructure models, conceptualized as discrete fiber networks (DFNs) of load-bearing components. Given the computational challenge of full-scale modeling, Representative Volume Elements (RVEs) are used as statistically representative mesoscale (μm) units to derive tissue behavior at the macroscale (mm) (2-6). Establishing the reliability of RVE models is critical for upscaling to the tissue level. However, a direct connection between in-silico and in-vitro mesoscale nonlinear mechanics remains underexplored, with validation limited to macroscale tissue behavior.
Jansen et al. (7) analyzed the role of network architecture in the nonlinear mechanics of collagen. Their in-silico comparisons with mesoscale rheological testing data on collagen networks polymerized at varying temperatures, resulting in differing structural properties, offered insights into the structure-function relationship. Their model, however, is limited to 2D, with the network represented as a triangular lattice. While this approach represents a significant advancement, it fails to capture the complexity of the 3D environment critical for understanding the localized mechanical properties of the extracellular matrix surrounding cells. Experimental evidence highlights that macroscopic deformation gradients cannot fully predict fiber reorientation and arrangement during loading. Instead, localized processes play a significant role in shaping the global tissue response (8). To capture these processes, models must account for the 3D structural arrangement of biological networks.

In this work, we build upon previous generative algorithms (4, 9) to develop topologically controlled DFNs, and we incorporate them in RVEs of load-bearing elements that exhibit softening under compression (10) and are bending resistant. To ensure Hill-Mandel energy consistency, we impose periodicity on the micro-fluctuation field using periodic boundary conditions (PBCs) implemented in Abaqus Standard (2024). We evaluate the robustness of our method by replicating the same structural conditions, including fiber volume fraction, cross-link concentration, and length distribution of reconstituted collagen I networks as in (7). Specifically, we analyze the evolution of the differential modulus as the temperature of

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polymerization varies and find consistency between the computational and in-vitro results. We observe that collagen networks exhibit a two-phase stiffening response as the applied load increases. Initially, fibers undergo reorientation, aligning with the loading direction and contributing to geometrical stiffening. This is followed by an affine stretching of fiber chains, producing a linear elastic response with stiffness increased by an order of magnitude compared to the initial modulus. Our novel framework provides a robust platform for investigating the impact that varying microscale tissue configurations have on the tissue's mesoscale mechanical behavior.

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